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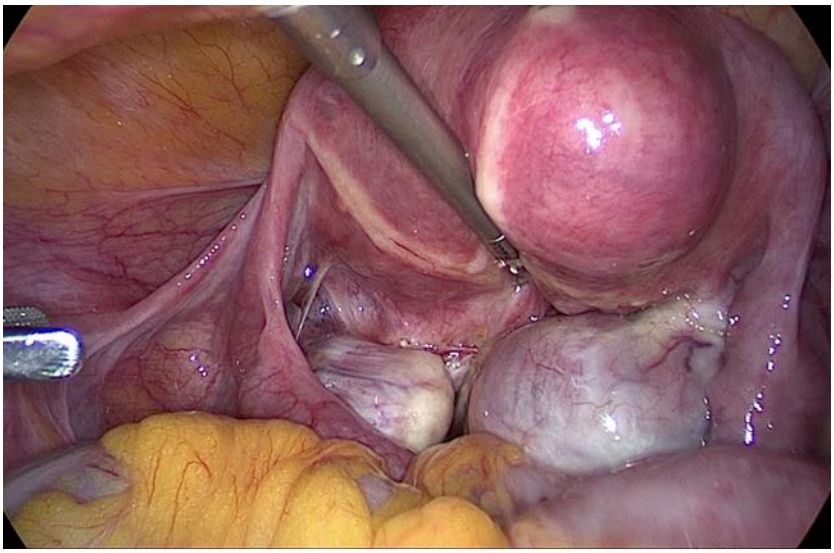

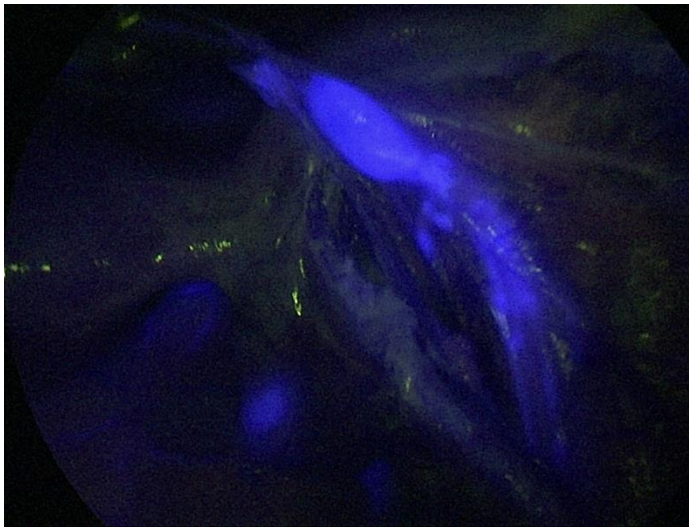

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How can we, as doctors, support each other to make good medicine available to more people?

As a global, specialized medical community, we bundle a lot of knowledge, experience but also cultures. In addition, the sometimes-extreme economic differences have to be reflected. It should not be forgotten that in associations like ours (ISGE) rather privileged people meet at first. But the good thing is that we can and may use this to support many. The question is how we do it well and at eye level.

In industrialized countries there is a perception that, many so-called developing countries are inherently poor and poorly developed. It should not be forgotten that former colonialism has been partly superseded by a kind of economic colonialism that supports corrupt elites because it benefits them. Above all, the "drippel-down" theory of neoliberalism has cemented the attitude towards the countries of the South. Developing countries tend to be very young in mean age, while developed countries are aging. Therefore, it is time for us to recognize the power of people and not see them as recipients of aid. It's not the time for charity, it's the time for participation.

It is important that we design training in such a way that it can multiply locally, as we as an organization have limited human resources. Financing is always a problem, so it is important that we succeed in getting support far from economic interests. In the economically prosperous countries, there are already too many training opportunities with which economic profit is made. Even an organization like ISGE needs funding, but our focus is on generating sources that enable funding for the common good.

ISGE works on learning concepts that respect local conditions, but also offer the highest possible standard. We are therefore pleased about the growing popularity by many colleagues who like our concept and would like to work on it. Be part of it and come to ISGE. If your local organization affiliates with ISGE, you are automatically an affiliate member and have almost all the options of a full member, so reach out to your local country organizations and encourage them to become an affiliate member.

I look forward to meeting you soon at one of our meetings, our trainings or on other occasions.

Best regards

Guenter Noé

Past President ISGE

Editor in chief

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The frontpage shows: 1) Myoma and kissing Ovaries 2) ICG right pelvic wall lymph node street

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The Trocar Issue 3 Volume 4/ Page 1-9 **ISSN: 2736-5530**

Ablation therapy: a new super-microinvasive treatment for uterine fibroids and adenomyosis

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Historically, the commonly used treatment for gynecological benign anatomical entities has been excisional, that is, surgical resection to remove the lesion. In the past 30 years, excisional treatment has gradually become minimally invasive. Laparoscopic and hysteroscopic surgery have become the treatments of choice for many gynecological diseases. It is also known as the era of minimally invasive gynecological surgery (1-4). Minimally invasive surgery, compared with traditional open surgery, is less painful, recovery is faster, produces smaller scars, and yields a higher patient satisfaction (5-7).

The improvement of the technology always promotes the development of lesser invasive treatment solutions, here the appearance of ablation therapy provides a less invasive option for uterine benign diseases such as fibroids and adenomyosis.

Ablation therapy, also called myolysis in case of myoma, is not a specific technology, it is a general denomination for a group of technologies, the basic principle of which is to use high temperature or low temperature to destroy the lesion (8-11). At this moment in time, thermal ablation is more commonly used, and cryoablation is also used in some tumors such as lung tumors (12-13).

The energy source for generating heat can be high-intensity focused ultrasound, microwave, radio frequency, or others. After the energy is generated, whether tissue degeneration and necrosis occur is related to the temperature of the target tissue after the energy is applied (14). If the local temperature in the tissue reaches 65 °C, it can achieve tissue damage within one second, leading to tissue degeneration and necrosis, and if the temperature reaches 54 °C, it takes 3 seconds to achieve tissue damage (15-16).

High intensity focused ultrasound (HIFU) is a method of tissue damage using

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ultrasonic energy, similar to the principle of a solar power cooker. A solar power cooker focuses sunlight on the cooker, while HIFU concentrates the energy of ultrasonic waves on the focal point in the tissues. This is a way to treat the tumor without touching it. Over the treatment path, because of the fact that the accumulation of energy does not reach a sufficient temperature needed to destroy tissues, it will therefore not cause damage to these tissues, and because the energy at the focal point is high, when it reaches above 65 °C, the tissue will be destroyed instantly (17-18).

At present, HIFU includes ultrasound-guided treatment (e.g., Haifu® Chongqing Medical Technology Co Ltd Chongqing China) and Magnetic Resonance Imaging (MRI)-guided Focused Ultrasound (MRgFUS) treatment (e.g., Exablate® Insightec STel Aviv – Yafo, Israel) (19). The two technologies have their own advantages and disadvantages. Ultrasound-guided high intensity focused ultrasound therapy is relatively convenient for adjusting the body position and designing treatment paths because of the real-time nature of the ultrasound signals. For MRgFUS, the image quality is better than the ultrasound-guided, there is also a temperature monitoring system during the treatment process, that can control the treatment boundary more accurately and ensure safety, but the operation time will be relatively longer (20) (Fig 1). The energy used by HIFU is ultrasound for the treatment of uterine diseases, fibroids and adenomyosis, Ultrasound can reach the uterus through the skin, the subcutaneous tissue, and the peritoneum. If the uterus is in the anterior position and very close to the abdominal wall, the treatment is easy to perform. If there are bowel loops in front of the uterus, then HIFU cannot be performed because ultrasound cannot pass through the air inside the bowel loops. Sometimes the intestines can be pushed aside by a full bladder, and ultrasound can travel through the bladder to perform the treatment. Since HIFU treatment works in a " telekinetic" fashion, its advantages include no scars, minimal trauma, quick recovery, and almost no bleeding during the treatment process.

The treatment can be carried out in outpatient clinics, but pathological examinations are not available during the treatment process, nor can it be combined with laparoscopic or hysteroscopic techniques. In addition, in order to avoid nerve injure during the treatment process, general anesthesia or regional block anesthesia cannot be used. Intraoperative sedation and analgesia are the only options, and most patients may experience a certain discomfort during the treatment process.

Figure 1: Temperature monitoring during MRgFUS

Microwave ablation is practiced by using a 16-18G sized needle like antenna to generate high-temperature energy within the punctured target tissue, causing destruction to the target tissue. There is water circulation within the microwave antenna sheath that does reduce the temperature of the rod. Therefore, on the puncture path the tissue temperature will not reach the destructive effect, this system can avoid damage to normal tissue.

Microwave ablation for the treatment of uterine-related diseases is usually performed under the guidance of abdominal ultrasound. The abdominal ultrasound probe guides the microwave antenna to puncture the uterus through the skin. Like HIFU, when the anterior positioned uterus is close to the abdominal wall, it can be treated by percutaneous microwave ablation. Different from HIFU, during percutaneous microwave ablation, the bladder, with the patient in lithotomy position, can be used and a uterine manipulator can be placed to change the position of the uterus during the treatment, in doing so a safe treatment pathway can be achieved. In some patients, when the uterus is in retroversion, or the lesion is relatively close to the posterior wall, an abdominal ultrasound-guided transcervical puncture or a transvaginal ultrasound guided transcervical puncture can be performed to reach the target area for treatment.

Laparoscopic microwave ablation can be performed on posterior adenomyotic lesions. Here a greater degree of destruction of the adenomyotic lesions can be achieved. Another difference from HIFU is that the microwave ablation is usually performed in the operating room, and the anesthesia can be general anesthesia or regional block anesthesia. The patient will not feel any pain during treatment. Another advantage is that a needle biopsy can be performed simultaneously to obtain pathology. Compared with HIFU, percutaneous microwave ablation has a puncture point, but the puncture needle hole is very tiny, and basically there is not much bleeding during the treatment process. Compared with laparoscopic surgery, there is no pneumoperitoneum effect, and the trauma is therefore much more reduced (Fig 2).

Figure 2. The tiny puncture needle hole in percutaneous microwave ablation

Another type of ablation energy is radiofrequency. Its working principle is to use high-frequency current to generate molecular oscillations to destroy target tissue. The principle and the method of percutaneous puncture are similar to percutaneous microwave ablation. At present, there are companies in the Chinese market that design transcervical radiofrequency ablation probes that can penetrate through the cervix to the target

tissue. An advantage is that the probe is reusable. Compared with microwave, the energy of radio- frequency is slightly lower, and it works slower on larger lesions with a diameter above five cm. One advantage of radio frequency is that it can automatically terminate the ablation through impedance detection. Once the resistance of the target tissue reaches a certain threshold; it will stop working.

Ablation therapy is guided by ultrasound or MRI. Generally speaking, lesions with diameters smaller than two cm usually cannot be accurately located and cannot be ablated, while lesions with diameters larger than ten cm can increase the difficulty of the treatment, especially for HIFU therapy. It will take too long a time and often requires GnRH-a pretreatment.

Before treatment, in addition to evaluating the size and location of uterine fibroids and adenomyotic lesions using ultrasound, it is necessary to check whether there are intestinal loops on the puncture path before implementing high intensity focused ultrasound. If there are intestinal loops that cannot be pushed aside, HIFU cannot be performed. Instead, when microwave or radiofrequency methods are used, if the abdominal path cannot be set up, a cervical or vaginal puncture route to avoid interference of the intestines can be tried.

Preoperative plain scan and contrast enhanced MRI can differentiate uterine fibroids from undetected uterine leiomyosarcomas (Fig 3-6). High Diffusion Weighted Imaging (DWI) signal intensity, low Apparent Diffusion Coefficient (ADC) and uneven enhancement are the signals of uterine sarcomas (21). The T2 weighted i image (T2WI) signal of MRI can also evaluate the difficulty of ablation. If the T2WI signal is high, it indicates that the water content in the fibroid is high, and it is often more difficult to perform ablation than in those with T2WI low signal intensity (22).

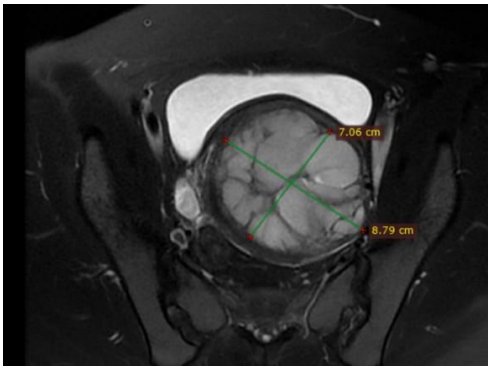

Figure 3: MRI revealed a tumor of about 9 cm

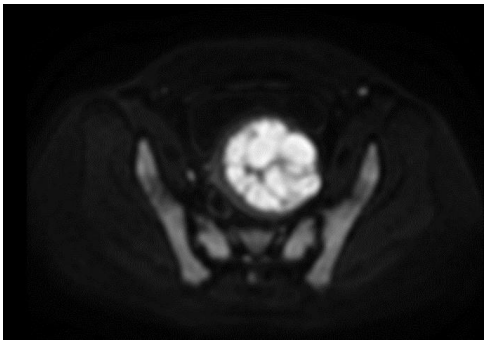

Figure 4: DWI revealed high signal intensity

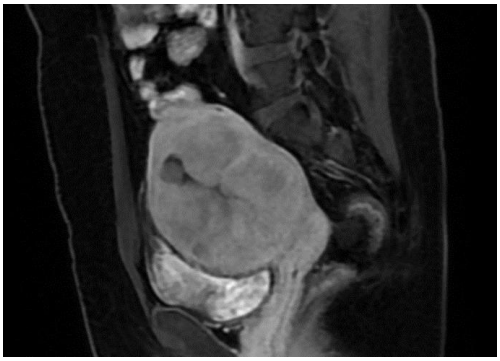

Figure 5: Contrast-enhanced MRI revealed that there was necrosis inside the tumor.

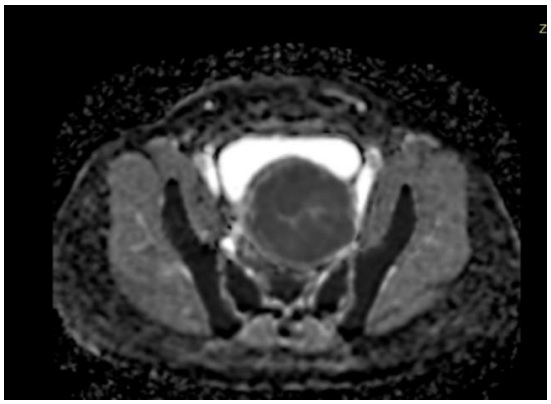

Figure 6: MRI revealed that the ADC value of the tumor was low

For uterine fibroids, if microwave or radiofrequency ablation treatment is performed, a 14 G biopsy needle can be used to obtain tissue for pathological diagnosis before treatment. In contrast HIFU treatment often makes it inconvenient to perform simultaneously a biopsy for pathology due to the patient's body position.

For patients with submucosal fibroids or other intrauterine lesions such as endometrial polyps, it is convenient to perform hysteroscopic examination and treatment simultaneously during microwave or radiofrequency ablation. Therefore, for patients with multiple uterine leiomyomas, we often prefer to use hysteroscopy to remove the type 0-2 lesions simultaneously, while for type 3-7 lesions, ablation can be used. For patients with menorrhagia, it is also convenient to perform endometrial ablation simultaneously to reduce menstrual flow and relieve symptoms. Likewise, hysteroscopic examination or treatment cannot be performed concurrently with HIFU due to patient's position and lack of anesthesia.

Different is the ablation treatment of some malignant tumors. The ablation of malignant tumors requires the implementation of over-range ablation, that is, the area of ablation necrosis should not only include the tumor, but also include the tissue of about half to one cm around the tumor to ensure the effectiveness and thoroughness of the treatment. In parenchymal organs, such as lung, liver, and thyroid, because of the protection of surrounding tissues, over-range ablation is usually safe.

For ablation of benign uterine diseases, the first priority is to ensure the safety of the treatment. The organs surrounding the uterus, such as the intestines and bladder should not be injured by ablation, otherwise this will gender or cause a complication. For patients with fertility requirements, the ablation treatment also needs to ensure that the scope of ablation is limited to the inside of uterine fibroids or adenomyotic lesions to avoid damage to the endometrium or the uterine seromuscular layer, otherwise there may be uterine adhesions, infertility, or uterine rupture during pregnancy after treatment (23-24).

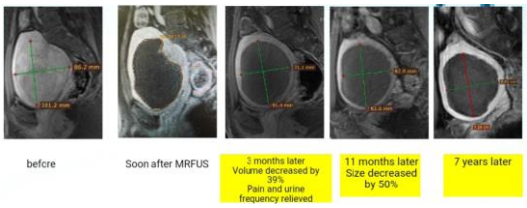

Figure 7. Non-Perfused Volume (NPV) area after ablation

Different from excisional treatment, the postoperative lesion cannot be seen by ultrasound or MRI. After ablation, the lesion

will gradually undergo necrosis and will be absorbed by the blood circulation, leading to atrophy of the lesions. If ultrasonic detection is used, it is often impossible to detect necrosis inside the lesion. By contrast enhanced ultrasound or contrast enhanced MRI, necrosis inside the lesions can be detected. Usually, we use non-perfused volume (NPV) to describe the proportion of necrosis after ablation (25) (Fig 7). The larger the NPV, the more symptoms will be cured. After ablation, usually the lesions gradually shrink, and symptoms are gradually cured (Figure 7). Uterine necrotic lesions often appear as degenerated fibroids on postoperative ultrasound.

Because the lesions do not completely disappear after ablation, we generally do not use the recurrence rate to evaluate the treatment efficacy. If it is considered that the presence of adenomyosis or uterine fibroids on ultrasound is a recurrence, then we can assume that the recurrence rate is almost 100%. With ablation therapy, we usually prefer to use the re-operation rate to evaluate the efficacy after treatment.

When it comes to the complications of ablation therapy, injury to adjacent organs caused by overtreatment is an important aspect. In addition to the injury to the endometrium (Fig 8) or the seromuscular layer (Fig 9) of patients wishing fertility,
injury to other organs is also an important aspect , including bowel loops (1-3‰), bladder, skin and subcutaneous tissue. The
injury to the bowel is often delayed, occurring 5-10 days after ablation. Heavy bleeding may occur after treatment due to vessel injury or uterine bleeding in some cases. Skin burn may happen during HIFU and microwave treatment (Fig 10). Nerve injury is a unique complication of HIFU therapy, which is related to the backfield energy of focused ultrasound behind the target tissue, which is also the reason why we use intravenous sedation and analgesia during high intensity focused ultrasound therapy. However, there are still a small number of patients with transient nerve involvement, manifested as sensory or motor disturbances in the legs.

Infection after ablation therapy is relatively higher than resection treatment, especially when ablation combined with some therapeutic procedures in the uterine cavity. Fever, abdominal pain, and odor discharge are the main symptom after infection. Antibiotics are necessary for the treatment. Dilation and curettage or hysterectomy are needed when antibiotics cannot control infection. Prolonged watery discharge is common when ablation affects the endometrium.

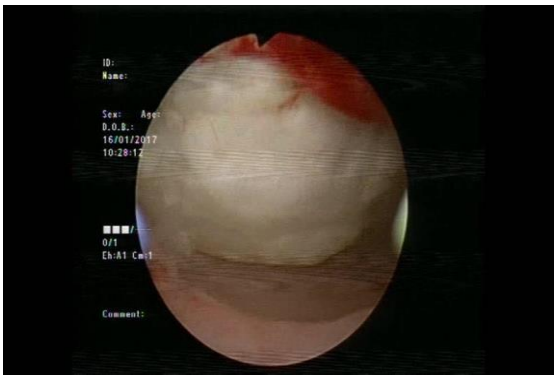

Figure 8. Endometrial damage by HIFU (figure courtesy of Dr. Ma Ning, Beijing Fuxin Hospital).

Figure 9 Laparoscopy View of uterine damage caused by HIFU

Figure 10. Skin injury cause by microwave ablation

Whether ablation therapy can be performed for patients with fertility wish needs further research. Current effective research suggests that ablation therapy is safe, but there are also reports of uterine rupture during pregnancy after ablation therapy (24-26-29-30). For patients with fertility wish, it is key to control the range of ablation therapy and not to over-treat when performing ablation therapy. During the treatment process, it is necessary to ensure that the integrity of the endometrium and seromuscular layer is not damaged to the maximum possible (Fig 11). It is better to have an insufficient ablation than secondary damage. After implementation of the ablation therapy, it is generally considered, empirically, that the patient can try to conceive one to three months after the treatment. A study on pregnancy after MRgFUS found that the complications of pregnancy after MRgFUS were comparable to those in the general population (31). Of course, due to the rarity of pregnancy complications more data have to be generated.

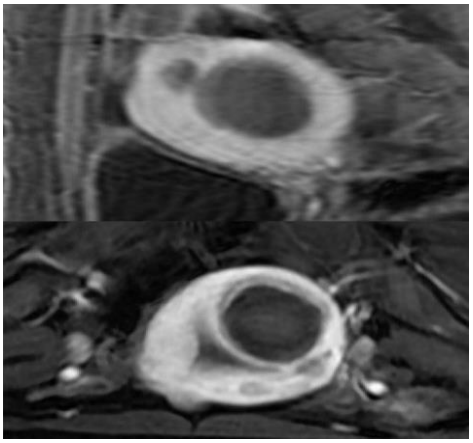

Figure11. Enhanced MRI did show the ablation zone after MRgFUS

Compared with traditional laparoscopic surgery or open surgery, ablation treatment causes less damage to the patient, less pain, almost no blood loss or very minimal bleeding, and shorter time to recovery and return to work. Most treatments can be performed in outpatient or at day surgery centers without a long hospitalization. Due to the fact that benign uterine diseases such as uterine fibroids and adenomyosis are age- related diseases, the lesions tend to shrink and symptoms are reduced with the decrease of estrogen after menopause.

Therefore, for these benign diseases of the uterus, in addition to the traditional

resection therapy, ablation therapy undoubtedly provides a new direction for the treatment. In our opinion, ablation therapy provides us with an alternative treatment for benign uterine disease alongside endoscopic surgery. It can also be considered as the next generation of surgical technology, which deserves to be mastered by more gynecologists.

Of course, compared with resection therapy, ablation therapy also has some disadvantages. For example, the lesion will not disappear completely after treatment. The chance of secondary surgery is relatively high, and the chance of secondary infection after treatment is relatively high.

Nevertheless, ablation therapy still provides a very good direction for the conservative treatment of benign gynecological tumors such as uterine fibroids and adenomyosis.

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The role of hysteroscopy in patients with recurrent implantation failure before starting in vitro fertilization: a systematic review and meta-analysis

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Abstract

Objective
Recurrent Implantation Failure (RIF) remains the most challenging in-vitro fertilization (IVF) problem to treat. This is because the overall success rate is only approximately 30%. Hysteroscopy remains the gold standard for diagnosing and treating intra-uterine anomalies. This study aimed to evaluate the role of hysteroscopy (HSC) in improving pregnancy outcomes in patients with RIF.

Methods
A systematic search was performed in PubMed, ScienceDirect, Embase, and Cochrane using MeSH terms, if applicable and in accordance with the PRISMA guidelines, to determine the role of hysteroscopy compared to patients who didn't undergo hysteroscopy. The Newcastle– Ottawa scale (NOS) was used to assess the risk of bias in this analysis, and Review Manager
5.4 was used to calculate the result of 95% CI for the outcomes. The endpoints of interest were clinical pregnancy rate, live birth rate, implantation rate, and miscarriage.

Results
A total of 3 randomized controlled trials (RCT) and 5 cohort studies with 4,679 patients were included. Pooled analysis showed that patients who underwent HSC were associated with higher clinical pregnancy - [OR 1.64, 95%CI (1.32-2.03)], live birth - [OR 1.50, 95%CI (1.17-1.92)], and implantation rate [OR 1.42, 95%CI (1.02-1.98)] but no significance in miscarriage rate. Further subgroup analysis suggests HSC had a significantly greater effect on clinical pregnancy rate for patients with abnormal HSC findings [OR 1.20, 95%CI (1.01-1.42)], but no significant difference in live birth - and miscarriage rate.

Conclusion
HSC plays a significant role in improving the clinical pregnancy rate, especially in patients with abnormal HSC findings. HSC also improves implantation rate, live birth -, and clinical pregnancy rates in patients with RIF. Since the number of the study is still limited, further investigations are still needed to confirm the results.

Key words: Hysteroscopy, recurrent implantation failure, in vitro fertilization, pregnancy outcome

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Introduction:

Infertility is a major issue that affects millions of couples worldwide. In the United States, around 7.5 million couples, or 1 in 8, are affected by this condition (1). The situation is not any better in Indonesia, where a study revealed that 21.3% of couples have trouble conceiving or sustaining a pregnancy, affecting roughly one in every five couples (2). Fortunately, a solution to this problem is assisted reproductive technology (ART). Among the most frequently techniques used in ART is in vitro fertilization (IVF). Studies have shown that IVF is an excellent solution for treating infertility (3-5). It is crucial to understand that the success rate of IVF cycles resulting in live births is approximately 25-30%. Among the numerous obstacles encountered during IVF, treating recurrent implantation failure (RIF) represents the most formidable challenge due to its low success rates of around 30% for women with RIF. While ovum collection and fertilization are often successful, an inexplicable discrepancy exists between the number of embryo transfers and the number of ongoing pregnancies lasting over 12 weeks (6). The reason for this failure to implant is not yet fully comprehended, although it appears to be influenced by both the embryo itself and the uterine cavity (7,8). Some abnormalities in the uterine cavity, such as polyps, myoma, adhesions, and sometimes endometriosis, are thought to be associated with impaired implantation and reduced chance of pregnancy (9). Several studies have reported the influence of intrauterine pathologies on pregnancy rates in women who will undergo IVF (10). Therefore, it is advisable to perform an examination for intrauterine pathologies before starting IVF (11,12). Since hysteroscopy (HSC) can give a good view of the uterine cavity, it is regarded as the reference standard for detecting these uterine abnormalities (13,14). HSC are reported to significantly find more abnormalities in patients with a history of ART failure (15-17). Two randomized controlled trials (RCT) confirmed the value of HSC in women with RIF by showing an increase in clinical pregnancy rate as high as 13%. In clinical practice, hysteroscopy is often performed on infertile women scheduled for the first IVF cycle. However, several studies have shown no significant effect of routine HSC on live birth rates (17-19). Due to conflicting findings regarding the use of HSC in patients with RIF, this study was aimed to determine if HSC before starting an IVF cycle in women with RIF may improve the clinical pregnancy rate, implantation rate, and live birth rate, this study was also aimed to see whether HSC reduces the miscarriage rate in IVF patients.

Materials and Methods

Systematic Reviews and Meta-Analyses (PRISMA) (20). This research collects and uses previously published studies. Therefore, there is no need for ethical approval. The submitted protocol was registered on the International prospective register of systematic reviews-PROSPERO (www.crd.york.ac.uk/prospero).

Search Strategy and Selection Criteria

Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed, EMBASE (Excerpta Medical Database), Science Direct and the Cochrane Library were searched without any language restriction from January 2002 until February 2023, using the following keywords: 'in vitro fertilization' or 'in-vitro fertilization' and 'infertility' and 'hysteroscopy' and 'recurrent implantation failure' or 'embryo implantation' or 'treatment failure' and 'uterine disease' and 'pregnancy'. Citation tracking was performed to identify additional publications. Our study searching protocols are presented in Supplementary Table S1.

All identified studies were screened by title and abstract. The inclusion criteria in this study were randomized controlled trial studies, non-randomized two-arm prospective studies, and two-arm retrospective studies. The study population was women with normal ultrasound examination of the uterine cavity and women who had recurrent implantation failure, defined in this study with at least 2 failed IVF embryo transfer attempts. Before starting IVF cycles, patients underwent HSC diagnostic. Meanwhile, the control population did not have a HSC before starting IVF. On the other hand, the exclusion criteria in this study were one-arm studies, article reviews, case reports, proceedings, and personal comments, studies with no data of outcome interest, and studies that aimed to assess the efficacy of HSC-associated scratching, biopsy, or treatment were also excluded. Two investigators independently identified studies that met the inclusion criteria, and the third investigator was consulted on whether any disagreements or to resolve any differences. A discussion was conducted to make the final decision.

Data Extraction; Quality Assessment

Data extraction and quality assessment were carried out independently by two investigators. Standard forms were used to extract the

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following information from each study: the study authors; study design and methodology; total and mean age of the patients; intervention used for the patients; IVF cycles failed; definition of RIF; clinical pregnancy rate; live birth rate; miscarriage rate; and implantation rate. In cases of missing data in the main results or something unclear, the authors of the original publication were contacted via email.

The risk of bias assessment for the included studies was conducted based on the study type. The randomized control trial study (RCT) was assessed using the Cochrane Risk of Bias tool (RoB) (21). The RoB consists of seven domains: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. Other sources of bias included potential bias related to the specific study design, stopped early due to some data-dependent process, and extreme baseline imbalance. The information extracted from the paper was judged on the possible risk of bias in each domain and was rated as "low risk," "unclear," or "high risk." For non-randomized studies, the risk of bias was analyzed by the Modified Newcastle-Ottawa Scale for Cohort Studies (22). The scale contains eight items within three domains. The possible total point for domain selection is 4 points, 2 points for comparability, and 3 points for outcome domain. The quality of the study was classified as "good" if the total was 7-9, "moderate" if the total score was 4-6, and otherwise as "poor." Two reviewers independently conducted the risk bias assessment, and any disagreement was resolved by discussion with the third reviewer. The overall quality of the non-randomized studies was good and presented in Table 1 as the risk of bias individually. The summary of RCTs quality is shown in Figure 1.

Outcome Measurement:

This study aimed to see whether there is any role for hysteroscopy in patients with recurrent implantation failure before starting in vitro fertilization considering clinical pregnancy rate, live birth rate, implantation rate, and miscarriage rate. Clinical pregnancy was defined as thirty-five days after embryo transfer and ultrasound examination showing a gestational sac, live birth rate was defined as the number of deliveries that resulted in a live-born neonate, and implantation rate was defined as the number of gestational sacs determined by ultrasound by the number of embryos transferred.

Data Synthesis and Analysis Quality Assessment

The meta-analysis was performed using Review Manager 5.4. The risks in terms of the outcomes of interest were computed and will be processed using Review Manager 5.4 and will later be presented with odds ratios (ORs) with 95% confidence intervals (CIs). Heterogeneity analysis between study populations was calculated using the I^2 statistic. The I^2 statistic was defined as follows: 0-24% as no heterogeneity, 25%-49% as moderate heterogeneity, 50-74% as considerable heterogeneity, and 75%-100% as extreme heterogeneity (23). Data are summarized across groups using the Mantel-Haenszel (M-H) risk ratio (RR) fixed effect model if $I^2 < 25\%$. The random effect model is used if $I^2 > 25\%$ (24). Funnel plots were used to evaluate publication bias. Analysis was carried out using Review Manager 5.4.

Results

Literature Search:

The flow diagram of the study selection process is shown in Figure 2. A total of 1039 studies were found during the initial screening through database searching and other sources. Two hundred ninety-three studies were removed due to duplicates, leaving 746 studies. These were scrutinized further for title and abstract and 673 studies that did not meet the inclusion criteria were excluded. The remaining 73 full-text articles were finally reviewed. As many as 65 studies were excluded due to different objectives and study designs (n=15), review articles (n=16), not a recurrent IVF but rather the first IVF cycle studies (n=17); no endpoints or different outcomes of interest (n=8); and case report studies (n=9). Finally, only eight studies were included in the meta- analysis (25 – 32)

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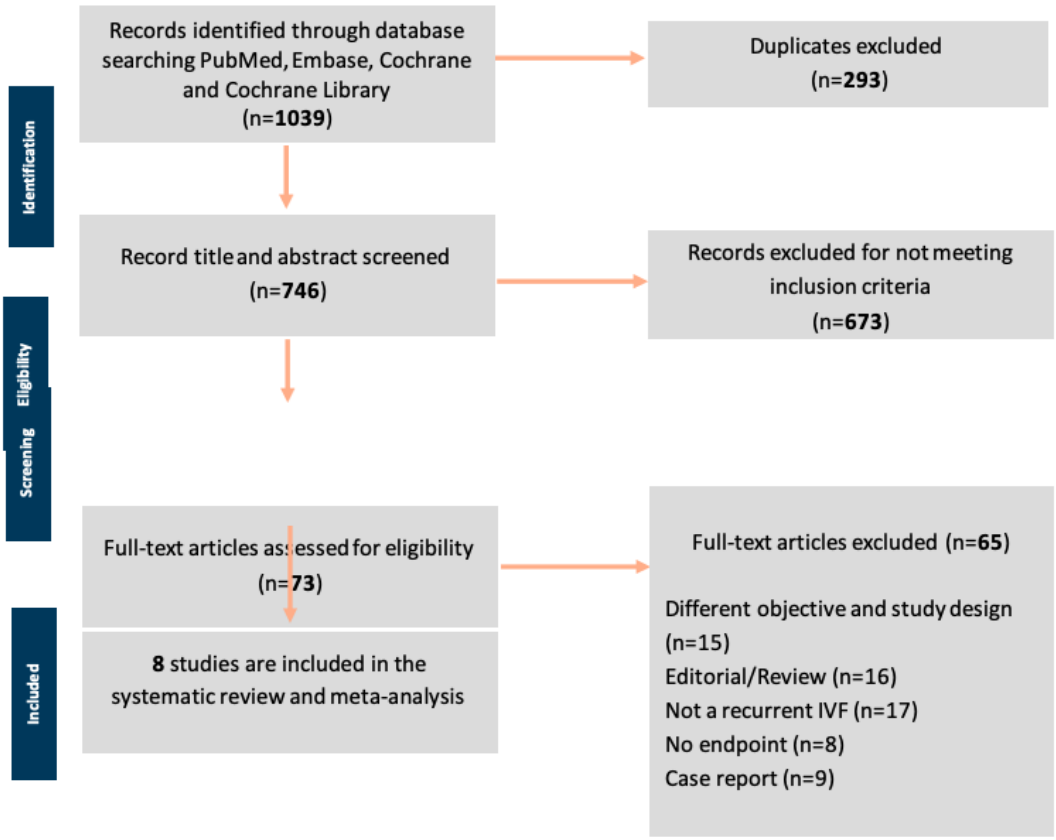

Figure 2. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram.

Characteristics of Included Studies

In this meta-analysis, eight studies met the predetermined inclusion criteria comprising three RCT studies, two retrospective studies, and three cohort studies. The basic summary of study characteristics included in this review, study design, the total of patients and the percentage of patients forming the population of each intervention, mean age, mean failed IVF cycles, the definition of RIF, and clinical pregnancy definition from each of the studies are represented in Table 2.

The basic summary data concerning the hysteroscopic examination procedure, ovarian stimulation procedure, and embryo transfer procedure is available in Table 3.

There are three studies with a RCT design. All of the studies did use computer- generated randomized systems, therefore these are rated as studies having a low risk of bias. Tarek et al., and Raju et al., needed clarification about the blinding outcome assessment domain because there was no statement about blinding the assessor. Similarly, in the study by Raju et al. and Demirol et al., there is insufficient data for the blinding participant and personnel domain to declare the risk of bias. As bias due to allocation concealment, all studies were considered high risk. The hysteroscopic procedure was explicitly unconcealed, which cannot be masked between the control and experiment groups. Tarek et al. published a study protocol that explained clearly the study outcome, thus getting a low risk of selective reporting. Meanwhile, the study protocol for the rest of the studies were unavailable.

All cohort studies were of quality, with a score of 7-9. The analysis by Hosseini et al. made no point in selecting a non-exposed cohort due to the fact of using an historical cohort as control compared to the present cohort, which means that the control cohort group did not resort from the same population The excellent quality in the selection domain must consist of inclusion and exclusion criteria to ascertain the representativeness of the cohort, pick the non-exposed group from the same cohort, have a good record of exposure, and ensure no outcome is present at the start of the study. Except for Hosseini et al., the rest of the studies fulfilled those criteria. The comparability domain examined the baseline data of exposure and control group, which expect to have no significant difference. The research by Makraris et al. was rated 2 points due to matching the control and exposure group. Of a population of

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1475 in this study, only 828 were included in the analysis because only 828 patients have been compared between the hysteroscopy and non-hysteroscopy groups. In contrast, the rest of the studies showed comparability of the cohort in their characteristic table. All included studies had a good outcome domain. The assessment of the outcome and length of follow-up of the study was described clearly in the method. The adequacy of the follow-up cohort from all studies was fulfilled due to no reporting attrition in the study of more than 10% of the participants.

Overall, the eight studies included 4679 patients with RIF, 1869 patients underwent hysteroscopy before starting IVF, and 2163 patients were allocated in the control group (patients without hysteroscopic evaluation before starting ovarian stimulation for IVF treatment). In this population, the average age of patients ranged from 25.39 to 38 years, with an average number of previous failed IVF cycles ranging from 2.4 to 4.04. The broad definition of RIF in each study protocol were patients who underwent two or more failed IVF cycles with a good-quality embryo, and clinical pregnancy was determined by using an ultrasound examination with hearth beating. During hysteroscopic examination, generally a rigid hysteroscope is generally used with a sheath diameter of 4 to 5 mm and a fore oblique lens of 22-30 degrees.

Seven of the eight studies, included in this meta-analysis, reported clinical pregnancy rate data (25-31). In the forest plot, the results of this analysis have a considerable heterogeneity between the seven studies included (Chi^2=12.61, I^2=52%), overall, this pooled analysis shows that the clinical pregnancy rate is significantly higher in patients who underwent hysteroscopy (HSC) when compared to the control group, which in this case is composed of patients with RIF who got IVF treatment without prior HSC examination [OR 1.64, 95% CI (1.32-2.03) p<0.001, (figure 3). Here we can also see the included results of the subgroup analysis of the non-randomized trial studies. The subgroup analysis shows that patients undergoing HSC have a higher clinical pregnancy rate [OR 1.67, 95% CI (1.31-2.13) p<0.0001]. The same was seen in the results of the RCT research analysis here also the clinical pregnancy rate was significantly higher in the HSC group [OR 1.60, 95% CI (1.03-2.49) p=0.04]. Both these results are presented in Figure 3.

We also did analyze further a subgroup between patients with normal and abnormal hysteroscopy findings to see if there is any difference in clinical pregnancy outcome. Five studies were included in the analysis, with no heterogeneity noted (Chi^2 = 1.03, I^2 = 0%). This analysis did find that patients with abnormal hysteroscopy findings and treated accordingly have a marginally significantly higher clinical pregnancy rate [OR 1.20, 95% CI (1.01-1.42) p=0.04]. The forest plot is presented in Figure 4.

Data Synthesis

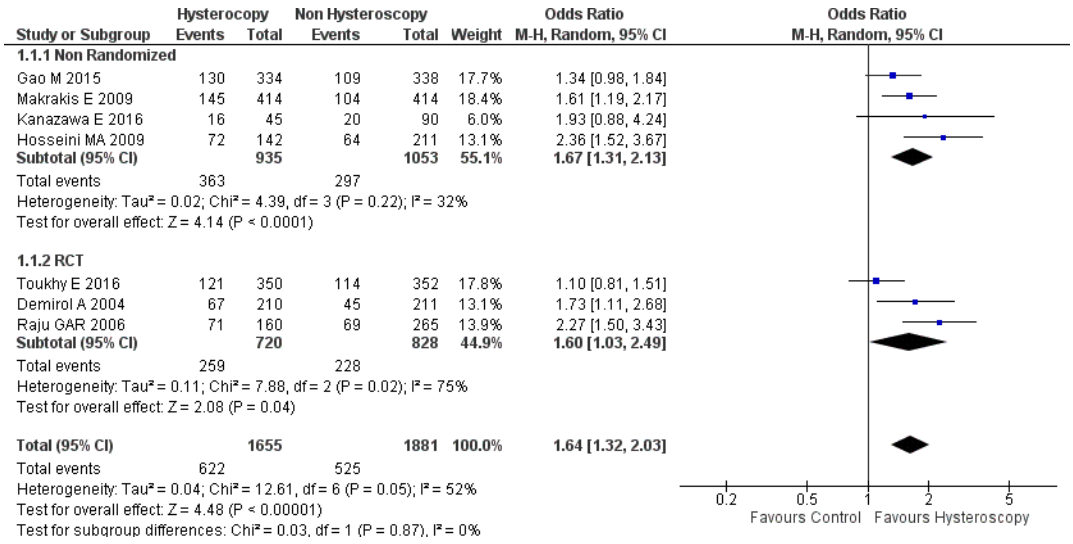

Figure 3. Forest plot of clinical pregnancy rate. Odd ratio of clinical pregnancy rate between

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patients with RIF who underwent hysteroscopy before IVF and did not undergo hysteroscopy before IVF. Test for overall effect: Z = 4.48 (p<0.0001) heterogeneity: I^2 = 52%. CI, confidence interval; RCT, randomized clinical trial.

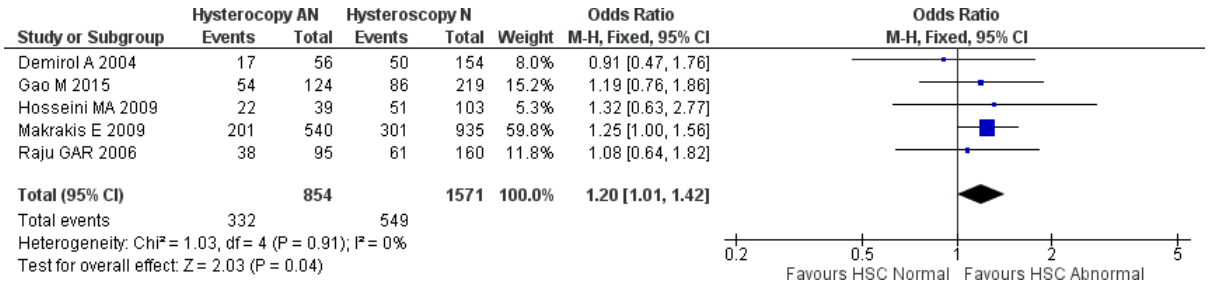

Figure 4. Forest plot of clinical pregnancy rate between normal and abnormal hysteroscopy findings in patients with RIF who underwent hysteroscopy before IVF. Test for overall effect: Z = 2.03 p=0.04 heterogeneity: I^2 = 0%. HSC: hysteroscopy.

Five studies provided data regarding the live birth rate; three were non-randomized trials, and two were RCTs (27-29,31,32). Overall, a moderate heterogeneity was found between the five studies (Tau^2 = 0.03, Chi2 = 7.04, I^2=43%). The pooled forest plot analysis showed that patients with RIF who underwent HSC before starting IVF have a higher live birth rate [OR 1.50, 95% CI (1.17-1.92) p=0.001]. Subgroup analysis of the non-randomized trials showed the same result, patients in the HSC group have higher live birth rates [OR 1.52, 95% CI (1.20-1.94) p=0.0007). But for the RCTs, the result showed no significant difference with OR 1.49, 95% CI (0.75-2.94), p=0.25. All the results are presented in Figure 5.

We further subgroup analysis between patients with abnormal and normal hysteroscopy findings to see whether there is any live birth rate difference. The analysis included three studies with no heterogeneity (Chi^2 = 0.73, I^2 = 0%). The forest plot found no significant difference between normal and treated abnormal hysteroscopy findings for live birth rate [OR 0.90, 95% CI (0.65-1.25) p = 0.53). The results are presented in Figure 6.

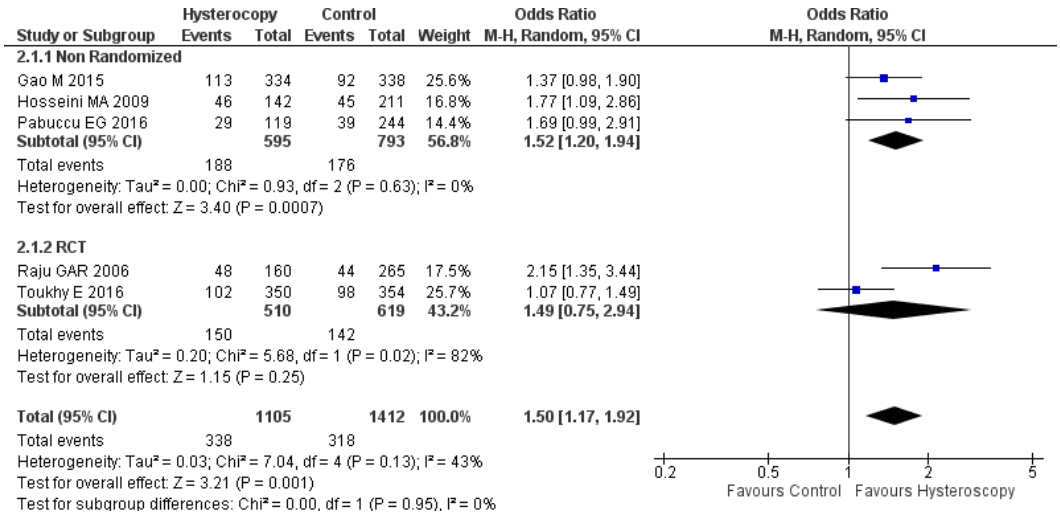

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Figure 5. Forest plot of live birth rate. Odd ratio of live birth rate between patients with RIF who underwent hysteroscopy prior to IVF and the patients who did not undergo hysteroscopy prior to IVF. Test for overall effect: Z = 3.21 (p=0.001) heterogeneity: I^2 = 43%. CI, confidence interval; RCT, randomized clinical trial.

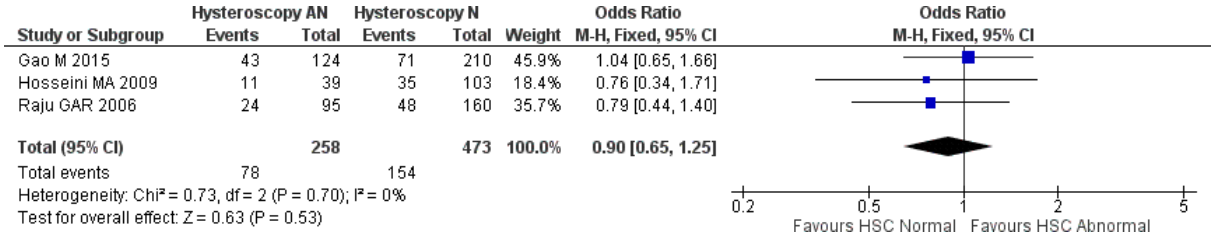

Figure 6. Forest plot of live birth rate between normal and abnormal hysteroscopy findings in patients with RIF who underwent hysteroscopy prior to IVF. Test for overall effect: Z = 0.63 p=0.53 heterogeneity: I^2 = 0%. HSC: hysteroscopy.

A total of four studies reported data related to the implantation rate, where 3 were non-randomized trials, and 1 was an RCT (28-31). This analysis shows considerable heterogeneity (Tau^2 = 0.06, Chi^2 = 6.91, I^2 = 57%). In the forest plot provided in Figure 7, it can be seen that RIF patients who underwent HSC before IVF had a higher implantation rate [OR 1.42, 95% CI (1.02-1.98) p = 0.04]. The definition of implantation in this study is the number of gestational sacs divided by the number of embryos transferred. A subgroup analysis from a non-randomized trial also showed a higher implantation rate in patients undergoing HSC [OR 1.64, 95% CI (1.11-2.42) p=0.0005). Unfortunately, no RCT subgroup analysis can be done. because only one study provided data regarding implantation rate.

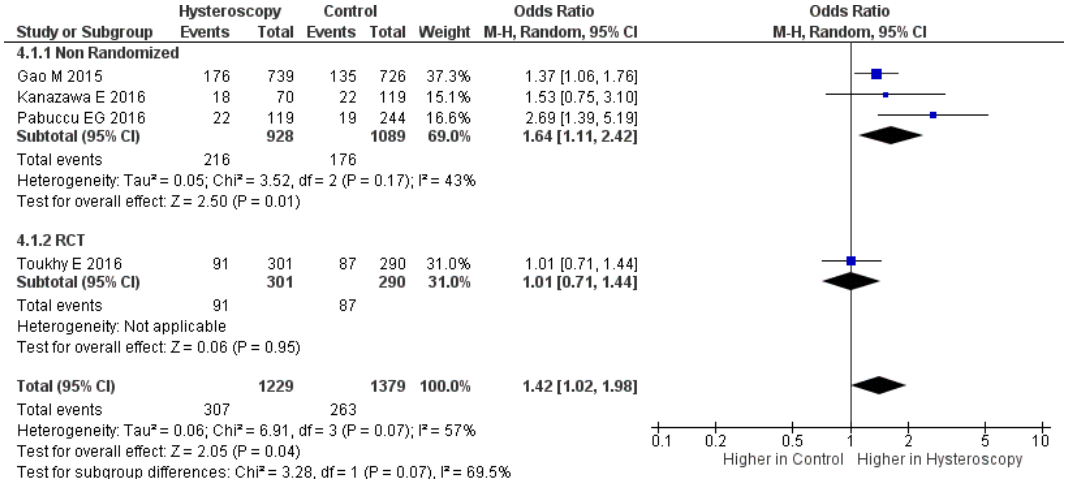

Figure 7. Forest plot of implantation rate. Odd ratio of implantation rate between patients with RIF who underwent hysteroscopy prior to IVF and the patients who did not undergo hysteroscopy prior to IVF. Test for overall effect: Z = 2.05 (p=0.04) heterogeneity: I^2 = 57%. CI, confidence interval; RCT, randomized clinical trial.

Seven studies reported miscarriage rate data; four were non-randomized, and the other three were RCTs. From the forest plot, the analysis had no significant heterogeneity among the studies (Chi2 = 7.84, I2=23%) (25,27,32). Pooled analysis showed that patients with RIF who underwent HSC before starting IVF had no significant miscarriage rate compared to patients with RIF who did not undergo HSC [OR 1.27, 95% CI (0.97-1.65) p=0.08]. Still, when we see the forest plot, the miscarriage rate does shift towards the control side, indicating that the miscarriage rate may be higher in the control group, but it is not statistically significant. The subgroup analysis of the non-randomized trial and RCT group also showed no significant difference [OR 1.45, 95% CI (1.00-2.12) p=0.05] and [OR 1.10, 95% CI

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(0.75- 1.61) p=0.64] respectively. All the results are provided in Figure 8. We also did further analyze the subgroup between normal and abnormal hysteroscopy findings. Three studies provided data regarding the difference between normal and abnormal hysteroscopy findings for miscarriage rate. No significant heterogeneity was found between the three studies. Pooled analysis shows no significant difference between normal and abnormal hysteroscopy findings for miscarriage rate [OR 0.91, 95% CI (0.52-1.59) p=0.75]. The results are provided in Figure 9.

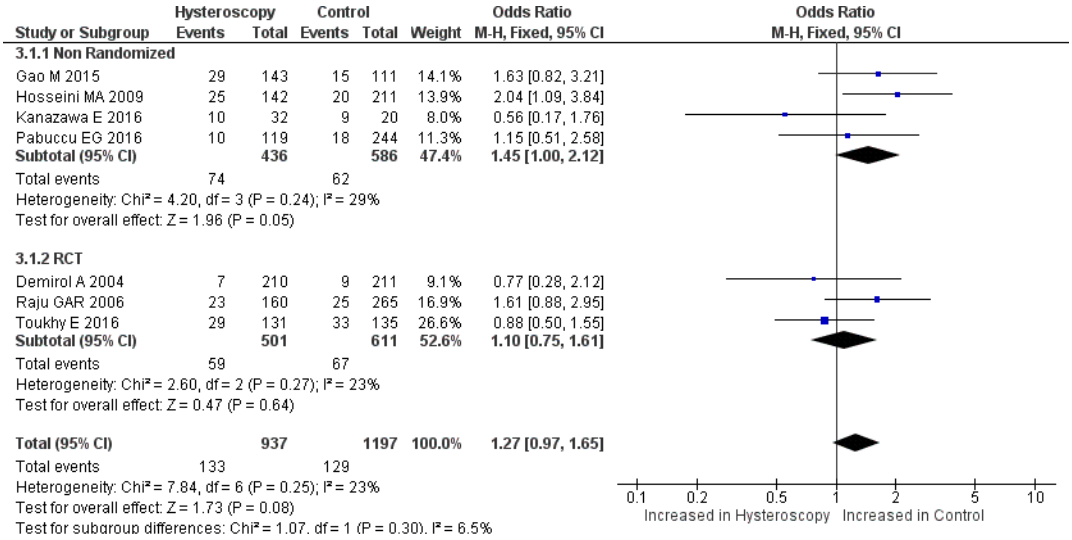

Figure 8. Forest plot of miscarriage rate. Odd ratio of miscarriage rate between patients with RIF who underwent hysteroscopy prior to IVF and the patients who did not undergo hysteroscopy prior to IVF. Test for overall effect: Z = 1.73 (p=0.08) heterogeneity: I^2 = 23%. CI, confidence interval; RCT, randomized clinical trial.

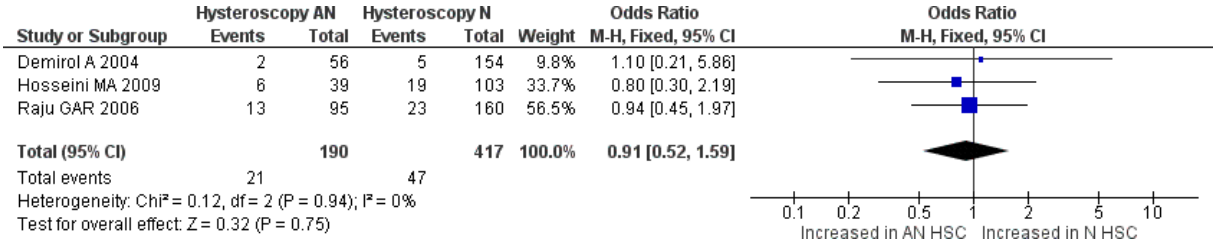

Figure 9. Forest plot of miscarriage rate between normal and abnormal hysteroscopy findings in patients with RIF who underwent hysteroscopy prior to IVF. Test for overall effect: Z = 0.32 p=0.75 heterogeneity: I^2 = 0%. HSC: hysteroscopy.

Discussion

There are two main findings of this meta-analysis study. First, patients with RIF who underwent HSC prior to the IVF procedure were associated with improved clinical pregnancy -, live birth -, and implantation rate. Second, the subgroup analysis of patients with normal vs. abnormal HSC findings suggests that HSC had a significantly greater effect on the clinical pregnancy rate for patients with abnormal HSC findings. The broadly used RIF definition of the studies included patients who had two or more failed IVF cycles with good-quality embryos, with an average number of previous failed IVF cycles ranging from 2.4 to 4.04. Overall, our results demonstrate that HSC has a role in improving pregnancy outcomes in patients with RIF.

IVF has widely known as the most common ART procedure performed worldwide (33). In the late 70s, the first successful IVF treatment in humans was performed in England, with a laparoscopic retrieval of a single oocyte from the ovary. The oocyte was fertilized in vitro and transferred into her uterus as an embryo (34). Since then, IVF technology has advanced and become more widely available. In most cases, ART is used to treat infertility. Infertility is

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frequently correlated with anatomical and physiological abnormalities of the ovaries, fallopian tubes, and uterus. Based on the intrauterine pathologies, IVF can be performed by bypassing the affected area. For example, IVF bypasses the fallopian tubes directly in patients with tubal factor infertility (33-36). Thus, evaluating the intrauterine pathologies for IVF success is crucial.

Repeated or recurrent implantation failure (RIF) is a problem that has baffled many experts for quite a long time in the IVF environment and has been attributed to embryo quality and decreased endometrial receptivity. One of the suspected causes of RIF is specific issues in the uterine cavity, such as the inadequacy of endometrial thickness, adhesions, and anatomical abnormalities. Endometrial and uterine pathologies such as endometrial hyperplasia, polyps, leiomyoma, and endometriosis have been reported to occur in 18%-50% of women with RIF (17,36,37). Because of this, it is recommended to examine intrauterine pathologies before starting IVF. Several options that are often performed and are not invasive are a combination of transvaginal sonography, hysterosalpingography and hysteroscopy. But unfortunately, hysterosalpingography has low specificity, high false-negative, and high false-positive rates. Although transvaginal sonography is a noninvasive option, the results are less sensitive (6,10,38,39).

A more effective method for simultaneously evaluating the uterine cavity and providing treatment is hysteroscopy (40). As a result, HSC is the gold standard for evaluating the uterine cavity (13,14). In women with unsuccessful IVF treatments, HSC examination of the uterus is beneficial. A recent study reported that in patients whose transvaginal sonography examination results were normal, it turned out that during HSC examination, there were minor intrauterine abnormalities as high as 30%-45%, and abnormalities found during HSC were significantly higher in patients who had a history of ART failure (15,17). This explains why many specialists perform HSC as the initial routine exam on patients with infertility despite the guideline recommendation (41).

A continuous process, starting with a successful implantation, establishing a clinical pregnancy, and ending with the delivery of a live baby, demonstrates the success of IVF. In our analysis, RIF patients that previously underwent HSC examination had higher clinical pregnancy rates [OR 1.64, 95% CI (1.32-2.03) p<0.001]. Subgroup analysis also did reveal that patients with abnormal hysteroscopy and had been treated for the latter did have higher pregnancy rate and a higher live birth rate [OR 1.50, 95% CI (1.17-1.92) p=0.001] but no significant difference could be demonstrated between patients with abnormal hysteroscopy findings compared patients with normal hysteroscopic findings.

The RIF patients who did undergo HSC before IVF also had a higher implantation rate [OR 1.42 (95% CI 1.02-1.98, p = 0.04]. These results align with a study conducted by Gao M, where it was found that RIF patients who underwent HSC had a significantly higher implantation rate (28). Uniquely, the study did not find a significant difference in the implantation rate in patients between abnormal and abnormal HSC findings. This can be caused because HSC can see minor lesions such as endometrial dysfunction and hyperplasi, polyps and adhesions that may occur due to ovarian stimulation and repeated intrauterine operations; this procedure can cause minor tissue damage (26). Besides that, HSC is said to be able to favor subsequent pregnancy outcomes. During HSC, cervical dilatation occurs, which allows the correction of cervical stenosis and facilitates the ET process, and uterine distention fluid can help flush the uterine cavity. The absence of a significant increase in the implantation rate in patients with abnormal HSC findings could be due to immune factors or poor embryo development (42).

The conclusion is that hysteroscopy has a fertility-enhancing effect, which is also thought to occur independently of the correction of intrauterine abnormalities. Hysteroscopy is also believed to improve ART outcomes through an endometrial injury that helps embryo implantation (42).

Strengths and Limitations

The strengths of our analysis were that we did include RCT studies with a high level of evidence; we also included two-arm cohorts and retrospective studies, of an overall good quality. Our results were generally consistent across the studies when we saw the primary endpoints, which ensured consistency in each study. This meta-analysis has several limitations, apart from the relatively small number of studies that could be included. Important is to note that patient demographics and procedure differences, that should have been accounted for in this analysis, may influence the outcome and which may also increase heterogeneity. It should also be remembered that some of the results of this study have considerable heterogeneity; this is quite difficult to correct in a meta-analysis study because we cannot control every population in each study. Therefore, there is a possibility of bias that we

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cannot control.

Conclusion

Overall, this meta-analysis shows that hysteroscopic examination in patients with RIF before IVF significantly improved clinical pregnancy -, implantation-, and live birth rates. Also, to our knowledge, this meta-analysis is the first to look at differences in patients with abnormal and normal hysteroscopic findings, but unfortunately, no significant differences could be brought to evidence. Although many studies have been related to the role of hysteroscopy in patients with RIF before starting IVF treatment, additional studies are still needed, especially large-scale RCT studies.

Table 1. Modified Newcastle-Ottawa Scale for Cohort Study

No	Author, years	Selection				Comparability	Outcome			Overall score	Quality of study
		Representativeness of the exposed cohort	Selection of non-exposed cohort	Ascertainment of the exposure	Outcome was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Enough follow up time	Adequacy of follow up of cohorts		
1	Makrakis E, 2009	1	1	1	1	2	1	1	1	9	Good
2	Hosseini, 2014	1	0	1	1	1	1	1	1	7	Good
3	Gao M, 2015	1	1	1	1	1	1	1	1	8	Good
4	Kanazawa E, 2016	1	1	1	1	1	1	1	1	8	Good
5	Pabuccu EG, 2016	1	1	1	1	1	1	1	1	8	Good

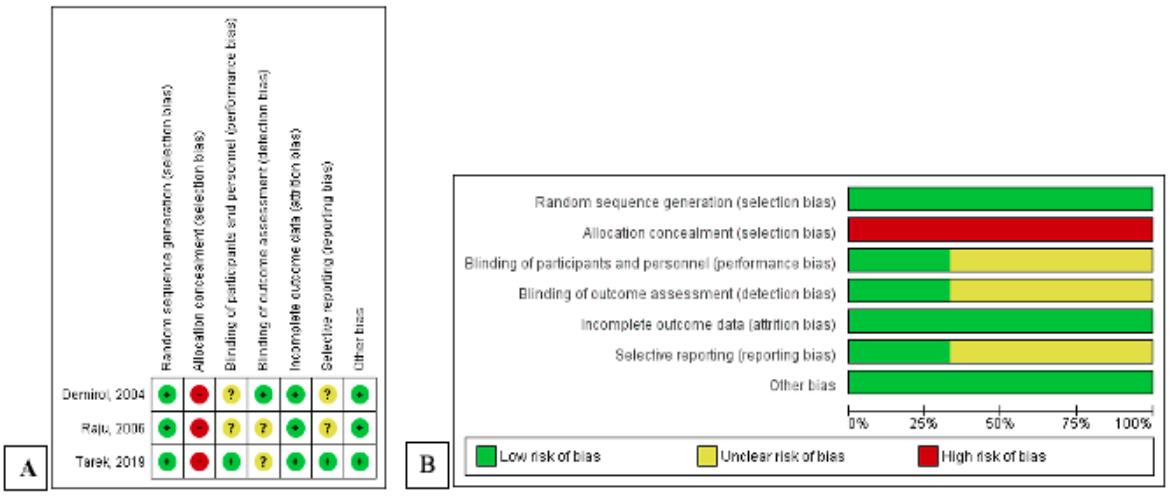

Figure 1. Quality assessment of RCT. (A) Risk of potential bias of individual RCT studies. (B) Risk of bias summary of all RCT studies. RCT: Randomized controlled trial.

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Table 2. Base Summary of Study Characteristics

No	Author	Country	Study Design	Total Patients		Intervention	Age (Years), SD	IVF Cycles Failed, SD	Definition of RIF	Clinical Pregnancy
1	Demirol A, 2004	Turkey	RCT	421	154	Hysteroscopy Normal	35.4, 0.6	2.6, 0.4	Patients who had undergone 2 or more failed IVF cycles in which two or more good-quality embryos transferred	Clinical pregnancies were confirmed by TVS at 6–7 weeks of gestation.
					56	Hysteroscopy Abnormal	36.2, 0.1	3.1, 0.1		
					211	Control	34.3, 0.8	2.8, 0.2		
2	Makrakis E, 2009	Greece	Prospective Matched Case-Control	1475	414	Hysteroscopy	35.38, 3.96	NA	History of 2 consecutive implantation failures despite the transfer of at least 1 good-quality embryo derived from fresh IVF cycles or 1 fresh IVF and its subsequent frozen/thaw cycle	NA
					414	Control	25.39, 3.95	NA		
3	Hosseini MA, 2014	Iran	2 Arms Cohort	353	142	Hysteroscopy	32.6, 4.2	2.5	≥ 2 ART cycles with fresh and good quality (according to previous ART history of the patient) and quantity (at least eight) of embryos transferred.	Each pregnant woman was followed up with an ultrasound scan until the fetal heart was documented (clinical pregnancy) and until delivery.
					211	Control	32.7, 4.3	3		
4	Gao M, 2015	China	2 Arms Cohort	672	334	Hysteroscopy	31.72, 3.55	NA	More than 2 consecutive ET failures with at least one good-quality cleavage embryo on day 3 in each ET	Clinical pregnancy was defined by TVS-confirmed intrauterine gestational sac and fetal heartbeat.
					338	Control	31.74, 4.08	NA		
5	Pabuccu EG, 2016	Turkey	2 Arms Retrospective	363	119	Hysteroscopy	30.7, 5.3	4.04, 1.5	Two or more unsuccessful ART/embryo transfer cycles despite the availability of good-quality embryos	NA
					244	Control	31.92, 4.4	3.06, 1.21		
6	Kanazawa E, 2016	Japan	2 Arms Retrospective Cohort	173	45	Hysteroscopy	38	NA	Patients who have failed implantation after repeating fair or good embryo transfer more than twice.	Clinical pregnancy was confirmed by ultrasound evidence of a gestational sac after a positive pregnancy test (urine β-human chorionic gonadotropin [β-hCG] level > 25 IU/L).
					128	Control	37	NA		
7	Toukhy E, 2019	United Kingdom	Multi Centre RCT	702	350	Hysteroscopy	32.7, 3.1	2.7, 0.9	Patients with two to four in vitro fertilization treatment cycles ending in an embryo transfer but no pregnancy and who were undergoing a further treatment cycle of in vitro fertilization	Observation of fetal cardiac activity on ultrasound scan four or more weeks after embryo transfer
					352	Control	32.7, 3.2	2.7, 1.0		
8	Raju GAR, 2006	India	RCT	520	160	Hysteroscopy Normal	27.4, 0.6	2.8, 0.3	Two or more failed IVF cycles in which two or more good-quality embryos were transferred per procedure	Clinical pregnancy was made after visualization of fetal heart pulsation four weeks later by transvaginal sonography (TVS).
					95	Hysteroscopy Abnormal	29.04, 0.92	2.4, 0.4		
					265	Control	26.72, 0.46	2.6, 0.1		

TVS: Transvaginal ultrasonography; ET: Embryo transfer; ART: Assisted reproductive technology; IVF: In vitro fertilization; hCG: Human chorionic gonadotropin; IU: International unit; RCT: Randomized controlled trial; NA: Not available

Table 3. The Base Summary of Hysteroscopy Examination Procedure, Ovarian Stimulation Procedure, and Embryo Transfer Procedure

No	Author	Hysteroscopy Examination	Ovarian Stimulation Procedure	Embryo Transfer Procedure
1	Demirol A	The hysteroscopy was performed in the early proliferative phase using a saline distention medium and a 5 mm continuous flow office hysteroscopy. The scope is based on a rod lens system with a diameter of 2.9 mm and a 30-degree view. The continuous flow sheath has an oval profile and maximum 5 mm diameter with an incorporated 5Fr working channel; the mechanical instruments used were grasping forceps with teeth and scissors. Intrauterine pressure was maintained at a constant 25/235 mmHg using an electronic pump for irrigation and aspiration. Semi-rigid operative hysteroscopic instruments such as scissors, grasping forceps, and biopsy forceps were used for the treatment.	IVF treatments were carried out on the menstrual cycles after office hysteroscopies. Patients were placed on an ovarian stimulation protocol that began with daily subcutaneous injections of leuprolide acetate 1 mg on day 21 of that cycle and continued until day 3 of the next menstrual cycle. If ovarian suppression was achieved (oestradiol < 40 pg/ml), 225 IU/day of gonadotrophin was started on day 3 or 4, and the dose arrangement was performed based on individual response. An ovulatory dose of 10,000 IU human chorionic gonadotrophins was given when at least two follicles of 18 mm diameter or more were observed.	Transvaginal ultrasonography (TVS)-guided oocyte retrieval was performed, embryo transfer was performed on day 3, and a maximum of four embryos, selected according to their quality, were transferred. Progesterone vaginal suppositories gave luteal support.
2	Makrakis E	Hysteroscopies were performed with the vaginoscopic approach under sedation using a 2.9 mm, 30-degree angle	Controlled ovarian hyperstimulation with a long protocol (mid-luteal beginning of gonadotropin-	Regarding frozen/thaw cycles, embryo thawing, and transfer were

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		hysteroscope with an external sheath of 5.5 mm diameter, providing inflow, outflow, and 5F working channels. Without introducing a speculum or tenaculum, and after vaginal and cervical disinfection, the hysteroscope was inserted in the vagina, the external cervical os was identified, and the scope was inserted through the cervical canal into the cavity with gentle movements, respecting the anatomy of the genital tract. Uterine cavity distention was achieved with normal saline installation. In patients with cavity distortion/pathology, appropriate treatment was applied simultaneously.	releasing hormone [GnRH] analog and stimulation with recombinant follicle-stimulating hormone [FSH] after confirmation of down-regulation), a short protocol (GnRH analog from cycle day 2 and recombinant FSH from cycle day 3), or a flexible antagonist protocol (recombinant FSH from cycle day 2 and addition of a GnRH antagonist when the leading follicles reached dimensions of 14–15 mm), with transvaginal ultrasound-guided oocyte retrieval 35 hours after the administration of 10 000 IU of human chorionic gonadotropin. The IVF or ICSI was performed with the respective male partner's spermatozoa, and sequential culture media were used in all cases.	synchronized according to the serum luteinizing hormone surge on a natural cycle. All ETs were performed with a Wallace catheter under ultrasound guidance. The number of transferred embryos depended on the female age and on embryo availability and quality (assessed with a 2-grade embryo score).
3	Hosseini MA	Hysteroscopy in the dorsolithotomy position and under general anesthesia was performed in the menstrual cycle just before ovarian stimulation or endometrial preparation by the attending physicians of the department. A rigid hysteroscope (continuous flow; 30° forward oblique view) with an outer diameter of 4 mm using 0.9% normal saline via a pressure pump was applied. The uterine cavity was adequately distended with the preset pressure between 80 and 100 mmHg. If there is any pathology, they were removed using mechanical instruments such as, forceps and scissors.	After complete desensitization with a long protocol using buserelin, ovarian stimulation with recombinant gonadotrophin, Gonal F, and human menopausal gonadotrophin based on age, weight, and the ovarian reserve was started. Transvaginal ultrasound was performed every 3–5 days to monitor follicular development, and final oocyte maturation was triggered with 10 000 IU human chorionic gonadotrophin (hCG). Then, oocytes were collected transvaginally 36–38 h later.	Up to four good-quality embryos were transferred transcervical 3 days later. Luteal phase support was by progesterone suppository Cyclogest. Serum β-hCG was checked 14 days after embryo transfer, and a transvaginal ultrasound scan was performed 2 weeks later to detect a gestational sac.
4	Gao M 2015	All HSC procedures were standardized, using a 6-mm outer-diameter continuous-flow rigid hysteroscope with a 22° direction of view. Normal 5% glucose or saline solutions distended the uterine cavity with a distention pressure maintained at approximately 20 kPa. A high-sensitivity cold-light-source fiber optic television camera and monitoring system collected HSC observations and image recordings. During HSC operation, all the images were observed continuously, and typical images were recorded fragmentally.	NA	Embryo transfer with either frozen or fresh embryos within 6 months after recruitment. ET was performed with at least one good-quality cleavage embryo on day 3. The criteria for good-quality cleavage embryos on day 3 were defined as being of 7 cells or more, equally sized blastomeres, less than 20% fragmentation, and no multinucleation.
5	Pabuccu EG 2016	All patients were examined during their early follicular phase, 1–6 months before starting a new ART cycle, via the	ICSI and all sperm injections were performed with fresh specimens. One ART cycle of each patient was included	During the study period, one embryo was transferred to patients aged <35,

		vaginoscopic approach as previously described. No routine pre-operative analgesia, antibiotics, sedation, or cervical preparation was used. A rigid hysteroscope (continuous flow; 30° forward oblique view) with an outer diameter of 4 mm using 0.9% normal saline was used. Following adequate distension of the uterine cavity, a systematic inspection was performed. Standard gynecologic surgical procedures were used to treat the recognized pathologies, such as removing all polyps and adhesions. A senior physician performed all the procedures.	in the study. All the OS cycles were conducted using the short antagonist protocol with recombinant or human menopausal gonadotropins (150–300 IU/day s.c.). Ovarian stimulation, oocyte retrieval, and embryo transfer procedures were performed as described elsewhere. Top-quality embryos were defined as those with ≥7 evenly sized cells and ≤10% fragmentation on day 3 and with a ≥3 AA quality of blastocyst morphology on day 5.	while two embryos were transferred to those ≥35 years following local legislation.
6	Kanazawa E 2016	Hysteroscopy was performed before the transfer cycle.	Hormone-replacement therapy in each group was our standard endometrial preparation protocol for FET cycles with transdermal estrogen patches for approximately 16 days. A transvaginal ultrasound was then performed, and if the endometrial thickness was >7.0 mm with a triple-line appearance, the patients were started on a regimen of 600 mg/day micronized progesterone, vaginally till 9 weeks of pregnancy and continued transdermal estrogen patches till eight weeks of pregnancy.	Embryo transfer with a Kitazato catheter under transvaginal ultrasound guidance was performed by four skilled doctors between 3 and 5 days later, depending on the embryo's stage of development. The embryos were classified according to Veeck's grading and Gardner's grading. Up to two embryos were transferred, including two-step embryo transfer.
7	Toukhy E 2019	Outpatient hysteroscopy was performed using a rigid 30° view 2.9 mm diameter hysteroscope with an atraumatic tip in a vaginoscopic approach. The hysteroscope could be assembled with accessory sheaths in an active or passive position. Each hysteroscopy was started with the single-flow 2·9 mm instrument to inspect the cervical canal and uterine cavity. If necessary, the accessory diagnostic (3.7 mm) or operative (4.4 mm) sheath was moved forward to establish a double-flow mode and allow operative intervention using 5 French instruments (crocodile forceps, biopsy forceps, and scissors). An isotonic solution (0.9% Normal saline or Ringer lactate) was administered via a pressure-controlled pump or simple pressure cuff system to provide the lowest pressure required to distend the uterine cavity for adequate visualization. No routine pre-operative analgesia, antibiotics, sedation, or	The in vitro fertilization treatment cycle commenced in the menstrual cycle immediately following the outpatient hysteroscopy. The ovarian stimulation protocols used for the in vitro fertilization treatment cycles were described previously. Briefly, follicle-stimulating hormone injections were started at 150-450 IU daily for multi-follicular ovarian stimulation. Final oocyte maturation was induced using 5,000-10,000 IU of human chorionic gonadotrophin when at least two 18 mm follicles were seen on ultrasound scanning. Ultrasound-guided oocyte retrieval was performed 34-38 hours following human chorionic gonadotrophin administration. Progesterone supplementation was used for luteal phase support and continued for up to eight weeks gestation if the pregnancy had occurred.	Embryo development and quality after fertilization were assessed until transfer or freezing. One and three embryos were transferred into the uterine cavity according to each participating center's protocol.

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		cervical preparation was used. A standardized protocol, data collection tool, and accurate description of possible abnormalities were provided to each participating center.		
8	Raju GAR 2006	Hysteroscopy was carried out at Krishna endoscopy on an outpatient basis without anesthesia. Midazolam 0.1 mg/kg was given intravenously as a sedative when needed. All hysteroscopies were performed in the early proliferative phase using a 1.9 mm hysteroscope, which has a 30 view with a 3 mm continuous flow sheath. The flow sheath has a maximum 5 mm diameter with an incorporated 5 Fr working channel. Associated mechanical instruments used were grasping forceps with teeth and scissors. Uterine distention was accomplished with glycine, and 80 mmHg constant intrauterine pressure was maintained using an electronic pump. At the end of the procedure, a sample of endometrium was taken for histological evaluation by aspiration using a 4 mm cannula. The patients were discharged after 15–60 min of the procedure, and no further complications were observed.	Down-regulation was initiated using an intramuscular injection of Decapeptide 3.75 mg on day 21 of the cycle. Adequacy of down-regulation was confirmed by measuring E2 (≤ 50 pg/ml) and LH levels (< 1 ng/ml). Controlled ovarian stimulation was achieved using recombinant FSH (Recagon, Organon), and the dose was adjusted based on individual response. Human chorionic gonadotropin (hCG) at 10,000 IU was given after two follicles of 18 mm or more were visualized in the ultrasound scan. Oocyte retrieval was scheduled 36 h later by transvaginal ultrasonography (TVS).	After fertilization, embryo transfer was performed on day 3, and the number of embryos transferred was kept constant in all patient groups. Progesterone vaginal suppositories gave luteal support. Two weeks after embryo transfer, serum human chorionic gonadotropin (hCG) was measured to confirm pregnancy and a diagnosis of clinical pregnancy was made.

IVF: In vitro fertilization; TVS: Transvaginal ultrasonography; ET: Embryo transfer; hCG: Human chorionic gonadotropin; IU: International unit ART: Assisted reproductive technology; GnRH: Gonadotropin-releasing hormone; FSH: Follicle-stimulating hormone; ICSI: Intracytoplasmic sperm injection; HSC: Hysteroscopy; NA: Not available

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Diagnostic dilemma after unusual vagino-scopic finding of vaginal ulcers in a post-hysterectomy patient with vaginal bleeding – a case report.

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Abstract

Vaginal ulcers can occur due to various causes such as infections, aphthous ulcers, malignancy, post- radiation therapy, or autoimmune disorders like Behcet syndrome or can be due to rare entities which may cause diagnostic confusion. We present an unusual case of vaginal ulcer in a post-hysterectomy patient presenting with vaginal bleeding. There are very few cases reported in the literature of vaginal ulcers in this context. Diagnosis is made only by excluding other common causes of genital ulcers. To the best of our knowledge, vaginoscopic pictures of vaginal ulcers are not available in the literature, not to mention lack of scientific data to support physicians in establishing the correct etiologic diagnosis. This case-report aims at demonstrating the pathology by vaginoscopy as well as providing a review on the various conditions causing it.

Key words

Vaginal ulcer; Post-hysterectomy; Non sexually acquired genital ulceration; Vaginoscopy;

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Introduction

Vaginal ulcers are breaks in the mucous membranes of the vagina that can cause symptoms such as itching, pain, bleeding upon touch, or the production of discharge. However, they can also be asymptomatic. Genital ulcers can be single or multiple and may be painful or painless. Dryness, scaling, and excoriations preceding the ulceration suggest dermatitis. Recurrent ulcers may indicate conditions like herpes simplex virus (HSV), Behçet disease, or fixed drug eruption. Inguinal lymphadenopathy suggests a likely infection, while uveitis, arthritis, and a family history of these conditions may indicate Behçet disease. The appearance of new ulcers after taking certain medications suggests a fixed drug eruption. Oral mucosal involvement is seen in aphthosis. Dysuria may be caused by the location of the ulcer or sexually transmitted urethritis. Constitutional symptoms (generalized symptoms affecting the whole body) can occur in conditions such as herpes simplex, secondary syphilis, lymphogranuloma venereum (LGV), and systemic lupus erythematosus.

Non sexually acquired genital ulceration (NSAGU) refers to ulcers that do not have an identifiable cause based on clinical, histopathologic, serologic, and microbiologic findings. However, Epstein Barr virus (EBV) has rarely been identified in the base of the ulcer (1-4). NSAGU is characterized by sudden painful genital ulceration and is often misdiagnosed as a sexually transmitted infection, leading to unnecessary investigations. It may be considered a variant of complex aphthosis or a separate condition. The onset of NSAGU may be preceded by an acute systemic illness. It is often under-recognized by healthcare providers, and its underlying causes are not fully understood (1-4). NSAGU is a benign condition that can present as an acute or recurrent event but does not progress. Currently, there are no consistent treatment protocols described for NSAGU.

Case report

This is a case report of a 56-year-old woman, gravid one para one, with a medical history of a total abdominal hysterectomy and bilateral salpingo-oophorectomy performed 14 years before for adenomyosis and severe endometriosis. Post operative period then was uneventful and she was put on leuprolide injections for 3 months post-operatively. She visited the outpatient clinic with a complaint of a 3 –days-ongoing vaginal bleeding, without associated pain. There was no history of vaginal discharge or itching in the perineal region, nor oral aphthous ulcers or any other significant diseases. The patient was not sexually active and also reported a medical history of multiple arthralgia, for which she had received some allied medicine.

The patient was admitted and examined under anesthesia. Diagnostic vaginoscopic technique was performed using a 2.9 mm office Bettocchi hysteroscope with outflow and inflow sheaths mounted. The distending medium was normal and a Karl Storz SPIES camera with spectra A filter was used to evaluate the vascularity (Karl Storz Se & Co KG Tuttlingen Germany). Three punched-out ulcers on the posterior vaginal wall were revealed, measuring 2x1 cm, 3x2 cm, and 2x2 cm, with a healthy vault (fig 1-2).

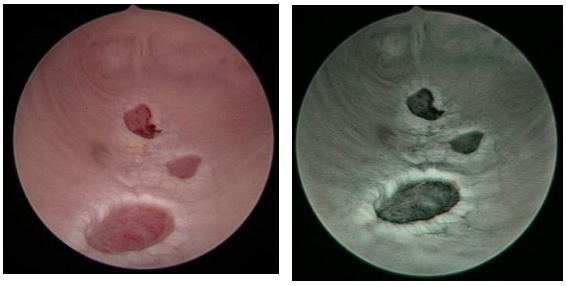

Figure 1 2. Vaginoscopic picture of ulcers (fig 1 natural aspect – fig 2 SPIES appearance)

Measurements were estimated by comparison with the distance separating the tips of the open jaws of the five French grasping forceps which is about six mm. Biopsies were taken from the lower ulcer margins, and the ulcer bed was subsequently sutured to allow for hemostasis. Histologic examination of the vaginal ulceration showed active chronic inflammatory granulation tissue and fibrosis

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with the defect partially reaching the muscularis. Deeper tissues exhibited fibrosis and a perivascular lymphoplasmacytic infiltrate, without evidence of vasculitis (Fig 3-5). The diagnosis of benign inflammatory ulcer was thus confirmed.

Tests for chronic inflammatory bowel disease (Crohn's disease) and Behcet disease were performed and came back negative. (Ziel-Neelsen (ZN) stain for acid-fast bacilli (AFB) and periodic acid-Schiff (PAS) stain for fungal infection were also negative. No microorganisms were found or cultured.

The prescribed treatment consisted of

1. Oral cefuroxim axetil 500 mg twice a day for 7 days.

2. Oral metronidazole 400 mg three times a day for 7 days

3. Ibuprofen 400 mg is association with paracetamol 325 mg trice a day for 3 days

4. Pantoprazole 40 mg twice a day for 7 days.

The follow up was done on days three, seven, 14 and 30.

The ulcers did heal well with the alleviation od the symptoms and restitutio ad integrum was witnessed by vaginal examination within two weeks. The vaginal bleeding did stop right after the suturing. The patient did respond well to the treatment.

Discussion

In a discussion about this rare case, the lack of literature on vaginal ulcers is considerable. Several conditions need to be considered in the process of differential diagnosis.

The patient has presented with acute genital ulceration. Several possible causes have been considered and ruled out based on clinical features and laboratory tests. Excoriations, trauma-induced ulcers, are unlikely due to the normal surrounding skin and absence of a history of trauma. Genital herpes, characterized by small vesicles that quickly rupture into shallow erosions, is unlikely due to the absence of typical prodromal symptoms and vesicles. Primary syphilis is also improbable as the ulcer associated with it is typically painless, has a clean base, and shows little to no pus or crust. Moreover, laboratory test for syphilis was negative.

Behçet's syndrome, a multisystem disease with aphthous ulceration, is highly unlikely given the absence of ocular or systemic complaints (5) and negative lab tests for the syndrome.
Crohn's disease, which can manifest with aphthous ulcers, is improbable as the patient has had a single episode of genital ulceration without other bowel or bladder complaints. Crohn's disease can affect the skin with or without bowel involvement, and vulval oedema may accompany ulceration in addition to typical sinuses and fistulae (6).
Squamous cell carcinoma and vulval intraepithelial neoplasia are unlikely due to the acute nature of the ulceration, and histopathology reports are suggestive of inflammatory lesions without any premalignant features (fig 3-5).

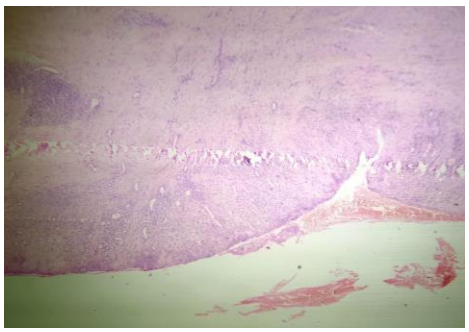

Figure 3. focus of the ulceration

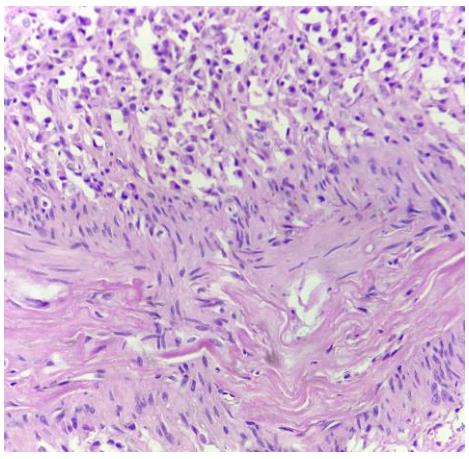

Figure 4. Deeper tissue reveals perivascular

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lymphoplasmacytic infiltrate (high power)

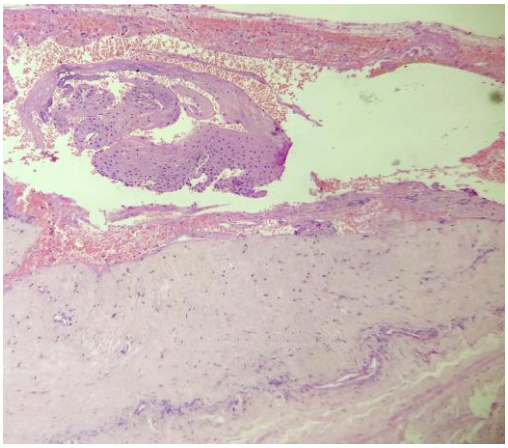

Fig 5 Deeper tissue reveals perivascular lymphoplasmacytic infiltrate (low power)

The most probable diagnosis is NSAGU, a benign condition with an unknown cause. Episodes are often triggered by viral infections, particularly when there is viral prodrome (1-4). However, no cause has been clearly identified in patients with recurrent ulcers who do not have an underlying condition such as Crohn's disease or Behçet's syndrome. NSAGU ulcers share characteristics with oral aphthous ulcers, being painful and sharply marginated (punched out).

The authors would like to highlight the clarity of the vision at vaginoscopic examination with the hysteroscope, to the best of our knowledge these pictures are not available anywhere in the literature. The clarity of the layers of the vagina and of the vascularity is clearly shown. These pictures can hopefully help researchers, who are looking at treating vaginal ulcers and similar pathology, in the future.

Investigations

The diagnosis of NSAGU relies on clinical observations. However, conducting a skin biopsy to confirm the diagnosis can be distressing for the patient and may yield non-conclusive results. It is crucial to investigate the presence of primary herpes simplex virus and secondary bacterial infection. This investigation should involve obtaining skin swabs for polymerase chain reaction (PCR) testing and culture.

In an emergency situation, it is essential to identify aphthous ulceration. Therefore, investigations are necessary to rule out alternative causes of genital ulceration. Biopsies from ulcers are needed to exclude malignancies.

Management

The management of NSAGU varies depending on the severity, and there are no formal treatment guidelines. For mild cases, the primary approach involves avoiding irritants such as tight clothing, perfumed soaps, pads, and liners. Analgesia and topical treatments are also recommended.

Corticosteroids, which have anti-inflammatory properties, can be beneficial. Potent topical corticosteroids are generally safe to use, and when applied in an ointment form for a short duration (two weeks or less), they do not cause side effects.

In our specific case involving a patient experiencing vaginal bleeding, the management included operative vaginoscopy with biopsy and suturing of the ulcer base. This procedure helped relieve the patient's symptoms. Additionally, prophylactic antibiotics were effective in controlling secondary bacterial infection and flare-ups.

Conclusion

There are various types of lesions that can occur in the vaginal and vulvar regions. The approach to diagnosing these lesions depends on the underlying cause. In this particular case, the diagnosis was made by ruling out known causes. When evaluating patients with such lesions, it is important to inquire about other systemic illnesses, paying close attention to symptoms related to the eyes, nervous system, gastrointestinal tract, and genitourinary system. A comprehensive physical examination, including the examination of oral and skin lesions, should be conducted by the physician. The latter should then make a differential diagnosis and implement a multidisciplinary treatment approach for the patient.

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Fallopian Tube Recanalization (FTR) Outcome in Bilateral Non-Patent Tubes at Dr. Moewardi Hospital Surakarta: Case Series

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Abstract:

Introduction:
Tubal obstruction is one of the common causes of female infertility and almost always needs artificial reproductive technology. Anatomical improvement of the tubes using surgical procedure are expected to restore their function. However, it raises the risks, cost, and morbidity. Previous studies show good technical success rates for fallopian tube recanalization (FTR) using minimally invasive transcervical tubal catheterization.

Objectives:
To report the outcomes of three cases of infertility due to bilateral non-paten tubes with performed FTR.

Case Operation Procedure:
We retrospectively evaluated the three cases of FTR procedures performed from July to November 2022 at Dr. Moewardi Hospital. The three cases had undergone a basic infertility evaluation and established diagnosis of infertility due to bilateral non-patent tubes. Infertility due to anovulatory and male factors were excluded. Minimally invasive transcervical tubal catheterization-hysterosalpingography with high pressure contrast injection followed by fluoroscopy were performed.
The success of the technique was established if both patent tubes were obtained at the end of the procedure. Clinical pregnancy was established if gestational sac obtained on transvaginal sonographic examination within 10 weeks post-procedure.

Discussion:
The fallopian tube, as a place of fertilization in the reproductive process, is very dependent on the health of its anatomy and physiological function. In studies of infertility in women, tubal factor infertility is the most common cause of infertility. Case-1 was a five years primary infertility, the

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technique was successful but patient did not conceive.
Case-2 was a one-year primary infertility, the technique was successful, and patient achieved a spontaneous pregnancy eight weeks after the procedure.
Case-3 was a five years secondary infertility, the technique was successful, but no pregnancy was obtained.

Conclusion:
There were three technical successes in the three cases that underwent FTR, one of which became pregnant.

Key words:
fallopian tube recanalization, fluoroscopy

Introduction:
Tubal factor infertility is a factor of infertility in women which can be caused by post infection fibrosis, spasm of the tubal ostium, and tubal obstruction. This tubal abnormality can occur at one side of the tube or bilaterally Trisna et al., 2019 (1). Diagnosis of tubal abnormalities can be done to determine tubal patency through laparoscopy to hysterosalpingography (HSG) Hardel et al., 2022 (2). This condition can be corrected by various tubal recanalization procedures under assistance of endoscopy, interventional treatment with radiology, or assisted treatment with traditional Chinese medicine (TCM) Liu et al., 2017 (3). In various studies, interventional radiological procedures are more recommended to be performed because it is minimally invasive and cost-effective with good outcome Mohan et al., 2018 (4).

Case Operation Procedure:

Case 1:
A P1A0 woman of 28 years old arrived at RSUD Dr. Moewardi to undergo an infertility treatment. Patient is seen with a moderate general condition, composmentis History, the patient has one child aged 5 years Clinical exam: supple abdomen, no tenderness, no vaginal bleed or discharges. The patient was diagnosed with bilateral non-patent tubes, a five years secondary infertility. Laboratory results: creatinine 0.6 mg/dl, blood sodium 134 mmol/l, blood chloride 108 mmol/l, hemoglobin 11.1 g/dl, hematocrit 33 percent, erythrocytes 3.77 million/µl.
During fallopian tube recanalization, injections of hyoscine butyl bromide (30 mg every 8 hours) and ketorolac tromethamine (12 mg every 12 hours) were given. Prior to the FTR procedure, ECG recordings were performed on the patient and normal blood pressure was obtained. Furthermore, preparation of the vulva was carried out with liquid betadine and alcohol. The patient is positioned in the lithotomy position for insertion of the speculum. The salpingography canula is inserted into the cervix and contrast is given, so that the contrast fills the cervical canal of the uterine cavity. It can be seen that the contrast doesn't fill the fallopian tubes, the uterus is in anteflexion position. Cervical canal elongation was obtained. The recanalization procedure was performed with a 4Fr vertebral catheter and
0.032 x 150 cm wire to the left fallopian tube, the results showed total occlusion of the left fallopian tube (6.38 mm). The patient complained of pain so she was immediately given an IV injection of 1-gram metamizole sodium monohydrate. The patient complained of nausea, so she was given an IV injection of 4 mg Ondansentron. The second maneuver was performed with a 5Fr vertebral catheter and

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0.035 x 150 mm wire to the left fallopian tube. The patient did complain of severe pain by the time the procedure is completed. Then fluoroscopy was performed with Iodixanol contrast 32- 60 cc for a duration of 20.49 minutes at a dose of 61 mGy. The patient was transferred to the ward. The patient was allowed to go home on the same day and scheduled for follow-up in 3 months later. When the patient was allowed to go home, the vital signs were normal.

Case-2

A 29-year-old P0A0 woman who had been infertile for two and a half years arrived at RSUD Dr. Moewardi to undergo an infertility treatment program. The patient came in a good general condition, compos- mentis, and vital signs within normal limits. The patient was diagnosed with primary infertility and had a history of anxiety problems. Furthermore, HSG will be repeated on the patient and she is given 1x2 Clomiphene citrate therapy. A few days later, the patient was diagnosed with non-patent tubal infertility The results of awareness assessment E4M6V5, blood pressure 120/80 mmHg, pulse 86x/minute, temperature 36.4^{o}C, and respiratory rate 20x/minute regularly. Laboratory examination of the patient showed blood sodium 137 mmol/l, blood potassium 4.2 mmol/l, blood chloride 100 mmol/l, non-reactive HBsAg, hemoglobin 14.1 g/dl, hematocrit 42 %, leukocytes 9.500 /µl, platelets 267.000 /µl, erythrocytes 4.80 million/µl, blood-type B with positive rhesus, PT 12.7 second, APTT 27.0 second, INR 0.930, blood glucose 106 mg/dl, total protein 7.0 g/dl, albumin 4.5 g/dl, globulin 2.5 g/dl, creatinine 0.6 mg/dl, urea 17 mg/dl, and abnormal results were obtained on SGOT 35 µ/l and SGPT 35 µ/l.

Seven months prior, the patient underwent an HSG in a private hospital and clinical exam did reveal a flat external uterine orifice, an erosion, a vaginal discharge. HSG was performed, 3 times: 5 cc, 4 cc, and 4 cc. With the patient in antero-posterior position photos were taken, right oblique, left oblique with as a result: normal uterine size and shape, both tubes are not visualized, no spillage is seen from both tubes, no hydrosalpinx, normal uterine impression, both tubes non-patent.

It was decided to perform a hysterosalpingography. Prior to the FTR procedure, an ECG record was performed on the patient and a blood pressure of 167/91 mmHg and a pulse of 100 x/minute were obtained. The usual preparation of the site as above mentioned were performed. Hysterosalpingography was performed using a metal salpingography cannula, contrast medium was injected, it was seen that the lumen of both fallopian tubes were filled with contrast and spillage was observed figure 1. After this first procedure, the patient underwent a fluoroscopy with Iomeprol 400 mg 15 cc contrast for 36 minutes with a dose of 61 mGy and fluoro dose area product 13505 mGycm2

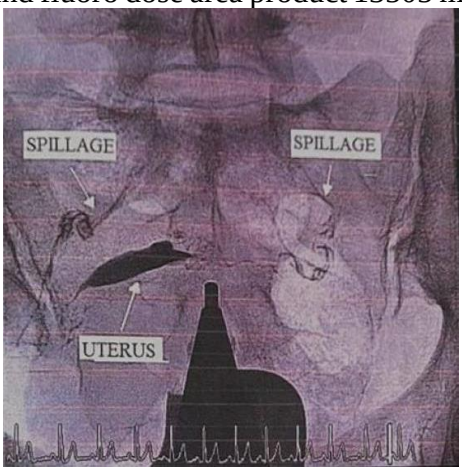

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Fig 1 Clear spillage is seen after the procedure.

Case 3

A 28-year-old woman came to RSUD Dr. Moewardi by referral from a private hospital with a diagnosis of bilateral non-patent fallopian tubes. The patient came in with a good general condition, compos mentis, and vital signs within normal limits.

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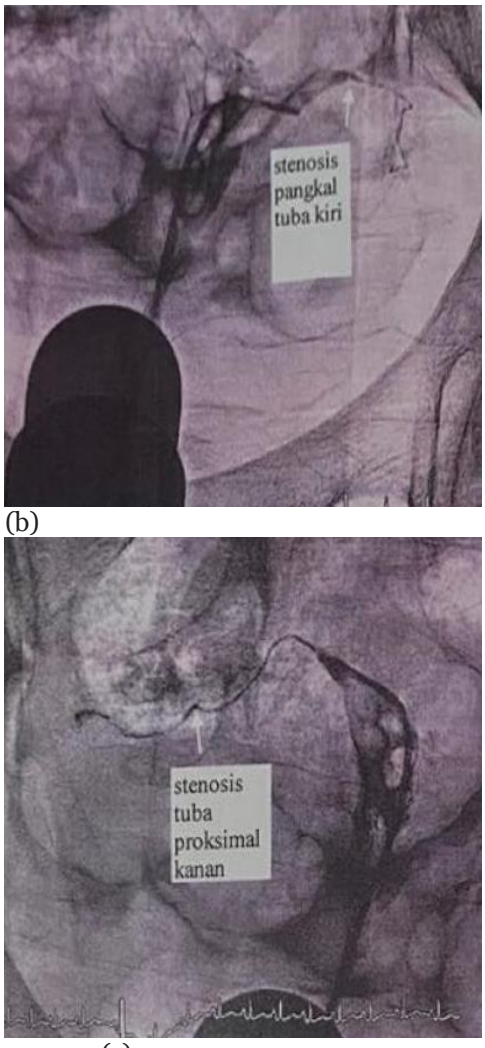
The patient underwent a chest X-ray and it was found that the size and shape of the hearth were normal, there were no infiltrates nor nodules in both the pulmonary fields, normal broncho vascular markings, sharp right and left costophrenic sinuses, normal right and left hemidiaphragms, trachea in the middle, good bone system, in conclusion both heart and lungs do not show abnormalities.

The patient's laboratory examination showed hemoglobin 12.2 g/dl, hematocrit 37 %, leukocytes 5.7000 /µl, platelets 311.000 /µl, erythrocytes 4.67 million/µl, blood-type A rhesus positive, albumin 4.9 g/dl, creatinine 0.7 mg/dl, urea 21 mg/dl, blood potassium 4.5 mmol/l, non-reactive HBsAg, non-reactive anti-HIV-I. Abnormal results were found for total protein 5.9 g/l, blood sodium 130 mmol/l, and blood chloride 107 mmol/l.

A few weeks earlier, the patient underwent an HSG examination and the results showed the bony structure to be normal, no soft tissue mass nor swelling was seen, +/- 10 cc of water soluble contrast was inserted into the uterus through a catheter attached to the OUE, the contrast appeared to fill cavum uteri cervical canal, no contrast is seen filling the right nor the left fallopian tube, the cervical canal appeared normal, regular mucosa, uterus in anteflexion, size of uterine cavity looks normal, no spillage right and left, so that the conclusion leads to a bilateral cornual spasm.

The decision was made to perform surgery in the form of a recanalization procedure of the fallopian tubes. Prior to the FTR procedure, a normal ECG was recorded and a blood pressure of 135/85 mmHg with a pulse 86 x/minute were obtained.

Hysterosalpingography was performed resulting in bilateral patent tuba, a stenosis was seen at the base of the left tube figure 2 b and c



(b)

(c)

Fig 2 b and c Stenosis on both tubes revealed.

and proximal to the right tube (c), contrast was injected into the right tuba. Insertion of the 4 Fr Vertebral Diagnostic Catheter is performed, followed by hysterosalpingography (figure 2. d - e) (d). Insertion of the 0.032-inch Guidewire through the 4 Fr Vertebral Diagnostic Catheter, followed by hysterosalpingography (e). The procedure is completed, the 4 Fr Vertebral Diagnostic Catheter and the wire are removed. Fluid intake: 100 cc, output bleeding: 10 cc, urine: 200 cc. Then a fluoroscopy was performed on the patient with Iomeprol 400: 60 cc contrast in 6 minutes 58 seconds with a dose of 210 mGy and fluoro dose area product 21608 mGycm2. Resulting in bilateral patent tubes figure 3.

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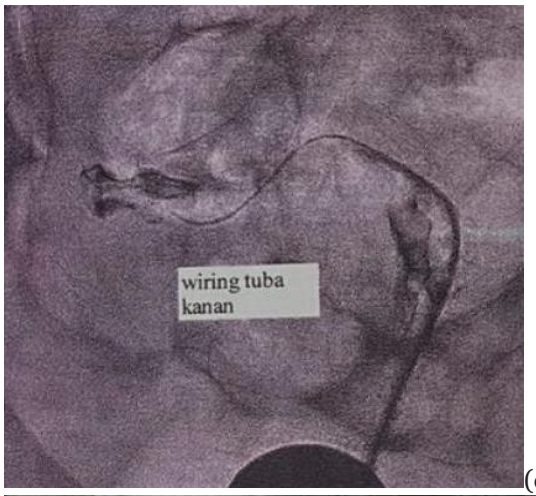
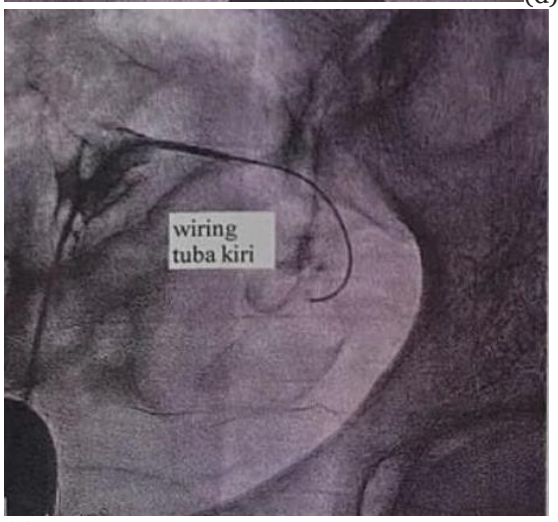


(d)



(e)

Fig 3 d and e catheters in place

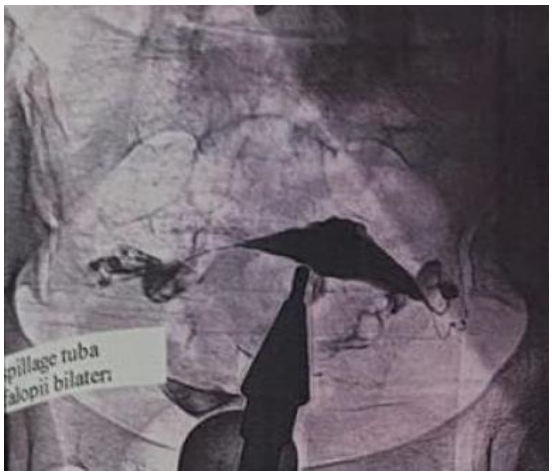


Fig 4. Patent tubes after the procedure

Discussion

The fallopian tube, as a place of fertilization in the reproductive process, is very dependent on the healthy condition of its anatomy and physiological function. Disturbances in the anatomy and function of the fallopian tubes can create pathological conditions in women, including infertility, infection, and ectopic pregnancy Su et al., 2022 (5). In studies on infertility in women, tubal factor infertility is the most common cause of infertility. So that the diagnosis and assessment of tubal abnormalities can help couples who are going through a pregnancy program to find out the causes of infertility and treat them Dun & Nezhat, 2012 (6)). In a study from the UK, several causes of tubal factor infertility included chlamydia infection, PID, to salpingitis Price MJ et al., 2016 (7).

Diagnosis and examination of the fallopian tubes can be done through Hysterosalpingography, Hystero- salpingo-contrast sonography, and gynecological endoscopy. This examination can assess tubal patency or tubal compliance without obstruction which supports the function of the fallopian tubes in pregnancy. HSG has a higher sensitivity (65%) and specificity (83%) in assessing tubal patency than gynecological endoscopy. A faster diagnosis and less exposure to radiation can be done with hystero-salpingo-contrast sonography (6) Tubal obstruction can inhibit fertilization and the passage of embryos so that treatment is needed to restore the patient's reproductive function.

One of the methods to treat non-patency in the tube is Fallopian-Tube Recanalization (FTR). In various studies, currently recanalization of the fallopian tubes increases with 50% the chance of conception in individuals after tubectomy and with 68% in salpingitis patients Mohan et al., 2018 (4). This figure has increased a lot since the FTR was first

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introduced in the 19th century. Tanaka et al. 2011 (8) described the development of FTR since the surgical approach for the treatment of proximal obstruction was conceived. In the 19th century, FTR was developed into falloposcopy for the treatment of cornual obstruction and endoscopic catheterization. Kohi et al, 2021 (9))
stated in his study, that currently, FTR is a minimally invasive procedure with a hysterosalpingogram for evaluation. A. Tanaka et al., 2017 (10) in a recent study reported that the tubal recanalization method with a combination of hysteroscopy and laparoscopy was successful in increasing pregnancy to birth. Another study described other methods of implementing FTR, namely FTR with radiological interventions that can be carried out more minimally invasive (Mohan et al., 2018 (4). The main point is, Fallopian Tube Recanalization begins with diagnostic steps such as HSG or Salpingography in the lithotomy position. This procedure is performed to assess tubal patency and the location of the tubal obstruction. HSG is performed with the addition of contrast through the cervix as to assess the proximal obstruction of the fallopian tube. The recanalization maneuver is performed with a 5-French or 3-French catheter. If there has been spillage of contrast in the peritoneal cavity, the tubal obstruction has been resolved (4,9). Anesthesia is required during the procedure to minimize pain and discomfort for the patient. In the cases discussed, fluoroscopy was still performed to ensure the success of FTR. This method can maximize the success of FTR and minimize the risk of complications from the FTR procedure. Kohi described the outcomes of FTR, including 84% of pregnancies occurring 1 year after FTR and 41% of them through full-term births (9) . A woman's chance of getting pregnant after the FTR procedure is 27%, with another 4% having an ectopic pregnancy. In the cases that have been described, the outcome of the FTR procedure was indicated as successful after visible contrast spillage in the peritoneal cavity. In one of the cases, the pregnancy occurred spontaneously after 8 weeks, and the other two cases did not result in pregnancy.

Conclusion

The fallopian tube as a place of fertilization has a very big role in the reproductive process. Disturbance of the fallopian tubes can cause several pathological conditions in women. One of them, namely tubal obstruction that can inhibit fertilization and the passage of conception results from fertilization on the uterine wall, so that treatment is needed to restore the patient's reproductive function. One of the methods to treat non-patency in the tube is Fallopian-Tube Recanalization (FTR). FTR can increase the chances of women who were previously infertile to be able to experience pregnancy.

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HIFU therapy Review of current status.

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Keywords

HIFU (High Intensity Focus Ultrasound), ultrasound-guided HIFU (USgHIFU), Adenomyosis, Infertility, GnRH A,

Introduction

In recent years, HIFU therapy has become a viable surgical alternative for patients who still wish to have their uterus. However, adenomyosis is a disease that is very sensitive to the hormone estrogen, and HIFU therapy will not change the performance of hormones in the body. The risk of recurrence still exists. GnRH-A is a hormone that is commonly used for the treatment of adenomyosis, which can lower estrogen levels to menopausal levels and increase the atrophy of adenomyotic cells in the myometrium. This study provides several systematic reviews and meta-analyses of HIFU combined with GnRH Agonist (GnRH-A) in adenomyosis and provides proof-based medical evidence for clinical applications.

3.2023005

Review

Adenomyosis is a gynecological disease characterized by ectopic endometrial tissue in the myometrium which often occurs in women during the reproductive age, between 30-40 years. The prevalence of adenomyosis currently ranges from 20-35%. The patient's main clinical symptoms include abnormal uterine bleeding, menstrual pain (dysmenorrhea), and impaired fertility (infertility). The pathological mechanism for the occurrence of adenomyosis is an

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imbalance of steroid hormones, causing a local inflammatory process that is the cause of changes in cell proliferation which may lead to neuro-angiogenesis in myometrial tissue (1-4).

Current therapy for adenomyosis includes oral therapy, progesterone, contraceptive pills or anti-inflammatory medication as well as GnRH-A injections and adenomyomectomy that can be performed by minimally invasive laparoscopic surgery or laparotomic surgery (5).
Surgical action for the removal of the uterus (hysterectomy) is the main option for women who no longer want children, but hysterectomy for adenomyosis which occurs in infertile couples is not a good choice for women who still want children. Although Uterin Artery Embolization (UEA) treatment can improve patient symptoms, its effect on ovarian function and pregnancy are still uncertain (4,5).

High Intensity Focused Ultrasound (HIFU), an emerging non-invasive surgical technique for the treatment of benign tumors, has been used for adenomyosis since 2008. Under ultrasound or magnetic resonance (MRI) examination, HIFU energy can penetrate the abnormal target tissue and remove the lesion through thermal effects and cavitation and allows the preservation of normal tissue around the lesion. The cavitation process is a condition in which HIFU will create a predefined temperature raise in the targeted cells so that the liquid in the cells is heated until it becomes liquid vapor, which results in the formation of bubbles, filled with vapor in the liquid (6,7). The bubbles eventually explode and the released vapor penetrates into the surrounding tissues through a mechanism that initially softens and then gets absorbed by healthy body tissue.

The Criteria of Selection

The studies that are included in this meta-analysis do meet the following criteria: Vannuccini and Petraglia: this study compares HIFU combined with GnRH-A vs. HIFU solely in patients with adenomyosis (8,9). The HIFU group combined with GnRH-A is defined as the experimental group, the HIFU group itself is defined as the control group, the objects of the study are women aged 18–50 years, women with focal or diffuse adenomyosis diagnosed by ultrasound examination, MRI, or computed tomography (CT), patients who have not received any treatment for adenomyosis within three months prior to the study. Abbott Outcome indicators: The main outcome indicators are changes in uterine volume while adenomyotic lesions are defined as the main outcome. The secondary outcomes are the visual analog scale score (VAS) for dysmenorrhea, menstrual volume score, serum CA125 level, and recurrence rate.
The exclusion criteria are the following:
animal experiments, case reports, conference
abstracts, conference proceedings, editorial letters, guidelines or comments, repeated study, studies in which the full text is not available, patients with uterine fibroids or other gynecological diseases, whose clinical symptoms are similar to adenomyosis and study less than 3 months HIFU ablation (10).

Results

Of the 390 articles, 9 studies were obtained from data of 766 patients analyzed in this

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meta- analysis (11-19). Of the nine studies, one of them was using MRI for the imaging diagnosis of adenomyosis, six were using transvaginal ultrasound or MRI, and the two ones did not report specific imaging diagnostic methods. Although these studies provide information about the diagnostic imaging methods used, they do not provide specific imaging criteria for the diagnosis of adenoma.

Changes in the physiology of adenomyosis

Changes in uterine volume

Among the nine studies included, only three reported a method of generating random-location sequences, which was the random number table method. The analysis demonstrated the change of uterine volume as the rate of uterine volume reduction after HIFU in 232 patients. The results of the meta-analysis showed that the rate of uterine volume reduction in the HIFU group with GnRH-A was higher than that in the HIFU only group at 12 months after the procedure (13-20).

Changes in volume of adenomyotic lesions

Three studies (239 cases) reported changes in lesion size before and after HIFU ablation which showed that the volume of lesions in the experimental group was smaller than that in the control group in 3 and 6 months after the procedure. Although the results of the study showed no significant difference in VAS score for dysmenorrhea in both groups ($p > 0.05$). (11, 12, 17). A total of five studies (367 cases) used VAS to evaluate patients with dysmenorrhea. The results of the meta-analysis showed that the VAS score for dysmenorrhea in the HIFU group with GnRH-A was lower than the HIFU group alone after the procedure (11, 13, 14, 17, 18).

Menstrual Volume Score

Three studies (243 cases) used the menstrual volume score to evaluate menstrual bleeding. The results of the meta-analysis showed that the menstrual volume score of the HIFU group with GnRH-A was lower than that of the HIFU group itself after the procedure (14,16,19).

Levels of Serum CA125

Three studies (252 cases) evaluated patients' levels of serum CA125. The results of the meta-analysis showed that serum CA125 levels in the HIFU group with GnRH-A were lower than the HIFU group alone after the procedure (11, 17, 18).

Recurrence Rate

Three studies (314 cases) compared the recurrence rates of the experimental and the control groups. The results of the meta-analysis showed that the relapse rate in the HIFU group with GnRH-A was lower than that in the HIFU group itself (15, 16, 19).

Pregnancy Outcome

One study reported patient pregnancy outcomes at 6 months after treatment. There were five pregnancies reported after the HIFU intervention combined with GnRH-A (n = 45), three of which delivered naturally and two ended in abortion. In the merely HIFU group (n = 46), there were four reported pregnancies following HIFU ablation, one resulting in natural delivery, one resulting in miscarriage and two ending in abortion (20).

Discussion

The results of this meta-analysis on the data from 766 patients showed that, HIFU combined with GnRH- A compared to mere HIFU group, for the treatment of adenomyosis had greater effectiveness in

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reducing uterine volume and adenomyotic lesions and alleviating symptoms.

Adenomyosis is a common and difficult gynecological disease that seriously affects women's health and quality of life. Effective symptom relief, relapse prevention, and increased pregnancy rates are problems that have to be solved. Compared to currently available therapies, HIFU is a non- invasive and innovative technology for adenomyosis while still at risk of recurrence.

The therapeutic mechanism of HIFU produces thermal and cavitation effects causing the target tissue temperature at the focal point to rise above 60–100◦C, causing non-coagulation necrotic lesions. At the same time, the surrounding structures are not damaged. Previous studies found that uterine smooth muscle tissue in adenomyotic lesions was sensitive to HIFU. HIFU treatment was an effective and ideal treatment for adenomyosis. A retrospective study by Lee et al. enrolled 889 patients with adenomyosis who underwent ultrasound-guided HIFU (USgHIFU). The results revealed that the uterine volume reduction rate was 60.1% at 3, 6, and 12 months after the procedure, respectively. This was consistent with the results of a recent systematic and meta-analysis showing a substantial effect in reducing uterine volume after HIFU treatment for adenomyosis in 12 months (20).

GnRH-a therapy can effectively relieve pain in adenomyotic patients by reducing the regulation of GnRH receptors in the body, thereby reducing the level of gonadotropins secreted by the pituitary gland which results in decreased ovarian function.

HIFU combined with GnRH-A can help maintaining the effect of HIFU therapy and reduce relapse rates. Most of the studies involved, suggest that patients should be given GnRH-A three times after HIFU ablation. The first GnRH--A is given on the first to third day of the first menstruation after HIFU therapy. Then, the interval between the two GnRH-A injections is maintained at 28 days.

The results of the existing study show that the all symptoms of both groups are improved after the procedure, but the VAS or dysmenorrhea scores and menstrual volume scores in the HIFU group combined with GnRH-A are lower than in the mere HIFU group. The levels of serum CA125 are also decreased. Although the results of the VAS score for dysmenorrhea show that HIFU combined with GnRH-a can better alleviate dysmenorrhea in each patient, there is still excessive heterogeneity. The relationship between adenomyosis and infertility is not clear, but adenomyosis can affect a woman's fertility, this is mainly related to disruption and thickening of the myometrial junctional zone (JZ), and hypo acceptability of the endometrium. In recent years, due to the continuous improvement of various ultrasound diagnostic methods and the increasing age of women seeking infertility treatment, the rate of women with a diagnosis of adenomyosis among infertile women has increased. Traditionally, infertile patients with adenomyosis are treated with GnRH-A or they may have adenomyosis (adenomyomectomy) removed surgically. Studies have shown that HIFU is a safe and effective procedure for infertile women and it does not increase obstetric risk (21,22).

Conclusion

The results of this meta-analysis show that compared with mere HIFU treatment and

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HIFU accompanied by GnRH-A therapy performed on adenomyosis, obtained a greater level of effectiveness in reducing uterine volume the volume of adenomyotic lesions and alleviating symptoms. However, because the number of studies included is too small, further research that has a long-term evaluation is needed.

Tab 1 Characteristics of the studies

Researchers	Research Design	Data	Research Groups	Control Group	Numbers of Respondents	Age of Respondents	Follow up	Diagnostic Examination	Total Energy	Average Power
Yang and Xie	Retrospective	Random	HIFU+GnRH-A	HIFU	38	41,6±6,3	12	USG TV/ MRI	NA	NA
Guo et al	Prospective	NA	HIFU+GnRH- A	HIFU	45	41,6±4,7	12	USG TV/ MRI	398,26±0,39	392,79±63,3
Jiang et al	Prospective	NA	HIFU+GnRH-A	HIFU	46	40,6±4,4	3	USG TV/ MRI	298,26±2,66	294,32±7,3
Xu et al	Retrospective	Random	HIFU+GnRH-A	HIFU	42	38,3±7,3	12	USG TV/ MRI	NA	50-400
Guo et al	Prospective	NA	HIFU+GnRH-A	HIFU	55	41,0±4,7	6	MRI	298,26±2,66	350-400
Xio-Ying et al	Retrospective	Random	HIFU+GnRH-A	HIFU	38	41,6±6,3	12	USG TV/ MRI	398,2 ± 0,3	392,7 ± 63
Yang et al	Retrospective	Random	HIFU+GnRH-A	HIFU	40	40,6±5,3	12	NA	NA	NA

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Delayed laparoscopic hysterectomy for placenta accreta in a postpartum setting: a case report

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Objective
To demonstrate technique of a delayed laparoscopic hysterectomy in the management of placenta accreta in a postpartum setting.

Design:
Stepwise demonstration of the technique with narrated video footage

Setting:
The incidence of placental accreta spectrum disorder has risen over the years due to the increasing number of caesarean sections being performed. A caesarean hysterectomy for placenta accreta is usually performed through a laparotomy. There is a lack of consensus in performing this procedure laparoscopically due to the increased risk of bleeding and the size of the uninvoluted postpartum uterus.
A laparoscopic approach may be considered for delayed surgical management of abnormal placentation, the key factors for success are a multidisciplinary approach, availability of skilled laparoscopic surgeons, appropriate equipment and resources and a tertiary hospital setting.1 Only case reports have been published about the laparoscopic management of these placental adhesive accreta spectrum disorders.2-3

Patients or participant: Written consent was obtained from the patient and an ethics approval was granted from the local Ethics Committee through Townsville University Hospital, Australia

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Case Report:
We present the case of a 42-year-old Para 5 patient referred from a regional hospital with ongoing vaginal bleeding 4 weeks following a caesarean section for placenta 1accreta, the diagnosis was made intra-operatively at caesarean section and adherent placenta was only partially removed owing to blood loss totaling 1500 ml. She had a BMI of 37 with a complex obstetric history, including a first delivery at 24 weeks for incompetent cervix, followed by 4 lower segment caesarean section for her subsequent deliveries. Her past medical history includes a gastric sleeve for weight loss, appendicectomy and a D&C.

Laparoscopic hysterectomy was performed with three 5mm laparoscopic trocars and a 10mm port using a 30-degree endoscope. In this video, we describe our technique for a delayed laparoscopic hysterectomy of placenta accreta in a postpartum setting. Intra-operatively, bilateral ureteric catheterization was performed. The uterus was a bulky 18-week size uterus that was occupying the pelvis limiting access to the pelvic side walls. There was also a residual placental bulge on lower segment with a moderately adherent bladder from the Caesarean section. Blood loss was 100mls and specimen were removed from the vagina. No complications were encountered during the hysterectomy. The patient was discharged home day 1 following the procedure.

There were several key strategies to success:
Ureteric catheterization and ureterolysis
Adequate development of potential pelvic spaces
Ligating the uterine artery at its origin
Late insertion of uterine manipulator after ligation of bilateral uterine arteries

Conclusion
This video highlights the ability to perform a delayed (post-partum) laparoscopic hysterectomy for placenta accreta, a minimally invasive alternative to the usual laparotomy

Introduction

Placenta accreta spectrum disorder (PASD) is defined as the abnormal attachment of all or part of the placenta to the uterus (1,2) Depending on the invasion of trophoblast past the normal decidual-myometrial junction zone it can be classified into superficial placenta accreta, where it attaches itself to attaches to the myometrium without invasion, increta where there is myometrial invasion, and percreta which involves penetration through the uterine serosa, potentially into surrounding organs (3).
It is a fairly rare condition, with a recent meta-analysis suggesting a prevalence rate of 0.01-1.1%, albeit increasing in incidence over the last few years (4,5). The incidence may be attributed to the increase in rates of caesarean sections, placenta previa, utilization of assisted reproductive technologies, surgeries of the uterus causing endometrial scarring, and advanced maternal age in pregnancy (6,8). This condition poses a significant risk patient's mortality and morbidity, with complications

such as massive hemorrhage, caesarean hysterectomy, cystotomy, ureteric trauma, infection, multisystem organ failure, disseminated intravascular coagulation, intensive care admission and death (4,5,9).
In this case study we are looking at a technique of delayed hysterectomy in the post- partum period, using minimally invasive laparoscopic surgery as an alternative approach (10).

Case

The patient was a 42-year-old G8P5 with a complex obstetric history who was referred to our tertiary unit for potential retained products of conception after an elective lower segment caesarean section.
Her obstetric history included:
G1: Neonatal death at 24 weeks of age from cervical incompetence.

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G2: Live birth at 39 weeks of age after an elective cerclage
G3: Live birth at 36 weeks of age following a double embryo transfer
G4: First trimester miscarriage at 8 weeks managed with suction dilatation and curettage
G5: Miscarriage at 5 weeks
G6: Live birth at 37 weeks of age. Elective lower segment caesarean section but placenta was found to be very adherent at time of delivery.
During her last elective caesarean section, the placenta was only able to be partially evacuated, as it was morbidly adherent. A Bakri balloon was required to tamponade the
lower segment, following a postpartum hemorrhage of 1500 ml. Despite having initial bleeding that was minimal, four weeks post-partum she started having intermittent erratic vaginal bleeding.
Ongoing ultrasound surveillance revealed vascular retained products of conception with a large heterogenous echogenic mass in the lower segment with an almost complete incursion into the myometrium posteriorly as well as posterior cervical stroma. Following a lengthy discussion with the patient with management options, the patient made an
informed decision to proceed with a laparoscopic hysterectomy.
She also had iron deficiency anemia during her pregnancy and had iron transfusions at gestational age of 4 weeks. She also has a BMI of 37. Her past surgical history included spinal fusion C 4/6 at age 13, knee construction, appendicectomy, gastric sleeve surgery, perianal abscess draining. She underwent a delayed laparoscopic hysterectomy and bilateral salpingectomy
with ovarian conservation for placenta accreta with procedural methods highlighted below, with no further complications and was discharged the next day.

Method

An anesthetic assessment was undertaken to ensure fitness for surgery. The vascular and urology team were also notified beforehand.
On the day of surgery, a cystoscopy was first performed to exclude placenta percreta and bilateral ureteric catheterization was performed. Intraoperatively, the uterus was 18 weeks of size bulky in appearance stretching from one lateral pelvic side wall to the other.
Anatomic abdominal survey including the fallopian tubes and ovaries was normal. A residual placental bulge was noted on the lower segment ostensibly from the abnormal placentation. There were multiple omental adhesions to the anterior abdominal wall.
Abdominal entry with Veress needle at Palmer's point was used to establish pneumoperitoneum. The round ligament was divided and the para vesical and pararectal spaces developed to isolate the uterine artery at the origin from the internal iliac artery which was identified in relation to the obliterated umbilical ligament. Bilateral ureterolysis
was commenced at the pelvic brim past the ureteric tunnel. The medial pararectal space of Okabayashi was further developed to further lateralize the ureters. Subsequently the
vesicouterine space was developed along with the medial and lateral para vesical spaces to mobilize and dissect the densely-adherent urinary bladder using a 'low-lateral' approach.
The uterine vessels were coagulated using an advanced Bipolar device. As the right superior vesical artery was contributing to an unusually enlarged vaginal artery it was secured it as well. Before continuing with bladder dissection, the uterus was completely de-vascularized. The uterine manipulator was inserted only after this point. A primary colpotomy was performed to further skeletonize the uterine vessels and these were coagulated at the traditional coagulation point.

A PDS 1 suture was used for uterosacral
suspension reconstituting the peri-cervical ring, pubo-vesical and rectovaginal fascia. The V-loc 0 suture was used for two layered vault closure. The uterus was delivered easily through the vagina without morcellation. Bleeding from peritoneal bleeders was secured with surgical clips; the generalized vault ooze needed pressure and FLOSEAL hemostatic agent. Total estimated blood loss for this procedure was 100ml.

Discussion and Conclusion

Some of the risk factors this patient had that may have attributed to having placenta accreta

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are complex obstetric history that involved multiple cerclage due to cervical incompetence, multiple invitro fertilization techniques for conception, advanced maternal age as well as parity. The mainstay of managing placenta accreta is a prenatal assessment of location,
depth of invasiveness, using ultrasonographic imaging modality as well as MRI and a multidisciplinary approach of delivery planning (11,12).
Generally speaking, there are four ways to manage Placenta Accreta Spectrum disorder, the extirpative method, caesarean section hysterectomy, conservative management, and one-step conservative surgery (12). Conservative uterus preserving methods such as methotrexate administration and long-term antibiotics were considered.
Conservative management although currently portrays conflicting studies, and
considerations for novel approaches for preservation of fertility, still poses significant risk of complications in women in the post-partum period with an increased risk of morbidity,
mortality, infections and requiring delayed hysterectomy (13,14,15,16). A hysteroscopic resection was considered but was deemed would be a difficult approach due to the large exophytic mass obstructing the lower segment.
An open caesarean hysterectomy remains the reference treatment for placenta accreta, considering reproducibility, rate of morbidity and complications in the other options mentioned (9,12). Although this may be the
preferred method of management, there are studies that show relativity high morbidity rates, with significant outcomes of needing
transfusion, cystotomy, ureteral injuries and infection (9,10,17).
There have been several case reports that highlight laparoscopic method of managing placenta accreta which have demonstrated good outcomes, with minimal bleeding and injury to the bladder (18,19,20). The key factors for success are a multidisciplinary approach, availability of skilled laparoscopic surgeons, appropriate equipment and resources and a tertiary hospital setting (18,19,20).
Surgically, the techniques to reduce complications include ureterolysis, ligating the uterine arteries along with other contributing branches at the origin from the internal iliacs, and delayed manipulation of uterus only after stepwise devascularization has been achieved. Ureterolysis along with ureteric catheterization is a vital step in this procedure to minimize risk of ureteric trauma owing to their proximity to the widened and broad lower uterine segment. Furthermore, delayed insertion of a uterine manipulator also assists with reducing blood loss (21Complete internal iliac artery ligation controls the blood that flows through the placenta via the cervical and vaginal arteries and therefore is considered superior to just uterine artery ligation (22).
In conclusion, placenta accreta spectrum disorder is a condition attendant with significant perioperative morbidity which can be offset to a certain extent with early recognition with ultrasound or MRI, proactive perioperative planning, a multidisciplinary approach and targeted surgical technique to ensure the best post-partum outcomes.
Compared to laparotomy, delayed laparoscopic hysterectomy for placenta accreta spectrum disorder is a safe and effective alternative as it results in a lesser intraoperative blood loss, wound infections, postoperative pain, earlier mobilization, shorter hospital stay, as well as a faster return to normal activities (23

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Complete septum removal with a new combined technique: Intrauterine Bigatti Shaver (IBS®) and scissors. (Video Article)

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Abstract

Uterine malformations are defined as deviations from the normal anatomy resulting from embryological maldevelopment of the Mullerian ducts (1). The prevalence of a uterine malformation is estimated to be 24.5% in patients who experienced miscarriage and infertility (2). Hysteroscopic metroplasty is currently considered the first-choice surgical therapy (3). Several studies reported that metroplasty increased the delivery rate and reduced the risk of spontaneous abortion (4, 5, 6, 7). However, due to the lack of randomized control studies, these results are still debatable. A recent randomized control study by Rikken et al. (8) reported that septum resection did not improve the reproductive outcome. Unfortunately, due to small trial size this result could not be confirmed. In literature there has been a wide agreement to perform hysteroscopic metroplasty in patients with two previous spontaneous abortions and no other cause for pregnancy loss (9). Cararach et al. (10,11) reported a better reproductive outcome in metroplasty performed with scissors compared to resectoscopy. Duffy et al. (12) speculated that the vascular damage resulting from electricity induced thermal damage could impair uniform endometrial healing over the resected area. Our proposed technique, by using mechanical energy via scissors and Shaver to completely remove the septum, aims to improve the quality of the result and to reduce the risk of complications.

Key words: Operative hysteroscopy; Uterine septum; Intrauterine Bigatti Shaver; Hysteroscopy; Uterine malformations

Study Objective:

To assess the efficacy of the surgical treatment for a complete septum (Class U2b) removal with a combined technique: "Shaver and scissors".

Design:

Description of the surgical steps and prognosis related to this new approach.

Setting:

"SELEC Sino European Life Expert Centre" of Jiao Tong University, Shanghai.

Patient:

Our patient was a 31-year-old woman, 0-0-2-0, with a previous history of two first trimester miscarriages in the last two years. A 3D transvaginal ultrasound showed the presence of a complete septate uterus (U2b - ESHRE/ESGE

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classification) confirmed by diagnostic hysteroscopy (13). The uterine cavity was divided by a septum up to the level of the internal cervical ostium.

The histological exam showed the presence of a benign polypoid simple hyperplastic endometrium. A new combined hysteroscopic approach to correct the uterine malformation with the Shaver technique and scissors was performed.

One month after metroplasty a diagnostic hysteroscopy was planned in the first half of the menstrual cycle to evaluate the completeness of our surgical approach.

Intervention:

The operative hysteroscopy was performed with the Intrauterine Bigatti Shaver (IBS®) (KARL STORZ SE & Co. KG). The 24 Fr Shaver optical system (KARL STORZ SE & Co. KG) with the flute beak SB blade (KARL STORZ SE & Co. KG) was used (14). The rotational speed of the blade was set between 1500 and 2100 rotations per minute (rpm) with a suction flow of 250 ml per minute.

As reported during the diagnostic hysteroscopy, a complete septum with a simple
hyperplastic polypoid endometrium was present in the uterine cavity. During the first step of the procedure the SB blade with a rotational speed of 2100 rpm was used to completely remove all the polypoid endometrium from both cavities.

This action reduced all the endometrial overgrowth improving the septum view.

Second, scissors were used to completely dissect the septum up to the uterine fundus. For the third and final step, the Shaver SB blade was used to completely remove the upper and lower septum remining and to completely
restore the volume of uterine cavity. To remove the residual septa rough edges left attached to the anterior and posterior wall, the Shaver Blade rotational speed was reduced to 1500 rpm. A perfect clear visual field was maintained during the whole procedure, and no bleeding was reported. The operative hysteroscopy lasted almost 10 minutes without any intraoperative complications. To prevent adhesion formation a Mate-Regen® by Bioregen was left in place at the end of the procedure. The patient was discharged from the hospital two hours after the operation.

Main Result:

The histological exam after the metroplasty confirmed the presence of a benign simple polypoid hyperplastic endometrium. A diagnostic hysteroscopy performed during the patient's follow up appointment three months after the operation, showed a normal uterine cavity without any remnant of the residual septa and a healthy, adhesion-free, regular proliferative endometrium.

Conclusion:

Presently the Shaver technique has been widely used in the treatment of all kinds of intrauterine pathologies (15). Polyps, adhesions, placental remnants, adenomyosis and all types of myoma up to 3.5 cm have been completely and safely removed with this new technique (16,17).

The major advantage of mechanical tissue removal systems is their ability to remove only the functional layer of the endometrium without affecting the basal layer.

This aspect is of primary importance for infertility patients. In addition, as no
electricity or heat production are involved in the resection process, there is a reduction in postoperative adhesion formations, leading to a faster recovery of the normal healthy endometrial layer. There are many techniques available for the surgical treatment of uterine malformations, but at present there is insufficient evidence to recommend the best corrective technique.

The additional use of the Shaver technique in a case of septum removal has not yet been reported. This case report shows that the combination of the Shaver technique with scissors could become the first-choice procedure to treat partial or

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complete uterine septa. The Shaver technique was able to remove all the thick endometrium, thereby allowing scissors to precisely cut the septum without bleeding and with the best possible visibility. In addition, the Shaver could remove all remnants of the septum to promote a regular and uniform endometrial healing. As clearly shown in our video, this method is a very fast, clear, precise, and safe technique to completely treat septa malformations. The Bigatti Shaver technique improves the quality of the result and reduces the risk of complications.

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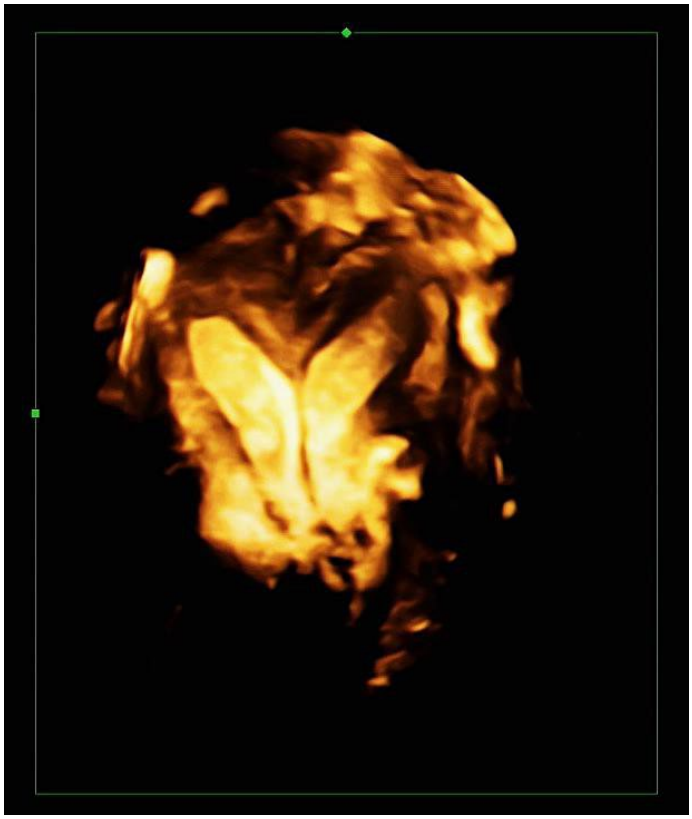

Fig.1 - 3D Ultrasound Image of Complete Septate Uterus - Class U2b.

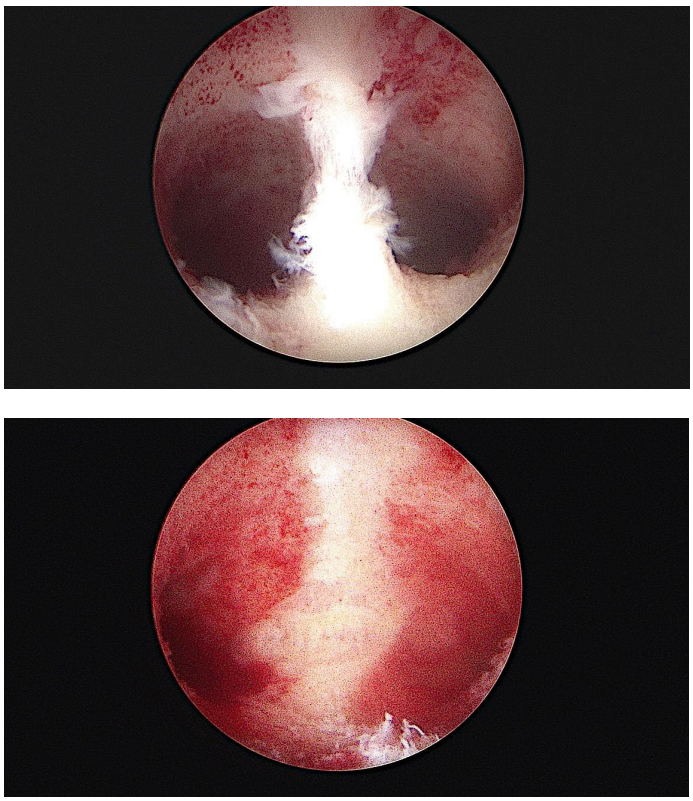

Fig2. A) Complete septum before Shaver and scissors technique B) Normal uterine cavity after treatment.

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Temporary Ligature of the Uterine Artery "Shoelace Knot"

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Study Objective:

To demonstrate the technique of temporary ligature of the uterine artery applied to minimally invasive uterine procedures to reduce blood loss. Design:

Step-by-step instructional video demonstration of surgical technique

Setting:

Department of Gynecology and minimally invasive unit Hospital Vita Batel Curitiba, Paraná, Brazil.

Interventions

The main steps of the uterine artery ligation by the posterior approach at laparoscopy are described in detail.

Case Report

A 35-year-old woman, G2/P0, with a history of infertility. She had complaints of dysmenorrhea, dyspareunia, and dyschezia, desiring pregnancy. The ultrasonography exam shows multiple myomas FIGO 3-6.

The patient underwent a laparoscopic myomectomy under general endotracheal anesthesia. Pneumoperitoneum was achieved by entry of a Veress needle into the umbilicus.

The laparoscopic trocars were placed according to the French technique initially as follows: a 10-mm camera port in the umbilicus, a 5-mm port in the right anterior superior iliac spine, a 5-mm suprapubic port, and a trocar. 5 mm in the left anterior superior iliac spine.

Posterior uterine artery ligation approach:

Step 1: Identification of anatomical landmarks (pelvic wall and the ureter attached to the peritoneum of the ovarian fossa).

Step 2: Opening of posterior peritoneum should be made medially to the infundibulo pelvic ligament, as the

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assistant grasps the infundibulo pelvic ligament creating a peritoneal tent.

Step 3: Identification of the ureter by its peristalsis and dissection, having access to the lateral pararectal space (Latzko space)

Step 4: Identification of the uterine artery, the first medial branch of the anterior division of the internal iliac.

Step 5: Blunt dissection around the uterine artery and ligation. The temporary occlusion is performed with 2-0 polyester suture with a double thread loop creating a shoelace knot (1,2). Both uterine arteries were ligated with the technique described. The posterior approach, just above the ureter, is indicated for myomectomy.

Myomectomy of multiple fibroids was completed and the uterine incision was sutured in two layers with polydioxanone sutures. Once the suturing was carried out, the knot was untied by pulling one end of the thread to restore the blood supply to the uterus. The intraoperative blood loss was 40 ml and the total time of the operation was 120 minutes.

Discussion

As previously described by Pisat and Desai et al temporary ligation of the uterine arteries at the time of myomectomy is a useful technique to minimize intraoperative blood loss and blood transfusion in patients who wish to preserve fertility (1,2).

Conclusion

The technique of temporary uterine artery ligation with a shoemaker's knot is a simple, reproducible, economical, and accessible procedure for the minimally invasive surgeon with knowledge of the anatomy being mandatory.

Standardization of the technique steps may help reduce the laparoscopic learning curve.

Key words: Laparoscopy, Myomectomy, Uterine artery ligation

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Hysteroscopic Septal Incision Using Scissors Following Laparoscopic Injection of Vasopressin Over the Uterine Fundus.

(Video)

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Abstract

Objective: To demonstrate the advantage of hysteroscopic septal incision using scissors following laparoscopic injection of vasopressin over the uterine fundus.

Design:

A video case report (Video 1).

Setting: Hysteroscopic septal resection, an accepted treatment modality for septate uterus, is done using scissors, unipolar or bipolar resectoscope, and laser (1,2). Bleeding, fluid overload, uterine perforation, intra-uterine adhesions, and uterine rupture in forthcoming pregnancy due to undue use of electro-cautery and laser are some reported complications (3). Although, scissors have been found to be advantageous when compared to resectoscopy (4), bleeding encountered with the former can hinder vision.

Key words:

Uterine Septum, hysteroscopy, hysteroscopic metroplasty, Septum resection

Intervention:

This video presents the technique of septal incision using scissors following laparoscopic injection of diluted vasopressin.

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Key surgical steps are:

1. Diagnostic hysteroscopy with laparoscopy to confirm presence of uterine septum.

2. Laparoscopic injection of 1:10 diluted vasopressin, in the midline of the uterine fundus using Pisat's VVIN (5).

3. Hysteroscopic incision of the uterine septum using cold scissors.

4. Procedure is deemed complete when both ostia appear to be in the same vertical plane, and are visualized in a single view when the telescope is at the internal os.

5. Clear field of vision is maintained throughout the procedure as there is no bleeding from cut edges.

Conclusion:

Laparoscopic injection of vasopressor solution over the uterine fundus makes hysteroscopic incision of uterine septum with scissors a straightforward and a relatively inexpensive procedure. Lack of bleeding provides a clear view and thus avoids the need of a resectoscope and its associated complications.

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Laparoscopic ovarian cystectomy for ovarian endometrioma – step by step technique (Video article)

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[2] Division of Minimally Invasive Gynecologic Surgery, Department of Obstetrics and Gynecology, University of Florida College of Medicine, Gainesville, Florida, United States.

Abstract

The surgical technique is essential to adequately manage the disease. The objective of this video is to show a meticulous technique to be necessary to adequately manage of Laparoscopic cystectomy for the treatment of ovarian endometrioma. This video reports in detail our current technique for laparoscopic cystectomy for ovarian endometrioma and all the tricks to permit a good answer to reproduction, and even improvement of the technique by other surgeons.

Key words:

Endometrioma; laparoscopic technique, endometriosis, ovarian, laparoscopy

Objective:

To describe a reproducible safe laparoscopic technique for the excision of ovarian endometriomas.

Design:

Video presentation

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Case Report:

Perfect surgical technique and knowledge of the anatomy is essential to adequately excise endometriosis. The ovarian endometrioma may be found in up to 44% of women with endometriosis.

The steps of a laparoscopic ovarian cystectomy for ovarian endometriomas are described in this video utilizing a reproducible technique with the aim of reducing trauma to ovarian injury. 10 key steps are highlighted.

Step 1: Patient preparation and establishment of peritoneum.

Step 2: Use of uterine manipulator

Step 3: Systematic diagnostic laparoscopy, endometriotic lesions mapping, and ovariolysis

Step 4: Aspiration and irrigation of endometriotic cyst contents.

Step 5: Identification of the endometrioma cleavage plane.

Step 6: Dissection of the ovarian endometrioma utilizing divergent forces

Step 7: Dissection of the deep aspect of the endometrioma near the ovarian hilum.

Step 8: Hemostasis.

Step 9: Excision of broad ligament and pelvic sidewall peritoneum.

Step 10: Extraction

Conclusion:

The ovarian endometrioma is seen in up to 44% of women with endometriosis. Premature surgical menopause and decreased anti-Mullerian hormone (AMH) after ovarian cystectomy is a concern that must be discussed with patients.

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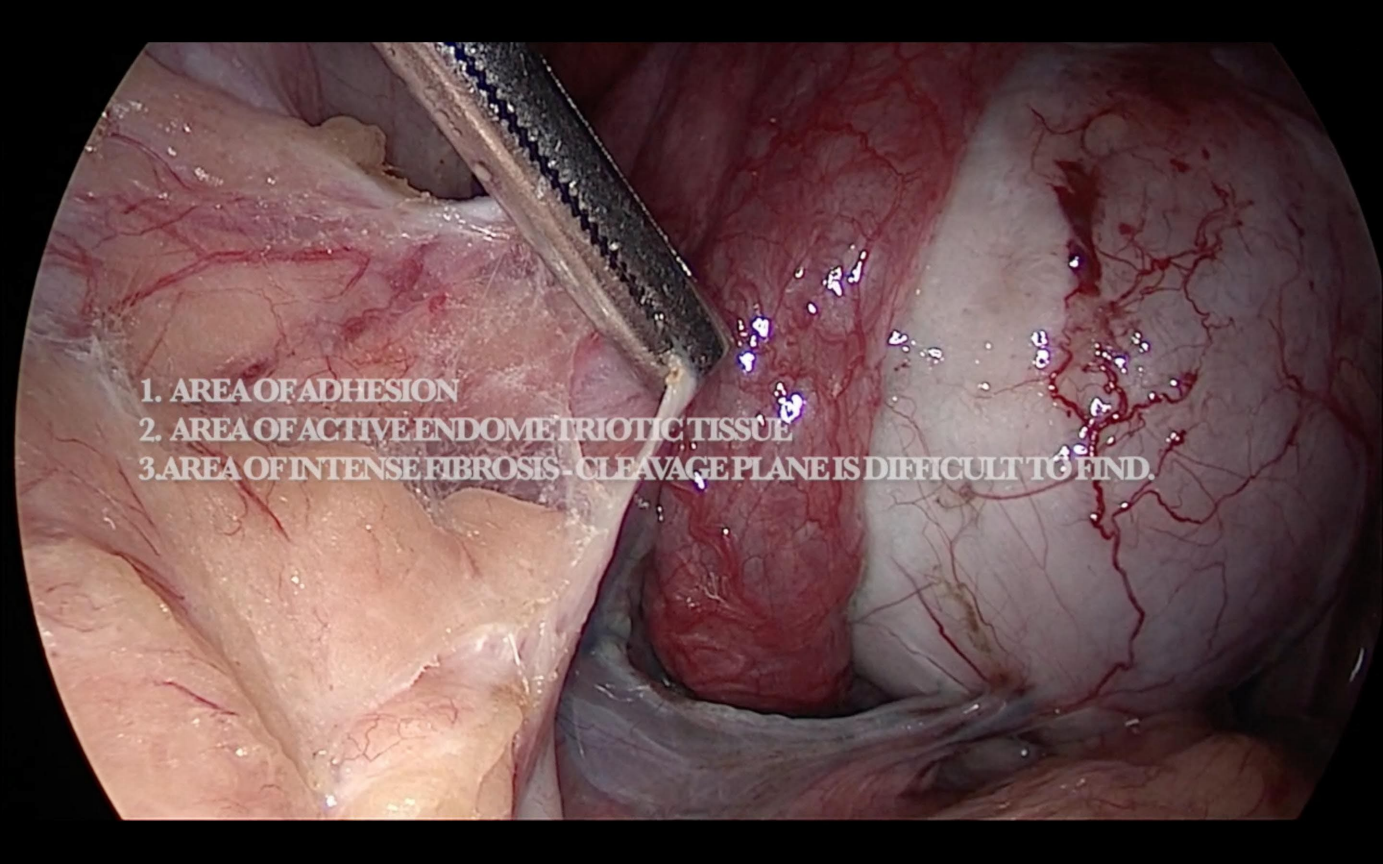
1. AREA OF ADHESION
2. AREA OF ACTIVE ENDOMETRIOTIC TISSUE
3.AREA OF INTENSE FIBROSIS - CLEAVAGE PLANE IS DIFFICULT TO FIND.

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10.36205/trocar3.2023007	Complete septum removal with a new combined technique: Intrauterine Bigatti Shaver (IBS®) and scissors. (Video Article) Xia Yin, Giuseppe Bigatti
10.36205/trocar3.2023008	Temporary Ligature of the Uterine Artery “Shoelace Knot” Pamela Delgadillo Tovar , Amira Quevedo, Isabella Naomi Furuie, Reitan Ribeiro, Fiorella Santos Carlos Henrique Trippia, Monica Tessmann Zomer, William Kondo
10.36205/trocar3.2023009	Hysteroscopic Septal Incision Using Scissors Following Laparoscopic Injection of Vasopressin Over the Uterine Fundus. (Video) Sanket Pisat, Pranay Desai
10.36205/trocar3.2023010	Laparoscopic ovarian cystectomy for ovarian endometrioma – step by step technique (Video article) Fiorella Santos Cajahuanca,Amira Quevedo, Isabella Naomi Furuie, Pamela Delgadillo Tovar, Monica Zomer, William Condo.