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The role of ovarian suspension in preventing post-surgical ovarian adhesions in patients with stage III-IV pelvic endometriosis: a systematic review

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Author Disclosure

Dr. Pierluigi Giampaolino, Dr. Luigi Della Corte, Dr. Gabriele Saccone, Dr. Amerigo Vitagliano, Dr. Giuseppe Bifulco, Drs. Gloria Calagna, Dr Jose Carugno and Dr. Attilio Di Spiezio Sardo have no conflicts of interest or financial conflicts to disclose.

Précis

Ovarian suspension is an effective option to prevent postoperative ovarian adhesion formation in patients with stage III-IV pelvic endometriosis.

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ABSTRACT

Endometriosis is a benign complex gynecological condition with high morbidity that affects women of reproductive age. Pelvic adhesion formation represents a serious clinical challenge in the management of patients with endometriosis. Several interventions have been proposed over the last few years aiming to reduce post-operative ovarian adhesions formation. The aim of this study is to summarize the evidence of the efficacy of ovarian suspension in the prevention of post-operative ovarian adhesions formation in women undergoing laparoscopic surgery for stage III-IV endometriosis.

The research was conducted using electronic databases. A review of the abstracts of all references retrieved from the search was conducted. Selection criteria for the systematic review included all randomized controlled trials (RCTs) and non-randomized studies (NRSs) of premenopausal women diagnosed with stage III-IV pelvic endometriosis who underwent ovarian suspension or no ovarian suspension (control group). RCTs were eligible for meta-analysis.

Eight studies were included in the systematic review: 2 RCTs and 6 NRSs. In all studies, ovarian suspension was performed during surgery for stage III-IV endometriosis. The site of the suspension was the anterior abdominal wall in 76.8% of the cases. Five studies reported the use of Polypropylene (Prolene® Ethicon Inc., Somerville, NJ, USA) as suture for the suspension. Removal of the suspension suture in the post-operative period was reported in six studies. Pooled data based on meta-analysis of RCTs showed that women who underwent ovarian suspension had a significantly lower incidence of postoperative adhesions formation in particular of moderate-severe adhesions.

Ovarian suspension may reduce the rate and severity of postoperative adhesions formation in women undergoing laparoscopy for the treatment of stage III-IV endometriosis, but RCTs with larger samples size are needed.

Keywords: endometriosis; postoperative ovarian adhesions; minimally invasive gynecology surgery; ovarian suspension.

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INTRODUCTION

Endometriosis is a chronic disease characterized by the growth of endometrial-like glands and stroma outside the uterine cavity [1,2]. It affects up to 10% of women of reproductive age, with a higher prevalence (40-60%) in women with dysmenorrhea, subfertility (21-47%) and/or pelvic pain (71-87%). [1-6]. The American Society for Reproductive Medicine, classifies endometriosis as stage I (minimal), II (mild), III (moderate) or IV (severe) based on the type (i.e. number, location, and depth) of implants and on the presence of filmy or dense adhesions. In particular, stage III endometriosis is characterized by many deep infiltrating implants, small endometriomas on one or both ovaries, and some filmy adhesions while stage IV by many deep infiltrating implants, large endometriomas on one or both ovaries, and many dense adhesions [3,7].

Laparoscopic excision of endometriotic lesions and lysis of adhesions is the recognized gold standard treatment for endometriosis [8], obtaining a reduction of pain and improving the quality of life in 70–80% of patients [9]. Nevertheless, the disease and symptoms frequently recur within 2-5 years from surgery [10]. Moreover, a high rate of post-operative adhesions formation has been reported, especially in patients with stage III/IV endometriosis (prevalence of 50-100% at second look laparoscopy) [11-14]. Post-operative adhesions typically involve the ovaries and the pouch of Douglas [15], causing chronic pelvic pain, dyspareunia, intestinal obstruction and infertility [11].

Several interventions have been proposed for reducing the formation of post-operative ovarian adhesions [16,17], including temporary ovarian suspension to the abdominal wall [18]. This procedure was first performed in 1970 during an abdominal laparotomic surgery to protect the ovaries from irradiation in a woman who had to undergo radiotherapy for Hodgkin's disease [19] and has since been used to protect the ovaries from pelvic irradiation when needed [20]. Lately, with increasing experience and refining of the techniques, ovarian

suspension has also been performed to prevent ovarian adhesion formation in the surgical treatment of severe endometriosis [21, 22].

Despite different studies have evaluated the role of ovarian suspension for the prevention of ovarian adhesions after laparoscopic surgery for endometriosis, there is still lack of a summary of evidence on this topic. Therefore, the aim of our study is to summarize the current evidence on the effectiveness and risks of ovarian suspension for the prevention of postoperative adhesion formation in the surgical management of women with stage III-IV endometriosis.

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METHODS

Search strategy

The research was conducted using the following electronic databases, MEDLINE, EMBASE, Web of Science, Scopus, ClinicalTrial.gov, OVID and Cochrane Library. The studies were identified with the use of a combination of the following text words: “endometriosis,” “laparoscopy,” “ovarian suspension,” “ovariopexy,” “adhesions” from the inception of each database to September 2017. We included all published randomized controlled trials (RCTs) and non-randomized studies (NRSs).

Study selection

Selection criteria included RCTs and NRSs (observational prospective, retrospective cohort studies, case-control studies, case series) on premenopausal women diagnosed with stage III-IV endometriosis (confirmed at the time of surgery) evaluating the impact of ovarian suspension on post-operative adhesion formation. Two surgical procedures were evaluated: the first included the transient ovariopexy to the anterolateral abdominal wall, and the second procedure consisted of permanent ovariopexy to the ipsilateral round ligament with a resorbable suture. Studies that included patients undergoing unilateral/bilateral oophorectomy and/or hysterectomy were excluded from the analysis.

Data extraction and risk of bias assessment

All review stages were conducted independently by two reviewers (PG, LDC). The two authors independently assessed electronic search, eligibility of the studies, inclusion criteria, the risk of bias, data extraction, and data analysis. Disagreements were resolved by discussion with a third reviewer (GB).

The risk of bias in each trial included in the meta-analysis was assessed by using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* [19]. Seven domains related to risk of bias were assessed in each included trial since there is evidence that are associated with biased estimates of treatment effect: 1) random sequence generation; 2) allocation concealment; 3) blinding of participants and personnel; 4) blinding of outcome assessment; 5) incomplete outcome data; 6) selective reporting; and 7) other bias. Review authors' judgments were categorized as "low risk," "high risk" or "unclear risk" of bias. The review was reported following the Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) statement [24].

Data analysis

Meta-analysis was planned only for RCTs, whereas for NRSs only a descriptive analysis was performed. The data analysis was completed using Review Manager 5.3 (Copenhagen: The Nordic Cochrane Centre, Cochrane Collaboration, 2014). Between-study heterogeneity was explored using the I^2 statistic, which represents the percentage of between-study variation that is due to heterogeneity rather than chance. A value of 0% indicates no observed heterogeneity, whereas I^2 values of $\geq 50\%$ indicate a substantial level of heterogeneity.

The summary measures were reported as summary relative risk (RR) with 95% of confidence intervals (CI) using the random effects model of DerSimonian and Laird.

Potential publication biases were assessed statistically by using Begg's and Egger's tests. A p-value <0.05 was considered statistically significant.

Tests for publication bias were not carried out if the total number of publications included for each outcome was less than ten. In this case, the power of the tests is too low to distinguish chance from real asymmetry.

All analyses were done using an intention-to-treat approach, evaluating women according to the treatment group to which they were randomly allocated in the original trials. The primary outcome included the prevalence and the severity of ovarian adhesions after ovarian suspension, defined as the total number of adhesions having impact on the ovaries of each patient and evaluated by means of ultrasound [16, 22, 24, 25, 27], laparoscopy [22, 26, 29] and/or transvaginal hydrolaparoscopy [28]. The severity of ovarian adhesions was graded using the Operative Laparoscopy Study Group (OLSG) criteria (0: no adhesion, 1: smooth and avascular, 2: dense or vascular, 3: cohesive) and the revised American Fertility Society (AFS) scoring.

Secondary outcomes included the evaluation of post-operative complications and post-operative pelvic pain assessed by Visual Analogue Scale (VAS) score. The VAS classified no pain as 0 and the worst imaginable pain as 10. A pain score of 1–3 was described as mild, 4–7 as moderate and 8–10 as severe.

Data from each eligible study were extracted without modification of original data and transferred onto a custom-made data collection form. Relevant data not present in the original publications were requested from all the principal investigators.

RESULTS

Study selection and study characteristics

Among the 24 articles initially identified, eight were included in the systematic review (Figure 1). Two were RCTs [16, 29], one was a pilot RCT [15] and five were NRSs [17, 22, 26-28] (Table 1). The non-randomized studies (NRSs) included 4 retrospective studies [17, 22, 26, 27] and 1 prospective cohort study [28]. The total number of patients examined was 795. In all described cases, the ovarian suspension was performed in patients diagnosed with stage III-IV endometriosis.

The site of the suspension was the anterior abdominal wall in 610/795, 76.8%) [17, 22, 25-27, 29], only one author described the suspension technique to the ipsilateral round ligament (185/795, 23.2%) [29]. Five studies, for a total of 502 patients, reported the use of Polypropylene (Prolene® Ethicon Inc., Somerville, NJ, USA) as suture material for the suspension [17, 25-27]. Six reported the removal of the suspension suture in the post-operative phase, with different reported timing of removal [17, 22, 25-27] (Table 1).

In the majority of the included studies, the ovarian suspension was temporary, commonly for a period of 36 to 48 hours, with a transient ovarian suspension range between 36 and 120 hours. In two studies ovarian suspension was permanent (Table 1).

All studies reported data on the post-operative evaluation of pelvic adhesion formation (Table 2). As previously reported, the evaluation of post-operative adhesions was performed using transvaginal ultrasound (TVU) [16, 25, 27, 29], laparoscopy (LPS) [17, 26], TVU plus LPS [22] and transvaginal hydrolaparoscopy (TV-H-LPS) [28]. Three studies reported the evaluation of post-operative pain [16, 28, 29], and 3 reported data on post-procedure pregnancy rate [17, 22, 26].

Ovarian suspension technique

The technique employed to perform the ovarian suspension to the abdominal wall was similar in all studies [16, 17, 22, 25, 26, 28, 29], except for Pellicano et al. [28]. All procedures were performed laparoscopically [16, 22, 25-29], excluding Carbonnel et al. [17], who used both laparoscopy and laparotomy to carry out the ovarian suspension. Although a different type of suture was used by Authors, as specified in the discussion section, a one-stitch simple technique was performed after ovarian cystectomy: the needle was introduced into the peritoneal cavity through the lower anterior abdominal wall and was recovered intracorporeally, grasping with a hemostat clamp the end of the thread. The needle was then passed through the ovarian medial side and passed out of the abdomen through the abdominal wall near the introduction point. The ovary was temporarily suspended to the peritoneum of the lower antero-lateral abdominal wall next to the ipsi-lateral round ligament of the uterus. Approximately 2 to 3 cm was left between the ovary and the pelvic sidewall to avoid fixation and adhesion formation between them. One knot was performed extracorporeally and was gradually tied, thus approximating transiently the medial ovarian side to the anterior pelvic wall. The stitch was then removed between one day and a half and seven days after the procedure.

In the case of ovarian suspension to the ipsilateral round ligament, the technique employed was similar to the one mentioned above, with the difference that the suture was carried out approximately 1 cm from the inguinal canal, to separate the ovary about 1.5–2 cm from the ovarian fossa. In this circumstance, the surgeon performed a single running suture, using an absorbable monofilament suture (Vicryl Rapid 2.0, CT-1 needle, Sommerville, NJ, USA, Ethicon), tied with intracorporeal knots (Figure 2).

Type of suture

Most of the Authors employed synthetic, nonabsorbable, polypropylene monofilament or a braided, nonabsorbable polyester suture (0 Prolene® Ethicon Inc., Somerville, NJ, USA and 0 Mersuture® Ethicon Inc., Somerville, NJ, USA, respectively) [16, 17, 22, 25-27].

Two Authors performed the suture using a single running suture with an absorbable monofilament suture (Vicryl Rapid 2.0, CT-1 needle, Somerville, NJ, USA, Ethicon): this choice was made to separate the ovary from the injured peritoneal surfaces during the healing process which is often longer than 7 days, avoiding the development of adhesion within the first 5–7 days after surgery. Moreover, Vicryl Rapid 2.0 suture has the peculiarity of losing tensile strength in 5–7 days, as well as having a fast reabsorption process [28, 29].

Assessment of post-operative adhesions

The utilized methods to determine the presence and location of postoperative pelvic adhesions were different: transvaginal ultrasound (TVU) [16, 25, 27, 29], laparoscopy (LPS) [17, 26], TVU plus LPS [22] and transvaginal hydrolaparoscopy (TV-H-LPS) [28]. The presence of adhesions evaluated by TVU were classified as minimal, moderate and severe using the following criteria: only minimal adhesions were considered to be present when a gentle pressure was not able to separate some (1/3) of the surrounding structures from the ovary but the ovary could be mobilized from the majority (2/3) of the surrounding structures; adhesions were classified as moderate when one-third to two-thirds of ovarian mobility was reduced because of adhesions to the surrounding structures; and severe adhesions were characterized by fixed ovaries unable to be mobilized with gentle pressure or separated from many of the surrounding structures. The evaluation through LPS and TV-H-LPS was conducted taking into account the presence of filmy, dense and/or vascular adhesions between the ovaries and nearby organs and/or the pelvic sidewall. The timing of evaluation

was ranged between 2 and 12 months after surgery. Data on pelvic adhesions formation rate were reported in Table 2.

Quantitative analysis

Two trials were included in the meta-analysis [16, 29], generating a total of 194 patients. The overall risk of bias of the included trials was low (Figure 3). Both studies had a low risk of bias in “random sequence generation,” “incomplete outcome data,” and “selective reporting.” Adequate methods for allocation of participants were used. Given the intervention, none of the included trials were double-blind. All randomized women were included in an intention-to-treat analysis. Publication bias, assessed using Begg’s and Egger’s tests, showed no significant bias ($P=0.69$ and $P=0.78$, respectively).

Pooled data showed that women who received ovarian suspension had a significantly lower incidence of overall postoperative adhesions (RR 0.78, 95% CI 0.63 to 0.96; Figure 4) and of moderate-severe postoperative adhesions (RR 0.50, 95% CI 0.34 to 0.73; Figure 5).

Qualitative analysis

The analysis of nRCTs included 636 women [17, 22, 26-28]. The pilot RCT included 16 patients [25]. Data about the incidence of post-operative ovarian adhesions after the ovariopexy is conflicting. Although two Authors [25, 26] proved an adhesion formation reduction of less than 50% (41,7% and 43,7% respectively), Ouahba et al. demonstrated a significant reduction in the severity of post-operative ovarian adhesions showing only in 4/12 ovaries (33.3%) the presence of organized dense and vascular adhesions between the ovary and the pelvic sidewall, with 5/12 ovaries adhesion-free and 3/12 ovaries with only filmy adhesions to the ipsilateral tube [26]. Carbonnel et al. [17] showed a reduction of 50% (19/38 ovaries free from adhesions) while both Abuzeid et al. [22] and Pellicano et al. [28] reported

a significant reduction of post-operative ovarian adhesions formation rate, respectively of 20% (2/10) and 40,7% (22/54).

Postoperative complications

Regarding post-operative complications, 3 studies reported absence of adverse events [22, 25, 28]. Only three Authors [17, 27, 29] described immediate postoperative complications in 6 patients: two of them reported fever, other two ovarian abscess and the remaining two hemoperitoneum, occurred few days after the surgery. Serrachioli et al. [29] reported 2 patients with post-operative fever due to urinary tract infection in the ovarian suspension group and 3 among controls; three patients had a large intra-operative blood loss which resulted in post-operative hemoglobin $< 10\text{g/dL}$ (1 among ovarian suspension group and 2 among control group), but no blood transfusion was required. Carbonnel et al. [17] and Poncelet et al. [27] reported respectively 2/297 (0.7%) and 2/336 (0.6%) immediate ovarian complications: 1 ovarian abscess (caused by *Klebsiella pneumoniae*) and 1 hemoperitoneum. These complications may be considered as major complications; indeed, in both cases, the abscess was drained by posterior colpotomy at the time of diagnosis, while a second laparoscopy performed on post-operative day 1 was needed to resolve the hemoperitoneum.

Post-operative pain

In the studies that have evaluated pre- and post-operative pain, both Pellicano et al. and Seracchioli et al. did not observe any difference in terms of postoperative pelvic pain between the groups, measured by VAS scale [28, 29], while Hoo et al. found a significant improvement in patient's pain scores after surgery despite the relatively high prevalence of postoperative pelvic adhesions [16]. Moreover, Hoo et al. [16] showed that the mean post-operative VAS score was lower than the mean pre-operative VAS score (5.79 vs 1.98).

According to Hoo et al., it is likely that post-operative pelvic adhesions is in part responsible for the persistent pelvic pain following laparoscopy for endometriosis, and that other unknown factors may also contribute to pelvic pain [16]. Although it is not clear why there has been an improvement in pain symptoms regardless of ovarian suspension, Seracchioli et al. reported that ovarian suspension seems to reduce pain induced by the pressure of vaginal probe, explaining this result, according to Hammoud et al., considering ovarian adhesions as a cause of pain due to distortion of normal anatomic relationships and to the stretching of the peritoneum/organ serosa at the adhesion's attachment sites [29, 30].

Pregnancy Rate

Fertility and pregnancy rate after ovarian suspension were evaluated in three studies. Ouhaba et al. (2004) reported that 53,3% of patients who underwent ovarian suspension conceived in average 11.5 months after the surgical procedure, (range 4-24 months) [26]. Carbonnel et. al (2011) showed similar results (55%), with a median time of conception of 8.6 ± 1 months: 36% of patients conceived spontaneously while 64% required assisted reproductive technologies (ARTs) [17]. In the three considered studies, about half of the women undergoing ovarian suspension were able to conceive after the procedure [17, 22, 26].

DISCUSSION

Main findings

Several strategies for adhesion prevention in patients with stage III-IV endometriosis are described in the literature. We have taken into account both transient and permanent ovarian suspension. To the best of our knowledge, this is the first systematic review with meta-analysis on this topic.

Our study revealed scarce data in the current literature about ovarian suspension as an adhesion-prevention strategy after surgery for endometriosis. We identified only eight studies addressing this practice. Of them, only two were randomized trials.

This lack of scientific evidence could be explained due to the fact that the use of ovarian suspension for the prevention of ovarian adhesion formation in patients with endometriosis is a relatively recently described procedure in the field of laparoscopic surgery. Accordingly, 6 (75%) of the 8 included studies were published starting from 2011, indicating that the use of ovarian suspension, as an adhesion prevention strategy in patients with severe endometriosis, is a recent innovation of gynecologic endoscopy, although its practice is progressively increasing.

Several interventions have been studied aiming to reduce postoperative pelvic adhesions and its complications. Both medical therapy and surgery are the main treatment options for endometriosis. However, the most effective treatment for severe pelvic endometriosis is surgical [16], being the laparoscopic approach the best option [31]. Nevertheless, new strategies are needed to maximize the impact on the disease, reducing pain and the potential risk of complications caused by post-operative adhesions formation.

Medical therapeutic options include oral contraceptives, progestogens, androgenic agents, and gonadotropin-releasing hormone analogues [3, 32, 33]. In an effort to prevent post-operative adhesion formation, intraperitoneal administration of anti-adhesive solutions,

such as icodextrin and hyaluronic acid, anti-inflammatory agents, polyunsaturated fatty acids, chemokine inhibitors and even anti-estrogens, has been studied [13]. Despite the development of many novel anti-adhesion agents, adequate surgical technique seems to be the most effective strategy in preventing adhesion formation [34].

The basic concept of transient “oophoropexy” during surgery for severe endometriosis arises from the purpose to keep the ovary away from the injured surrounding peritoneum during the immediate post-surgery peritoneal healing based on findings of animal studies which showed a reduction in adhesion formation when separation of injured peritoneal surfaces was maintained for at least 36 h [35], oophoropexy may represent a good option to avoid periovarian adhesions formation. The main proposed site of the suspension was the abdominal wall and the timing of post-operative adhesions evaluation ranged from 3 to 12 months after surgery.

Recent improvements in ultrasound technology allowed to use it as a reliable technique for the detection of pelvic adhesions and to evaluate their severity. Gentle pressure with the vaginal probe and an abdominal compression with the examiners free hand have been used to assess the presence of ovarian adhesions: the presence of adhesions was diagnosed when it was impossible to separate the ovary from the peritoneum of the pelvic sidewall and/or pouch of Douglas. Currently, laparoscopy remains the gold standard for the diagnosis and staging of deep infiltrating endometriosis (DIE) [36]. The surgical treatment of these lesions represents a challenge for surgeons, because of the high rate of intraoperative/postoperative complications. Although laparoscopy allows a direct access to the lesions, an accurate preoperative assessment of DIE implant location and extension is crucial; for these reasons, new modified standard transvaginal sonography techniques, which differ from standard ultrasonography by the introduction of a contrast medium into the vagina or rectum, are being considered [36, 37].

The Operative Laparoscopy Study Group (OLSG) Scoring System has been used to quantify the results after oophoropexy in two studies [17, 26]. Carbonnel et al. and Hoo et al. showed 50% of suspended ovaries had absence or only thin adhesions at the second-look laparoscopy [17, 26]. Pellicano et al. demonstrated a large difference between patients undergoing ovarian suspension to the ipsilateral round ligament and patients without additional procedures. In his study, 66,7% of patients of the ovarian suspension group had no postoperative ovarian adhesions versus only 19,2% of the control group [28]. Only one study described transvaginal outpatient hydro-laparoscopy as post-operative ovarian adhesions assessment modality performed 60-90 days after surgery [28], while in all other studies the evaluation of adhesion formation was done with ultrasound or second-look laparoscopy [17, 22, 25-28, 29]. Serrachioli et al. classified ovarian adhesions diagnosed by TVU into mild, moderate and severe, founding an increased ovarian mobility from the surrounding structures, as uterus and bowel, a reduction of postoperative severe adhesions and a reduction of ovarian pain under the pressure of the vaginal probe in the ovarian suspension group [29]. Moreover, all studies assessing adhesions at second-look laparoscopy showed absence of adhesions in a proportion of patients ranging from 40% to 80%.

Regarding the type of suture material, the most commonly used suture was synthetic, nonabsorbable, polypropylene monofilament (0 Prolene® Ethicon Inc., Somerville, NJ, USA), and a braided, nonabsorbable polyester suture (0 Mersuture® Ethicon Inc., Somerville, NJ, USA). Many Authors used absorbable sutures avoiding the need for suture removal and perhaps the possibility of infection. [25].

All the authors described the procedure as well tolerated and safe. No major complications were reported. Three Authors [17, 27, 29] reported minor postoperative complications. Out of 795 patients who underwent ovarian suspension, only 2 cases of ovarian abscess formation caused by *Klebsiella pneumoniae*, 2 cases of hemoperitoneum, 2

cases of fever ($T > 38^{\circ}\text{C}$) and 1 case of excessive intraoperative blood loss resulting in a post-operative Hb $< 10\text{mg/dL}$, occurring few days after the surgery, were reported [17, 27, 29] (Table 2). The patient with fever required antibiotic treatment for 7 days [29]. The patient diagnosed with ovarian abscess (caused by *Klebsiella pneumoniae*) had it drained via posterior colpotomy on post-operative day 8 whereas the patient who had hemoperitoneum was treated via laparoscopy on the first postoperative day [17, 27]. Although these complications occurred after the procedure, it is likely that excessive blood loss, fever and hemoperitoneum were related to the complex laparoscopy per se rather than the ovarian suspension part of the procedure. The only complication secondary to the ovarian suspension could be the ovarian abscess, demonstrating the safety of this technique.

The pelvic pain intensity was evaluated using the VAS score preoperatively and 3-6 months after the procedure. No difference was found by Pellicano et al. [28] and Seracchioli et al. [29] while Hoo et al. [16] reported an improvement in women's pain scores after surgery. The correlation between oophorectomy and post-operative pelvic pain is not clear because painful symptoms experienced by patients after laparoscopic procedures are likely multifactorial and may depend on the extent of the surgical procedure. Moreover, the ovary has visceral innervation, that is different from somatic type pain commonly complained by patients during the postoperative period [38].

The evaluation of fertility and pregnancy rate after this procedure is difficult to interpret because of the scant available data. Although the Authors [17, 22, 26] showed encouraging results (Table 2), the pregnancy rate should take into account several factors like the advanced reproductive age of patients, potential male factor infertility, and history of pelvic inflammatory disease in addition to endometriosis, as showed by Abhuzeid et al. [22], as well as the use of assisted reproductive technology (ART) in women unable to conceive spontaneously.

We acknowledge limitations of this review resulting from the high heterogeneity between studies, the presence of only 2 RCT as well as the different methods employed (TVU, LPS, TVU plus LPS and TV-H-LPS) to evaluate post-operative adhesions formation. Indeed, four of the eight studies only used ultrasound to score post-operative adhesions, including the only 2 studies in the meta-analysis [16, 25, 27, 29], while one study used both ultrasound and laparoscopy for post-operative adhesion scoring [22]. Moreover, the two RCT showed differences in terms of suture types and, consequently, ovarian suspension times.

Conclusions

Our data support the use of ovarian suspension as a safe, simple, feasible and effective strategy to reduce the incidence as well as the severity of postoperative ovarian adhesions formation in women undergoing laparoscopic surgery for stage III-IV endometriosis. Oophoropexy represents an adhesion formation preventive option in the surgical management of patients with stage III-IV endometriosis. Given the scant available scientific evidence, further studies are needed to confirm our findings.

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Table 1. Characteristics of the studies included in the review

	Abuzeid 2002 ²²	Ouahba 2004 ²⁶	Carbon nel 2011 ¹⁷	Hoo 2011 ²⁵	Poncel t 2012 ²⁷	Hoo 2014 ¹⁶	Pellican o 2014 ²⁸	Seracch ioli 2014 ²⁹
N. of patient s (type of study)	20 (RS)	20 (RS)	218 (RS)	16 (pilot RCT)	193 (RS)	55 (RCT)	185 (PCS)	88 (RCT)
Age of patient s (mean)	32 years	31.5 years	32.4 years	34.6 years	32.4 years	32,6 years	26.5 years	33.2 years

Site of suspension	Anterior abdominal wall	Anterior abdominal wall	Anterior abdominal wall	Anterior abdominal wall	Anterior abdominal wall	Anterior abdominal wall	Round ipsilateral ligament	Antero-lateral abdominal wall
Surgery type	LPS	LPS	(193) LPS (25) Laparotomy	LPS	LPS	LPS	LPS	LPS
Indication	Endometriosis stage III-IV	Endometriosis stage III-IV	Endometriosis stage III-IV	Endometriosis stage III-IV	Endometriosis stage III-IV	Endometriosis stage III-IV	Endometriosis stage II-III	Endometriosis stage III-IV
Suture (measure)	Polypropylene (3.0)	Prolene (3.0)	Prolene (0) Mersuture (0)	Prolene (0)	Prolene (0) Mersuture (0)	Prolene (NA)	Vicryl Rapid (2.0)	Vicryl (2.0)
Post-op removal (timing of removal)	Yes (fifth/seventh day)	Yes (fourth day)	Yes (fifth day)	Yes (36-48 h after surgery)	Yes (fifth day)	Yes (36-48 h after surgery)	No	No
Post-op adhesions evaluation (n° patients)	TVU, LPS (5)	LPS (8)	LPS (24)	TVU (16)	TVU (136)	TVU (52)	TV-H-LPS (50)	TVU (20)

RS: retrospective study; RCT: randomized controlled trial; PCS: prospective cohort study; LPS: laparoscopy; TVU: transvaginal ultrasound; NA: not available; TV-H-LPS: transvaginal hydrolaparoscopy; OA: ovarian abscess; HE: hemoperitoneum

Table 2. Outcomes of the studies included in the review.

	Abuzeid 2002 ²²	Ouahba 2004 ²⁶	Carbonnel 2011 ¹⁷	Hoo 2011 ²⁵	Poncellet 2012 ²⁷	Hoo 2014 ¹⁶	Pellicano 2014 ²⁸	Seracchioni 2014 ²⁹
Timing of post-op adhesion evaluation	N/A	5 months after surgery	12 months after surgery (mean)	3 months after surgery	N/A	3 months after surgery	2-3 months after surgery	6 months after surgery
Post-operative ovarian adhesions formation	2/10 (20)	7/12 (58.3)	19/38 (50)	18/32 (56.3)	N/A	20/52 (38,5) vs 27/52 (51.9)	22/54 (40.7)	30/45 (66.7) vs 38/45 (84.4)

rate [n° ovaries (%)]								
Severity of post-operative ovarian adhesions (%)	N/A	4/12 (33.3)	N/A	N/A	N/A	5/52 (9.6) vs 10/52 (19.2)	N/A	17/45 (37.8) vs 34/45 (75.5)
Evaluation of post-op pain (VAS score)	N/A	N/A	N/A	N/A	N/A	Yes	Yes	Yes
Pregnancy rate (%)	8/20 (40)	8/15 (53.3)	58/105 (55)	N/A	N/A	N/A	N/A	N/A
Immediate post-op complications	None	N/A	OA (1); HE (1)	None	OA (1); HE (1)	N/A	None	Fever (2); blood loss (1)

N/A: not available; OA: ovarian abscess; HE: hemoperitoneum

Figure 1. Flow diagram of studies identified in the systematic review. (*Prisma template [Preferred Reporting Item for Systematic Reviews and Meta-analyses]*).

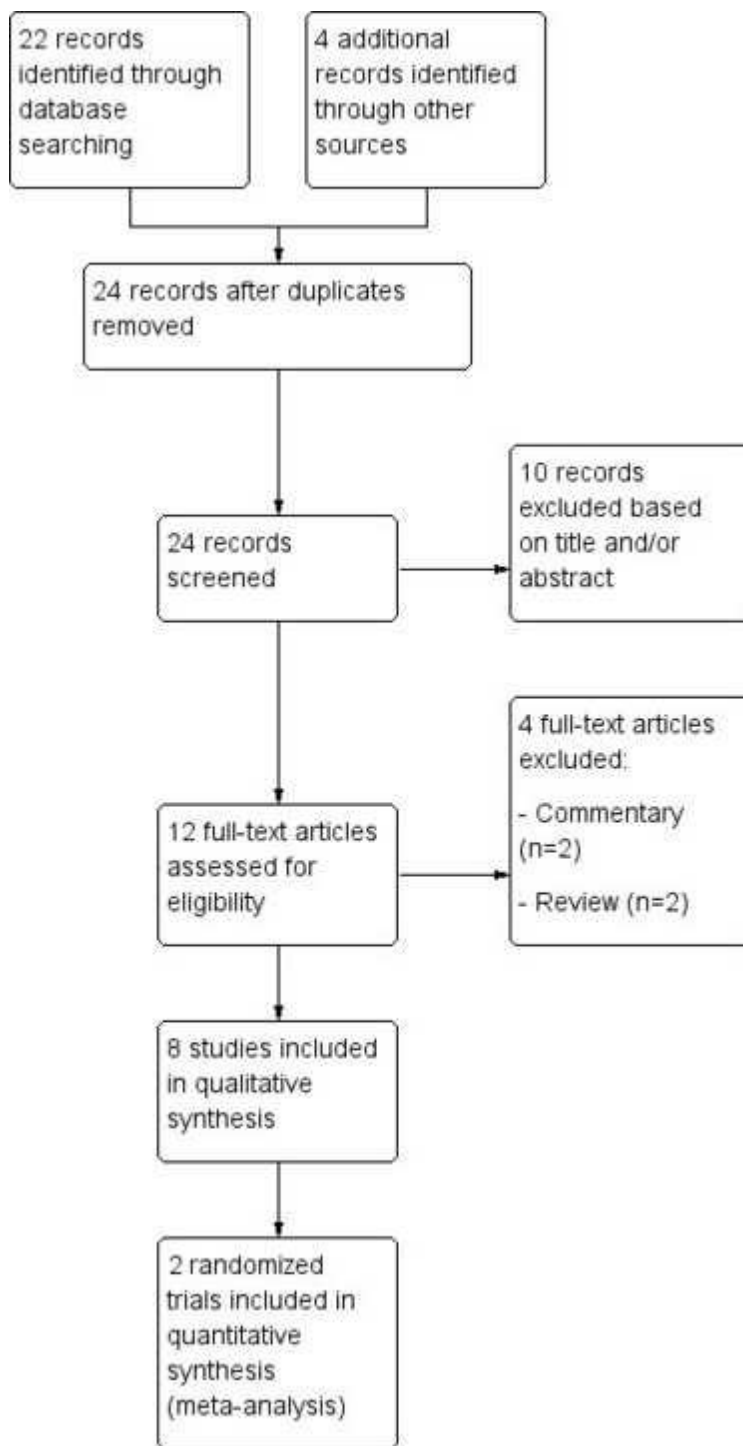


Figure 2. Ovarian suspension to the ipsilateral round ligament.

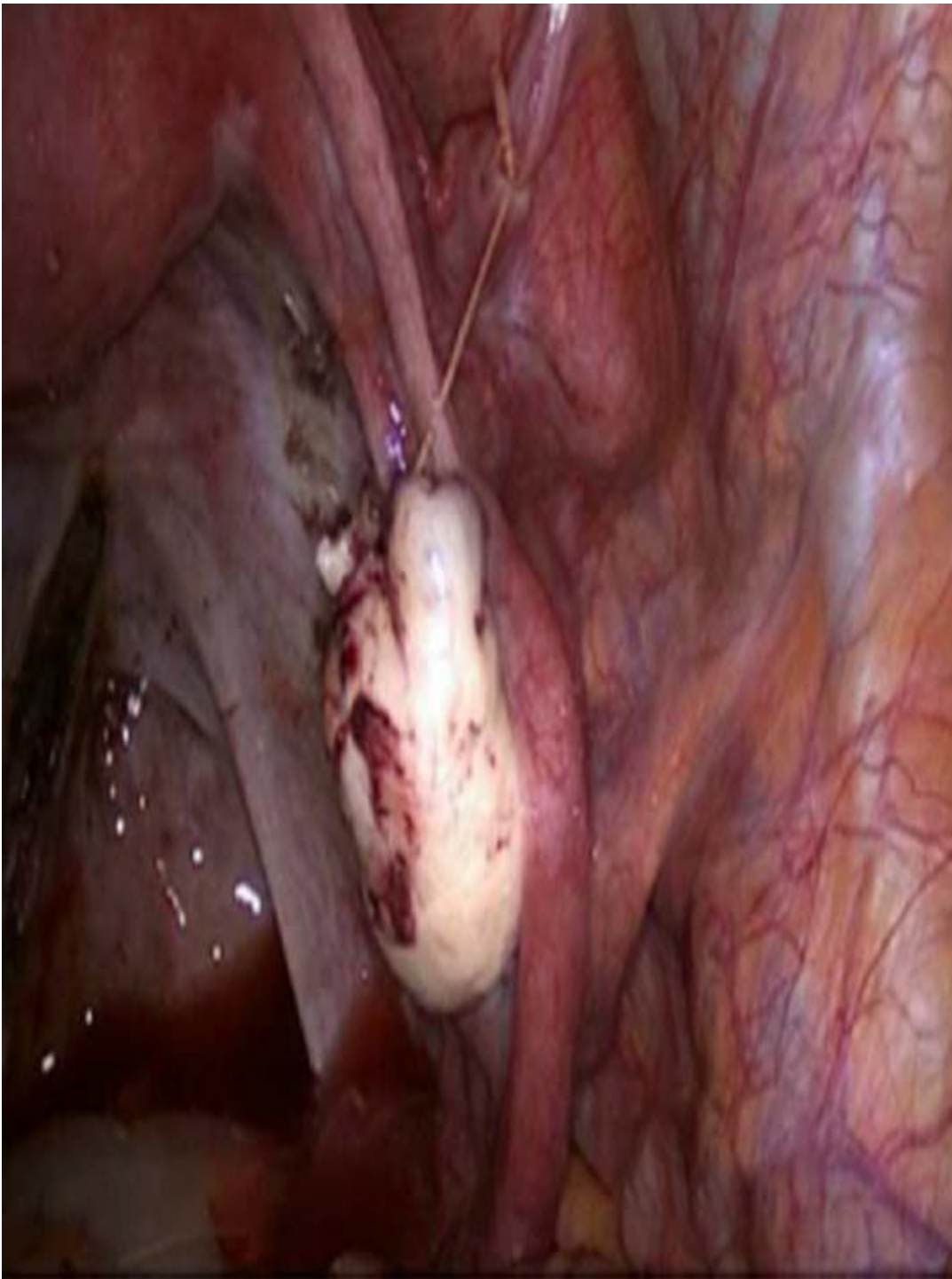


Figure 3. Assessment of risk of bias. (A) Summary of risk of bias for each trial; Plus sign: low risk of bias; minus sign: high risk of bias; question mark: unclear risk of bias. (B) Risk of bias graph about each risk of bias item presented as percentages across all included studies.

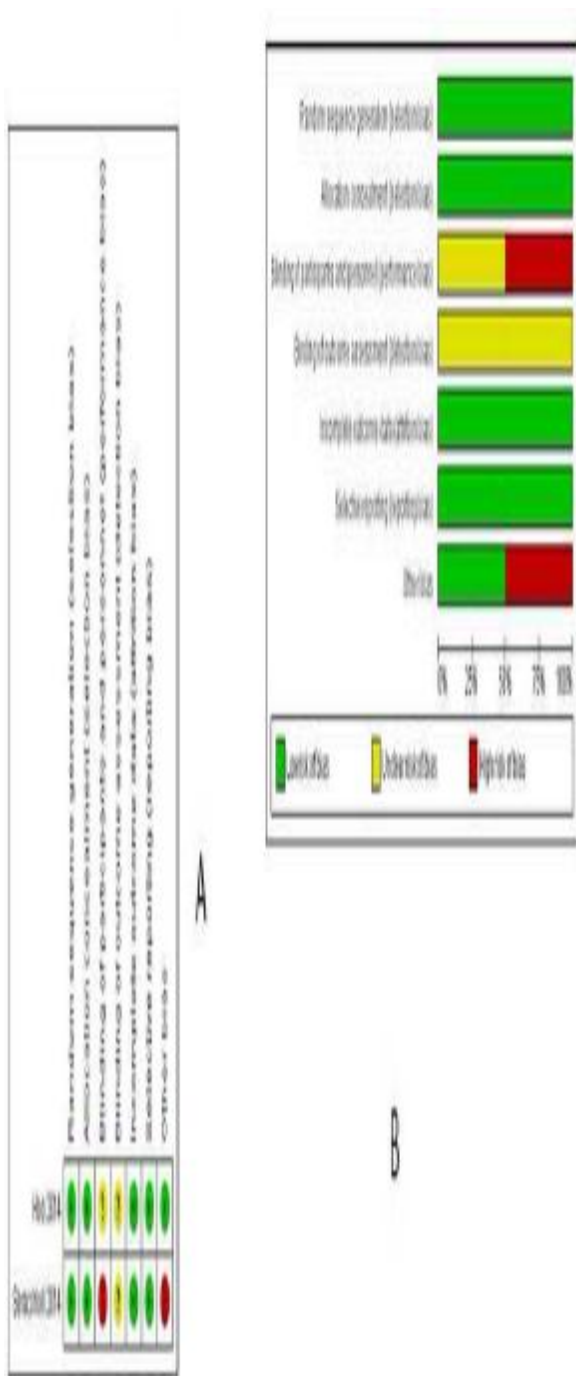


Figure 4. Forest plot for the risk of postoperative adhesions.



Figure 5. Forest plot for the risk of moderate-severe adhesions.



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