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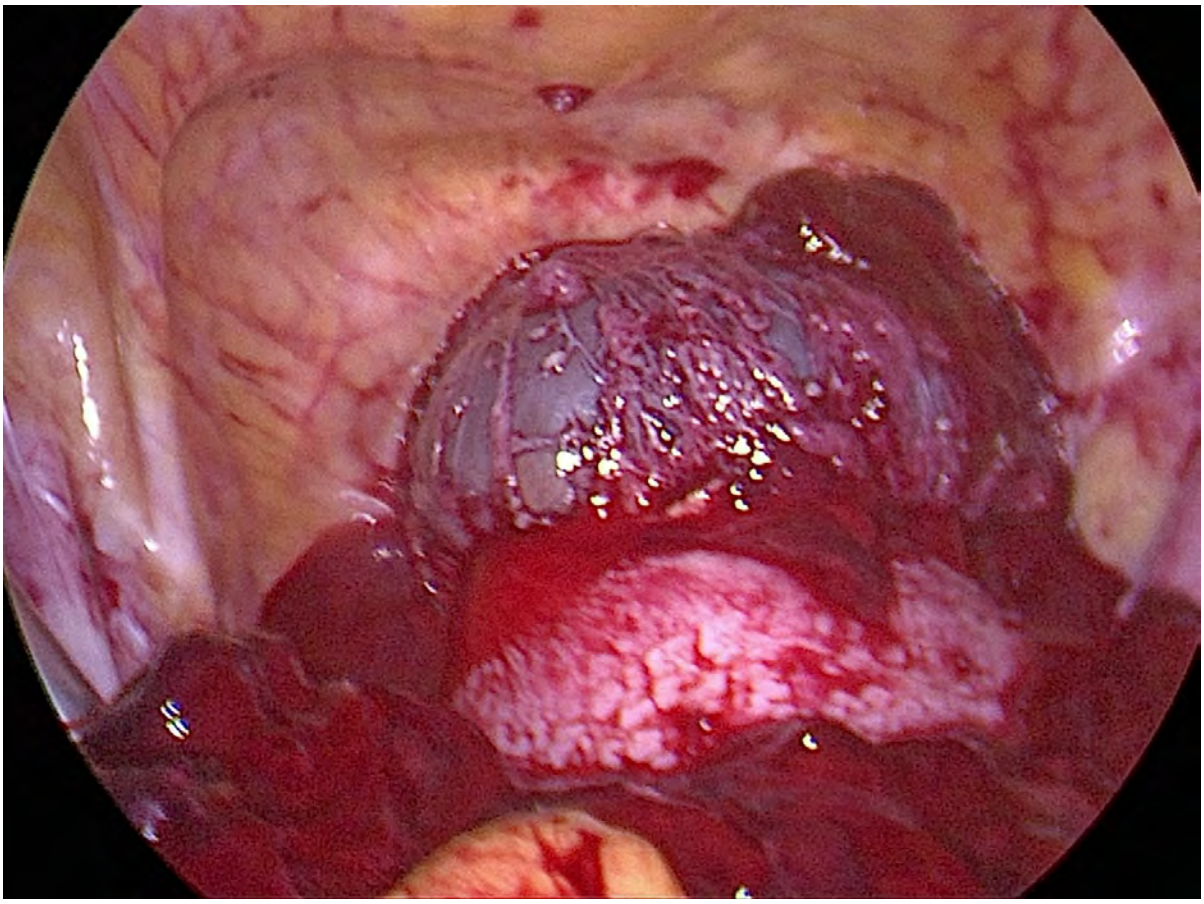

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Where are we going in 2024?

ISGE has been able to successfully continue on its path in 2023. As always in life with ups and downs. Our congress in Bali was a great success and thanks to intensive work, the accreditations are also progressing. In a time of global upheaval, conflict and the threat of climate change, it is still important that we as a community of physicians continue to dedicate ourselves to our goal, unfazed by the external circumstances.

Medical education or medical care should be a basic human right. Unfortunately, we are still a long way from that. Unfortunately, states are too often preoccupied with their strategic interests, so billions of people continue to lack operational care. The medical industry has not yet adapted to the needs of large parts of the world. This requires simple solutions that can be produced locally. Medical technology must be implemented in the countries because it takes too long to procure from the developed countries, corruption eats up money and is ultimately too expensive.

I am sure that talent and knowledge are plentiful all over the world. Therefore, there is a need for projects that enable medical products and technology to be manufactured locally. This is where governments and industry are called upon. Otherwise, our efforts to trace doctors remain only a very small contribution, as sustainability is lacking.

As doctors, we can impart knowledge and training, but our colleagues need tools that are always available and can be used even in difficult areas of their countries. The high standards and guidelines in industrialized countries make the products more expensive, to such an extent that in many countries they cannot be financed or are only available to a very small group. As doctors, we have little influence, but we should use every option to advocate for these goals as well.

ISGE will continue to work on its mission of education in 2024 as a community of international physicians and to make medicine available to more people. Anyone who supports us in this goal is welcome.

Happy New Year on behalf of the Editorial Board

Günter Noé

Index: Issue 4 Volume 4 The Trocar — December 2023

The frontpage shows: ruptured cesarian scar pregnancy

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THE INTERNATIONAL SOCIETY FOR GYNECOLOGIC ENDOSCOPY
PROMOTING VAGINAL SURGERY

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Editorial: Vaginal hysterectomy: another unique skill about to be lost

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The literature in Gynaecology for the last 30-40 years highlights the low percentages of hysterectomies performed vaginally, where there are no obvious contraindications. When compared to the other routes of hysterectomy, in terms of performance, duration, cost and complication rates, the vaginal route offers more rapid recoveries, more rapid return to daily activities, and is more cost effective.

The laparoscopic route of hysterectomy appears, recently, to be replacing vaginal hysterectomy as the preferred route, a transformation driven by trade and the ever-expanding fascination with technology. This change in preference has resulted in generations of surgeons that lack the skill set necessary to perform basic vaginal hysterectomy. These surgeons will therefore refrain from performing a routine vaginal hysterectomy, when it should be the preferred route.

Historically the first hysterectomy performed was a vaginal hysterectomy (VH). VH

dates back to ancient times, and was probably performed by Themison of Athens in 50BC (1) and definitively performed by Soranus of Ephesus in 120 years AD (1). VH was also mentioned in Alshahavarious' writings of 11th century: "if uterus has prolapsed externally and could not be reinserted, it should be surgically excised" (2). These hysterectomies were carried out sporadically and only for the reason of uterine prolapse or uterine inversion. However,

the bladder and the ureter were often torn and the patient rarely survived.

Vaginal hysterectomy found in the descriptions of Berengario de Capri of Bologna in the Middle Ages (1470-1550) (3) and the first planned VH was performed by Conrad Lagenbeck of Gottingen in 1813. His patient made an uneventful recovery and lived for 26 years after the vaginal hysterectomy (4). The first recorded subtotal hysterectomy was performed by Charles Clay in 1843, in Manchester, England (1).

One of the strongest proponents of vaginal hysterectomy was Noble Sproat Heaney of Chicago who in 1934 reported a series of 627 VH for benign pelvic disease resulting in death in only three cases (3). During this period, the first part of the 20th century the VH had fallen out of favour as the general surgeons, not being familiar with the vaginal surgery, favoured the abdominal route. The first total abdominal hysterectomy (TAH) was performed by Richardson in 1929 in the United States of America (USA) (1). Despite Richardson's recommendations, subtotal hysterectomy remained the preferred surgical technique until the late 1940's, supracervical hysterectomies were preferred due to theoretical reduced risk of bladder and ureter injury, as well as avoiding opening the vagina, the risk of contamination with vaginal flora was eliminated. The advent of antibiotics, blood transfusion, modern anesthesia and the recognition that cancer occasionally developed in the cervical stump, encouraged the surgeons to carry out TAH. For the next 50 years or so no further conceptual advances in the technique were introduced until the advent of endoscopic surgery. During this period the technique of TAH has improved. The introduction of Pfannenstiel incision with cosmetic results and safety led to the explosive increase of the number of TAH seen today.

The introduction of Laparoscopic assisted vaginal hysterectomy (LAVH) in 1984 by Kurt Semm (5,6), and the Total Laparoscopic Hysterectomy (TLH) in 1989 by Reich in 1989 (7,8), revolutionized the surgical approach to hysterectomies. Both the above authors intention was to decrease the number of hysterectomies performed abdominally and not to replace the VH as seen today. We shouldn't forget that these conceptual advancements necessitating new skills and equipment represent a new technique for an old procedure- the VH.

With the introduction of Laparoscopic Hysterectomy (LH) in the last part of the 20thcentury, the concept of minimally invasive hysterectomy (MIH) emerged. The question is why VH, a long-practice procedure dating back to Themison in 50BC, meeting all the parameters of MIH namely, avoidance of large painful abdominal scars, less need for analgesia, rapid recovery and return to daily activities among other benefits, does not hold preferential place amongst surgeons with the AH and LH routes being the first choice?

Hysterectomy remains one of the most common operative procedures for benign uterine diseases performed today in developed countries (9,10), yet the route of hysterectomy for benign uterine conditions continues to excite controversy and debate. It can be performed abdominally, vaginally, or laparoscopically, with or without robotic assistance. The surgical approach of hysterectomy is the most important factor responsible for postoperative morbidity. Many studies have compared the surgical approach and complications according to the type of surgery to determine which method is best for the patient. The conclusion suggests that abdominal hysterectomy is inferior to VH and LH. The advantages provided by LH/RH and VH over open abdominal hysterectomy (AH) include less

postoperative pain, less need of analgesia, shorter hospital stay, and more rapid recovery and return to daily activities (11-15). Additionally, there are fewer intra-operative and postoperative complications reported with vaginal hysterectomy as compared with abdominal hysterectomy (AH) or laparoscopic hysterectomy (LH) (16-18). However, AH for benign uterine conditions remains the chosen route worldwide. This preference, is largely due to a lack of experience in VH, resulting in surgeons' reluctance to perform VH, especially in patients without uterine prolapse, with uterine fibroids, previous caesarean sections, previous laparotomies, as well as in nulliparous women. Correctly challenging these contraindications may lay the foundation for implementing different approaches towards an increased number of VHs (19-24).

In spite of the benefits offered by VH, globally, 70- 80% of hysterectomies have been shown to be carried out via the abdominal approach, according to all large-scale surveys (25-37), except when treating uterovaginal prolapse, for which the vaginal route is generally preferred. This latter indication accounts for about 10% of all hysterectomies conducted worldwide (38). The rate of LH has been shown to be increasing, without a significant reduction in AHs. This increase in LH has thus been incurred at the expense of VH while, ideally, it is the VH rate that should increase at the expense of the AH rate.

It is a common perception that the decreasing VH rate, which came about as a consequence of the dependence on LH, may be at least partially attributed to the impact of the industry that manufactures and promotes the laparoscopic equipment. The introduction of robotics has changed the rates in favor of robotic hysterectomy (RH). In the hospitals where the RH was introduced in United States of America (USA), the number of RHs increased with a further decline not only in VH but also in conventional LH (39). It seems like hysterectomies which can be performed vaginally or laparoscopically are now done robotically.

Assessing current trends in resident hysterectomy training it is obvious that VH is not promoted as should be when deciding the route of hysterectomy. When deciding the route of hysterectomy, the preference and proficiency of the surgeon may be the most decisive factors. As a result, if LH is performed more often than VH, gynecologists in the future will be unfamiliar with VH, leading to a more profound decrease in the implementation of VH. This was demonstrated in a survey amongst residents performed in the USA in 2011, by Antosh et al (40). In this survey, only 41.7% of residents reported VH as their preferred route of hysterectomy, as compared to 47.1% who preferred laparoscopic approaches (40). Similar findings were reported by Burkett et al. who concluded that there is an increase in endoscopic approach, including robotic hysterectomy (RH), while VH is becoming inappropriately replaced and underutilized (41).

This highlights a fundamental problem currently facing clinical gynecology, namely insufficient VH training/practice due to the inadequate experience of junior trainers in VH, and the consequent lack of appreciation of the benefits afforded by VH. It is evident from the literature that the vaginal route should be considered the preferred choice. VH skill should not be sacrificed in favor of LH or RH. Academic institutions worldwide are urged to review a strategy in order to retain the skill of VH, via appropriate training programs. Surgeon training and experience have often been deemed particularly influential leading factors for the selection of the most appropriate approach to hysterectomy. Failure

to achieve proficiency during training as a registrar due to the lack of training and experience in VH has been raised by several authors as being an important obstacle in performing VH. Lack of experience in vaginal surgery leading to gynecologists having a dependence on the abdominal and/or laparoscopic routes when contemplating hysterectomy (42-45).

Aside from personal training, other factors that are considered prerequisites for a successful VH are vaginal accessibility, together with the size and mobility of the uterus (46). The ACOG has stated that VH is indicated for patients with a mobile uterus of less than 12 weeks gestational size (47). The International Society for Gynecologic Endoscopy promoting vaginal surgery (ISGE), introduced evidence-based guidelines for selection of women who can had undergone uncomplicated VH as well as practical guidelines for safe performance of VH (48,49). Incorporation of these guidelines into the residents training programme, can increase the rate of VH and result in an overall decline in open AH and LH (50).

We demonstrated in an academic institution in South Africa, that when formal institutional guidelines and surgical decision algorithm are introduced into the residents training program this promotes the vaginal approach to hysterectomy in patients with benign disease and non-prolapsed uterus (49). In our Institution, the proportion of hysterectomies performed abdominally decreased from 91.2% to 51.6% and those performed vaginally increased from 9.8% to 48.4% from the beginning of the study in July 2001 to its end in December 2014. The VH to AH ratio, therefore, was increased from 1:9 to 1:1. Based on this, it seems that as much as 40 % of feasible vaginal procedures were replaced by a more invasive approach, AH/ LH, when guidelines and surgical decision algorithm were not used (50). This study is in agreement with other large studies, which indicate that, the implementation of a clinical pathway and hysterectomy guidelines can be associated with a decrease in the proportion of hysterectomies performed abdominally (42,46,51). By increasing the rate of VH in our institution, we achieved greater exposure and training at resident level, providing the possibility of true proficiency that could be passed to others. Future studies will indicate the effects of these clinical and education strategies in increasing the rates of VH worldwide.

Conclusion

Literature review reveals that when hysterectomy for benign uterine disease is undertaken, VH should be considered as the ideal surgical approach amongst minimally invasive hysterectomies. Despite evidence supporting the benefits of VH, current statistics indicates that VH is underutilised. The decreased utilisation of VH is undesirable because VH is the least invasive approach with shorter operating time and is less costly. The introduction of the guidelines proposed at our institution into the registrar training program can lead to a decrease of hysterectomies performed abdominally and an increase in hysterectomies performed vaginally which may be achieved without inappropriate increase in laparoscopic or robotic hysterectomy. Minimally invasive gynaecologic surgeons around the world should focus on the VH training, skills and proficiency among residents. It is true that all of hysterectomy cannot be performed by VH, but for patients with similar indications and uterine weight, all of hysterectomy should not be performed by laparoscopic or robotic hysterectomy. Based on the benefits offered by VH, I consider that nobody can call himself or herself a minimally

invasive gynaecologic surgeon if not able to perform a VH in selected patients with benign uterine diseases and non-prolapsed uterus. The evidence overwhelming in favour of VH hence, all efforts should be directed to revive VH. VH should not be sacrificed on the altar of any further debate or dispute.

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Preoperative diagnosis of leiomyosarcoma: practical guidelines of the International Society for Gynecologic Endoscopy (ISGE)

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Abstract

Introduction: Uterine leiomyomas are the most common benign gynecologic tumors afflicting women. Different types of minimal invasive gynecologic surgical procedures (MIGS) exist to treat leiomyomas. Tissue retrieval procedures came into disrepute since the Food and Drug (FDA) statements of 2014. The incidence of leiomyosarcoma in women is estimated to be 0,13 to 0,29 % whilst in patients undergoing power tissue retrieval an incidence of 1,2 % was observed. The aim of this prospective observational trial with retrospective analysis is to define the real incidence of leiomyosarcoma in women operated in Europe by MIGS.

Material and methods: From January 1998 through December 2004 in four Italian centers 2050 laparoscopic myomectomies for myomectomy or hysterectomy have been performed and two leiomyosarcomas have been found. One recognized and converted during surgery and one non diagnosed but recognized at frozen section. In a second phase from January 2005 to May 2015; 990 myomectomies

- laparoscopic, laparotomic or hysteroscopic - and hysterectomies for myomas have been performed in two centers (Italy and Belgium) using the International Society for Gynecologic Endoscopy (ISGE) preoperative screening protocol: clinical history, clinical examination, ultrasound scanning, blood testing. The low-risk patients to undergo the projected surgery and the high-risk patients to be screened by magnetic resonance scan (MRI) before surgery if back to low risk by MRI these patients did undergo the projected surgery. Other patients diagnosed as high risk for potential leiomyosarcoma were treated with an oncological regime.

Results: In total of 3040 myomectomies over a seventeen-year period in 6 centres in Europe (five in Italy and one in Belgium) have been performed. Three sarcomas have been diagnosed two in the first phase one during surgery and one immediately after surgery (frozen section). In the second phase one leiomyosarcoma has been detected using the ISGE recommendations prior to surgery. Detection rate of 0,10% or 1:1000 with one undetected (1:3040).

Conclusion: An improvement can be made in detecting leiomyosarcoma prior to surgery using preoperative history, blood testing (LDH) and imaging techniques, mainly vaginal ultrasound scanning and on indication MRI - the ISGE recommendations. In this study concerning patients undergoing MIGS, the incidence of leiomyosarcoma is of 0,10%. This is less than the estimated rate (0,13% – 0,29%) and much less than the rate found at power tissue retrieval (1,2%).

Keywords

Leiomyosarcoma, diagnosis preoperative, ultrasound, MRI, MIGS, ISGE guidelines.

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Introduction:

Fibroids, also known as leiomyoma, fibro myoma or uterine fibroids are the most common benign tumours in women (1). Historically fibroids have been operated by laparotomy. At this day and age Minimal Invasive Gynecological Surgery (MIGS) including hysteroscopic myomectomy, laparoscopic myomectomy , with or without robotic approach, vaginal myomectomy, vNOTES myomectomy, with or without robotic techniques and hysterectomy performed by conventional laparoscopy or robotic-assisted, vaginal route or vNOTES are preferentially used. This shift to MIGS is explained by the reduction of the hospital stay, a reduced intra – and postoperative morbidity and a reduced delay to normal activity of the patient (2-12) In order to remove the fibroid or the uterus from the abdominal cavity some kind of volume reduction, to be able to remove the tissues, is mandatory. This can be achieved by power tissue retrieval

(12). This technique does increase the risk of spreading both benign and malignant cell in the abdominal cavity and even in the MIGS entry wounds (13-25) The US Food and Drug Administration (FDA) communication on patients' safety dated April 17th 2014 did change the approach of the surgeons to myoma surgery as it did urge them not to use tissue retrieval techniques based on power morcellation in treating the supposedly benign tumors. It did stress the concern that these techniques could be spreading cells of occult leiomyosarcomas and therefore reduce the survival rate of the patients (26,13-18,20-22). It also stated that samples obtained by power tissue retrieval could reveal to be difficult to interpret by pathologist due to the impact of the techniques on the specific tissues to be examined (26). This safety communication did lead to a cascade of statements by different entities warning against but not prohibiting power tissue retrieval Health Canada (27), the Society of Gynecologic Oncology (SGO) (28), the American College of Obstetricians and Gynecologists (ACOG) (29), the American Association of Gynecologic Laparoscopists (AAGL) (30), the European Society for Gynaecological Endoscopy (ESGE) (31), the European Society of Gynecological Oncology (ESGO) (32), the Asia-Pacific Association for Gynecologic Endoscopy and Minimally Invasive Therapy (APAGE) (33), the Australian Gynaecological Endoscopy and Surgery Society/The Royal Australian College of Obstetricians and Gynecologists (AGES/RANZCOG) (34), the British Society for Gynaecological Endoscopy (BSGE) (35), the French College of Obstetrics and Gynecology (36), and the German Society for Gynecology and Obstetrics (DGGG) (37). The FDA analysis went out from the estimate that 1/350 women undergoing hysterectomy for myoma could have an occult leiomyosarcoma this in contrast to the findings of the American Cancer Society estimating that only 1600 cases of newly diagnosed uterine cancers in 52.000 registrations reveals to be a uterine leiomyosarcoma (38). On top of these FDA warnings Seidman et al (2012) did observe that in 1,2% of the power tissue retrieval cases unexpected diagnoses of atypical or malignant smooth muscle had been made, in cases diagnosed preoperative as benign fibroids (39). In a prospective study Sizzi et al did find one case in 2050 myoma tissue retrievals (0.04%) (40). In its 2021 statement the Italian Association of Medical Oncology (AIOM) stated for the impact to be of < 2/100000 women/year with an average age of detection at 56 years (41). In view of the above data the overall risk of an occult uterine leiomyosarcoma appears low. However, patients needing to undergo a MIGS and require intracorporeal tissue retrieval are in need of an appropriated preoperative evaluation to exclude a potential occult malignancy. The aim of this study is to prove that the ISGE guidelines do offer the clinician a workable flowchart to discuss the preoperative findings with the patients as to offer a workable solution for both patient and surgeon (42). This by confronting the data of a prospective Italian observational study, reanalyzed retrospectively with a prospective observational study using the ISGE recommendations as a preoperative diagnostic flow chart (40,42).

Methods

The results of the first prospective observational study have been reevaluated looking at the presence of leiomyosarcomas. In the second prospective observational study patients needing a myomectomy, for clinical symptoms or fertility indications, or a hysterectomy for symptoms were subjected to the ISGE recommendations as follows: a first consultation was held with the individual patient where the different ISGE guidelines were explained in detail

and the patient did sing a consent form after understanding and agreeing with the proposed guidelines. Patients who did not sign the consent from were excluded from this study. As this last study was a prospective observational study dealing with normal surgical interventions and the patients did give their consent prior to the study the personal data do resort under the privacy, later GDPR, regulations and ethical approval was not asked for (43,44).

Clinical exam considerations

All patients needing a myomectomy of hysterectomy with MIGS did undergo a structured interview concerning their medical history. Projected against the known leiomyosarcoma risks (Table 1) Black race is a common risk factor for both LM and LMS. In black vs. white women, the LM incidence is 2- to 3-fold greater and the LMS incidence as well as the incidence of carcinosarcoma is 2- fold higher (45-48). In contrast, increasing age, particularly postmenopausal status, is an important risk factor for uterine sarcomas, while LM typically shrinks following menopause. Below the age of 40, sarcoma in a presumed LM is extremely rare (31). Tamoxifen used for five years or more, pelvic irradiation, hereditary leiomyomatosis and renal cell carcinoma (HLRCC) syndrome due to germline mutations of fumarate hydratase, and a history of childhood retinoblastoma constitute other risk factors for uterine sarcoma, which do not present statistically significant association with LM. The clinical manifestations of LM and LMS are often indistinguishable (29,30). Abnormal uterine bleeding (AUB) (most frequently, in the form of heavy menstrual bleeding), dysmenorrhea, lower abdominal pain, lumbago, pressure symptoms (e.g. pollakisuria, dysuria, bowel symptoms) and palpable mass on the site of lower abdomen are symptoms and signs for both LM and LMS (29,49–52). Uterus and lesion size, uterine contour, mobility and any other examination finding cannot accurately distinguish a LM from a LMS (49,50,53-55). Rapid lesion growth has been traditionally valorized as a sign of a potential malignancy (56) however, neither large tumors (49,54) nor rapidly enlarging uterine masses (53,55,57–60) have been demonstrated as useful malignancy indicators in premenopausal women. On the other hand, in postmenopausal patients, particularly in women who are not on hormone replacement therapy, new or growing lesions require evaluation and malignant process exclusion. Furthermore, the lesion failure to respond to medical or non-excisional treatment, such as uterine artery embolization or myolysis performed by magnetic resonance-guided focused ultrasound (MRgFUS), is clinically highly important, despite the fact that it does not provide absolute evidence of malignant nature (61–67). The metastatic disease manifestations can be found in women with LMS, while spontaneous benign LM dissemination is very rare, except when power tissue retrieval methods are used, giving origin to disseminated peritoneal leiomyomatosis, intravascular leiomyomatosis and benign LM metastasizing to distant tissues (68).

Uterine sarcoma clinical risk criteria (adapted from ACOG and AAGL statements)	
Symptoms	
Abnormal Uterine Bleeding (including irregular, heavy and/or prolonged menstrual bleeding	
Dysmenorrhea	
Palpable Abdominal mass	
Lower Abdominal pain	
Lumbago	
Pressure Symptoms (pollakisuria, dysuria, bowel symptoms)	
Risk Factors	**Comment**
Black race	Two-fold LMS incidence rate comparing to The white race
Increasing age	Mean patient age at diagnosis:60 yrs. Lowest risk in women <35 yrs.; highest risk in women >65 yrs
Tamoxifen	Prolonged use (>5 years)
Pelvic Radiation	Association especially strong for carcinosarcoma
HLRCC syndrome	AD syndrome: sarcomas often found in younger women
Survivors of childhood RB	Higher risk for uterine sarcomas and sarcomas in general

Table 1: known leiomyosarcoma risk

The following initial exam does include a physical examination and a routine screening for cervical cancer

Routine screening for cervical cancer and endometrial sampling

Prior to treatment of presumed LM, routine screening for cervical cancer should be performed. Uterus morcellation should be avoided in women with cervical dysplasia (30). To rule out endometrial atypical hyperplasia or endometrial cancer in women with abnormal uterine bleeding, most guidelines suggest that patients should be selected for endometrial sampling based on a combination of the factors indicating an increased risk (e.g. patient's age, genetic and personal risk factors, endometrial echo-features) (69). Although the results of previous smaller studies (70,71), show that the sensitivity of endometrial biopsy to detect LMS is low, positive or suspicious results do have decisive impact on management of that individual patient (72).

Biochemical markers

Patients with LMS often have somewhat increased serum lactate dehydrogenase (LDH) levels (73) especially isoenzyme 3 (LDH3) (74). For instance, Goto et al. observed an abnormally increased level of total LDH and LDH3 in all patients with LMS (LDH3, sensitivity and specificity 90% and 92.3%) (74). These studies have not been reproduced. Elevated serum cancer antigen 125 (CA125) has been occasionally observed in LMS in advanced-stage disease (75,76). However, Menczer et al. did not evidence CA125 expression in any of 17 immunohistochemically examined LMS tumors, concluding that the origin of increased serum CA125 is not in neoplastic tissue (77) As there is significant overlapping levels of CA 125 between LM and early LMS this biochemical marker is of

no use in a flowchart to detect LMS preoperatively (75).

Imaging: Ultrasonography:

The vast majority of fibroids are discovered and evaluated via ultrasound scanning, using the trans-abdominal and transvaginal routes, due to its accessibility, relatively low costs and reliability (1). The Morphological Uterus Sonographic Assessment (MUSA) consensus paper, published in 2015, provides the terms, definitions and measurements for standardized evaluation and reporting of sonographic features of the myometrium and myometrial lesions (78). Sonographically, a typical uterine LM is a well-defined round formation within or attached to the myometrium, its echogenicity varies, often showing some internal hyper echogenicity, internal fan-shaped shadows and/or shadows at the edge of the lesion (78). Circumferential flow around the formation can be visualized by color or power Doppler, the MUSA group suggests that LM should be labeled as sonographically atypical if the lesion does not exhibit this vascular pattern. When a LM degenerates, it may show low echogenicity, a hyperechogenic rim and no internal vascularity, or mixed echogenicity, or hypoechogenic cystic areas (78 -81). LM with little or no recurrent and/or metastatic potential as well as uterine Smooth-muscle Tumors of Uncertain Malignant Potential (STUMP) have the same ultrasound characteristics as does an ordinary LM (78,82–87). Several studies focused their attention on the detection of sonographic parameters that could be used in distinguishing between a benign and a malignant uterine smooth muscle tumor (89-92) Uterine sarcomas are typically solitary, large lesions often exhibiting ultrasound features that are indistinct from those of LM (81,92, 93). Although they may also appear as irregularly and highly vascularized masses, with or without irregular anechogenic areas reflecting tumor central necrosis (1,88,91,94,95), there is no ultrasound characteristic that can reliably differentiate between LM and LMS. Exacoustos et al. proposed a subjective semi-quantitative assessment of the blood flow (vascular score), examined with directional power Doppler imaging, which was similar to that proposed for adnexal masses by the International Ovarian Tumor Analysis (IOTA) Consensus Group, revealing that the increased central and peripheral vascularity had a sensitivity, specificity, and positive predictive value (PPV) of 100%, 86%, and 19% in the diagnosis of LMS (94). However, a 19% PPV is not clinically relevant. This being the reason why the ISGE did propose a scoring system for the ultrasound evaluation of the LM with a cut off at score of 18 points (Table 2) (Figure 1). This guiding the physician to evaluate the individual situation in the by ISGE proposed flowchart (Table 3) (42).

Ultrasound criteria to evaluate uterine sarcoma risk
Level II Ultrasound criteria
Echo pattern (homogeneous or inhomogeneous with mixed echogenic and poor echogenic parts)
Necrotic, cystic, haemorrhagic changes
Presence or absence of central vascularization [a]
Distribution of tumoral vascularization: a high vascularity score [b]
Size (maximal diameter > 8 cm)
Presence or absence of calcifications

[a] Subjective color score: 1 – no color, 2 -minimal color, 3 – moderate color, 4 – abundant color
[b] The score for both central and peripheral region are combined (maximum vascular score 8)

Table 2 Ultrasound criteria to evaluate uterine sarcoma risk.

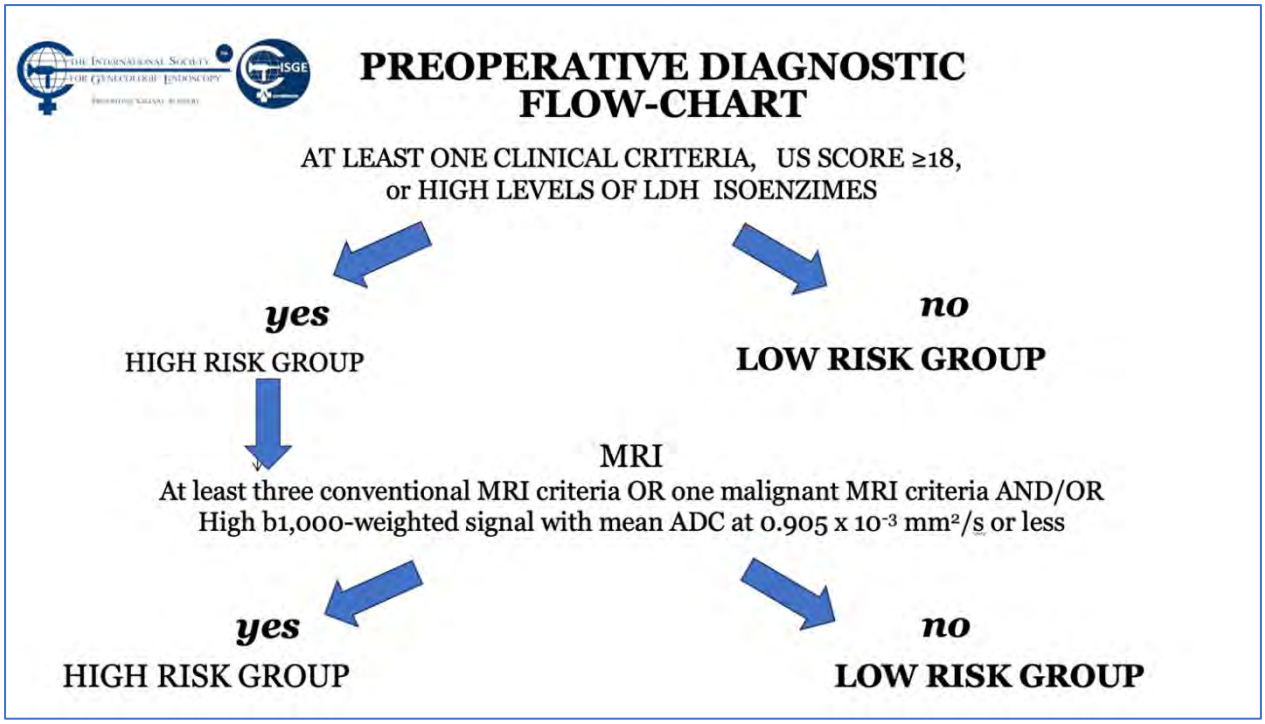


Table 3: ISGE Flowchart to distinguish LM from LMS

Imaging: Magnetic resonance imaging (MRI):

MRI provides a better image in delineating the exact location and characteristic of the fibroids; the down point is that this exam it is far more expensive and less accessible than ultrasound (1,89). Therefore, MRI should be considered only for women in whom the nature of the pelvic mass is uncertain after clinical and pelvic ultrasound, preferably vaginal ultrasound, assessment as recommended by the ISGE guidelines if the score is higher or equal to 18 points (Fig 1). The differentiation of LM from LMS

may be suggested by assessing tumor total necrosis and the presence of a peripheral rim, which corresponds to the obstructed veins showing low signal intensity on T2 and high signal intensity on T1WI (96). Tanaka et al. reported that the highest accuracy in diagnosing non benign smooth muscle lesions is expected when more than 50% of the tumor shows high signal on T2WI (97). Goto et al. compared conventional MRI findings along with post-enhancement behavior (dynamic MRI) of degenerated LM and LMS, revealing a specificity, accuracy and positive predictive value (PPV) of 96.9%, 97.1%, and 71.4% for MRI, and 87.5%, 90.5% and 71.4% for dynamic MRI (74). Both sensitivity and negative predictive value (NPV) were 100%. Sato et al. proposed the use of Diffusion-Weighted Imaging (DWI) and corresponding Apparent Diffusion Coefficient (ADC) values in the evaluation of myometrial tumors (98). DWI provides quantitative measurements for the ADC - ADC being a mathematic mapping not a real image - and these are considered to be influenced by nuclear to cytoplasm ratio and cellular density in solid tissues. Both DWI and ADC therefore do need a T2 image of the structure. Sato et al. affirmed that cases with low signal intensity on DWI may be regarded as uterine LM, while intermediate to high signal intensity may indicate uterine LMS. For this reason, in patients with parenchymal areas of intermediate to high signal intensity, ADC values were evaluated, revealing that the mean ADC value for the LMS lesions was significantly lower than that of the LM nodules (98). Neoplasms are characterized with high cellularity this reduces the free motion of water molecules on DWI imaging increasing the signal. On ADC MAPs the signal of these areas is hypointense (99).

Fig. 1: Practical scoring system of ultrasound features and age data

Results

From the first prospective study after retrospective analysis of 2050 patients two LMS

have been diagnosed at operation one and one immediately after surgery during the operation itself by frozen section and in both cases the operation has been converted to an oncological procedure.

During the second prospective observational study the ISGE recommendation: 1. Structured interview taking into account the different common risk factors of LMS (table 1) 2. Structured clinic clinical exam with exclusion of cervical malignancy and if needed intrauterine malignancy indicators 3. Vaginal ultrasound evaluation in accordance with the ISGE recommended scoring system for ultrasound (table 2, figure 1) and finally adherence on the ISGE flowchart (table 3) have been followed in 990 patients. One LMS was detected before surgery with as characteristics: patient 52 years of age, solitary lesion of 10.87 x 7;20 x 8.0 cm – large - ultrasound evaluation score 22/25 (figure 2, 7, 11). On ISGE flowchart HIGH RISK. One other patient was detected preoperatively as a Uterine Smooth-muscle Tumor of Uncertain Malignant Potential (STUMP). The patient of 52 years of age presented with a solitary lesion of 52.43 x 29.39x 4.58 cm with rapid increase of volume with strong inhomogeneous echotexture without cystic degeneration. The ultrasound score was 19/25. ISGE flowchart HIGH RISK (figure 3,10). A third patient, 32 years of age, was first considered to be possible LMS preoperatively but averred on histology to present an intramural leiomyoma with hyper cellular areas, focal sclerohyalinosis and fatty degeneration. Her ultrasound score was 20/25 (fig 4, 9). On ISGE flowchart initially HIGH RISK but converted after MRI to low risk. The final histopathology in the last patient was atypical leiomyoma with a high mitotic index. Three other patients age range between 38 and 43 presented with normal LDH and ISGE scores between 22 and 19 al these patients were cleared by MRI as LOW Risk in all cases pathology did detect less than 10 mitoses per high power field. As all ultrasound scores were over > 18 all patients were confirmed by MRI. None of the other 987 patients had an abnormal pathology report (ultrasound score </= 18).

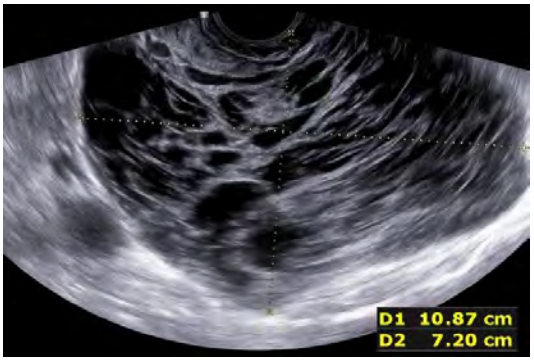


Fig. 2: Prospective study 2 Conventional ultrasound scanning Leiomyosarcoma detected preoperatively. US Score 22/25

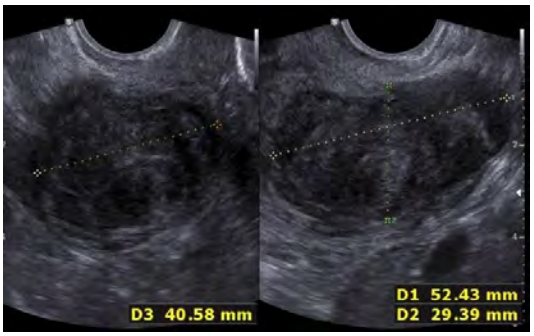


Fig. 3: Patient in phase two prospective trial Conventional ultrasound scanning detected with STUMP US score 19/25

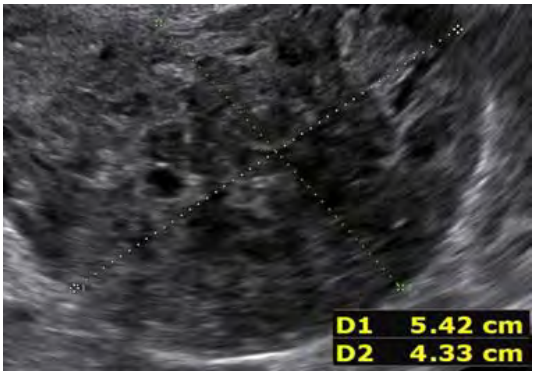


Fig. 4: 32-year-old patient in phase two prospective trial: Conventional ultrasound

scanning with Intramural leiomyoma with hypercellular areas, focal sclerohyalinosis and fatty degeneration. US score 20/25

Fig. 5: Example of peripheral vasculature Power Doppler

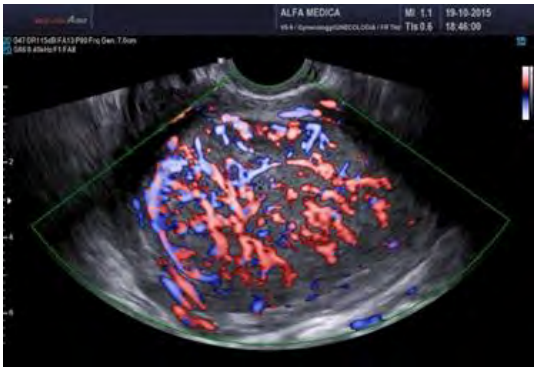


Fig. 6: LMS with marked peripheral and internal vasculature

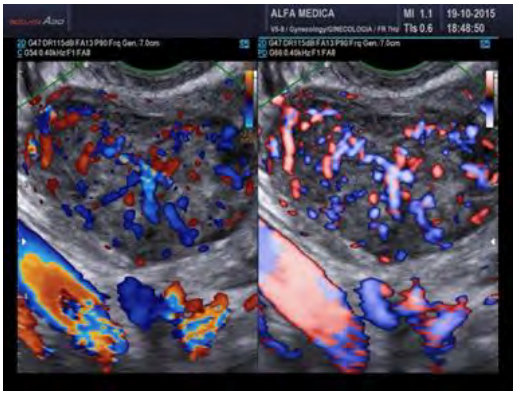
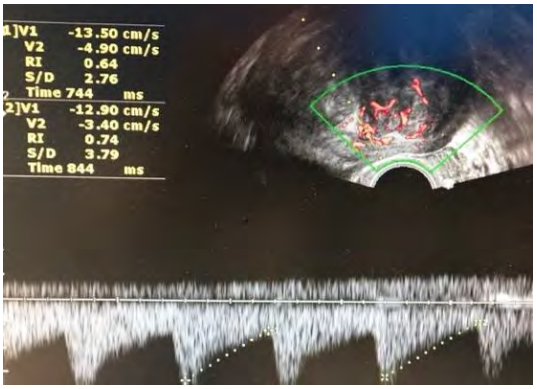


Fig. 7: LMS Note the heavy doppler signals not around the mass but also inside. (Doppler (left) and Power Doppler (right) intensities)



Fig

Fig. 8: LM: Normal peripheral vasculature at Doppler sometimesthe Resistance index (RI) can help out. Normal curves and RI of the vessels 0.74 (cut off for malignancy RI 0.45)

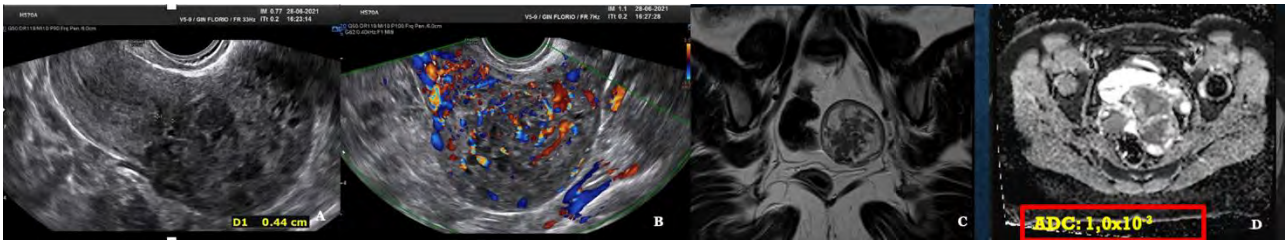


Fig. 9: Atypical myoma with high mitotic activity. **A** vaginal ultrasound greyscale. **B** Vascular halo but also internal vascularization. **C** T2 MRI. **D** ADC mapping with measurements in the high range. ADC $1,0x10^{-3}$

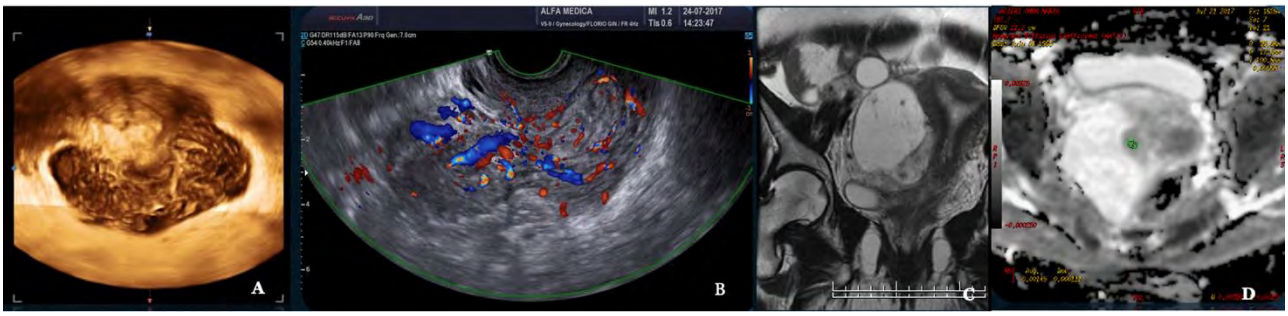


Fig. 10: Smooth muscle Tumor with Undefined Malignant Potential (STUMP) **A** Three D vaginal scanning **B** Doppler Ultrasound ISGE US score 22/25 **C** MRI T2 image. **C** ADC Mapping ADC in the high range: $1{,}1x10^{-3}$

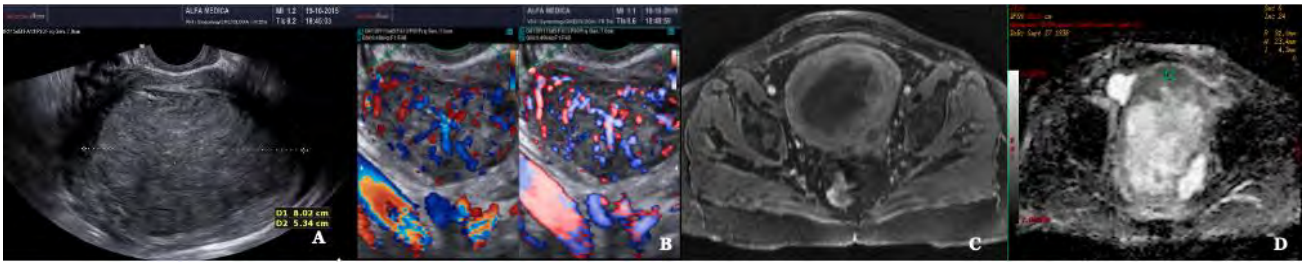


Fig. 11: Leiomyosarcoma **A** Conventional ultrasound scanning **B** Doppler enhanced ultrasound scanning (left) Power Doppler enhanced ultrasound scanning (right) **C** MRI T2 image **D** MRI ADC mapping ADC in the lower range: $0{,}9x10^{-}$

Discussion

In this study concerning patients undergoing MIGS, the incidence of LMS is of 0,10%. This is less than the estimated rate of (0,13% – 0,29%) in the literature and much less than the rate found at power tissue retrieval (1,2%). The conclusion from these numbers therefore is that some data in literature are overestimated and that the true incidence of LMS is between 0,10% and 0,29%. However, it is important to state that the final diagnosis of LMS can only be reached through the lesion's histological evaluation. From the numbers of the above prospective trial, it is shown that starting in patients over 30 years of age more mitoses per high power filed at pathology are found. Further it is essential to realize that the incision in the uterine serosa and myometrium, necessary to extract LM, by definition opens vascular and lymphatic channels, facilitating the spread of tumor cells if dealing with LMS. Any blood or tissue fragments spilled into the abdominal cavity as well as contact of any resected tissue with the peritoneum can potentially spread cancerous cells. By the time the tissue has been placed in a bag for morcellation, it may be already too late to prevent the spread of tumor (100,101). On the other hand, it could be considered to perform total laparoscopic hysterectomies instead of supra-cervical hysterectomies, with tissue retrieval of the specimen through the vagina, in a bag. There are no evidence-based medicine data showing that supra-cervical hysterectomy is better for the patient on the long run compared to total laparoscopic hysterectomy (102). Preference to supra-cervical hysterectomy can be justified only in case of pelvic organ prolapse repair after appropriate preoperative evaluation. Currently, there is not a single tissue-extracting

procedure that offers absolute patient protection. Thus, all methods should remain available (30). In all circumstances when preoperative evaluation of cervix, endometrium and/or myometrium results in an increased suspicion for malignancy, the surgeons should employ alternatives to tissue retrieval, including laparotomy (29–31,38). Inversely, low-risk patients may undergo and experience benefits from minimally invasive surgery avoiding per- and postoperative complications (103).

Surgeons and hospitals should always be aware that sarcomas are diagnosed, although very rarely, even in patients appropriately evaluated and selected for tissue retrieval-involving interventions (104,105). A new aspect of ultrasound is elastography. In the future this technique of reporting stiffness in tissues could be integrated into to preoperative ISGE guidelines (106). As MRI is not always easily accessible and available it should be reserved for those patients who are classified high risk after ultrasound scanning. Dealing with MRI it is important to consider the T2 image so that the DWI can be interpreted and the ADC can be mathematically constructed. It is the ADC mapped image that is the most reliable to diagnose LMS. ISGE does advise that the ultrasound scanning is made by the vaginal approach as to be as close as possible to the target tissue. Power Doppler enhanced vaginal ultrasound scanning helps to define the peripheral vascularization in LM (figure 5). It does also help to identify the internal vascularization (figure 6,7). Measurement of the Resistance Index (RI) of the vascular flow can in some cases help (fig8). ISGE also advises for the gynaecologist to perform the vaginal ultrasound examination her or himself or at least to closely observe the examination as to apply the scoring system him or herself. The use of the preoperative ISGE guidelines especially the ISGE flowchart seems to offer the individual physician tools to enable individualizing patients at risk for LMS.

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Which Surgical Approach is the Best for Patients with Symptomatic Isthmocele? A Systematic Review and Meta-Analysis for Laparoscopy, Hysteroscopy, and Transvaginal Surgery

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Abstract

Introduction: Uterine isthmocele is a pouch-like structure defect at the site of a previous cesarean scar. Due to an increase in cesarean rates over the years, prevalence of isthmocele has grown and is estimated to range from 19.4% to 88%. While it may not always cause symptoms, it can lead to disabling symptoms. Various studies have suggested that surgical management can be beneficial in reducing symptoms and improving obstetric outcomes. Nonetheless, there is still conflicting data on which surgical approach is best suited for patients with symptomatic isthmocele. This study aims to evaluate and compare each surgical approach for these patients.

Method: A systematic search was performed in PubMed, ScienceDirect, Embase, and Cochrane from January 2000 until June 2023 to compare surgical approaches outcome for symptomatic isthmocele patients. The research were using MeSH terms if applicable and following the PRISMA guidelines. MedCalc was used to see the overall proportion of each study and Review Manager 5.4 was used to calculate the result of 95% CI for the outcomes. Newcastle–Ottawa scale was used to assess the risk of bias. Primary endpoints of interest were improved symptoms, duration of menstruation post-treatment, and postoperative complications.

Results: Twelve Non-comparative studies and six comparative studies with 1389 patients were included. Pooled analysis of proportion showed an improvement of symptoms in 90.74% (75.02% - 95.19%) after

hysteroscopic surgery, 84.33% (52.55% - 93.27%) after laparoscopic surgery, and 65.71% (51.20% - 78.86%) after transvaginal surgery. Interestingly, in the pooled analysis of comparative surgery, laparoscopy significantly resulted in shorter menstruation duration than hysteroscopy MD 2.47, 92% CI (1.83 – 3.11) <0.001, I2: 0%. However, hysteroscopy had better outcomes in terms of operative duration, blood loss, and hospital stay.

Conclusion: This is the initial meta-analysis that compares various surgical options for treating symptomatic isthmocele. Overall, more than 60% of patients experienced an improvement in their symptoms. For those with enough residual myometrial thickness overlapping the isthmocele, hysteroscopic surgery was deemed the safest and most effective option. However, laparoscopy showed greater improvement in menstruation duration compared to hysteroscopy. Patients with thinner residual myometrium may benefit more from laparoscopy or transvaginal surgeries.

Key words: Symptomatic Isthmocele; Laparoscopy; Hysteroscopy; transvaginal Surgery

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INTRODUCTION

The cesarean section is a frequently performed gynecological procedure, with its occurrence steadily rising (1). It constitutes one-third of all deliveries globally. The World Health Organization advocates for an optimal cesarean section rate of 10-15% of all births. However, in South America (42.9%), Latin America (40.5%), North America (32.3%), and Europe (25%), the percentage of cesarean section deliveries exceeds this number (2,3). There is currently a global conversation surrounding the risks and outcomes associated with cesarean section births, and these risks are becoming more prevalent. Certain complications, such as scar dehiscence, placenta previa, and accreta, have already been extensively researched. However, other complications, like cesarean scar defects, isthmoceles, and niches, are just beginning to gain attention (4).

Isthmocele or caesarean scar defect (CSD) is a condition with a pouch-like defect in the front wall of the uterus connected to the uterus cavity. It is mainly caused by medical intervention or as an iatrogenic disease such as a cesarean section. The healing process of the uterine wall after the surgery does not restore the myometrial layers properly, leading to a fibrotic reaction resulting in a minor resistance locus (5). This was caused because the uterine isthmus of the myometrial layers after hysterotomy in the anterior wall did not heal appropriately. As the number of previous cesarean sections increases, so does the occurrence of isthmocele, a defect in the cesarean scar. Recent data shows that 60% of patients have an isthmocele after their first cesarean section and 100% after three cesarean

sections. Although isthmocele can be asymptomatic, it may cause adverse reproductive outcomes, pelvic pain, and abnormal uterine bleeding. During the menstrual cycle, a small amount of blood can accumulate in a pouch-like defect. This causes an inflammatory reaction and may contribute to irregular vaginal bleeding, pelvic pain (due to the effects of inflammatory cytokines on perilesional nerve fibers), and difficulties with embryo implantation that result in secondary infertility or subfertility. Also, isthmocele may increase the rate of cesarean scar pregnancy, a potentially life-threatening condition that deserves accurate management to avoid massive uterine bleeding (6,7).

Isthmocele can be presented in transvaginal ultrasound (TVUS) or sonohysterography (SHG) examination in non-pregnant women following a previous cesarean scar (CS). The location of the defect varies depending on the location of the CS, the stage of labor, changes in the uterine cervix, and the surgical technique. There are different ways to treat CSD, both surgical and non-surgical. It has been suggested that oral contraceptives, hormonal intrauterine device may help reduce AUB in isthmocele patients. Surgical methods include laparotomic, laparoscopic, and vaginal excision and repair, as well as resectoscopic revision with radiofrequency ablation of the isthmocele base and electrosurgery. The purpose of this review is to evaluate the evidence supporting the surgical treatment of isthmocele in women with abnormal uterine bleeding and infertility, as well as in preventing obstetric complications. Additionally, we will examine the potential risks and complications associated with these surgical treatments.

MATERIAL AND METHODS

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (8). This research collects and uses data from 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 CRD42023453117 (www.crd.york.ac.uk/prospero).

Search Strategy and Selection Criteria

To formulate a search question, we used the Population, Intervention, Comparator, and Outcome (PICO) framework as follows: Patients with uterine scar defects who experience symptoms and/or infertility (P), treated surgically for isthmocele (I), compared to those who remain untreated or treated non-surgically (C), with the goal of achieving symptom relief and/or conception (O). The final question is whether surgery is an effective solution for symptomatology and reproductive issues in patients with uterine scar defects and also to see which surgery technique is best for the patients.

Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed, EMBASE (Excerpta Medical Database), Science Direct and the Cochrane Library were searched from January 2002 until June 2023, using the following medical subject heading (MeSH) and in combination with the following keywords: "cesarean scar", "cesarean scar defect", "niche", "isthmocele", "treatment", "surgery", "outcome". Citation tracking was performed to identify additional publications. Our study searching protocol are presented in Supplementary Table S1.

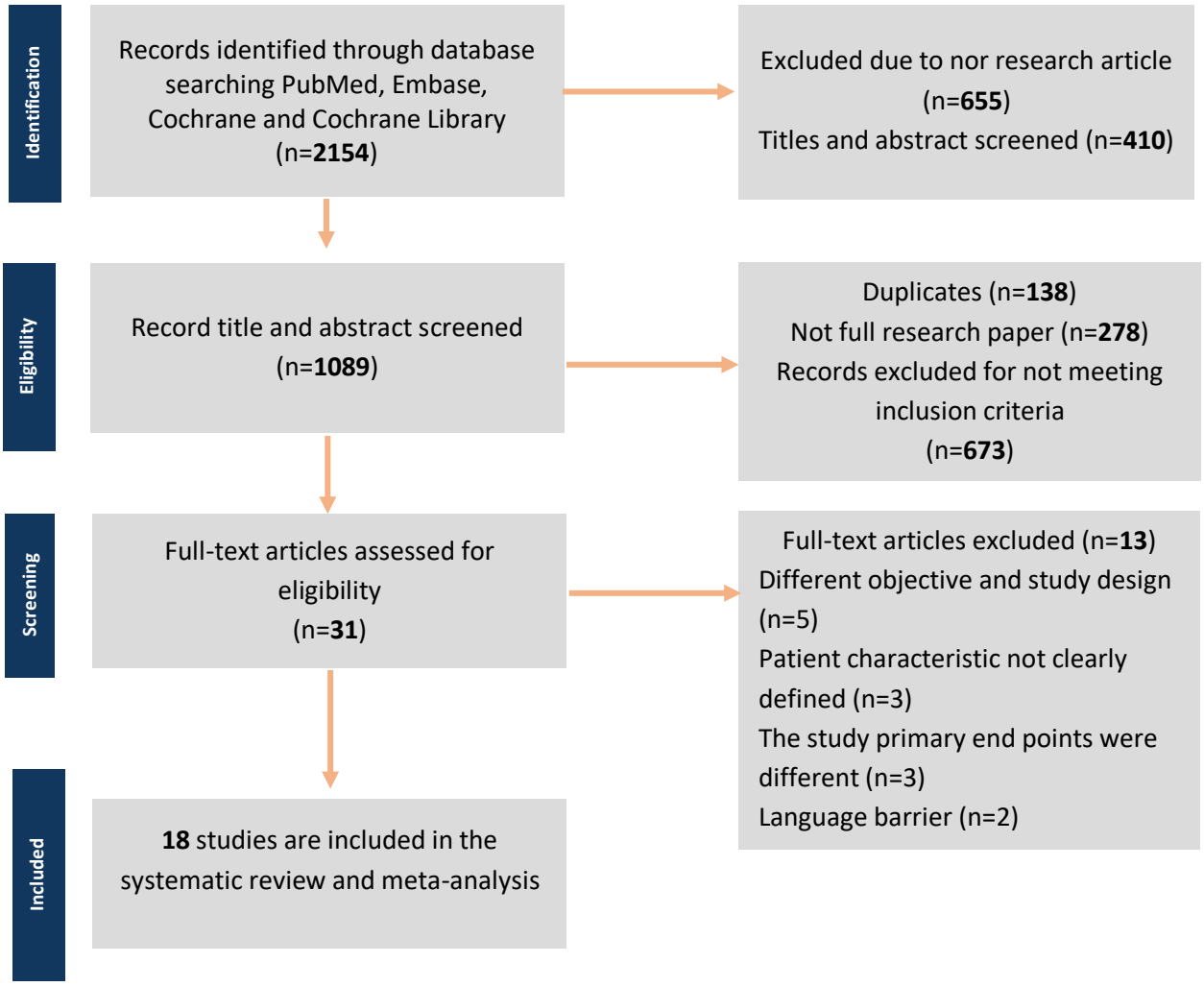
During the study, all articles were reviewed based on their title and abstract. The inclusion criteria consisted of original articles that were randomized controlled trials, prospective observational studies with or without a control group, and retrospective cohort studies that focused on the surgical treatment of CSDs. These articles also had to clearly define isthmocele and explain how it could be diagnosed, as well as provide details on how the surgery would be performed. Conversely, article reviews, proceedings, personal comments, studies with no data on outcome interest and that only featured case reports or case series were 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 and Quality Assessment

Data extraction and quality assessment were carried out independently by two investigators. Standard forms were used to extract the following information from each study: the study authors; study design and methodology; total and mean age of the patients; type of surgery; number of previous cesarean deliveries; duration of postmenstrual spotting before treatment; isthmocele diagnosis; how the surgery performed; post operative treatment; surgical outcome. Furthermore we extracted blood loss during operation, mean operative time, intra and post operative complications, length of stay post operative, duration of menstruation post treatment in surgical outcome section. 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 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) (9). 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 (10). 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-comparative studies was good with average point of 7.8 and presented in Table 1 as the risk of bias individually. Risk of bias assessment of comparative studies were available in supplement Table 2 and supplement Figure 2 for controlled trials studies.

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram



Outcome Measurement

This study aimed to evaluate the results of surgery in isthmocele patients who experienced specific complaints, such as hip pain and abnormal uterine bleeding. The study compared the outcomes of those who received surgical treatment to those who received no treatment or treatment without surgery. Based on The European Niche Taskforce by Jordan et al. (2019) an isthmocele, a cesarean scar defect, or uterine niche is an indentation of the uterine myometrium at the site of the Cesarean section (CS) scar with a depth of at least 2 mm and is preferably assessed by transvaginal ultrasonography (TVS) using gel or saline (11). Postmenstrual spotting was defined as two or more days of intermenstrual spotting or two or more days of brownish discharge at the end of menstrual bleeding when the total period of menstrual bleeding exceeds seven days.

Data Synthesis and Analysis Quality Assessment

The data in this study was analyzed using the MedCalc application version 22.0.01 (Ostend, Belgium) and Review Manager 5.4. The MedCalc

were use for non comparable studies, the analysis was conducted using the proportion method and a forest plot was created for meta-analysis. Patient subgroups were studied separately, including those undergoing hysteroscopic, vaginal, and laparoscopic/robotic treatment for isthmocele. The proportion of patients was analyzed with a 95% confidence interval (CI). Heterogeneity was assessed using I2 statistics. A low degree of heterogeneity was considered when I2 was less than 30%, moderate between 30-50%, and high if I2 was greater than 50%. The random effects model (DerSimonian and Laird method) was used for data analysis. Additionally, the influence of individual studies on the overall results was examined.

The meta-analysis was performed using Review Manager 5.4 were performed only for comparable studies. 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 I2 statistic. The I2 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. Data are summarized across groups using the Mantel-Haenszel (M-H) for odd ratio (OR) and inverse variance for mean difference, fixed effect model if I2 < 25%. The random effect model is used if I2 > 25% (12). Funnel plots were used to evaluate publication bias. Analysis was carried out using Review Manager 5.4.

RESULTS

Literature Search

During the systematic research process, the initial screening included 2154 studies with keywords related to the research. After screening for titles and abstracts, 410 studies were excluded. An additional 655 studies were excluded as they were not original research. Of the remaining 1089 studies, 1058 were excluded for various reasons such as being duplicates, incomplete research papers, or not meeting the inclusion criteria. Thirty-one full research papers were screened, and ultimately, but only 18 studies met the inclusion criteria. The study flow diagram of the selection process can be seen in Figure 1. From 18 studies included, 1389 patients with an average age of 33.98 years old were included in the meta-analysis. Twelve non-comparative research with a total of 886 patients included had an average age of 33.25 years old (13-23), while six comparative research with a total of 503 patients that included had an average age of 34.72 years old (24-29).

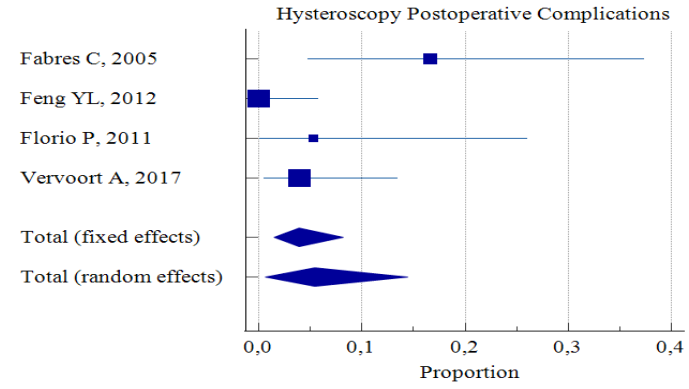
Characteristics of Included Studies

This meta-analysis is divided into two study groups: comparative and non-comparative. We collected data for the table of base characteristics, including study type, surgery type, number of patients included, mean age with standard deviation (SD), number of previous cesarean deliveries, duration of postmenstrual spotting before treatment, and its SD. The table for the base characteristics of non-comparative studies is presented in Table 3, while the table for comparative studies is shown in Table 4. The group was divided into two groups which were Non-comparative and comparative studies, this was carried out in order to keep the results of the meta-analysis fair and reduce selection biases. In addition, this was done because it was not possible to carry out comparisons of intervention and control when taking population samples from different studies. Non-comparative studies

were subject to proportion analysis as they only focused on one intervention. On the other hand, a forest plot of pooled comparative analysis was conducted for comparative studies, which had both intervention and control results within a specific population. In this study we also make a table summary for how the isthmocele were diagnosed in each study, how the surgery was performed, and were there any post operative treatment were given, the table were available in supplement table 5 for non-comparative studies and table 6 for comparative studies.

Out of the total twelve studies in the non-comparative study, eight studies (66.7%) were conducted in Asia, 3 studies (25.0%) in Europe, and one study (8.3%) in South America. Laparoscopic surgery was the focus of three studies, which included a total of 120 patients. Hysteroscopic surgery was the focus of four studies, with 169 patients included. Five studies were focused on transvaginal surgery, which included as many as 597 patients. Of the six comparative studies, four studies (66.7%) were from Asia and 2 studies (33.3%) were from Europe.

Data Synthesis: Non-comparative studies have consistently shown that surgery yields better outcomes when compared to no treatment. The result of pooled proportion analysis of these studies revealed that hysteroscopy, particularly, had better outcomes in addressing symptoms, with up to 90.80% of patients reporting an improvement after undergoing the procedure, 95% CI (84.49 – 95.15) and low heterogeneity (I2 = 4.97%), which indicates that all studies produced similar results. In this case, symptoms referred to abnormal postmenstrual uterine bleeding and pelvic pain. Hysteroscopy treatment improved these symptoms with low postoperative complications, with only 5.4%, 95% CI (0.64 – 14.43) I2 = 72.42%. In this case, postoperative complications refer to complications such as Ashermann syndrome, ectopic pregnancy, or vesico-uterine fistula. Figures 3 and 4 provide pooled proportion analyses of postoperative complications and symptom improvement of symptomatic isthmocele patients after hysteroscopy surgery.



Publication bias

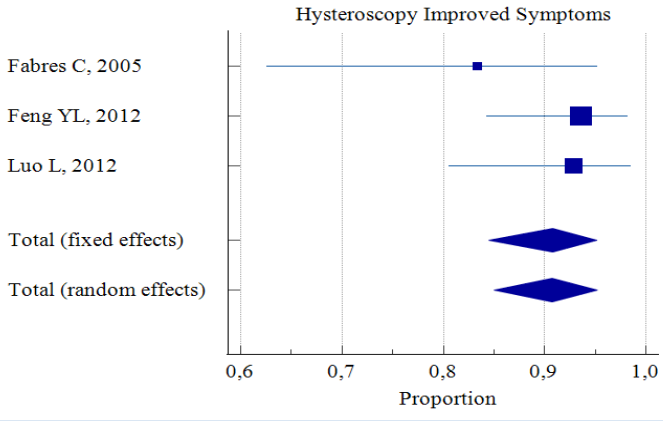
Egger's test	
Intercept	5,6872
95% CI	-7,6118 to 18,9862
Significance level	P = 0,2071
Begg's test	
Kendall's Tau	0,6667
Significance level	P = 0,1742

Test for heterogeneity

Q	10,8792
DF	3
Significance level	P = 0,0124
I^2 (inconsistency)	72,42%
95% CI for I^2	22,01 to 90,25

Study	Sample size	Proportion (%)	95% CI	Weight (%)	
				Fixed	Random
Fabres C, 2005	24	16,667	4,735 to 37,384	15,62	22,58
Feng YL, 2012	62	0,000	0,000 to 5,776	39,37	28,90
Florio P, 2011	19	5,263	0,133 to 26,028	12,50	20,71
Vervoort A, 2017	51	3,922	0,478 to 13,459	32,50	27,81
Total (fixed effects)	156	3,906	1,483 to 8,190	100,00	100,00
Total (random effects)	156	5,418	0,641 to 14,431	100,00	100,00

Figure 2. Proportion of Hysteroscopy Postoperative Complications



Test for heterogeneity

Q	2,1047
DF	2
Significance level	P = 0,3491
I^2 (inconsistency)	4,97%
95% CI for I^2	0,00 to 96,81

Publication bias

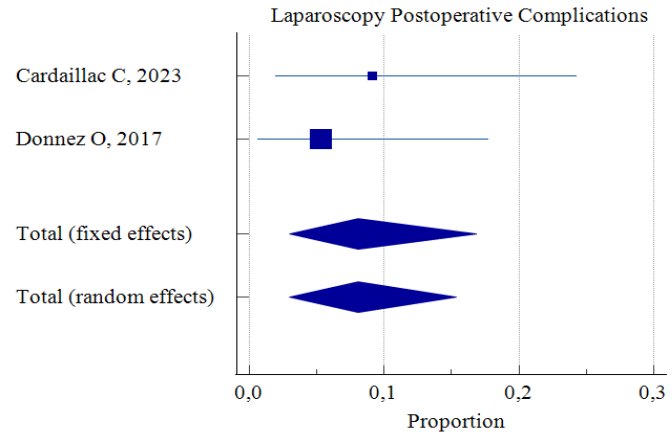
Egger's test	
Intercept	-4,3914
95% CI	-22,3362 to 13,5533
Significance level	P = 0,1981
Begg's test	
Kendall's Tau	-1,0000
Significance level	P = 0,1172

Study	Sample size	Proportion (%)	95% CI	Weight (%)	
				Fixed	Random
Fabres C, 2005	24	83,333	62,616 to 95,265	19,08	19,65
Feng YL, 2012	62	93,548	84,297 to 98,214	48,09	47,29
Luo L, 2012	42	92,857	80,517 to 98,502	32,82	33,06
Total (fixed effects)	128	90,800	84,498 to 95,148	100,00	100,00
Total (random effects)	128	90,743	85,020 to 95,199	100,00	100,00

Figure 3. Proportion of Hysteroscopy Improved Symptoms Post Treatment

When it comes to laparoscopic procedures, there are only three studies available for proportional analysis. Unfortunately, only two studies can be analyzed when it comes to the analysis of improved postoperative symptoms. This study utilized the random effect model method to account for the small number of studies and moderate heterogeneity found between the

studies. This method helps to eliminate bias factors from the sample size in each study. Our analysis found that 84.34%, 95% CI (72.55 – 93.27) and an I2 of 47.78%, have improved symptoms postoperative. These improvements were related to the duration of postmenstrual abnormal uterine bleeding and pelvic pain. Interestingly, both studies show that postoperative complications related to laparoscopic procedures are relatively small. Only 8.06% of patients reported complications after the procedure, with 95% CI (2.97 - 16.8) I2= 0.00%. It's worth noting that the analysis results show low heterogeneity, but this could be due to the limited number of studies included. Figures 5 and 6 provide pooled proportion analyses of postoperative complications and symptom improvement of symptomatic isthmocele patients after laparoscopy surgery.



Test for heterogeneity

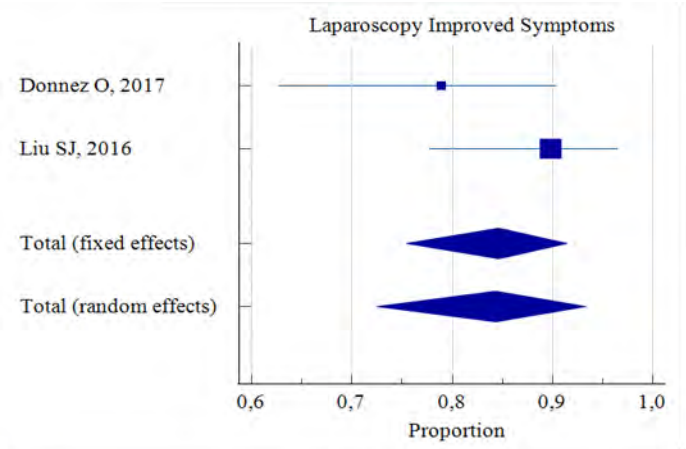
Q	0,3675
DF	1
Significance level	P = 0,5444
I^2 (inconsistency)	0,00%
95% CI for I^2	0,00 to 0,00

Publication bias

Egger's test	
Intercept	12,5087
95% CI	
Significance level	P < 0,0001
Begg's test	
Kendall's Tau	1,0000
Significance level	P = 0,3173

Study	Sample size	Proportion (%)	95% CI	Weight (%)	
				Fixed	Random
Cardaillac C, 2023	33	9,091	1,915 to 24,332	46,58	46,58
Donnez O, 2017	38	5,263	0,644 to 17,749	53,42	53,42
Total (fixed effects)	71	8,060	2,978 to 16,832	100,00	100,00
Total (random effects)	71	8,060	2,969 to 15,349	100,00	100,00

Figure 4. Proportion of Laparoscopy Postoperative Complications



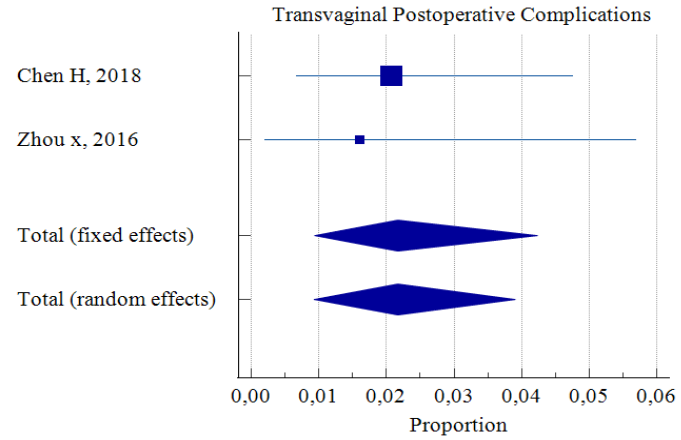
Test for heterogeneity	
Q	1,9149
DF	1
Significance level	P = 0,1664
I^2 (inconsistency)	47,78%
95% CI for I^2	0,00 to 0,00

Publication bias	
Egger's test	
Intercept	-15,8033
95% CI	
Significance level	P < 0,0001
Begg's test	
Kendall's Tau	-1,0000
Significance level	P = 0,3173

Study	Sample size	Proportion (%)	95% CI	Weight (%)	
				Fixed	Random
Donnez O, 2017	38	78,947	62,681 to 90,446	43,82	46,77
Liu SJ, 2016	49	89,796	77,772 to 96,603	56,18	53,23
Total (fixed effects)	87	84,654	75,461 to 91,421	100,00	100,00
Total (random effects)	87	84,338	72,551 to 93,275	100,00	100,00

Figure 5. Laparoscopy Improved Symptoms Post Treatment

Out of the five studies that concentrated on transvaginal surgery, only four of them could carry out pooled proportion analysis. The reason for this was that one study by Zhou J, 2016 used different units of variables from the other researchers. As a result, we chose not to include that particular study in the analysis. According to the findings of the pooled proportion analysis, compared to the two earlier surgical techniques, patients who underwent isthmocele treatment using the transvaginal surgery technique had the lowest proportion of improved symptoms, which was 65.71%, with a 95% CI of (51.20 – 78.86) and I2 = 89.59%. However, it is worth noting that this technique has a low rate of postoperative complications, which was 2.17%, with a 95% CI of (0.93 – 4.23) and I2 = 0.00%. The low complication rate could be as a result of the fact that only two studies were used for pooled analysis. Additionally, transvaginal surgery is a classic technique and the oldest surgical method, which most practitioners are familiar with. Figures 7 and 8 provide pooled proportion analyses of postoperative complications and symptom improvement of symptomatic isthmocele patients after transvaginal surgery.



Test for heterogeneity

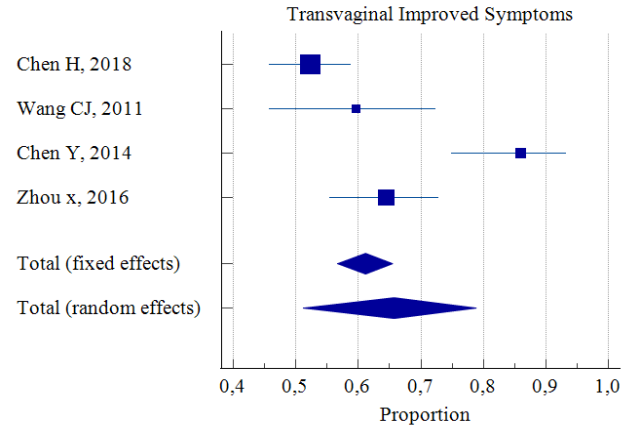
Q	0,03290
DF	1
Significance level	P = 0,8561
I^2 (inconsistency)	0,00%
95% CI for I^2	0,00 to 0,00

Publication bias

Egger's test	
Intercept	-0,7941
95% CI	
Significance level	P < 0,0001
Begg's test	
Kendall's Tau	-1,0000
Significance level	P = 0,3173

Study	Sample size	Proportion (%)	95% CI	Weight (%)	
				Fixed	Random
Chen H, 2018	241	2,075	0,677 to 4,775	65,94	65,94
Zhou x, 2016	124	1,613	0,196 to 5,705	34,06	34,06
Total (fixed effects)	365	2,168	0,938 to 4,234	100,00	100,00
Total (random effects)	365	2,168	0,931 to 3,905	100,00	100,00

Figure 6. Transvaginal Surgery Postoperative Complications



Test for heterogeneity

Q	28,8248
DF	3
Significance level	P < 0,0001
I^2 (inconsistency)	89,59%
95% CI for I^2	76,18 to 95,45

Publication bias

Egger's test	
Intercept	6,9282
95% CI	-12,4992 to 26,3556
Significance level	P = 0,2647
Begg's test	
Kendall's Tau	0,3333
Significance level	P = 0,4969

Study	Sample size	Proportion (%)	95% CI	Weight (%)	
				Fixed	Random
Chen H, 2018	239	52,301	45,765 to 58,779	49,18	26,99
Wang CJ, 2011	57	59,649	45,821 to 72,439	11,89	23,37
Chen Y, 2014	64	85,937	74,976 to 93,363	13,32	23,82
Zhou x, 2016	124	64,516	55,423 to 72,898	25,61	25,82
Total (fixed effects)	484	61,146	56,663 to 65,494	100,00	100,00
Total (random effects)	484	65,716	51,207 to 78,862	100,00	100,00

Figure 7. Transvaginal Improved Symptoms Post Treatment

Four studies were analyzed for comparing hysteroscopy and hormonal treatment. The pooled analysis showed that hysteroscopy had significantly better outcomes in reducing the mean duration of menstruation which were in days. The forest plot indicated a lower mean difference (MD) of 1.69, 95% CI (0.28 - 3.10), and a p-value of 0.02, while I2 was 91%. Two studies compared postoperative pelvic pain between hysteroscopy and hormonal treatment, and the

forest plot showed that the proportion of patients experiencing postoperative pelvic pain was significantly lower in hysteroscopy with an odds ratio (OR) of 0.15, 95% CI (0.04 - 0.54), and a p-value of 0.004, while I2 was 35%. Figures 9 and 10 display a forest plot comparing the mean duration of menstruation and pelvic pain post-treatment between hysteroscopy surgery and hormonal therapy.

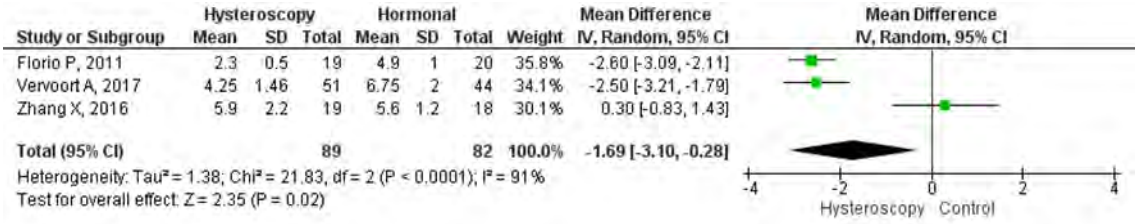


Figure 8. Pooled Analysis of Mean Duration of Menstruation Post Treatment Between Hysteroscopy Surgery and Hormonal Therapy in Patients with Symptomatic Isthmocele

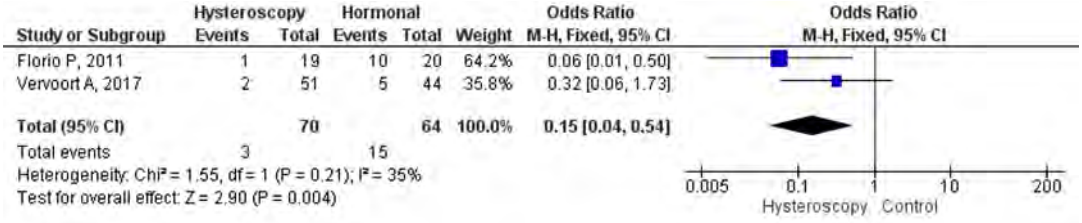


Figure 9. Pooled Analysis of Pelvic Pain Post Treatment Between Hysteroscopy Surgery and Hormonal Therapy in Patients with Symptomatic Isthmocele

However, only two studies directly compared the mean duration of menstruation after treatment, intraoperative, and postoperative complications between hysteroscopy and vaginal surgery. The results showed that hysteroscopy had a significantly lower mean duration of postoperative menstruation, MD 2.37, 95% CI (1.83 - 3.11), and a p-value of less than 0.001. Heterogeneity was low, with an I2 of 0%, fixed method was used due to the low heterogeneity found in the studies. Figure 11 shows a forest plot comparing the mean duration of menstruation post-treatment between hysteroscopy and vaginal surgery. Furthermore, this study analyzed intraoperative and postoperative outcomes between hysteroscopy and transvaginal surgery. For intraoperative outcomes, we analyzed the duration of the operation and the amount of blood loss during surgery, which were in min and ml respectively. For postoperative, we analyzed the length of stay post-surgery which were in days. The study also compared the results of each intraoperative and postoperative outcome between the surgical techniques to see which one had the best overall surgery outcomes. Our analysis showed that hysteroscopy had significantly lower operative duration MD 25.35, 95% CI (18.53-32.17),

p<0.001, I2=60%; lower mean blood loss MD 26.02, 95% CI (9.39-43.85), p=0.002, I2=95%; and also shorter length of stay MD 2.5, 95% CI (1.79-3.21), p<0.001, I2=0%. Overall, the forest plot showed that hysteroscopy had better outcomes for both intraoperative and postoperative complications. The forest plot may be seen in Figure 12.

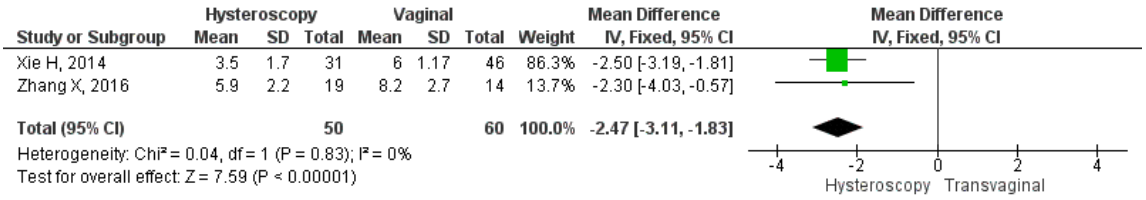


Figure 10. Pooled Analysis of Mean Duration of Menstruation Post Treatment Between Hysteroscopy and Vaginal Surgery in Patients with Symptomatic Isthmocele

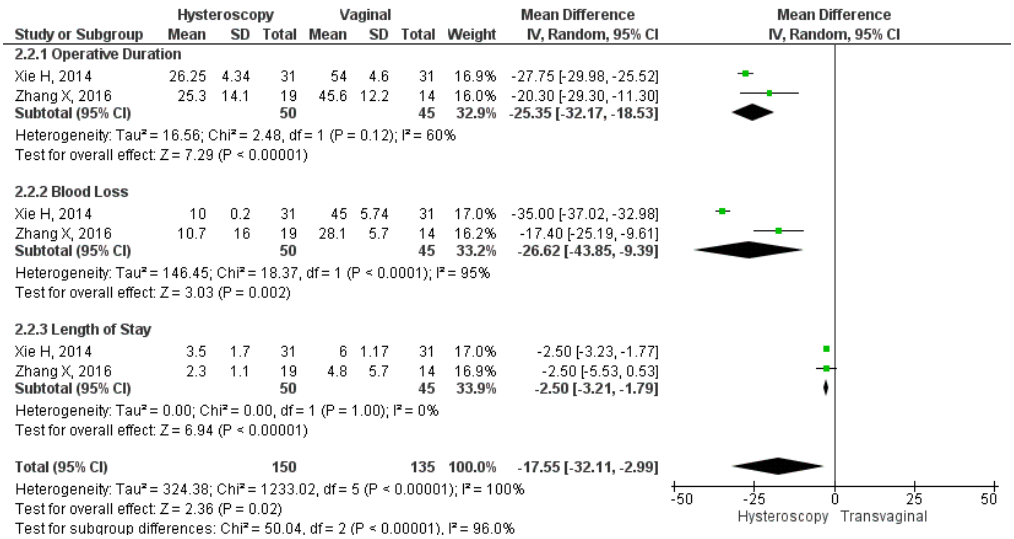


Figure 11. Pooled Analysis of Intraoperative and Postoperative Outcome Between Hysteroscopy and Vaginal Surgery in Patients with Symptomatic Isthmocele

Unfortunately, only two studies compared the mean duration of menstruation after laparoscopy and hysteroscopy surgeries. The results on the forest plot indicated that the laparoscopic procedure led to a significantly shorter mean duration of menstruation post-treatment, with an MD 2.46, 95% CI (1.83 – 3.11) p <0.001, I2=0%. Figure 13 displayed the forest plot, which compared the mean duration of menstruation post-treatment between laparoscopy and hysteroscopy surgeries. Furthermore, three studies were included that compared the intraoperative and postoperative outcomes of each technique. Hysteroscopy was

found to have significantly better outcomes for operative duration with an MD 63.25, 95% CI (41.51 – 84.99) P<0.001, I2=91%; lower mean blood loss, with an MD 66.22, 95% CI (32.88 – 99.57) p<0.001, I2=88%; and shorter length of stay, with MD 4.15, 95% CI (2.90 – 5.40) p<0.001, I2=67%. The forest plot in Figure 14 showed that although laparoscopy had a better outcome in terms of mean duration of menstruation post-treatment, the procedure had inferior intraoperative and postoperative measures if seen in operative duration, blood loss, and length of stay compared to hysteroscopy.

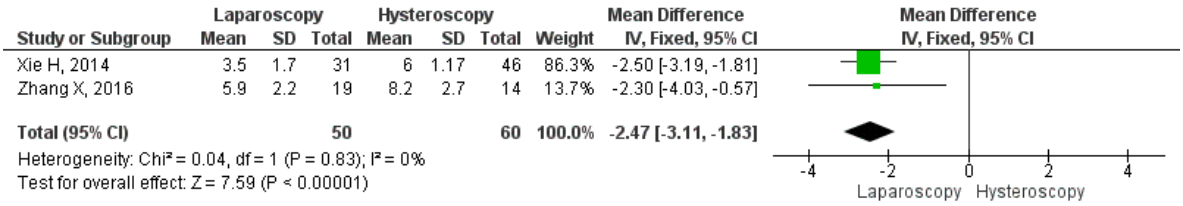


Figure 12. Pooled Analysis of Duration of Menstruation Post Treatment Between Laparoscopy and Hysteroscopy Surgery in Patients with Symptomatic Isthmocele

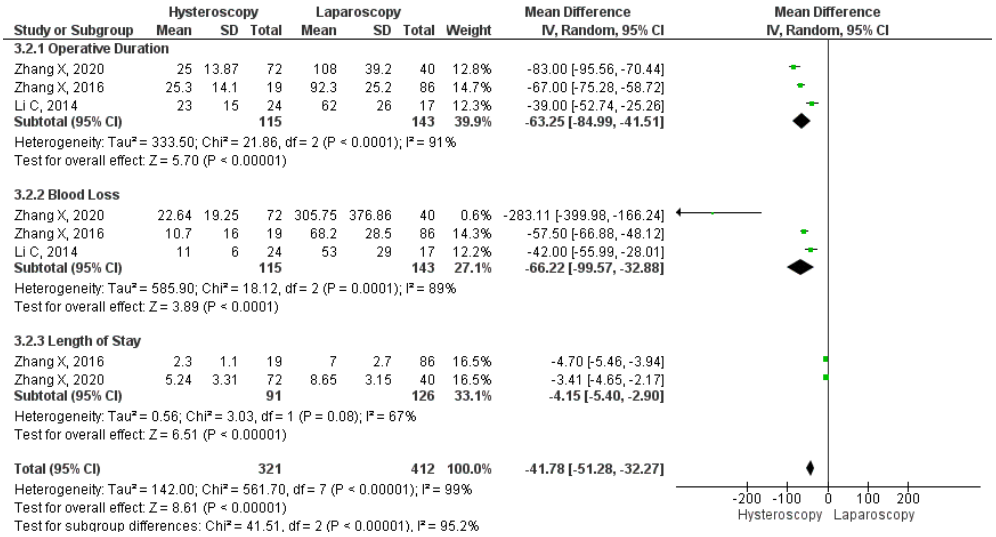


Figure 13. Pooled Analysis of Operative Outcome Between Laparoscopy and Hysteroscopy Surgery in Patients with Symptomatic Isthmocele

DISCUSSION

Isthmocele is a myometrial defect or a hypoechoic triangle in the anterior uterine wall at the site of hysterotomy presented in transvaginal ultrasound (TVUS) or sonohysterography (SHG) examination in non-pregnant women following a previous cesarean scar CS (30,31). The location of the defect varies depending on the location of the CS, the stage of labor, changes in the uterine cervix, and the

surgical technique (32). The isthmocele indicates insufficient healing of the myometrium at the location of a cesarean incision. The phenomenon's prevalence exhibits significant variation, ranging from 6.9 to 69%, contingent upon the characteristics of the studied population and the employed methodology (33). According to the findings of Antila-Långsjö et al., the prevalence of isthmocele following elective caesarean delivery (CD) was 41.4%, while it was found to be 58.6% in cases of emergency CD. This finding demonstrates a higher incidence of isthmocele in emergency cesarean deliveries than in elective cesarean deliveries. The primary causes for Emergency Cesarean Deliveries were prolonged labour, 44.0% of cases, and fetal hypoxia, accounting for 32.4%. A total of 371 women were included in the study, among whom 59 cases (15.9%) were diagnosed with intrapartum or postoperative infection. Their prospective observational cohort study included patients who were recruited either prior to undergoing the cesarean delivery procedure or within three days following the procedure.(34) Sonohysterography (SHG) has been found to possess a higher level of accuracy in the diagnosis of niches. The use of sonohysterography (SHG) has been found to result in a higher proportion of identified abnormalities (45% opposed to 22%) when compared to transvaginal ultrasound (TVS). Additionally, SHG has demonstrated the ability to detect larger niches and thinner residual myometrium. Additional specialized characteristics, such as concavity, atypical vascularity, visible serosa, and the presence of cysts or polyp-like structures, should also be included in the discussion. Superficial high-resolution ultrasound imaging (SHG) conducted at 6-12 weeks after childbirth, when the surgical incision has not fully healed, assists in the identification of scar tissue and minor indentations. This process is further supported by the presence of a thin endometrium during breastfeeding (35).

The study found that there was no notable difference in the incidence of isthmocele between emergency and elective CD OR 1.03, 95% CI (0.68 - 1.56). However, it did reveal a significant relationship between previous CD and isthmocele development OR 3.69, 95% CI (2.38 - 6.04) $p<0.001$. Furthermore, the multivariate analysis for emergency CD indicated that longer active labor before emergency CD was associated with a higher risk of isthmocele development OR 1.06, 95% CI (1.01 - 1.11) $p=0.032$. This factor was found to be an independent risk factor for isthmocele development. Hayakawa H et al. also discovered a similar outcome. A study conducted in Japan in 2006 revealed that there was no notable difference between the risk of elective or urgent CD and the incidence of isthmocele. The study also examined the correlation between isthmocele and suturing techniques. Follow-up was conducted one month after the procedure.

The study found that the lowest incidence of isthmocele was observed when using the single-layer myometrium closure with decidual suture technique OR 0.077 (0.012 – 0.49) p=0.007, followed by double-layer myometrium close OR 0.28 (0.085 – 0.94). However, no significant differences were found for single-layer myometrium closure. The study suggests that the disadvantage of a continuous single suture not precisely joining the tissues together must be weighed against the similar short-term maternal morbidity with a shorter operative period reported for single-layer closure, which explains its broad clinical acceptance (36).

Antila-Långsjö study also identified infections encompassed chorioamnionitis, endometritis, and postpartum wound infections. The diagnostic criteria for chorioamnionitis encompassed intrapartum fever and increased infection markers (such as C-reactive protein and leukocyte count), accompanied by maternal or fetal tachycardia (33). Various researchers have employed different timeframes for conducting clinical examinations to diagnose isthmocele. According to the findings of Gozzi et al., the prevalence of isthmocele, as determined by transvaginal ultrasound (TVS), was shown to be 44.4% among women who had previously undergone cesarean section (CS) six months prior (37). Dosedla et al. selected the time points of 6 weeks and 18 months postpartum to investigate the clinical manifestations of isthmocele (38). In contrast, previous studies explored isthmocele within varying time intervals of 6-12 weeks, 6-9 months, or 6-12 months postpartum, resulting in a more diverse timeframe and differing definitions of a niche (39). According to research conducted by Hayakawa H et al, there is a higher risk of isthmocele associated with premature rupture of membrane (PROM) OR 8.72, 95% CI (1.28-59.65) p=0.027 (35). Similarly, Park et al found a correlation between the incidence of isthmocele and PROM in a 2018 case-control study from Korea with OR 1.90, 95% CI (1.08-3.34) p=0.027. It is important to note that PROM is a significant risk factor for infection and can weaken the healing process of uterine closure. Patients with PROM may have an immature lower segment of the uterus, which can negatively impact the suture and wound healing process. Appropriate management should be implemented if PROM occurs during delivery to prevent infection and ensure proper healing and remodeling of the myometrial incision. Interestingly, one study has indicated no notable difference in the occurrence of isthmocele between urgent or elective cesarean deliveries in relation to infections like chorioamnionitis, postpartum wound infections, and endometritis (34,36). The disparities in the findings of this study could be attributed to the varying approaches to infection management across different centers, as the treatment of infections may impact the process of remodeling of the myometrial incision. It is

hoped that appropriate treatment of postoperative endometritis or myometritis would foster optimal healing.

Isthmocele has the potential to be classified as one of the primary etiological factors contributing to infertility. An association was observed between the inability to conceive and an increased prevalence of cesarean deliveries. Calzolari et al. conducted a study in which patients were categorized into two groups: fertile patients, who achieved pregnancy within 12 months after diagnosis of isthmocele, and infertile patients, who did not achieve pregnancy within the same timeframe. The authors reported that the association between BMI and infertility supports previous findings in the literature (40). Isthmocele may contribute to developing a uterine cavity that is physically less conducive to fertility. Additionally, it was revealed that the individuals who could not achieve pregnancy within a 12-month following the surgical procedure exhibited advanced age and a more severe isthmocele grade compared to those who could conceive. Age is a widely recognized risk factor for infertility, and earlier research has demonstrated a correlation between the severity of isthmocele, cervical dilatation, and infertility (40,41).

Currently, there are no diagnostic criteria that have been universally agreed upon (41). Some authors classified isthmocele based on the size of the defect, with a large defect if the myometrial reduction of >50% of the wall thickness or even >80% (42). In addition, residual myometrium (RM) 2.2 mm by TVUS and 2.5 mm by SHG may also describe a large defect (43). Marotta et al. adopted the cutoff of RM >3 mm as a large defect, and RM <3 mm as a small defect for management purposes (44). In the absence of symptoms, these radiologic findings may be discovered by chance or linked to clinical signs. They can therefore be categorized as either asymptomatic or symptomatic when presenting with abnormal uterine bleeding (AUB), pelvic pain, or infertility (45,46).

The treatment options for isthmocele include expectant or pharmacological treatment and surgical treatment such as hysteroscopic, laparoscopic, laparotomic, or transvaginal procedures (47). The treatment decision is based on the size of the defect, symptoms, secondary infertility, and pregnancy plans (29,48). Clinical observation and no surgical intervention are usually recommended for an incidental diagnosis of asymptomatic isthmocele and no plans for future childbearing (44). Numerous studies propose various surgical approaches for correcting the cesarean scar defect. Several studies have suggested that surgical management can help reduce symptoms and improve obstetric outcomes (49). The surgical procedure generally involves resectioning fibrotic tissue from the defect, presented as a flap beneath the triangular pouch. Resection of

the isthmocele edges, which connects the wall to the cervical canal, improves flow drainage and prevents menstrual blood retention (46). More advanced cases of isthmocele with RMT < 50% or <3mm usually require surgical resection through vaginal, laparoscopic, laparotomic or combined (abdominal/transvaginal) approaches (50). The vaginal approach to isthmocele repair is technically difficult due to the limited field of the operation. This technique requires the bladder preparation, opening the vesicovaginal space and resection of fibrotic cesarean scar. Intraoperative identification of the defect is the most difficult part of the operation. Additional devices like hysteroscope (backlight), Foley catheter, or Hegar dilators (“slip and hook” technique) are very useful for the mapping the defect during these procedures. The gentle tissue preparation and non-coagulating cutting, followed by two-layer closures (2-0 thread) appeared to be the most effective way of treatment. The improvement of reducing the symptoms was reported in nearly 90% (51,52).

Nonetheless, data on which surgical approach best suits patients with symptomatic isthmocele still needs to be clarified. Further in this systematic review and meta-analysis, we evaluate the benefits and challenges of hysteroscopy, laparoscopy, and transvaginal surgery approaches. The hysteroscopic surgery approach is a minimally invasive, non-time-consuming, and low-morbidity procedure that allows direct visualization and repair of the defect (30). The hysteroscopic management targets the simple triangular pouch with a minimum residual myometrium of 2.5-3 mm (48). It entails coagulating its roof following resection of either the distal edge alone (Fabre's technique), the distal and proximal edge (Gubbini's technique), or the whole canal by channel-like 360° resection (45). The pooled proportion analysis in our study showed an improvement of symptoms in 90.74% (75.02% - 95.19%) after hysteroscopic surgery. Our results also showed that hysteroscopy had better outcomes in operation duration, blood loss, and length of hospital stay than another surgery approach. A systematic review by Abacjew-Chmylko et al. reported 85.5% favorable outcome rates for hysteroscopic resection, ranging from 59.6% to 100%, with 72.4% of cases completely resolving AUB symptoms.46 The main risks of the hysteroscopic procedure are uterine perforation and bladder injuries. Resectoscope treatment by hysteroscopy is recommended to reduce this risk if the remaining myometrial thickness is greater than 3 mm (50).

Laparoscopic isthmocele repair is performed with excision of the scar tissue from the edges of the isthmocele followed by closure of the defect with sutures in two layers, the first being interrupted monofilament sutures. Laparoscopy provides optimal visualization in identifying the isthmocele and allows for the

repair and consequent increase in myometrial thickness (53-55). Donnez et al. examined gynecological, obstetrical, and myometrial outcomes after laparoscopic isthmoceles repair (15). MRI-detected symptomatic isthmoceles with myometrial thickness less than 3mm were treated laparoscopically in 38 individuals. The Lumenis-Sharplan CO2 laser was used for laparoscopic isthmocele removal. After excising the isthmocele, a Hegar probe was placed into the cervix to maintain cervical canal-uterine cavity integrity. A three-layer incision repair followed. After closing the first two layers with Vicryl sutures, the surgeon closed the peritoneum with Monocryl running sutures. Vervoort et al. advised shortening round ligaments when the uterus was retroflexed to decrease counteracting forces that could hinder wound healing. Hysteroscopy checked the repair, and histology examined the isthmocele (25).

After undergoing surgery, an MRI was done three months later to assess the thickness of my myometrium. The results showed that the mean thickness of my myometrium had increased from 1.43 0.7 to 9.62 1.8 mm. Additionally, 91% of patients reported being symptom-free, and among women who had infertility issues, 44% were able to conceive and deliver healthy babies at full term successfully. The significant increase in myometrial thickness demonstrates the effectiveness of undergoing a laparoscopic isthmocele repair in restoring the anterior uterine wall (15). If a patient has enough residual myometrial thickness over their isthmocele (RM > 3 mm), hysteroscopic correction might be the fastest, easiest, and safest surgical treatment. However, if a patient has thinner residual myometrial thickness (RM < 3 mm), laparoscopic correction is a better option to avoid the risk of uterine perforation and bladder injury. A study from Belgium with the mean value of the residual myometrial thickness in the study population of 1.77 mm reported that the laparoscopic approach was the preferred method (15,56-58).

In addition, using a laparoscopic surgical approach can increase the amount of myometrial tissue left for patients who plan to have children in the future. Although there is a significant reduction in myometrial thickness one month after surgery, compared to three to six months after surgery, this does not indicate that the therapeutic effect of the surgery has decreased over time. The thickness of the myometrial tissue is still significantly greater than the average thickness before surgery (p-value <0.001). This may caused by the resolution of the inflammatory changes and edema of the uterine myometrium at the surgical site (59). In this meta-analysis, it was found that the laparoscopic technique had a high success rate in improving patient outcomes (84.33%, 95% CI 72.55 – 93.27), second to only hysteroscopy (90.74%, 95% CI 85.02 – 95.19). Additionally, a pooled analysis using the Inverse Variance method

demonstrated that laparoscopy is also more effective in reducing the length of menstruation after surgery with MD lower 2.47, 95% CI (1.83 – 3.11) when compared to hysteroscopy. However, it is important to note that this analysis is limited by a small number of studies on laparoscopic techniques, emphasizing the need for further research to confirm these findings (60).

Minimally invasive surgery has become more popular due to its advantages over invasive techniques. It offers improved safety and a shorter recovery period. However, this procedure requires special equipment and may not be available in underdeveloped or medically underserved areas. Vaginal surgery, a traditional operative procedure, has been widely used for a long time and most gynecologists are skilled in its techniques (56). According to a retrospective study, both techniques had similar outcomes. The first technique involves dissecting the bladder from the cervix and uterus, then opening the vesicovaginal space to identify the isthmocele. The defect is removed, and the hysterotomy is closed in two layers. On the other hand, transvaginal isthmocele repair was found to be more cost-effective and has shorter operation time than laparoscopy. However, this method requires a surgeon who is highly experienced in vaginal surgery to avoid damaging adjacent structures and to accurately locate the isthmocele in the limited surgical view (61). It is crucial for obstetricians to be aware of the numerous factors that come into play when treating isthmocele, such as lost follow-ups after cesarean delivery, suturing technique, surgeon performance, and infection management. However, there are currently no established guidelines for determining the appropriate timing of follow-up and intervention. Some studies suggest a follow-up period of 3-6 months after the procedure, based on the understanding that wound healing takes at least six months. An earlier assessment may lead to overdiagnosis, but a delayed evaluation may result in a higher dropout rate due to subsequent pregnancies. Treatment is only recommended for symptomatic women with secondary infertility, previous ectopic scar, recurrent miscarriage, AUB, and bothersome post-menstrual spotting. The efficacy of treatment has yet to be confirmed. It is not recommended to routinely repair an incidentally diagnosed isthmocele in women who do not plan on having future children. According to the hypothesis proposed by Vervoort et al, there are several potential factors that may contribute to the development of isthmocele, a defect in the cesarean scar. These factors include a low incision through the cervical tissue, suboptimal suturing or incomplete closure of the uterine wall, and surgical techniques that promote adhesion formation. Specifically, non-closure of the peritoneum, insufficient hemostasis, and visible sutures may all contribute to this complication (62, 63).

In a recent study, it was discovered that utilizing a single full-thickness closure technique resulted in more complete closure than the single-layer decidua sparing closure technique. Interestingly, almost 95% of patients with isthmocele undergo single-layer closure without closing the peritoneum. The risk of isthmocele can be minimized by creating a strong myometrial scar through proper anatomical approximation without tissue strangulation. For optimal healing and lower risk of niche formation, it is best to include the deeper part of thick muscular edges in the first layer and the remaining superficial cut edges in the second layer. Non-perpendicular sutures, locking sutures, or a very tight second layer can lead to irregular myometrial closure and ischemic necrosis, resulting in poorly healed scars. The recommended technique for uterine closure is double-layer using non-locking sutures, which allows for thicker residual myometrium. Suboptimal surgical techniques including inadequate hemostasis, tissue ischemia, devascularization, and excessive tissue manipulation can contribute to poor scar healing and adhesions, ultimately forming an isthmocele (64,65). Prior to selecting a specific surgical approach, it is recommended to conduct a thorough preoperative evaluation with transvaginal ultrasound, sonohysterography, and/or magnetic resonance imaging (MRI) in order to examine the extent of myometrial coverage over the isthmocele. When considering the option of undergoing surgery, it is of utmost importance to consider the remaining myometrial thickness that encompasses the isthmocele in those who are experiencing symptomatic isthmocele.

Strength and Limitation

As far as we know, our meta-analysis is the first to assess comparative studies on how effective various surgical approaches are for treating isthmocele. However, our findings are limited due to the small number of patients in most studies, variations in patients' characteristics, poor quality of original research, and concerns about how isthmocele was diagnosed in different studies. During our comparative studies analysis we also encountered an obstacle where each study had different variables. This hindered us from making a proper comparison, despite all studies having the same primary outcome. Additionally, surgeons' varying skill levels may also affect the results of particular surgical techniques. These factors must be considered when weighing any surgical approach's benefits and risks.

CONCLUSION

According to this meta-analysis, surgery is a viable treatment option for patients experiencing symptomatic isthmocele. Over 65% of patients report improved symptoms after undergoing surgery. For patients with adequate residual myometrial thickness overlying the isthmocele (≥ 2.5–3.5 mm), hysteroscopic

correction may be the safest and most effective strategy. However, for those with a thinner residual myometrium over the defect (< 2.5 mm) or when hysteroscopic treatment is inconclusive, laparoscopic and vaginal surgeries may be the preferred options. This study showed that laparoscopic procedures have better outcomes compared to hysteroscopy. However, there are some challenges during the surgery, such as longer duration, increased blood loss, and longer hospital stay. Moreover, some centers or countries may have financial and equipment limitations. Nonetheless, vaginal surgery is still a feasible alternative in situations where resources are limited.

To summarize, it is still necessary to conduct high-quality comparative studies to determine the best surgical approach for treating symptomatic isthmocele. These studies will also help establish a specific threshold for residual myometrial thickness, below which hysteroscopic surgery should not be performed. Additionally, further research is needed to explore the potential benefits of surgical correction for asymptomatic isthmocele, including improved fertility and reduced risk of obstetrical complications.

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Vaginal plus laparoscopic approach for uterine reposition in a rare case of non-puerperal uterine inversion

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Abstract

Nonpuerperal uterine inversion (NPUI) is of extremely rare occurrence. It mostly results due to benign etiologies like leiomyomas but can be associated with malignancies as well. We report a case of chronic nonpuerperal uterine inversion where successful uterine reposition and repair was done by a combined vaginal and laparoscopic approach. A 35-year woman presented with complaints of heavy menstrual bleeding and dysmenorrhea. Her uterine inversion was promptly diagnosed on clinical examination and a definitive surgery was then performed. To begin with prolapsed submucous myoma was shaved off vaginally by cauterization and myoma bed was sutured with vicryl. Following this vaginal reposition was attempted which failed. Owing to this decision to perform Haultain's procedure was made. Midline vertical 3cm incision was made over the constriction ring. After the constriction ring was released an upward push from vaginal end combined with simultaneous upward traction on round ligament resulted in reposition of uterus. Uterine incision was sutured with continuous non interlocking barbed sutures. Postoperative period was uneventful and patient was discharged with advice regarding future conception. It should be taken into consideration as one of the differential diagnoses in females with mass protruding through vagina. A high index of suspicion is essential for prompt diagnosis and appropriate surgical intervention.

Key words: Nonpuerperal uterine inversion (NPUI), Laparoscopic Haultain's procedure, Uterine reposition and repair, Hysterectomy, Fertility outcomes following uterine reposition

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Introduction

Nonpuerperal uterine inversion (NPUI) is a rare clinical condition which poses challenge in diagnosis as well as surgical management. The precise incidence of nonpuerperal uterine inversion (NPUI) is unknown. NPUI may occur by the intrauterine tumor's weight, manual traction on the tumor, or elevated intra-abdominal pressure due to sneezing, coughing, and straining. Patients of NPUI present with foul-smelling vaginal discharge or irregular vaginal bleeding, anemia, abdominal cramps, pelvic discomfort, and fullness of the vagina or pressure in the vagina. Accurate clinical examination, imaging, histopathological evaluation, examination under anesthesia, laparoscopy all aid in the diagnosis of NPUI. Stages 2, 3, and 4 inversions are probably going to be more difficult, although stage 1 inversions can have more chances of successful uterine reposition. However, where uterine reposition fails hysterectomy remains the only option. Various surgical approaches for NPUI have been described so far which include abdominal, vaginal, combined abdominal-vaginal, laparoscopic. We report a case of chronic nonpuerperal uterine inversion where successful uterine reposition and repair was done by a combined vaginal and laparoscopic approach.

Case Description

A 35yrs female reported to us with history of heavy menstrual bleeding for 2 years. Her ultrasound report done 2 years back was suggestive of 3 cm submucous myoma for which she was advised surgery but she did not follow up for the same. Over 2years her complaints increased with dysmenorrhea. However, the dysmenorrhea increased significantly over last few months and patient noticed a mass coming out of the vagina 1 month back for which she went to her family physician. She was advised by family physician to do ultrasound which was s/o Uterovaginal prolapse. She was then referred to us for further evaluation and management. On local examination in OPD, a 5x6 cm mass was seen protruding from the vagina with another globular swelling 3x3cm in size attached to the larger mass at the cranial end. On per speculum examination, neither a uterine sound nor a gloved finger could be passed around the pedicle of protruding mass encircled by the cervical rim. Uterine fundus was not palpable on bimanual examination. This raised a clinical suspicion of uterine inversion due to a large submucous myoma. Also, two small dimples were seen equidistant from the midline at 3 o clock and 9 o clock position on the cranial swelling, which were suspected to be tubal ostia. Hence, the patient was counselled for laparoscopic surgical repair of the chronic inversion. On doing laparoscopy, no uterine fundus was seen and medial ends of all cornual structures were pulled in the center at

the constriction ring formed by uterine isthmus and cervix. This confirmed the diagnosis of uterine inversion. To begin with, the prolapsed submucous myoma was shaved off vaginally by cauterization and the endo-myometrial junction line which was actively bleeding was sutured with Vicryl™. Excessive use of cautery over the endometrial lining was avoided as the patient wanted future fertility. Bilateral ureters were visualized and traced caudally till the level of uterosacral ligaments. Lateralization of ureters was performed. Following this, vaginal reposition of the prolapsed fundus by pressure was attempted which failed. Owing to this, a decision to perform Haultain's procedure was made. The posterior part of the constriction ring was made prominent by inserting a sponge on holder in the vagina. Vasopressin was infiltrated over the posterior part of the ring in the midline using Pisat's Visual Vasopressor Injection Needle (VVIN).1 Midline vertical incision approximately 3 cm in length was made over the constriction ring. After the constriction ring was released an upward push from vaginal end combined with simultaneous upward traction on round ligament which resulted in reposition of uterus. Uterine incision was sutured with continuous non interlocking barbed sutures. Adhesion barrier was placed over the uterine incision line. Intra uterine pediatric foleys catheter was kept postoperatively for 3 days. Postoperative period was uneventful and patient was discharged with advice regarding future conception.

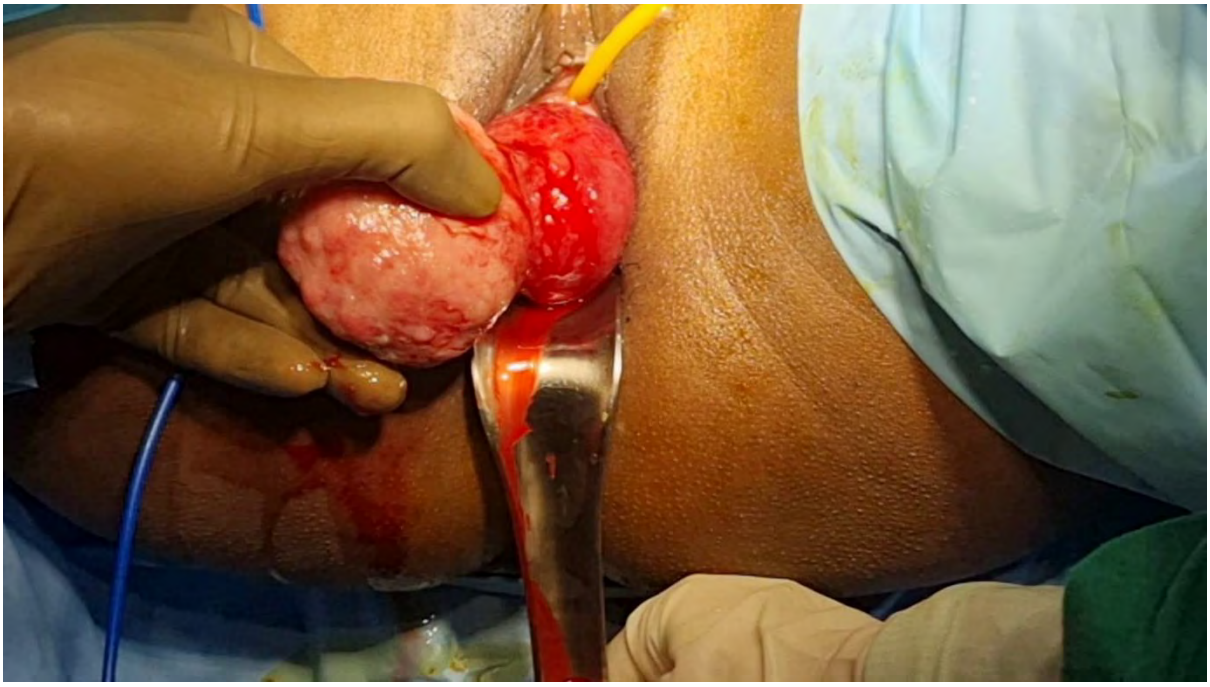

Figure 1. Submucous myoma with uterine inversion

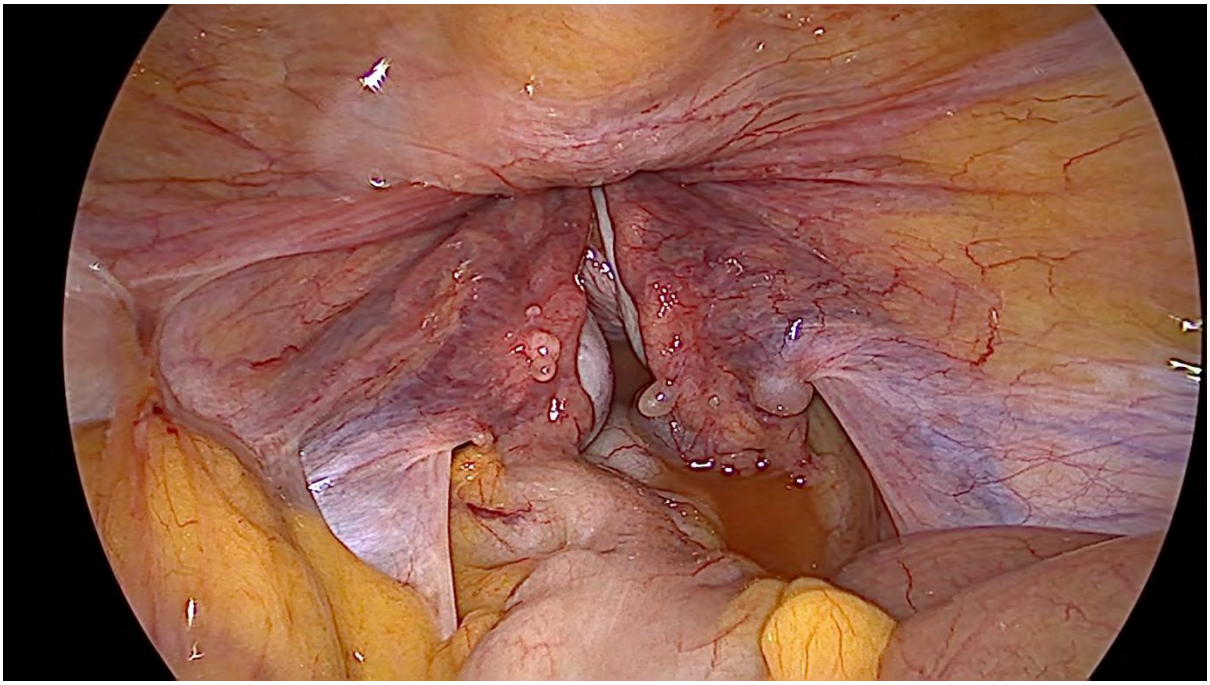

Figure 2. Laparoscopic view -Uterine fundus not seen, medial ends of all cornual structures pulled in the constriction ring

Figure 3. Vaginal myomectomy done to ease uterine reposition

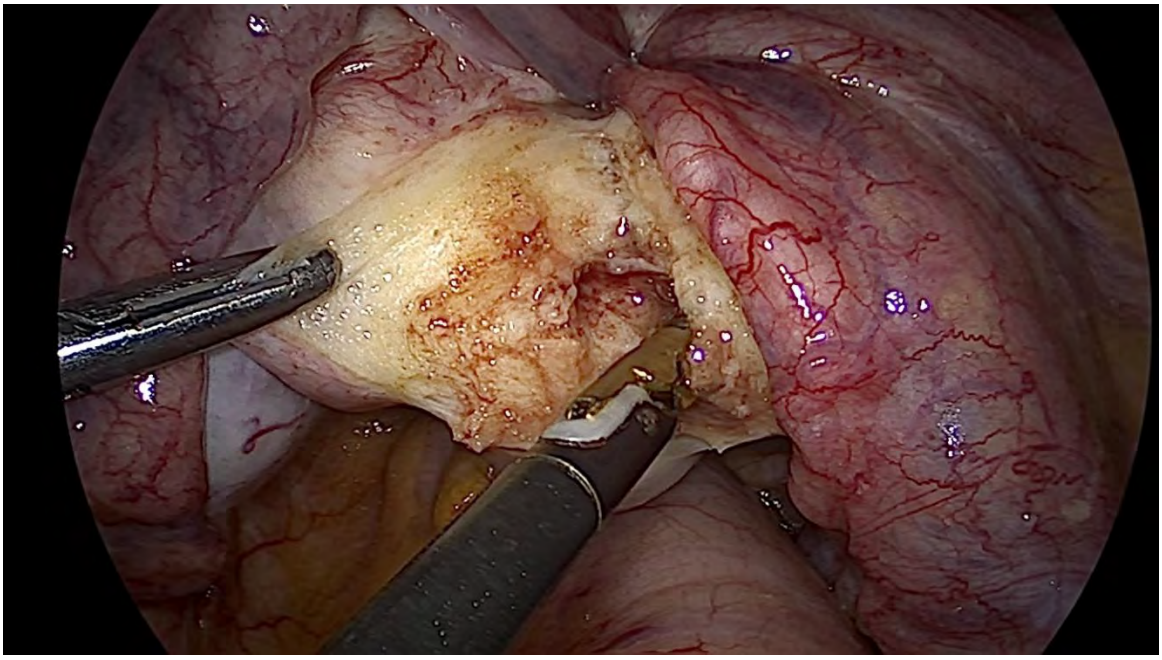

Figure 4. Uterine constriction Ring released with posterior incision on uterine isthmus and cervix

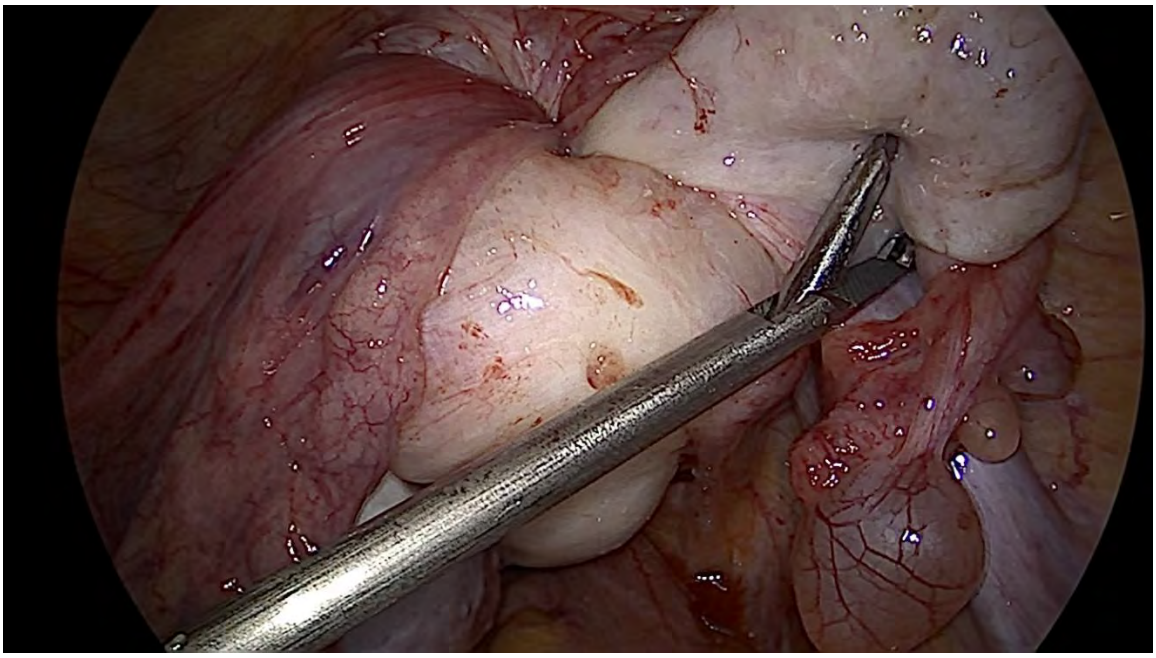

Figure 5. Upward traction on the medial ends of all cornual structures after release of constriction ring

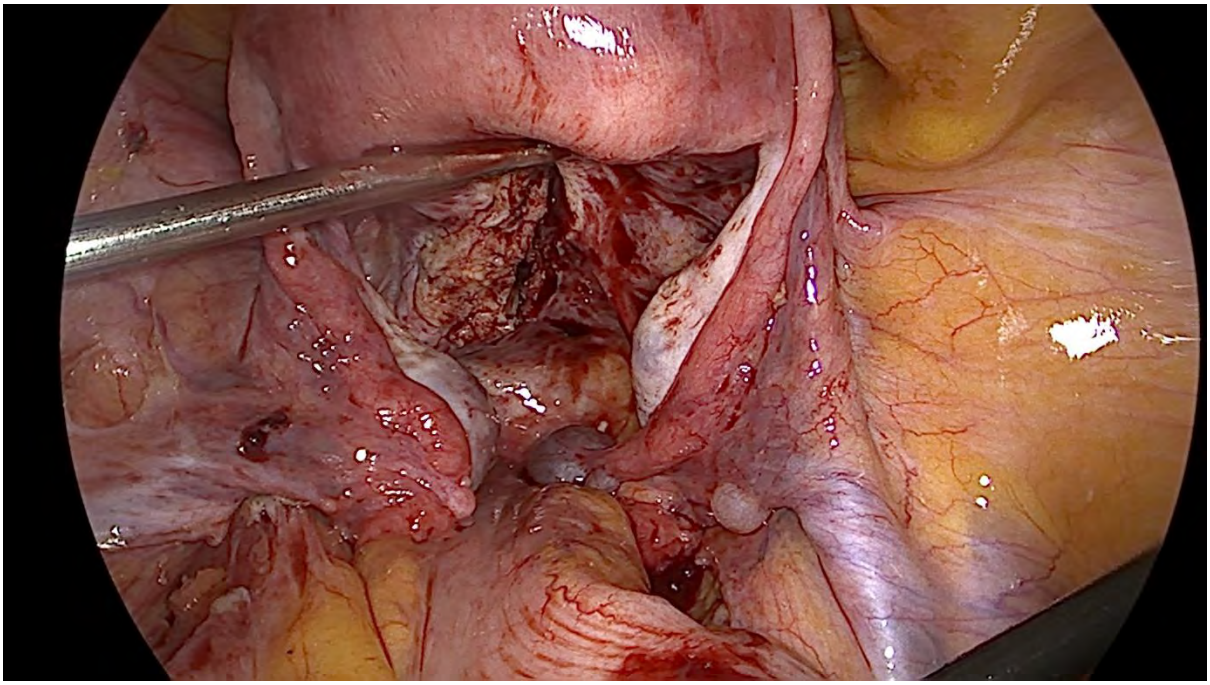

Figure 6. Uterus reposited back

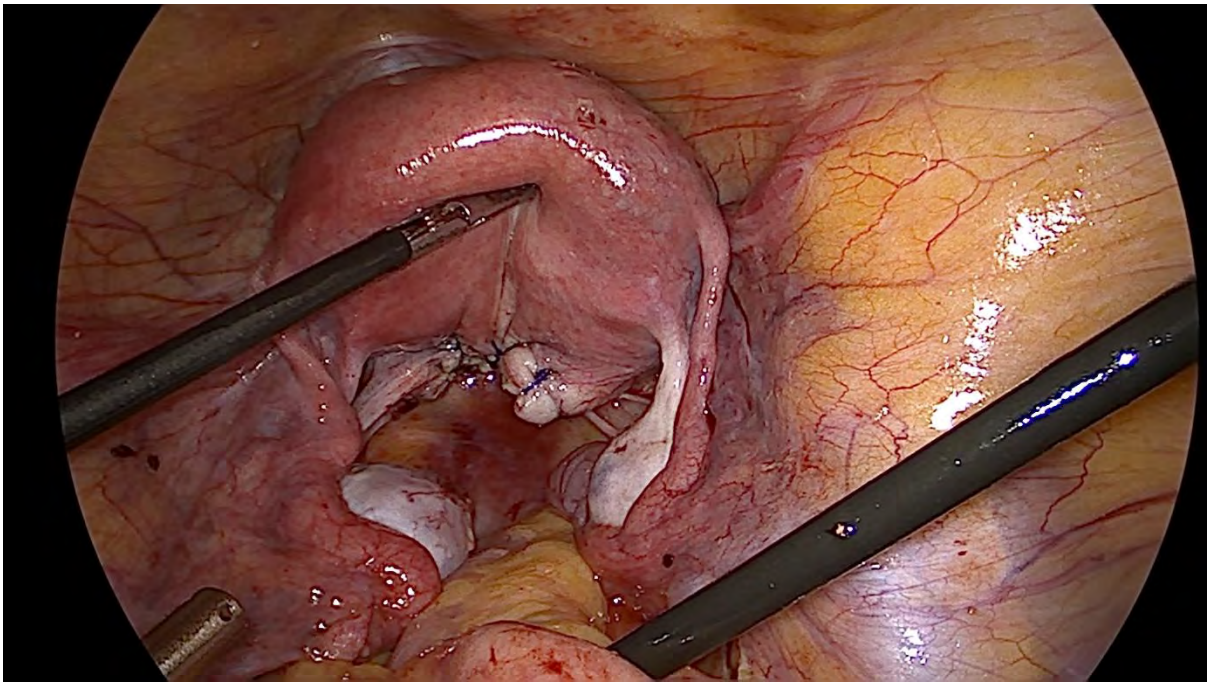

Figure 7. Uterine repair with barbed sutures

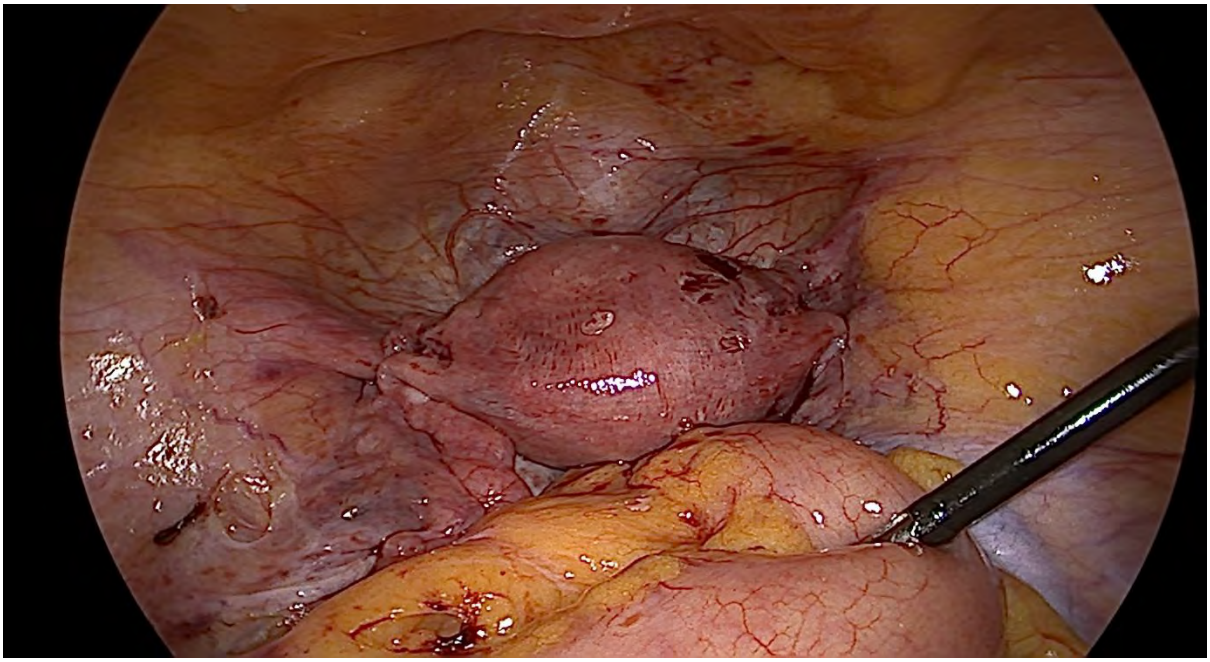

Figure 8. Final picture after uterine reposition and repair

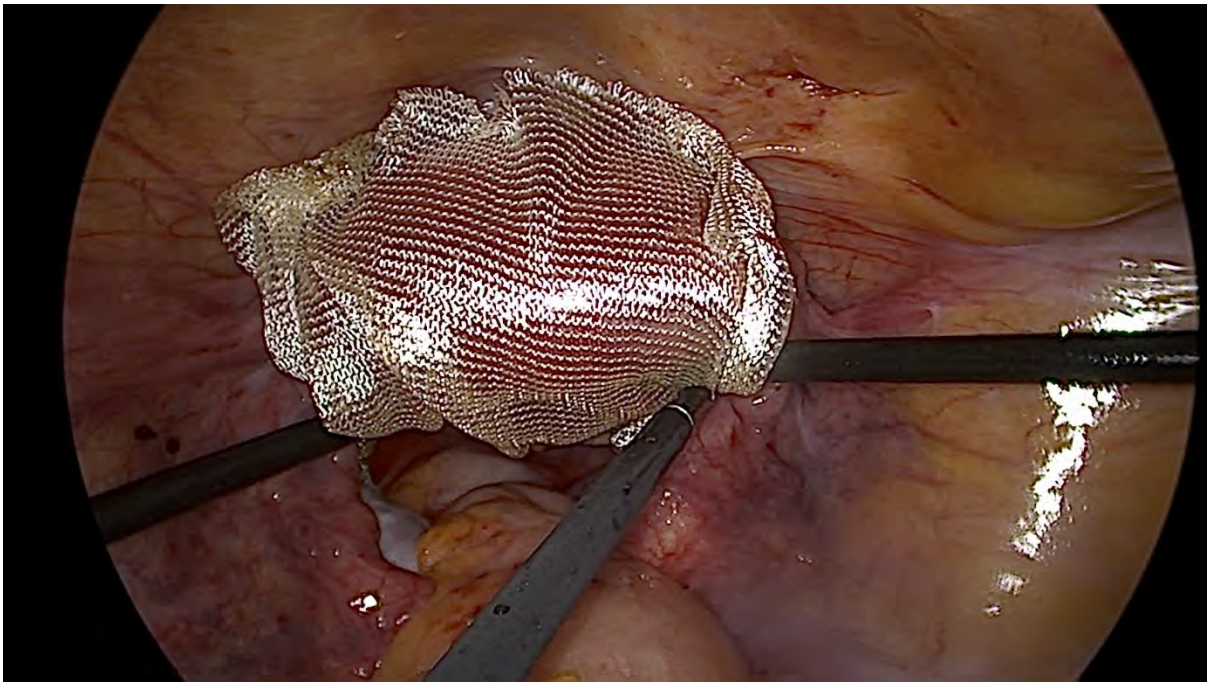

Figure 9. Adhesion barrier placed over reposited uterus

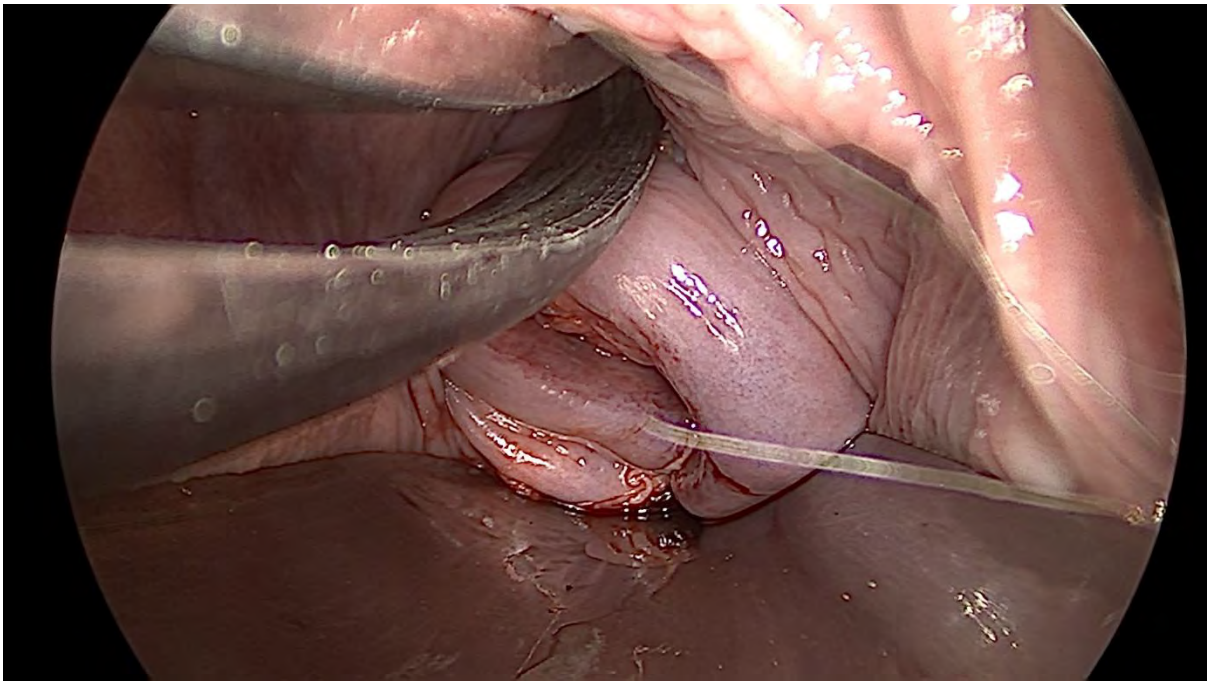

Figure 10. Picture of cervix following uterine reposition

Etiology

In a study by Herath RP et al, leiomyoma was the most frequent cause of NPUI, accounting for 86 (56.2%) of the cases.3 Another study by Takano et al observed 92% cases were associated with uterine tumors of which 71.6% were leiomyomas and 20% were malignant tumours.4 Amongst the malignant causes leiomyosarcomas are the most common, followed by endometrial carcinoma, rhabdomyosarcoma, malignant mixed müllerian tumor, and endometrial stromal sarcoma 5.

Diagnosis

The clinical diagnosis of non-puerperal uterine inversion is challenging and a high index of suspicion is necessary for accurate diagnosis. Important clinical signs that aid in diagnosis are absence of identifiable cervical rim around the proximal portion of the mass (in case of complete inversion), failure to find the opening of uterine cervix or probe the endometrial cavity, cupping of fundus on bimanual palpation (in incomplete inversion cases), no palpable uterine fundus on per rectal examination. Both the diagnosis of NPUI and the identification of its etiology can be aided by ultrasound imaging. Incomplete uterine inversions show sonographic signs of a "Y"-shaped uterine cavity in the longitudinal plane. The base of “Y” indicates the noninverted endometrial lining. Complete inversion in the longitudinal view on ultrasound results in a "U"-shaped structure, with the limbs of the "U" standing in for the entire inverted endometrial lining.

The diagnosis of NPUI using magnetic resonance imaging (MRI) has been found to be sensitive. U-shaped uterine cavity, thicker and inverted uterine fundus on a sagittal view, and a "bull's eye" arrangement on the horizontal section are the three distinct observations noted on MRI in cases of uterine inversion. In case of difficulty in clinical diagnosis and interpretation of imaging

findings comes the role of examination under anesthesia, laparoscopy and biopsy of the vaginal mass prior to definitive surgical management. Malignancies though rare have been associated with NPUI hence histological assessment of the mass is justified prior to definitive surgery unless there is an obvious cause like fibroid as in our case.

Management

Techniques of uterine reposition such as Huntington (traction on round ligaments abdominally), Haultain (abdominal – posterior incision), Spinelli (vaginal- posterior incision), and Kustner's (Vaginal- anterior incision) operations were traditionally described for puerperal inversions. Subsequently, the above procedures have been used to treat NPUI also. Our case was managed with a combined vaginal and laparoscopic approach for uterine reposition and repair. Vaginal myomectomy was done which resulted in debulking of the uterus. This was followed by laparoscopic Haultain procedure for uterine reposition and repair. As per a study conducted by Herath RP et al, Haultain procedure seems to be the most successful method to achieve repositioning in 18.0% cases of NPUI.2 This study also found that majority 48.8% were managed by only abdominal approach while 27.1% had both abdominal and vaginal approach. The majority 39.7% required abdominal hysterectomy while 15.0% had uterine repair after repositioning.3

Future Outcome

Unfortunately, future fertility has not been found to be satisfactory following uterine reposition in NPUI cases. A case was reported by Irani et al where the uterus was repositioned with the Haultain procedure but the woman failed to conceive for two years after the operation.6 Similarly Herath RP et al. failed to find any evidence of successful pregnancy following repositioning of a nonpuerperal uterine inversion.3 However, following successful uterine reposition in NPUI cases women should be counselled regarding associated risks in future pregnancy like uterine rupture, cervical incompetence. Pregnancies following NPUI repair may warrant need of prophylactic cervical cerclage and need for elective caesarian section near term. Also, in pregnancies following NPUI repair complicated with low-lying placenta morbidly adherent placenta is to be ruled out with imaging.

Discussion

Only one-sixth of all occurrences of uterine inversion are non-puerperal, and the majority of cases of uterine inversion occur during puerperium 2. The mechanism of non-puerperal uterine inversion is not clear. However, the chronic downward traction force exerted by the submucous myoma situated at the fundus caused inversion in our case.

Conclusion

NPUI is rare. It should be taken into consideration as one of the differential diagnoses in females with mass protruding through vagina. A high index of suspicion is essential for early diagnosis and appropriate surgical intervention so as to avoid devastating consequences.

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A Novel Technique for En Bloc Hysterectomy in the Treatment of Deep Endometriosis #Enzian C3 Bowel Nodules to Optimize Video: Step by Step Approach

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Abstract

Deep endometriosis with bowel involvement presents a significant clinical challenge, open necessitating complex surgical intervention. Traditional surgical methods often demand extensive operating items and pose inherent surgical risks. This article introduces a groundbreaking technique for en bloc hysterectomy designed to optimize operative efficiency, thereby reducing surgical time without compromising patient outcomes.

Objectives

To elucidate a novel, step-by-step surgical approach for performing an en bloc hysterectomy in the treatment of deep endometriosis bowel nodules, aiming to improve operative efficiency and reduce surgical complications.

Methods:

A comprehensive, multidisciplinary approach was employed, incorporating advanced laparoscopic techniques for en bloc resection of diseased tissue. Pre-operative criteria Mandatory nowadays was implemented mapping of the disease by MRI in Special protocol to identify C3 ENZIAN bowel nodule was implemented as well as Adenomiosis, deep endometriosis in the retro-cervical area and endometrioma with this full characteristic of the nodule were diagnose (length from the anal verge, percentage of bowel circumference etc.) with this we plan surgery in a multidisciplinary fashion and plan full excision surgery, in our criteria patient without desire of future pregnancy and adenomyosis unresponsive to medical treatment we perform hysterectomy and in cases like this Em bloc hysterectomy reduces surgical time and improve ffectiveness, this is because a:er full excision of deep endometriosis nodules in our previous described and published “reverse technique” we can leave the uterus attached totally to the bowel nodule and during colpotomy we access always if the nodule is over 7 cm over the anal verge the health plane of the recto vaginal space and the healthy Denonvilliers fascia, with this we can easily create the stapler line below the nodule during bowel segmental resection, this reduce surgical time, unwanted opening of the bowel during surgery and comorbidities, surgical steps were standardized.

Results

Preliminary data suggest a significant reduction in operative time compared to standard procedures,without a concurrent increase in surgical complications. Further, the en bloc method allows for a more comprehensive removal of endometrial-like tissue, minimizing recurrence risk and unwanted opening of the bowel during bowel segmental resection.

Conclusion

The proposed en bloc hysterectomy technique provides a paradigm shift in the surgical management of deep endometriosis with bowel involvement. With the potential for improved surgical outcomes and reduced operative time, this method warrants further investigation and validation through large-scale clinical studies.

Key words: en bloc resection; #ENZIAN; C1 Lesion; bowel resection

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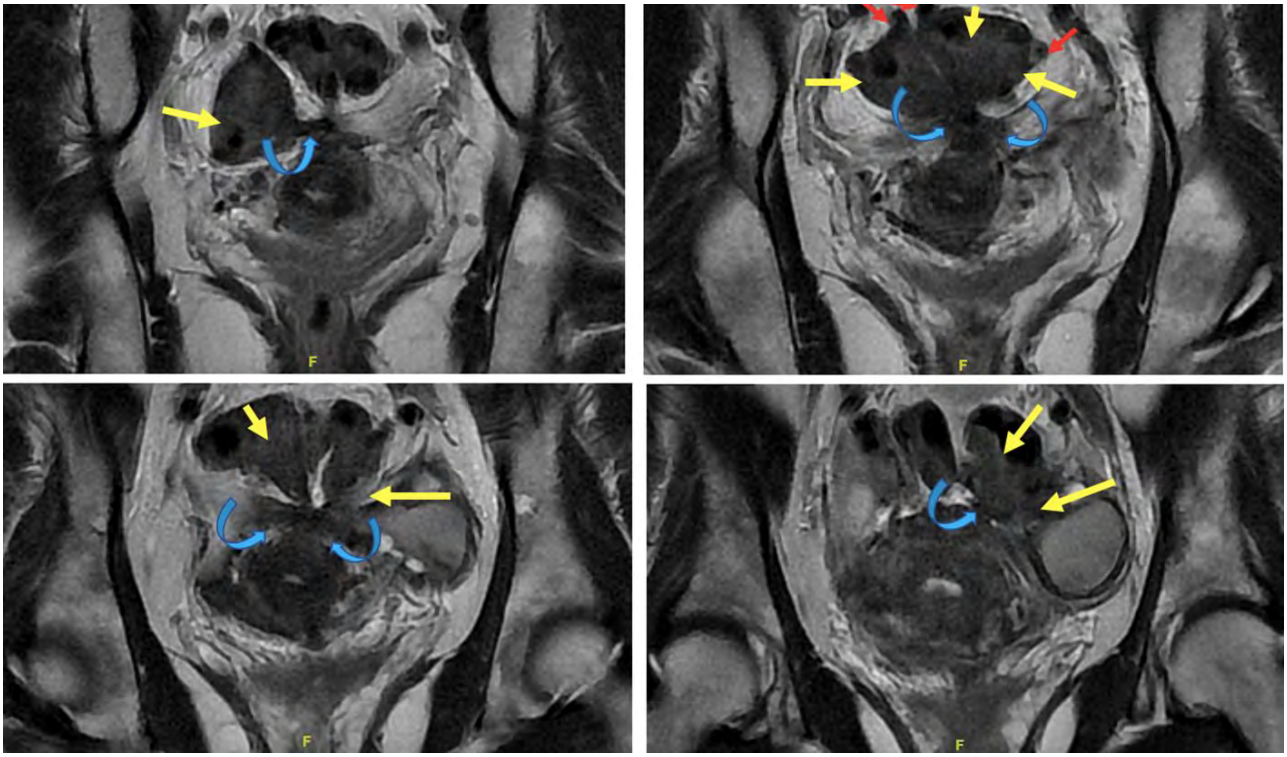
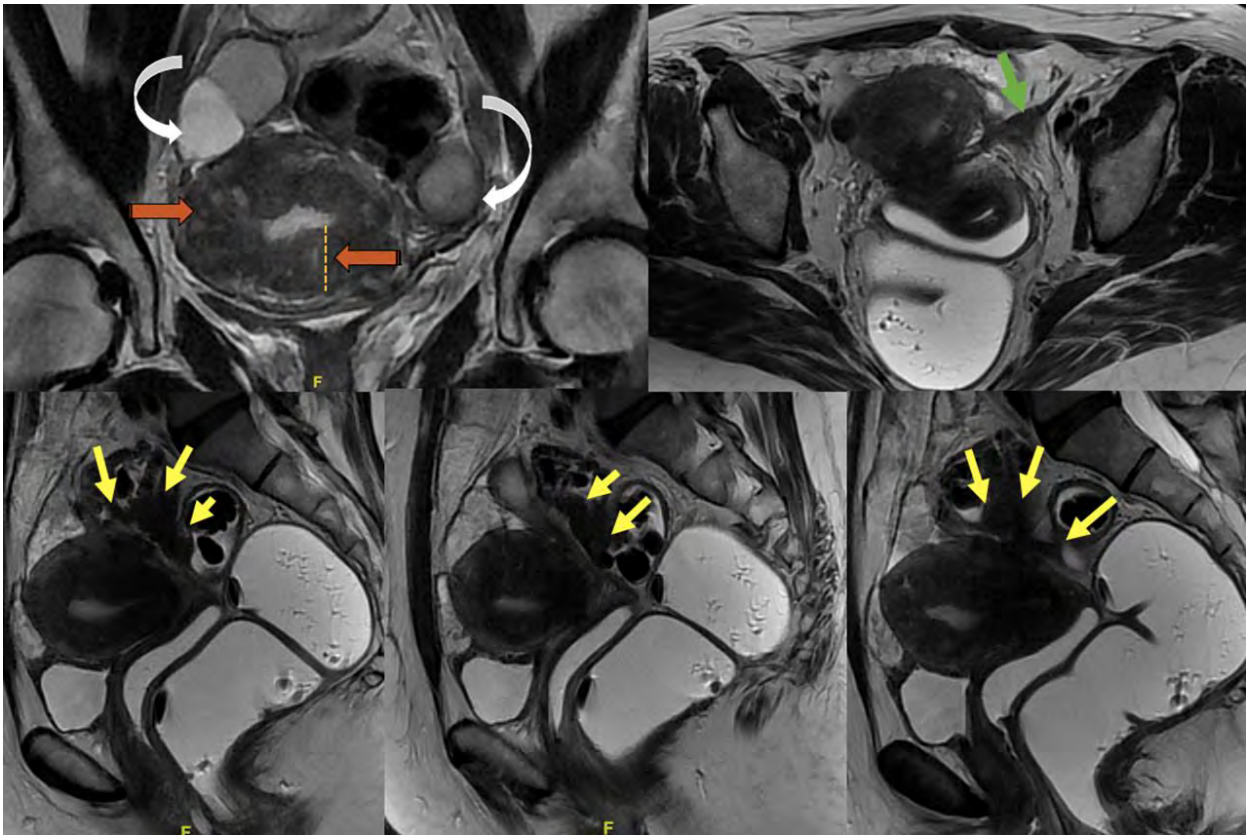


Magnetic Resonance Imaging (MRI) Endometriosis Mapping, T2-weighted sequence. Images acquired in the coronal plane reveal an extensive nodular fibrous plaque (blue curved arrow) retro-uterine involving the uterine torus with extension into the meso-rectal fat and multiple adhesive bands directed towards the wall of the sigmoid rectum. The nodular endometriotic plaque extends to the sigmoid rectum involving the muscular layer in a long segment, retracting it in various portions, forming a fixed loop morphology (yellow arrows), and multiple diverticula are observed in this sigmoid segment (red arrows).



Magnetic Resonance Imaging (MRI) Endometriosis Mapping, T2-weighted sequence. In image A, acquired in the coronal plane, extensive adenomyosis with interposed adenomyotic cysts is observed (orange arrows), with ovaries retracted due to endometriomas (curved white arrows). Image B shows thickening of the left round ligament (green arrow). In images C, D, and E, sagittal plane images with intravaginal and intrarectal gel reveal the nodular plaque (yellow arrows) involving the high sigmoid rectum at 17 cm from the recto-anal junction, adhering to the retro-uterine plaque, forming a "loop" morphology due to retraction in several segments.

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Surgical approach of the OHVIRA-like syndrome: a didactic video

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Abstract

Introduction.

Herlyn-Werner-Wunderlich (HWW) syndrome, also known as OHVIRA (obstructed hemivagina and ipsilateral renal anomaly) syndrome, is a rare congenital urogynecological malformation, typically characterized by the triad of uterine didelphys, obstructed hemivagina, and ipsilateral renal agenesis. The multiple anatomical variations of this syndrome challenge the prompt diagnosis and the therapeutic approach. Surgical treatment may not always be clear until completing diagnostic with endoscopic exploration. Case presentation. An adolescent female, virgin, with a history of left renal agenesia was addressed to the Mother and Children Department with complaints of chronic abdominal pain, worsened in the last weeks, mainly irradiated to the left iliac fossa. Physical examination showed a painful abdomen and normal external genital organs. Abdominopelvic ultrasound and MRI revealed a uterus didelphys and suspected a blind left hemivagina with 8 cm presumed hematocolpos. The association with a left renal agenesia was suggestive of an OHVIRA syndrome. A vaginoscopy followed by a laparoscopy were planned to complete the diagnostic. Unexpectedly, vaginoscopy didn't show either the hematocolpos, second hemivagina, or cervix, with no possibility then to drain it transvaginally. Laparoscopy revealed a probably obstructed left hemi-uterus associated with a large hematocervix and hematosalpinx; on the right side, a normal hemiuterus and adnexa with a functional right tube.

Peritoneal endometriosis was identified at multiple sites of the abdominal cavity. A left hemi-hysterectomy was decided intraoperatively, which is illustrated in this video as the surgical approach to a variant of HWW syndrome classified by Zhu L. 2015 as cervicovaginal atresia without communicating uteri (OHVIRA type 1.2.). An extensive adhesiolysis to progressively "enucleate" the dilated cervix from the surrounding peritoneum was performed until the complete resection of the rudimentary left uterus and tube without

complications. Desogestrel-only pill was then started to treat endometriosis and regular follow-up was established. Conclusion. HWW syndrome may be suspected in young patients with abdominal pain, a pelvic mass (suggestive of hematocolpos) and renal agenesia. Early diagnosis and timely proper management of this syndrome are crucial as they would prevent urogynecological complications such as endometriosis, infection, and infertility. Even if a conservative approach is recommended, some anatomical variants may require a hemi-hysterectomy.

Keywords:

Benign Gynecology, Gynecologic Surgical Procedures, Herlyn-Werner-Wunderlich (HWW) syndrome,

Laparoscopy, Obstructed hemivagina and ipsilateral renal anomaly (OHVIRA) syndrome

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Resection of Type 2 Myoma Located in the Fundus of the Uterus with Cold Knife Hysteroscopy System and Myosure® Tissue Removal Suite

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Abstract

Type 2 myoma located in the fundus of the uterus is relatively harder to remove compared to the myoma located in the anterior or posterior wall. We described a technique using cold knife hysteroscopy system and Myosure® tissue removal suite.

Myoma capsule was cut with a 3 mm scissor under direct hysteroscopy view. When the capsule is open, we use a 3 mm grasper to dissect, isolate and pull the myoma. After dilation of the cervix to Hega size of 20, A Lin's grasper is used to hold the myoma and rotate it from the myometrium under abdominal ultrasound monitoring.

To reduce the volume of the myoma, we use a Myosure® tissue removal suite to morcellate the myoma. When the myoma size is reduced, we use Lin's grasper to get the smaller myoma piece from the uterine cavity. A balloon was inserted into the uterine cavity to stop bleeding and prevent adhesion.

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Key words: TCRM; Myosure tissue removal suite; Type 2 myoma

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Two - steps procedure with the Intrauterine BIGATTI Shaver (IBS®) for a large, 6 cm degenerated G1 submucosal myoma removal: a case report Video article

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Abstract

Submucosal myomas represent 5.5% to 16.6% of all uterine fibroids (1). Several treatment options are available in clinical practice nowadays (2). Bipolar resectoscopy still remains the gold- standard surgical procedure to approach submucosal myomas (3). Fluid overload, uterine perforation and long learning curve are still unsolved, technical related, problems (4). With the advance of new surgical devices an alternative and completely mechanical approach to tissue removal has been developed. Currently there are three main tissue mechanical removal systems: Truclear®, Myosure® and Intrauterine BIGATTI Shaver (IBS®). Despite several advantages, such as shorter operative time, higher total resection rate and higher patient acceptability, myoma size and consistency still limit the use of tissue mechanical system for this indication (5). In 2014 Bigatti et al. reported that the IBS® was able to remove in a single-step procedure 93.5% of submucosal myomas up to 3 cm in diameter, 62.5% of which were type II (6). In 2023 Zhang Shu et al. by reducing the IBS® rotational speed from 2100 rpm to 1500 rpm and increasing the aspiration flow rate up to 500 ml/min achieved a more complete resection and a faster operating time especially for myomas between 3 and 5 cm in diameter (7). This case report shows a two steps procedure with the IBS® for the successful removal of a large 6 cm submucosal degenerated myoma.

Key words: submucosal myoma; Intrauterine BIGATTI Shaver; IBS®; Operative hysteroscopy.

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VIDEO Article:

Two - steps procedure with the Intrauterine BIGATTI Shaver (IBS®) for a large, 6 cm degenerated G1 submucosal myoma removal: a case report

Study Objective: To assess the IBS® efficacy for the treatment of a large 6 cm - G1 submucosal myoma.

Design: Description of the surgical steps and prognosis related to this approach. Setting: "SELEC Sino European Life Expert Centre" of JaoTong University, Shanghai Patient:

A 27-year-old nullipara woman was admitted to our hospital with a one-year history of abnormal uterine bleeding.On examination, the uterus was enlarged to 10-weeks of pregnancy in size. Her hemoglobin was low at 95g/L with a normal CA125 and Ca19.9 levels. Transvaginal ultrasound showed an 80mm×87mm×96 mm anteverted uterus with a type 1, 55mm×68mm×60mm submucous myoma inside the uterine cavity according to FIGO classification (8). Both ovaries were of normal size. At diagnostic hysteroscopy the presence of a G1submucous myoma almost occupying the whole cavity and inserted into the left side of the uterine fundus was confirmed (9). The red color and the tenderness of the myoma capsule gave us the impression of a partial necrotic degenerated myoma. The vascular patterns on and around the myoma appeared normal and therefore a biopsy of the fibroid prior to removal was not felt to be necessary.

Intervention:

An operative hysteroscopy utilizing the IBS® (KARL STORZ SE & Co. KG) was scheduled. The 24Fr. optical system with an SB blade of the shaver was used. A detailed description of the equipment has been published previously (10). The procedure was carried out under general anesthesia and the hysteroscopic distension medium chosen was normal saline. The rotational speed of the blade was set to 1500 rpm with an aspiration flow rate between 250ml/min and 500 ml/min. As described in our previous diagnostic hysteroscopy, the uterine cavity was completely distended by the presence of the G1 myoma with several organized blood clots. A two-stage procedure was required as the fluid deficit limit was reached during resection of the intracavitary portion of the fibroid (Fig.1).

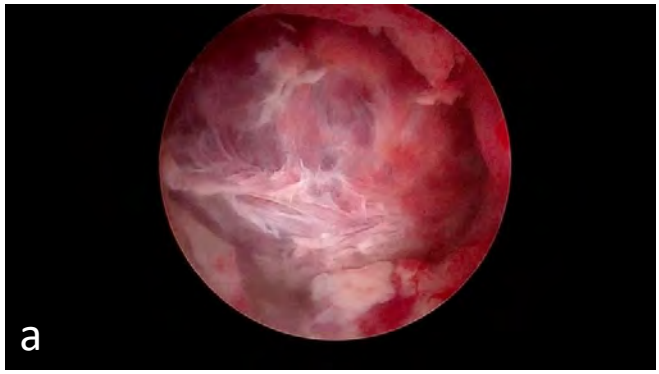

Figure1: Stage 1 procedure: a) 6 cm degenerated submucosal myoma b) Final image after the removal of the myoma intracavitary portion c) Total amount of tissue removed.

This procedure lasted around 25 minutes but as the fluid deficit reached 2000mL, the decision to stop and reschedule for complete resection at a second stage was taken. The histological examination confirmed the presence of a partial necrotic degenerated submucous myoma. After the first surgery the patient experienced an improvement in her menstrual flow with no more abnormal uterine bleeding. At transvaginal ultrasound two months after surgery a 2.5 cm residual myoma was found. The residual myoma was completely removed at second surgery (Fig.2).

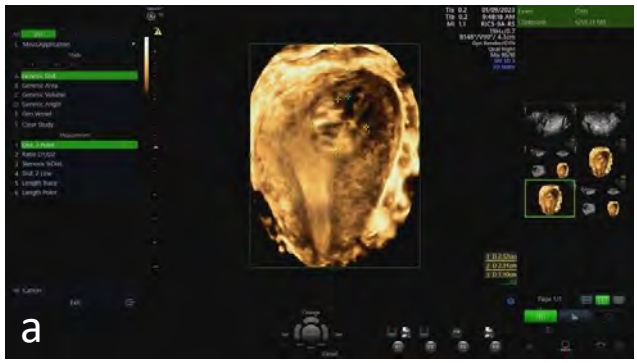

Figure 2: Stage 2 procedure: a) 3D US of the residual Intracavitary portion of the degenerated submucosal myoma b) Final image after the removal of the myoma residual intracavitary portion c) Total amount of tissue removed.

The IBS® was also used with an operative time of 20 minutes and a fluid deficit of 500 ml of normal saline solution. The procedure was almost bloodless with no anesthesia-related complications. To prevent adhesion formation, a Mate-Regen® gel by Bioregen was left in cavity at the end of the procedure. The patient was discharged from the hospital two hours after both operations.

Main Result:

At a three months postsurgical evaluation the patient reported normal cycles without intermenstrual abnormal uterine bleeding. Transvaginal ultrasound confirmed the completeness of the myoma removal with the presence of a normal endometrial thickness.

Conclusion:

The IBS® system has been shown to allow completion of most major operative hysteroscopic procedure in a single step (11,12,13). It has been shown to be precise, safe and with a short learning curve, The shave technique allows the removal of polyps and fibroids without affecting the basal layer and thereby reduces the risk of post-surgical adhesions. Due to its mode of action, electrosurgery which may cause thermal damage is not involved in the process. This is the reason why this technique should be the first choice in case of infertility patients. However, the removal of large submucosal myomas by the IBS® is still a challenging hysteroscopic operation. A rotational speed of 1500 rpm with an increased aspiration rate up to 500 ml/min increased our performance in the removal of intrauterine submucous myomas. This case report confirms the validity of the Shaver technique for this indication and therefore the need to promote further technical research on tissue mechanical removal systems to improve the success rate in case of removal of all kinds of large submucosal myomas.

Conflict of interest:

Dr G. Bigatti is a consultant for Karl Storz SE & Co KG and a developer of the IBS® device reports personal fees from Karl Storz SE & Co KG outside the submitted work. No support from the financial industry was received for this study.

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Minimally Invasive Gynecologic Surgery (MIGS) – History, Today and Future. A personal perspective over 5 decades.

Author: Liselotte Mettler, Kiel, Germany

Introduction

Over the past 50 years, MIGS has evolved in a relatively short period of time to overtake the centuries-old visionary and pioneering groundwork of our outstanding colleagues in all surgical disciplines. Minimal Invasive Surgery (MIS) began with the innovative approach of Philipp Bozzini who died in 1809 at the age of 36 years. He basically invented the illumination of body cavities using an extracorporeal light source to reflect light. The beginning of Endoscopic Surgery from a surgical perspective starts with Georg Kelling, who presented the first endoscopic procedure, viewing the stomach of a dog, using Nitze's cystoscope and an air insufflation apparatus at the Natural Scientists' Meeting in Hamburg, Germany in 1901. Departed innovative thinkers and visionary mentors, such as Raoul Palmer, Hans Frangenheim, Kurt Semm, Daniel Dargent, Patrick Steptoe, Jordan M. Phillips, Maurice Bruhat, Robert B. Hunt, Jochen Lindemann, Thoralf Schollmeyer, and our general surgical colleague Gerhard Buess, all struggled to introduce less disabling diagnostic and therapeutic endoscopic technologies into daily clinical use for the betterment of our patients [Table 1].

Table 1: Founding fathers of laparoscopic and hysteroscopic surgery

1) *Philipp Bozzini (1773-1809) and the light guide*
2) *Antonin Jean Desormeaux (1815-1894) and his endoscopes*
3) *Georg Kelling (1866-1945) and his air insufflation apparatus*
4) *Max Nitze (1848-1906), an early urological endoscopist who developed cystoscopy*
5) *Heinrich Kalk (1895-1973) and his insufflation apparatus which allowed abdominal biopsies of the liver, etc.*

6) *Raoul Palmer (1904-1985), the European father of endoscopy with the lithotomy position*

7) *Hans Frangenheim (1920-2001) built his first abdominal insufflator in 1959*

8) *Harold Hopkins (1918-1994) developed the rod lens system of modern endoscopes*

9) *Karl Storz (1911-1996) was responsible for the development of the cold light source in 1960*

10) *Patrick Steptoe performed many laparoscopies in Great Britain and developed the human in vitro fertilization and embryo transfer technique together with Robert Edwards*

11) *Hans-Joachim Lindemann (1920-2012) laid the groundwork for hysteroscopy based on the first book on hysteroscopy written by Duplay and Cladoin 1898*

12) *Jordan M. Phillips (1923-2008) was a propagator and "prophet" for gyne endoscopy worldwide*

13) *Kurt Semm (1923-2003) was the father of operative gynecological endoscopy and operative endoscopic surgery for all disciplines. He performed the first endoscopic appendectomy as a gynecologist in 1981*

14) *Gerhard Buess (1943-2012) was an intensive promoter of minimal invasive new surgical techniques in the field of operative endoscopy worldwide.*

15) *Thoralf Schollmeyer (1964-2014) was the Leader of the Kiel School of Gynecological Endoscopy from 2007 to 2014*

16) *Maurice Bruhat (1934-2014) was the leader of the Clermont Ferrand Endoscopic School in France*

Jacques Hamou, Dennis Querleu, Marc Possover, Frank Löffer, Christopher Sutton, and Harry Reich, the Nezhat brothers, under the lead of Camran Nezhat, - Nargesh Motashaw, Prashant Mangeshikar, Prakash Trivedi , Shailesh Putambekar and Akhil Saxena - under so many Indian and other dedicated colleagues around the world like Ibrahim Alkatout, Joerg Keckstein , Bruno van Herendael, Guenter Noe and Keith Isaacson are contemporary gynecological visionaries whose achievements have set the path which we now follow. The worldwide development and popularization of gynecologic endoscopy and endoscopic surgery in all medical disciplines began when Professor Kurt Semm became chief of the Department of Obstetrics and Gynecology at the University of Kiel, Germany, in 1970. I was then a first year resident in the OB.GYN Department in Kiel, Germany, but had an education of three years in General Surgery

in the Amazon Hospital in Pucallpa, Peru, when I joined him. After initial tubal sterilizations in Kiel in 1970, ovarian cyst- resections, ectopic pregnancies, and myomectomies followed and were performed successfully however, sutures and ligatures were difficult to acquire. Manufacturers were eager to produce only if

large quantities of surgical products were ordered. With the introduction of laparoscopic cholecystectomy by Erich Mühe in 1985 and Phillipe Mouret in 1987, industry realized the importance and potential commercial benefits of this endoscopic surgical development and became more interested in endoscopic surgery. There are many milestones in the chronological development of minimal invasive surgery which are very well detailed in our Practical Manual of Laparoscopic and Hysteroscopic Gynecological Surgery (1 and 2). The development of safe coagulation strategies by Kurt Semm and Video laparoscopy with better and better camera systems by Camran Nezhat (USA) set milestones (3).

Many national gynecological endoscopic societies as well as multidisciplinary societies of endoscopic or MIS/medicine (SLS, ITS, and SMIT, ESGE, ISGE, AAGL, APAGE) have since been formed. From 1970 to 1990, gynecological laparoscopic surgery continued to be developed in Kiel under Kurt Semm. Numerous national and international endoscopy courses took place in Kiel, Clermont Ferrand, Brussels, Lyon, Strasbourg, in various locations in the USA and worldwide. In 1990, the Kiel School of Gynecological Endoscopy was founded by Liselotte Mettler and continues today under the leadership of Ibrahim Alkatout. Since 35 years, Prashant Mangeshikar of Mumbai, India, visited this school with annual courses of 30–40 Indian gynecologists and general surgeons for 2 weeks of intensive endoscopic surgery and training. This means dedication and recognition of our Indian colleagues, who today are leading worldwide in their open and critical discussions of surgical endoscopic procedures in modern multimedia.

ISGE, APAGE, ESGE and AAGL direct with their many national and International Endoscopy courses and meetings the world standard in Gynaecological Endoscopic Surgery, whereas. SLS and SMIT support the interdisciplinary cooperation of all medical and surgical specialities

Specifications

Where are we standing today with the Catalogue of Organ-oriented Indications for Operative Laparoscopy/Pelviscopy and Hysteroscopy in Gynecology?

Can all surgical procedures be done endoscopically? (Pelviscopy is the term used by Kurt Semm for Gynecological Laparoscopy).

A variety of operating indications in our field has been established during the past 5 decades, including surgery on the uterus and the adnexa for benign and for malignant reasons. Many patients have benefited from the use of laparoscopy, particularly those with extra uterine pregnancies or endometriosis. Today, the field of endometriosis includes intensive cooperation with general surgeons, especially in the treatment of deep infiltrating endometriosis reaching into the bladder and bowels. There are less complications, shorter hospital stays, and faster rehabilitation. Laparoscopic interventions are now possible for intestinal tumors, female genital tract tumors, adhesiolysis, genital suspension operations, resection of rudimentary uterine horn, incision of lymphocele and during pregnancy. Furthermore, the endoscopic treatment of malignant disorders, including multiorgan procedures such as lymphonodectomies or pelvic exenterations, shows their progress. The very well discussed results of the LACC study brought cervical cancer surgery to acertain halt and reflection. However, newer studies have proofed that early cervical cancer surgery can only be performed laparoscopically in the hands of expert surgeons respecting two principals:

1. Application of a cervical vaginal tissue sleeve around the cervical tumor and 2. No use of intrauterine manipulators. This proofed to have the same results in cancer progression rates and long-term survival rates for the patients as open surgery (4 and 5).

An overview does not permit to go into selected examples of laparoscopic and hysteroscopic surgery, therefore I will only give one example on current endometriosis surgery based on the European #ENZIAN score for ENDOMETRIOSIS as preoperative and postoperative classification (table 2).

Current Endometriosis Surgery

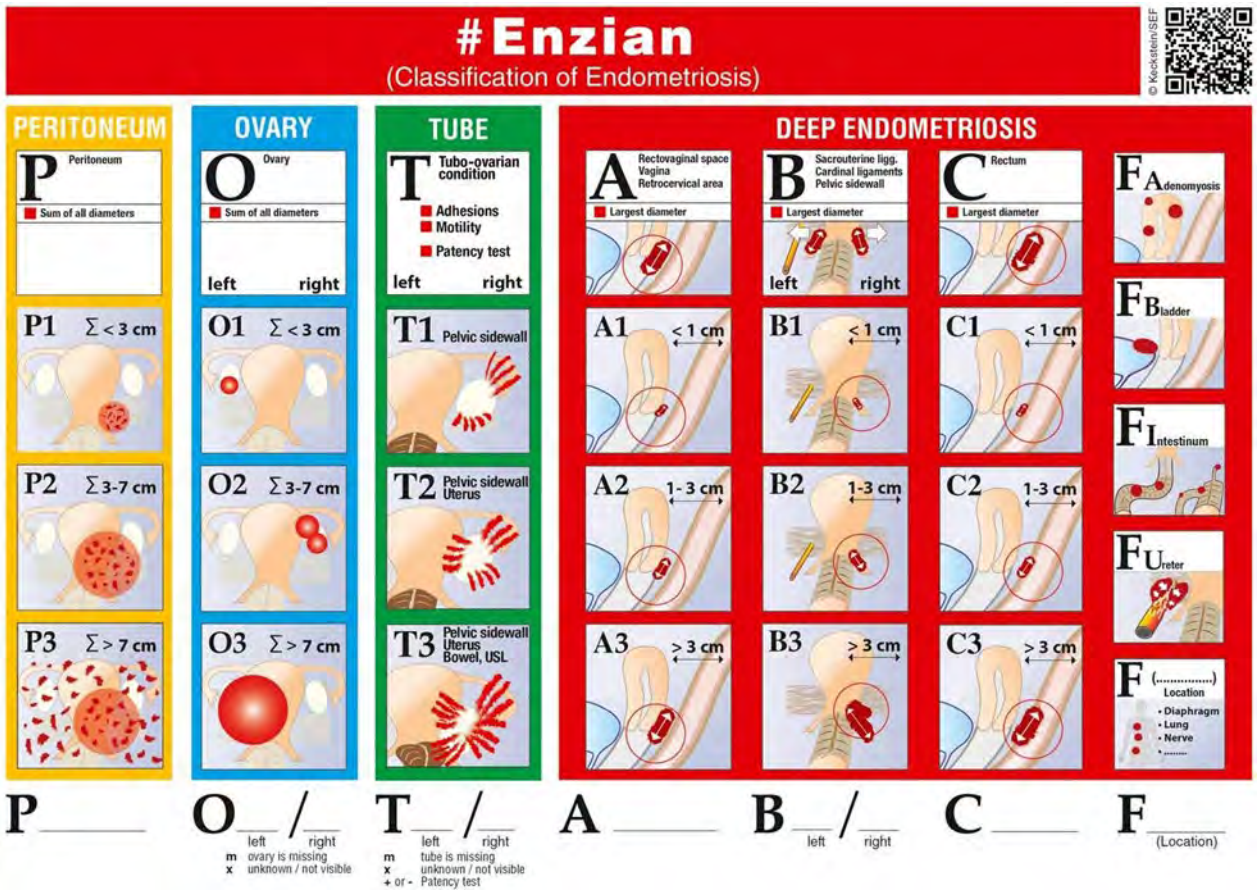

Table 2: #ENZIAN score

Endometriosis surgery has of course improved over the 50 years of laparoscopic diagnosis and treatment. However, histologically, the lesion remains the same. While we all know the endoscopic endometriosis classification (EEC), which we published again in 2006 and again 2017 (6) which is in good accordance with the IFFS, rASRM classifications, the fertility index

(endometriosis fertility index [EFI]) and ESHRE classification, we use since 2012 the #Enzian classification [Figure 2]. EEC Stages3 and 4 are further detailed with the #Enzian classification. Recently in Human Reproduction, EQUSUM was published merging the three most frequently used Endometriosis classifications which are: American Society for Reproductive Medicine (rASRM), #Enzian and EFI (6 and 7).

Quality and Safety Issues in Endoscopic Surgery

Although minimally invasive endoscopic surgery was generally pioneered and popularized by gynecologists over the past decades, teaching institutions failed to inspire and invest in endoscopic education and research, with the same enthusiasm and dedication as our general surgical and other colleagues did. Given the prevailing political, educational, industrial, and societal realities while facing most advanced economies, we are destined to grapple with a protracted period of fiscal restraint, consumer demands, and societal expectations.

In Canada, with a relatively small health market (population 34,482,779 million), health expenditure in 2019 was expected to reach $265 billion, although health spending actually decreased in proportionate terms. It was anticipated that, overall, health spending represented 11.5% of Canada's gross domestic product. Thus, every country has to set a certain amount of money for health and health-related technology aside.

Future Aspects

Goals of Good Surgery are identical whether we perform laparotomy, laparoscopy, vNOTES (vaginal Natural Orifice Transluminal Surgery) or endoscopic conventional or robot assisted procedures, regardless of the angle, location, or means of access:

- Recognition of relevant pathology
- Possibility of radical treatment in endometriosis and cancer
- Minimal trauma, bleeding, and tissue laceration
- Adhesion prevention
- Preservation of urogenital tract in women of reproductive age
- Utilization of the best instruments (with as many degrees of liberty as possible, robotic transmission, etc.).

Let us continue along the path of minimal trauma, maximum vision and good tactile feeling to ensure optimal surgical success until times with protons or other magical bullets open up new options to treat pathologies. It is conceivable that within the near future, pre-operative early recognition of pathological conditions with contemporary imaging technologies – the merger of imaging and endoscopy has already occurred – and better molecular-genetic recognition of disease – the human genome has already been described – will automize or even make extensive radical surgical procedures unnecessary.

We are already experiencing the next generation of genetics and metabolomics (?). These fields will render extensive surgeries unnecessary in

the future and we will rely only on minimal invasive surgery which requires three fundamental components: Skilled surgeons or well programmed robotic automated procedures, depending on the input of technical data and measurement together with spontaneous machine recognition = artificial intelligence. Instruments and apparatuses are the key features that enable a skilled surgeon to perform optimal, precise, and indicated surgical procedures with minimal inflammation, adhesions, and complications.

Exchange of knowledge

Thanks to the ready exchange of knowledge between military institutions, aviation, space technology, informatics, engineering, mathematics, biology, genetics, and medicine as well as human dedication to disease exploration, technological advancements are no longer bound in one field. Journals are our present optimal exchange of ideas. Every written article needs special dedication and educates the writer at the same time.

Technical developments

Technological advances with improved endoscopic instruments for hemostasis and non-traumatic procedures as well as suturing skills allow us endless choices and possibilities. Precise, endoscopic, and robotic surgery, most likely preprogrammed with intraoperative imaging will be the only surgical tool in 2050.

Bloodless surgery with articulated and robotic instruments with multiple degrees of liberty and precision coagulation will be possible. Computer-assisted instruments tips will allow the surgeon to position the angles to the desired tissue planes and give tactile feedback.

Conclusion

It must be stressed that the history of laparoscopy and hysteroscopy and its introduction in the surgical practice is a story of many researchers, who for years battled against prevalent general thinking and partly against rejection of their brainchild of performing 'gentle operations.' Many of the pioneers were ignored, called dreamers or regarded as crazy. It is only through their persistence, their tenacity, their strong personalities and their intense dedication to life and love, that they could stand firm in the face of adversities. For India let us fully acknowledge the immense input of Shailesh Puntambekar (8) and Meenu Agarwal (9) of Pune, India.

The history of laparoscopy is a unique mixture of various trends in different fields, spurred by the activities of established societies as well as opportunities of their publication and influenced by the world's progress, recession, war, piece and the love of the individuals for life. The influence of industry, which has kept pace and actively supported this development for years, is the driving force besides the heroes of doctors and engineers that bring up new ideas. Without suitable technology, this dissemination would not have been possible. Endoscopic development and its future does depend on new inventions, on the audacity of leading heroes, their input into this field but also on their management of life to continue to survive on a healthy and successful cooperation with the medical technical industry and the governments of our countries which grant us the freedom of research and development for the best of all our patients.

Today laparoscopic and hysteroscopic surgery represent modern ways of surgery and are on the way to be the leading interventions with least trauma and good surgical outcomes. We have to be open for new technologies as robotic surgery,

which is together with artificial intelligence at present - after its 20 years of development - the trend of the time.

Robotic surgery is the most dynamic development in the sector of minimally invasive operations at the present time in 2024. It should not be viewed as an alternative to laparoscopy, but as the next step in a process of technological evolution. The advancement of robotic surgery, in terms of

the introduction of the Da Vinci Xi, and other robots on the surgical market, permits the variable use of optical devices in all four trocars. Due to the new geometry of the "patient cart," an operation can be performed in all spatial directions without re-docking. Longer instruments and the markedly narrower mechanical elements of the "patient cart" provide greater flexibility as well as access similar to those of traditional laparoscopy. Currently, robotic surgery is used for a variety of indications in the treatment of benign gynecological diseases as well as malignant ones. Interdisciplinary cooperation and cooperation over large geographical distances have been rendered possible by telemedicine, and will ensure comprehensive patient care in the future by highly specialized surgery teams. In addition, the second operation console and the operation simulator constitute a new dimension in advanced surgical training. The disadvantages of robotic surgery remain the high costs of acquisition and maintenance as well as the laborious training of medical personnel before they are confident with using the technology, but there are roads in vision to overcome that and let this surgery take over in laparoscopic surgical procedures as the leading technology.

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