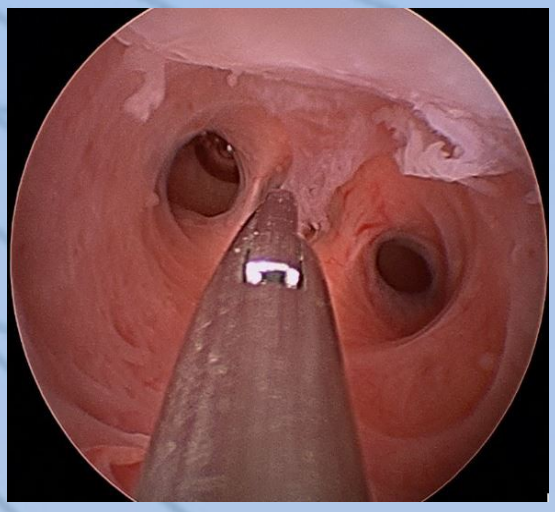
Hysteroscopy Newsletter



HYSTEROSCOPY Editorial teaM

Dear Friends and Colleagues,

It is my great pleasure to introduce this new issue of Hysteroscopy Newsletter, focused on Asherman syndrome and intrauterine adhesions.

I followed the project of Hysteroscopy Newsletter since the beginning, joining the Editorial Committee with other experts, and I am very glad to see its significant evolution: without any doubt, each new issue collects very important pieces of evidence-based information about different topics of hysteroscopy, with clear and rigorous guides for the clinical practice.

Interestingly, also the topic of this new issue underwent radical changes in the recent past. Indeed, we did giant step forwards to improve our knowledge of the etiology and etiopathogenesis of Asherman syndrome, even adding to the puzzle important elements from the molecular and cellular points of view.

In addition, the availability of modern 2D and 3D ultrasound, together with the potential use of fluoroscopy, allowed a paradigm shift for a precise diagnosis of intrauterine adhesions before hysteroscopic management.

Finally, the opportunity offered by new hysteroscopic devices opened new scenarios for the treatment of this condition, although we should always keep in mind that less energy we use, better outcomes we may obtain.

As reproductive surgeons dealing mainly with infertile women, I acknowledge also the promising preliminary data about hysteroscopic-guided platelet-rich plasma injection, as potential novel treatment when the endometrium is refractory to hormonal stimuli after hysteroscopic adhesiolysis.

In summary, much more work is yet to be done in the field, but I am quite sure that our group of worldwide recognized hysteroscopists will achieve significant advancements in the next future, due to a fine-tuned ability to see over the horizon of common clinical practice.

Ad maiora!

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If you are interested in sharing your cases or have a hysteroscopy image that you consider unique and want to share, send it to hysteronews@gmail.com

Etiopathogenesis of Asherman's Syndrome

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INTRODUCTION

Intrauterine adhesions are bands of fibrous tissue that occur inside the endometrial cavity frequently in response to endometrial injury. The severity of this condition can range from thin strings of filmy tissue to complete obliteration of the cavity with subsequent amenorrhea and infertility among other clinical devastating consequences. Clinical challenges include primary prevention of adhesions and prevention of recurrent adhesions after surgical treatment. In this chapter, will provide an overview of the ethiopathogenesis of intrauterine adhesions.

ETIOLOGY

The most common cause of Asherman Syndrome is trauma to the endometrium. This can be the result of a dilation and curettage (D&C) for spontaneous abortion or termination of pregnancy, a molar pregnancy, or a curettage in the postpartum period. Due to this knowledge, the rate of medical abortions to avoid surgical manipulation has risen in some parts of the world (1) . In a study of 1856 cases examined by Schenker and Maralioth, pregnancy was the predominant risk factor, and 66.7% of Asherman cases occurred after post-abortion/miscarriage curettage, 21.5% after postpartum curettage, 2% after cesarean section (2), and .6% after evacuation of hydatiform mole (3). Rare cases of IUAs have been seen in c-sections even after the use of B-lynch procedure in the event of postpartum hemorrhage.

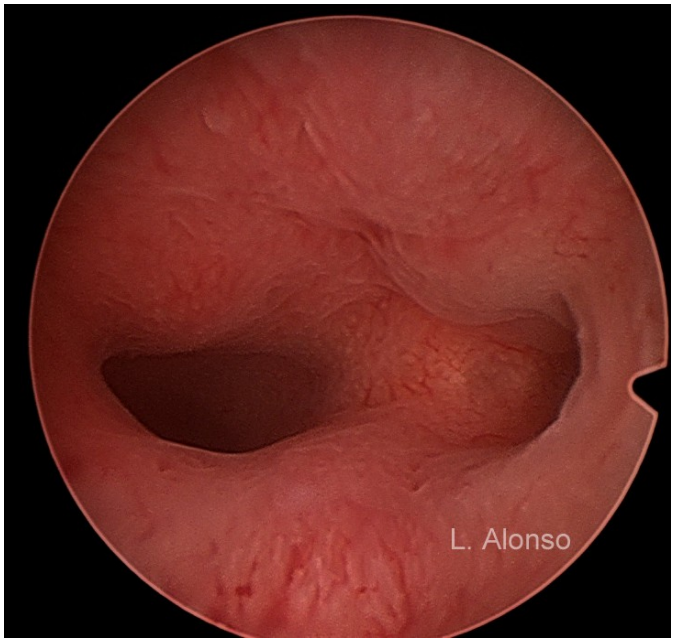
It remains unknown why pregnancy has a high risk of Asherman's. One of the theories is the low estrogen status of the patient before and after the procedure does not allow for adequate growth and stimulation of the endometrium (4).

Another possible reason for the higher risk brought by pregnancy is that the uterus may be in a more vulnerable state after pregnancy, thus causing the basal layer of the endometrium to be more easily damaged by trauma (4). This is supported by the observation that a large percentage of patients with Asherman report prior instrumentation after pregnancy. Studies show that the risk of adhesion development is higher when the procedure is performed in the 2nd thru fourth postpartum weeks (21.5-40%), and the risk is actually lower if endometrial manipulation is performed within 48 hours (2). One of the theories of increased adhesion formation in post-abortion D&Cs is that the placental remnants can encourage fibroblastic activity and collagen formation, causing adhesions before the endometrium can regenerate (3).

Patients who are not pregnant may also experience Asherman syndrome due to manipulation of the uterus or endometrium. As reported by Yu et al, Asherman Syndrome was seen after diagnostic curettage (1.3%), hysteroscopic resection of uterine septum (6.7%),hysteroscopic myomectomy (31-45%), abdominal myomectomy, insertion of IUD (.2%), and even after uterine artery embolization (1).

Asherman's is also seen after endometrial ablation (36.4%). This is logical as the ablation destroys the basal layer of the endometrium in order to prevent the regrowth of endometrium. Unlike in the above cases where patients may desire future fertility, the majority of individuals undergoing endometrial ablation do not wish to maintain childbearing ability. The rate of IUAs after ablation may be even higher as these patients will not come with a complaint of a decrease in menstrual flow as decreased menses is an expected effect of endometrial ablation.

Infection has also been proposed as a cause of Asherman's syndrome. The method by which infection can cause this is still hotly debated. In a report of 171 patients who underwent cesarean section, 28 developed endometritis; however, post-operative hysterosalpingogram (HSG) demonstrated no difference in intrauterine adhesions between the endometritis group and the rest of the group (4).



Despite being a rare etiology in the United States, genital tuberculosis has been identified as a more common and concerning cause of IUAs in developing countries such as India. In these patients, the uterine cavity is totally obliterated, and the endometrium is destroyed. These patients go on to experience amenorrhea and infertility (4). The damage caused by genital TB is so severe that attempts to repair the endometrial cavity are often futile (2).

Along with the above causes, another possible cause or risk factor for Asherman's is congenital anomalies of the uterus, specifically a septate uterus (4). No studies have been done to determine whether the anomaly was the cause of Asherman's. It is thought that the uterine anomaly places the patient at risk for multiple hysteroscopic procedures, thus placing the patient at higher risk of developing adhesions (4). Lastly, reports of Asherman's syndrome after pelvic radiation have also been reported (5).

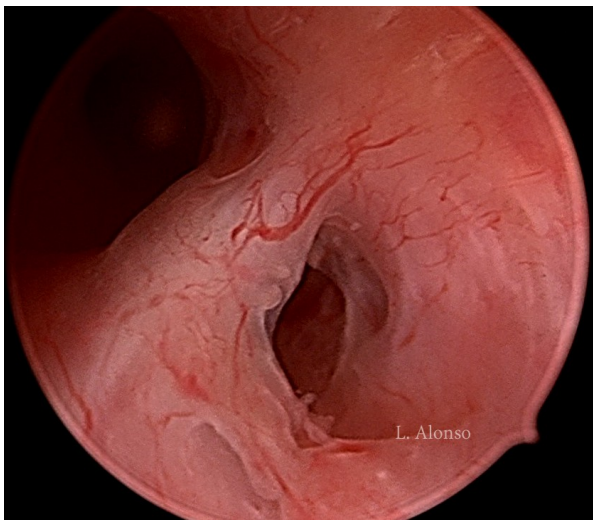
Risk Factors	Frequency
Miscarriage curettage	66.7% (1237/1856)
Postpartum curettage	21.5% (400/1856)
Caesarean section	2% (38/1856)
Trophoblastic disease evacuation	0.6% (11/1856)
Mullerian duct malformation	16% (7/43)
Infection (Genital tuberculosis)	4% (74/1856)
Diagnostic curettage	1.6% (30/1856)
Abdominal myomectomy	1.3% (24/1856)
Uterine artery embolization	14% (7/51)
Hysteroscopic surgery: Metroplasty	6% (1/15)

PATHOGENESIS

After trauma or the above mentioned causes of Asherman occur, the basal layer of the endometrium is damaged and becomes fibrosed, and the stroma is exchanged for fibrous tissue (5). Unfortunately, the molecular mechanisms regulating the pathogenesis of adhesions is not known at this time (4).

Changes at the cellular level occur, with the endometrium transforming to an inactive cubo-columnar epithelial layer (4). The distinction between the basal layer and the functional layer becomes nonexistent, and there is no longer a differentiation between the functional and basal layer of the endometrium as the functional layer is replaced by an inactive avascular layer in which fibrous synechiae forms across the cavity. The fibrotic synechiae disrupt the entire cavity, and on relook hysteroscopy, stromal calcifications and ossification are seen (2). The new fibrous layer of tissue is not responsive to hormone stimulation (4). The fibrous adhesions exhibit dense connective tissue and demonstrate no endometrial lining in comparison to the surrounding endometrium.

At the histological level, when full-thickness myometrial biopsies were taken, it was found that the uterine wall was 50-80% fibrous tissue in comparison to 13-20% of control subjects (4). In addition, Asherman's has also been noted with deep adenomyosis (1). With such a large amount of the endometrium being replaced by fibrous adhesions, it is thought that the myometrial activity is thus decreased, and the perfusion of hormones is inhibited as well.



Common cytokines known to be involved in the pathogenesis of adhesions include TGF-β, TNF-, IL-1, and IL-18 . Their exact role is yet to be determined. In a study by Wang et al, it was noted that NF-kB was significantly elevated in the endometrium of patients with Asherman's. NF-kB is a transcription factor that promotes the expression of IUA inflammatory markers and is seen as a major component of inflammatory disease (7). More studies are planned by this group to further determine the possible clinical role of NF-kB

Another possible cause for the pathogenesis of adhesions includes the cytokines b-fibroblast growth factor, platelet derived growth factor and transforming growth factor type 1 (6). Further work must be done to confirm their role in Asherman's as well.

Lastly, it has been hypothesized that there is a genetic component in the formation of IUAs, however, there is scant evidence of what genetic factors may be involved (6). Moving forward, several studies will be performed so that a better understanding of Asherman's is obtained, which may help physicians with treatment and prevention of this devastating pathology.

REFERENCES

1- Dreisler E, Kjer JJ. Asherman's syndrome: current perspectives on diagnosis and management. Int J Womens Health. 2019;11:191-8.

2- Malhotra N, Bahadur A, Kalaivani M, Mittal S. Changes in endometrial receptivity in women with Asherman's syndrome undergoing hysteroscopic adhesiolysis. Arch Gynecol Obstet. 2012;286(2):525-30.

3- Schenker JG. Etiology of and therapeutic approach to synechia uteri. Eur J Obstet Gynecol Reprod Biol. 1996;65(1):109-13.

4- Yu D, Wong YM, Cheong Y, Xia E, Li TC. Asherman syndrome--one century later. Fertil Steril. 2008;89(4):759-79.

5- Salazar CA, Isaacson K, Morris S. A comprehensive review of Asherman's syndrome: causes, symptoms and treatment options. Curr Opin Obstet Gynecol. 2017;29(4):249-56.

6- Conforti A, Alviggi C, Mollo A, De Placido G, Magos A. The management of Asherman syndrome: a review of literature. Reprod Biol Endocrinol. 2013;11:118.

7- Wang X, Ma N, Sun Q, Huang C, Liu Y, Luo X. Elevated NF-kappaB signaling in Asherman syndrome patients and animal models. Oncotarget. 2017;8(9):15399-406.

IUA Classification Systems

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INTRODUCTION

Different diagnostic modalities have been used for Intrauterine Adhesions (IUA) such as Hysterosalpingography (HSG), transvaginal USG, 3D USG, sonohysterography (SHG), MRI and Hysteroscopy. Hysteroscopy is presently the gold standard diagnostic and therapeutic modality for the IUAs.

Classification	Year	Summary of classification
Toaff and Ballas	1978	Classifies the IUAs into four grades based on HSG findings to determine the impact of the extent of IUA as well as their location in the uterus on the menstrual pattern of patients
March	1978	IUA were classified as minimal, moderate, or severe based on hysteroscopic assessment of the degree of uterine cavity involvement
Hamou	1983	IUAs were classified as isthmic, marginal, central, or severe based on hysteroscopic assessment
Valle	1988	IUAs were classified as mild, moderate or severe based on hysteroscopic assessment and extent of occlusion (partial or total) at HSG
American Fertility Society	1988	Complex scoring system of mild, moderate and severe IUAs based on extent of endometrial cavity obliteration, appearance of adhesions, and patient menstrual characteristics based on hysteroscopy or HSG assessment
European Society for Hysteroscopy	1989	Complex system classifies IUAs as grades I through IV with several subtypes based on a combination of hysteroscopic and HSG findings and clinical symptoms
Donnez and Nisolle	1994	IUAs were classified into six grades based on their location determined by hysteroscopy or HSG and postoperative pregnancy rate being the primary clinical outcome
Nasr	2000	Complex system generating a prognostic score by incorporating menstrual and obstetric history with findings at hysteroscopic assessment
MEC	2016	Simple and easy to use system dividing AS into mild, moderate, and severe grade based on the extent of uterine involvement at hysteroscopy

1- Toaff and Ballas classification (1978)

They were the first to classify AS in 1978 [1]. This classification was based on HSG and degree of menstrual disturbance.

-Grade 1: a single, small, filling defect within the uterine cavity, occupying up to about one-tenth (1/10) of the uterine cavity.

-Grade 2: a single, medium-sized filling defect occupying one-fifth (1/5) of the uterine cavity, or several smaller defects adding up to the same degree of involvement, located within the uterine cavity, whose outline may show minor indentations but no gross deformation.

-Grade 3: a single, large or several smaller, filling defects involving up to about one-third (1/3) of the uterine cavity, which is distorted or asymmetrical due to marginal adhesions.

-Grade 4: large-sized filling defects occupying most of the severely deformed uterine cavity.

The authors correlated above radiographic findings with the degree of menstrual dysfunction and graded as follows:

+: slight, but noticeable reduction in quantity and duration of the menstrual flow.
++: reduction in menstrual flow quantity and duration to half of the usual flow.
+++: scant menstrual flow for 1 or 2 d followed by brown spotting
++++: only brown spotting for 1 or 2 d

2- March Classification (1978)

Classification	Involvement
Severe	>3/4 of the uterine cavity involved, agglutination of walls or thick bands, tubal ostium areas, and upper cavity occluded -
Moderate	1/4–3/4 of the uterine cavity involved, no agglutination of walls- adhesions only, tubal ostium areas and upper fundus only partially occluded
Minimal	<1/4 of the uterine cavity involved, thin or filmy adhesions, tubal ostium areas, and upper fundus minimally involved or clear

March classification. March et al. in 1978 were the first ones to categorize IUAs based on hysteroscopic findings into minimal, moderate, and severe. The criteria used to grade the severity of AS was extent of adhesions present in the endometrial cavity and the degree of its occlusion.

This classification system is still used because it is simple to use and easy to remember. However, the shortcoming of this classification system is that there is no correlation with clinical symptoms and the post-treatment success was not defined [2].

3- Hamou Classification (1983)

Location of the adhesions	Isthmic Marginal Central
Size of the adhesions	<1 cm2 >1 cm2
Type of adhesions	Endometrial adhesions Fibrous/ connective tissue adhesions Myometrial adhesions

In 1983, Hamou et al. also included the extent and histologic nature of the adhesions as well as the evaluation of the surrounding glandular endometrium along with the degree of cavity distortion [3].

The **three types** of adhesions described in his study are as follows:

-Endometrial adhesions: white, vascularization similar to the surrounding endometrium

-Fibrous or connective tissue adhesions: transparent, bridge-like and poorly vascularized

-Myometrial adhesions: highly vascular and extensive adhesions

4- Valle Classification (1988)

Type of adhesion	Mild Moderate Severe
Extent of uterine cavity occlusion	Partial Total

The types of adhesions identified were as follows:

- **Mild:** filmy adhesions, composed of endometrial tissue causing partial or complete endometrial cavity occlusion.
- **Moderate:** fibromuscular adhesions, made up of endometrium causing partial or total occlusion of the endometrial cavity, can bleed on adhesiolysis.

- **Severe:** dense connective tissue adhesions, lack endometrial tissue and causing partial or total occlusion of the endometrial cavity, not likely to bleed on adhesiolysis.

In an attempt to reduce the shortcomings of the previous classification systems, in 1988, Valle et al. suggested that success of treatment, identified by improvement in menstrual pattern, and reproductive outcomes, also had to be correlated with the severity of disease. This classification system thus included both the extent of endometrial cavity involvement as well as the type of adhesions [4].

5- Donnez Classification (1994)

Degree	Location	
I	**Central adhesion** a. Thin filmy adhesion (endometrial adhesions) a. Myofibrous (connective adhesions)	
II	**Marginal adhesions** (always myofibrous or connective) a. Wedge like projection a. Obliteration of one horn	
III	**Uterine cavity absent on HSG** a. Occlusion of the internal os (upper cavity normal) a. Extensive coaptation of the uterine walls (absence of the uterine cavity, true Asherman's syndrome)	

Donnez and Nisolle classification. In 1994, Donnez and Nisolle re-emphasized the importance of using HSG in the classification of AS along with hysteroscopic finding and proposed a classification system based on both modalities. They broadly divided AS into three groups and six subgroups depending on the type of adhesion and the extent of uterine involvement as described in the table [5].

6- American Fertility Society Classification (1988)

The AFS introduced a comprehensive classification system that became the most widely accepted IUAs classification system across the globe. It included the clinical symptoms (menstrual pattern) as an indicator of disease severity, which was considered important as it gives an estimate

Extent of cavity involved	<1/3 **1 point**	<1/3–2/3 **2 points**	>2/3 **4 points**
Type of adhesions	Flimsy **1 point**	Filmy & Dense **2 points**	Dense **4 points**
Menstrual pattern	Normal **0 points**	Decreased **2 points**	Amenorrhoea **4 points**
Prognostic classification: HSG score			
Stage I (Mild)		1–4	
Stage II (Moderate)		5–8	
Stage III (Severe)		9–12	

about the amount of endometrium which was available for potential regeneration post-adhesiolysis and serves as an important marker for defining the prognosis post-treatment, thus helping in pre-treatment patient counselling. Scoring points (1–3) were given to each of the included characteristics and staging of AS was done (stage I/II/III: mild/moderate/severe) according to the score obtained. Additionally, a prognostic score to each patient was for the first time assigned by a classification system and hence it became a more objective way of classification [6].

7- European Society of Hysteroscopy Classification (1989)

Grade	Extent of intrauterine adhesion
I	Thin or filmy adhesion The adhesions are easily broken using only the hysteroscope sheath The cornual areas are normal
II	Single firm adhesion Connecting separate parts of the uterine cavity Visualization of each tubal ostium is possible Cannot be broken by hysteroscope sheath alone
IIa	Occluding adhesions only in the region of internal cervical os The upper uterine cavity normal
III	Multiple firm adhesions Connecting separate parts of the uterine cavity Unilateral obliteration of tubal ostium areas
IIIa	Extensive scarring of the uterine cavity with amenorrhea or decreased menstrual flow
IIIb	Combination of III and IIIa
IV	Extensive firm adhesions with agglutination of the uterine walls At least both tubal ostium areas are occluded

Another classification system was proposed by the European Society of Hysteroscopy (ESH) in 1989, incorporating the menstrual pattern of women with AS. However, the reproductive outcome of patients, which is one of the important aspects in cases of AS, was not included. Another disadvantage of this classification system was that, despite it being a very comprehensive system for

grading, its complexity makes it difficult to remember and use in clinical practice, thus limiting its utility [7].

7- Nasr Classification (2000)

Hysteroscopic findings	Scoring
Isthmic fibrosis	2
Filmy adhesions few excessive (i.e.,1/2 of the cavity)	 1 2
Dense adhesions single band multiple bands (i.e. .1/2 of the cavity)	 2 4
Tubal ostium both visualized only one visualized both not visualized	 0 2 4
Tubular cavity (glove finger appearance) (sound less than 6)	10
Menstrual pattern Normal Hypomenorrhea Amenorrhea	 0 4 8
Reproductive performance Good obstetric history Recurrent pregnancy loss Infertility	 0 2 4

Scoring	
Score of 0–4	Mild →Good prognosis
Score of 5–10	Moderate → Fair prognosis
Score of 11–22	Severe → Poor prognosis

Nasr classification. Nasr et al. (2000) described a very comprehensive scoring system including the clinical symptoms (both menstrual pattern and reproductive outcomes) of the patients and the hysteroscopic findings along with providing a prognostic correlation.

This system gives greater emphasis on the type of adhesions and the ability to visualize the tubal ostium over the involvement of the rest of the endometrial cavity.

Adhesions were pathologically classified into three categories: filmy/dense/tubular. The latter, which is the most severe form of the disease, indicates dense adhesions obliterating the entire uterine cavity, thereby obscuring both the tubal ostia. Isthmic fibrosis was identified as a separate entity and was given special importance as it could initiate a neuroendocrine reflex and cause endometrial deactivation and amenorrhea even when the rest of the cavity is free of adhesions [8].

8- MEC Classification (2016)

MEC classification. In 2016, the Manchanda's Endoscopic Centre (MEC) classification system

Grade	Category	Characteristics
Grade 1	Mild	Less than one-third of the uterine cavity is obliterated (filmy/dense adhesions)
Grade 2	Moderate	1/3–2/3 of the uterine cavity obliterated (filmy/dense adhesions)
Grade 3	Severe	More than two-thirds of the uterine cavity obliterated (filmy/dense adhesions)

was proposed in India, which categorized AS as mild, moderate, and severe disease owing to the extent of the endometrial cavity involvement. It encompasses both dense and flimsy adhesions in all categories. Its advantage is of being relatively simple and easy to use in clinical practice [9].

The reproductive outcomes based on this classification system were correlated with the severity of the adhesions in a retrospective analysis performed in 2018 by Sharma et al., who reported an increased number of live births after adhesiolysis in the moderate and severe categories of adhesions. [10]. The postoperative management protocols were governed and laid down by the severity of adhesions according to this classification system.

Conclusion

It is necessary to evaluate the extent of intra-uterine adhesions, in order to select the best treatment option in managing menstrual and infertility problems and analysing the postoperative success of adhesiolysis, hence classification systems are useful. Varied scoring systems are used to classify IUA, which are based on HSG, hysteroscopy, and hysteroscopic findings along with clinical data. HSG-based classifications have high false positive rate (39%) and it doesn't detect endometrial fibrosis and type and level of IUA, hence it's replaced by hysteroscopy.

By and large AFS classification is the most widely accepted among these scoring systems which is a clinic-hysteroscopic classification. Simple and easy to implement under clinical settings. MEC classification is the most recent classification system, which is hysteroscopy-based scoring system that has been developed in 2016 in India and is relatively simple, broad based and easy to implement under clinical settings.

A universally agreed upon classification system is needed to predict post-treatment reproductive outcomes according to the severity of the condition.

Diagnostic Methods in Asherman's Syndrome

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INTRODUCTION

Intrauterine adhesions were originally described by Friesch in 1894, but it was in 1948 when Joseph Asherman defined the association between structural amenorrhea and endometrial adhesions, publishing in 1950 a scientific article with the definition: "Traumatic intrauterine adhesions".

Asherman's syndrome represents the association between traumatic adhesions and amenorrhea and infertility, although the term has often been used to describe only the presence of intrauterine adhesions (UTI).

The common denominator for adhesions to occur is trauma to the basal layer of the endometrium. Although in most cases, this occurs after a uterine curettage, it has also been described less frequently after procedures such as laparotomic or hysteroscopic myomectomy, caesarean sections, difficult placental delivery, or metroplasties.

Beyond surgical causes, it is known that endometrial trauma can also be caused secondary to infection, pathogens that cause endometritis or endometrial tuberculosis, which can induce obliteration of the cervical canal and/or Fallopian tubes in more than 50% of cases.

The clinical manifestations are generally represented by decreased menstrual flow, amenorrhea, pelvic pain secondary to retrograde menstruation or hematometra, and poor reproductive outcomes, such as infertility or recurrent abortions.

The incidence of the syndrome remains unclear, estimates range from 6 to 40% after curettage. The prevalence of endometrial adhesions in women with fertility problems varies from 2.8% to 45.5% depending on the subpopulation.

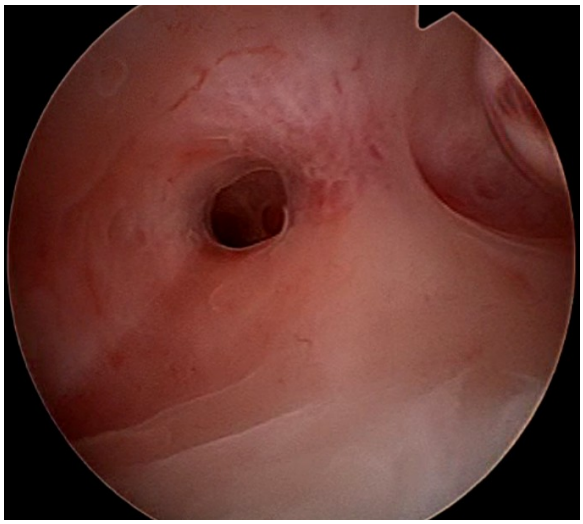
Different classification systems for this pathology have been proposed. The European Society of Hysteroscopy (ESH) considers according to the thickness of the adhesion, the degree of obliteration or compromise of the cavity and the tubal patency. However, the most commonly used system is the one proposed by the American Society for Reproductive Medicine (ASRM), which also includes menstrual bleeding.

The obstetric or surgical history and the current symptoms of the patient can lead to a clear diagnosis, especially in the group of patients studied for infertility. But it is essential to confirm this suspicion.

Once the diagnosis is made, it is important to determine the extent of the condition, in order to be able to propose the best therapeutic strategy. Treatment remains hysteroscopic lysis of adhesions. The comprehensive therapeutic goal not only involves restoring the intrauterine anatomy and potentially its physiology, but also to prevent its recurrence.

HYSTEROSCOPY

Diagnostic hysteroscopy is considered the gold standard for the diagnosis of intrauterine adhesions, since it allows to diagnose and classify them; determining the type of adhesions and the



degree of compromise of the cavity; as well as the treatment in the same intervention. However, office hysteroscopy is not available in all settings and performing an intervention under anesthesia as a first measure can be invasive.

Also, hysteroscopy is not without complications, especially when severe disease is present, in which case, the risk of complications such as uterine perforation is greater, when the possibility of accessing the uterine cavity becomes difficult or impossible as a result of obliteration of the lower uterine segment.

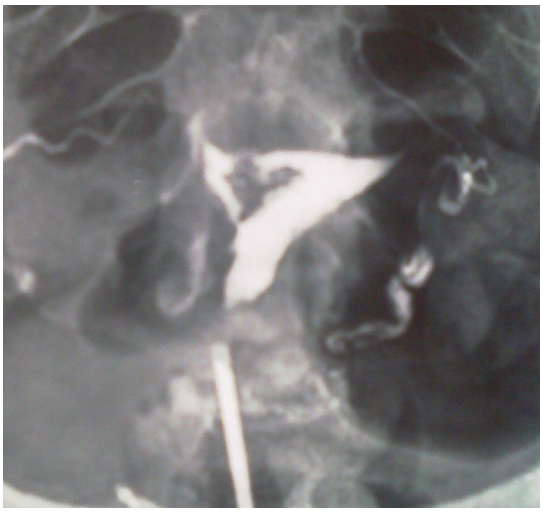
Diagnostic imaging methods are extremely useful in order to avoid undesired surgical risks and to establish an adequate therapeutic strategy for each particular case.

HYSTEROSALPINGOGRAPHY

Historically, hysterosalpingography (HSG) has represented the most widespread diagnostic tool for the detection of intrauterine adhesions. It is a widely used method to evaluate tubal patency in women with infertility. Intrauterine adhesions are represented by focal fill defects, such as homogeneous opacity surrounded by well-defined borders that do not vary with position.

In cases of greater involvement, the uterine cavity appears completely distorted and narrowed, and ostial occlusion may also be evident, as long as the cervical involvement does not prevent the possibility of performing the study.

This group of patients may be more prone to pain during injection of contrast due to poor uterine cavity compliance.



The result of the Soares study. et al. revealed that HSG had a sensitivity of 75% in the detection of intrauterine adhesions and positive predictive values (PPV) of 50%.

2D TRANSVAGINAL ULTRASOUND

Conventional transvaginal ultrasound is relatively inexpensive and is usually an available tool, frequently being the first-line study for endometrial evaluation.

The characteristic signs of suspicion are determined by the finding of hyperechoic areas within the endometrium. However, the sensitivity and specificity of 2D-TVUS for the detection of adhesions are not great (52% and 11%) thus, limiting its clinical use.

TRANSVAGINAL 3D ULTRASOUND

Three-dimensional transvaginal ultrasound (3D-TVUS) has been accepted as a non-invasive way of providing accurate information about the uterine cavity.

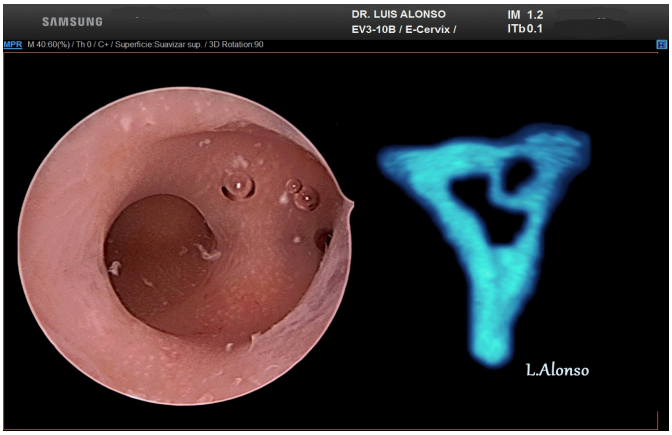
The possibility of multiplanar analysis, in which the three orthogonal exploration planes are simultaneously visualized, and better access to the coronal plane offer the advantage of being able to explore views that cannot be visualized with 2D ultrasound.

3D ultrasound can provide detailed information about the uterine cavity to more accurately determine the degree of endometrial involvement; since it offers the possibility of having images that show the relationship between myometrium and the endometrium, they allow to evaluate the cornual regions with greater precision and to visualize the cervical canal from the coronal plane. The possibility of evaluating the advantages of intraoperative ultrasound assistance has been raised, but this would not only lengthen surgical times but would also lead to a lower capacity for analysis.

In contrast, endometrial evaluation during the middle menstrual phase would allow a better analysis of the situation, in order to maximize surgical success and minimize complications.

A prospective study by Brujoo et al., which included 362 patients, with a hysteroscopic diagnosis of intrauterine adhesions, has shown that the preoperative evaluation of transvaginal 3D ultrasound was of great help to hysteroscopists in making intraoperative decisions during the performance of hysteroscopic adhesiolysis, achieving better surgical success rates, represented by restoring the morphology of the uterine cavity and reducing surgical risks.

Knopman et al. successfully reported the ability of 3D-TVUS to classify the severity of IUA, evaluating percentages of cervical tract and cavity obstructions. They reported that the sensitivity of identifying IUA by 3D-TVUS was 100%, while the sensitivity by HSG was only 66.7%.



A case series, Cohen, et al. studied 54 women with a primary diagnosis of Asherman's syndrome and compared 3D ultrasound with HSG to assess the accuracy of their diagnosis. Sensitivity was calculated using hysteroscopy as the gold standard. 100% of preoperative 3D images were found to be consistent with hysteroscopy results to assess disease severity, compared to 66.7% for HSG.

In another study published by the Taiwanese Association of Gynecology and Obstetrics, they attempted to classify the findings of adhesions diagnosed by 3D ultrasound by evaluating their hysteroscopic correlation, finding similar results. Another study evaluated 3D-TVUS, in combination with intrauterine saline infusion and 3D Doppler (3-DPD), finding sensitivity and specificity of 91.1% and 98.8%, respectively for all types of intrauterine lesions, including synechiae.

All these preliminary results show diagnostic capabilities comparable in efficacy with diagnostic hysteroscopy.

NUCLEAR MAGNETIC RESONANCE (MRI)

Magnetic resonance imaging has been considered as a supplementary diagnostic alternative, especially when adhesion involves the endocervix. Adhesions are visualized as low intensity images on T2.

CONCLUSIONS

Although the gold standard for the diagnosis of IUA continues to be hysteroscopy, today 3D ultrasound allows each case to be previously evaluated to obtain better therapeutic results and lower surgical complications rate.

These benefits are greater in more complex cases where HSG or diagnostic hysteroscopy are technically relegated by the lack of permeability of the cervical canal.

3D ultrasound can provide useful information on the location and degree of involvement.
The continuous improvement in the definition of the equipment and greater availability of this technology could make 3D-TVUS a key tool in the approach to this pathology.

REFERENCES

1- Burjoo A, Zhao X, Zou L, et al. The role of preoperative 3D-ultrasound in intraoperative judgement for hysteroscopic adhesiolysis. Ann Transl Med 2020;8:55.
2- Dreisler E, Kjer JJ. Asherman's syndrome: current perspectives on diagnosis and management. Int J Womens Health 2019;11:191-8_._ _
3- Gilman AR, Dewar KM, Rhone SA, et al. Intrauterine Adhesions Following Miscarriage: Look and Learn. J Obstet Gynaecol Can 2016;38:453-7.
4- Carugno J, Laganà AS, Vitale SG. Use of 3D ultrasound in the hysteroscopic management of Asherman syndrome. Ann Transl Med 2020;8(14):847. doi: 10.21037/ atm.2020.04.18
5- Soares SR, Dos Reis MMBB, Camargos AF. Diagnostic accuracy of sonohyster- ography, transvaginal sonography, and hysterosalpingography in patients with uterine cavity diseases. Fertil Steril 2000;73:406e11.
6- Worldwide AAMIG. AAGL practice report: practice guidelines for management of intrauterine synechiae. J Minim Invasive Gynecol 2010;17:1-7.
7- Bacelar AC, Wilcock D, Powell M, Worthington BS. e value of MRI in the assessment of traumatic intra–uterine adhesions (Asherman's syndrome) *Clin Radiol* 1995; 50: 803.
8- Cohen J, Copperman AB. e value of 3D ultrasound the diagnosis and treatment of Asherman's syndrome. *Fertil Steril* 2005; 84: S464.
9- Knopman J, Copperman AB. Value of 3D ultrasound in the management of suspected Asherman's syndrome. J Reprod Med 2007;52:1016e22.

Asherman Syndrome: Hysteroscopic Treatment

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Nigeria

INTRODUCTION

Asherman's syndrome (AS) is an acquired uterine condition that describes the occurrence of intrauterine adhesions (IUA) in association with symptoms related to menstrual irregularities, recurrent pregnancy loss, and infertility (1). The terms AS and IUA are often used interchangeably. While AS is said to be a rare entity in industrialized societies, the same cannot be said in developing countries, especially those with highly restrictive abortion laws, where it is a common indication for operative hysteroscopy (2).

The first recorded treatment of IUA was by Henrich Fritsch in 1894 (3). Intrauterine adhesions were traditionally managed by blind adhesiolysis. This did not allow for proper visualization of the adhesions and was associated with an increased risk of uterine perforation (4,5). Hysteroscopy is now considered the gold standard technique for the treatment of AS. The use of hysteroscopy for the treatment of Asherman's syndrome was first reported in the seventies (6-8). In 1978, Sugimoto described the findings of IUA in 192 women who underwent diagnostic hysteroscopy. Following hysteroscopic treatment, 74.5% (143) of them recovered previous menstrual flow (9).

Hysteroscopy offers a direct view of the adhesions as shown in figures 1 and 2, allowing for classification and subsequent precise breakdown of the adhesions (10).

AIMS OF HYSTEROSCOPIC TREATMENT

-Hysteroscopy aims to restore the anatomical shape and capacity of the uterine cavity.

- It aims to restore normal menstruation.

- Hysteroscopy also aims to ensure the normal continuity between the cervical canal, endometrial cavity, and tubal Ostia, thereby aiming to restore fertility.

EQUIPMENT FOR HYSTEROSCOPIC ADHESIOLYSIS

The rigid, optical hysteroscope with fluid distension media is used for operative hysteroscopy. The 0- and 30-degree viewing angle telescopes are commonly used with an outer diameter sheath ranging from 3.5mm to 6.5mm (11).

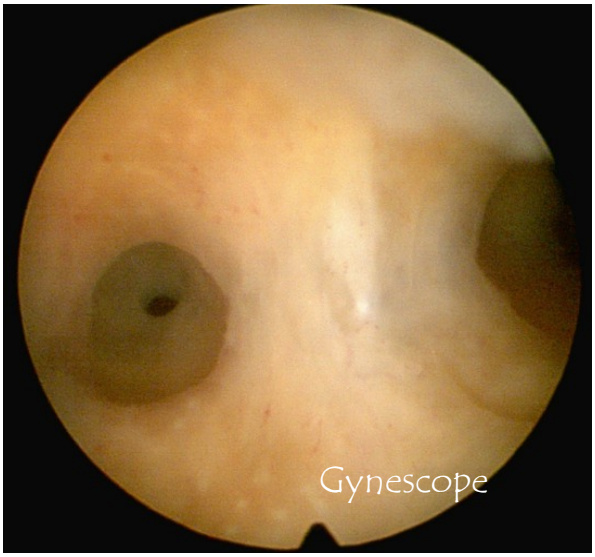

Figure 1

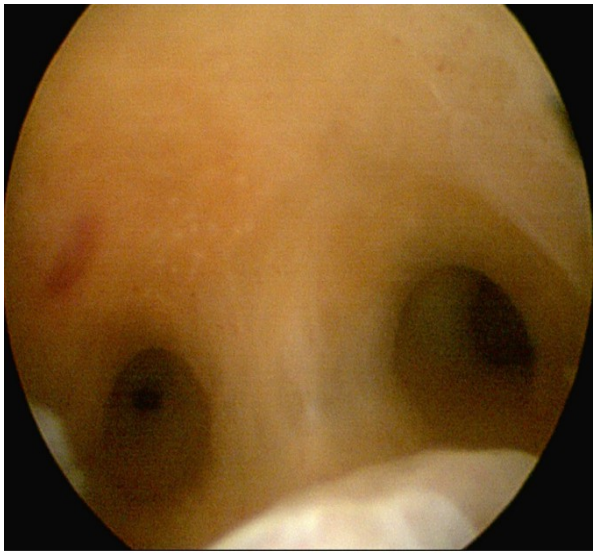

Figure 2

The choice between the use of hysteroscopy scissors (figure 3) or electrocautery is commonly at the discretion of the practitioner. Yang et al (12) in their recent meta-analysis of randomized controlled trials comparing cold scissors and electrocautery, concluded that cold scissors are more efficient in preventing IUA recurrence, increasing the menstrual flow, reducing intraoperative blood loss, and shortening the operating time than cautery.

The authors, working in an environment with highly restrictive abortion laws with considerably high unsafe abortion rates, have not had cause to use cautery in almost two decades and over 500 cases.

COMPARISON BETWEEN COLD SCISSORS AND ELECTROCAUTERY (1,11-13)

- Cautery would more likely cause damage to the endometrium compared with scissors, because of the extreme heat generated.

- If there is inadvertent uterine perforation, significant bowel or urinary bladder injury is more likely with cautery, particularly if activated.

- The cost of instrumentation is in favour of the cold scissors.

- Except in cases where a mini-resectoscope is used, the resectoscope generally requires more cervical dilatation.

- The use of cautery is associated with the ability to secure haemostasis, unlike cold scissors. However, intraoperative bleeding is generally not a significant problem due to the rapid flow of liquid which renders the operating field clear, coupled with postoperative uterine constrictions which occlude the bleeding blood vessels.

If electrocautery is chosen, monopolar or bipolar cautery can be used as both provide satisfactory results. Bipolar cautery however has the advantage that it is used with an electrolyte-containing fluid such as normal saline as distension medium. This has a better safety valve compared with non-electrolyte containing fluids such as 1.5% glycine, used with monopolar cautery.

Figure 3

The higher cost and possible damage to healthy endometrial tissue of laser vaporization using Nd-YAG (Neodynium-doped Yttrium aluminium garnet) and KTP (potassium-titanyl-phosphate) have limited its use for hysteroscopic adhesiolysis (14).

TECHNIQUE OF HYSTEROSCOPIC ADHESIOLYSIS

Hysteroscopic adhesiolysis is associated with a great risk of complications, especially uterine perforation (15). Mild to moderate cases can generally be managed on an outpatient basis without the need for anaesthesia while severe cases are managed in theatre under general or regional anaesthesia. The lead author however manages over 90% of cases (including the severe categories) in an office setting with the use of conscious sedation and intracervical block (2). The absence of nerve endings within the fibrous tissue means adhesiolysis can be performed with minimal pain.

In mild cases of IUA, pressure from the distension fluid might be enough to cause separation of the adhesions, others might be thin enough to be separated by the tip of the hysteroscopy sheath. Centrally placed adhesions are less vascularized and less dense compared with the laterally placed ones, they are therefore usually divided first. It is also prudent to separate distal adhesions first before the proximal (fundal) ones. While maintaining a clear vision at all times, care must be taken to search for possible routes into the uterine cavity. Dark areas that absorb more light might be indicative of an entrance into the

endometrial cavity and should be explored (11). It is also worth exploring any areas with the usual pinkish endometrial tissue or areas through which fluid can be observed being sucked into or emanating from.

The treatment of severe cases still poses a challenge. Numerous case reports describe ways in which gynaecologists have tried to manage severe cases of Asherman's syndrome. McComb and Wagner (16) described the management of six cases with severe Asherman, five of which had complete obliteration of the uterine cavity. Under laparoscopic guidance, the uterine wall was separated into two Hemi-cavities by inserting a 13 French Pratt cervical dilator. This resulted in the formation of a fibrotic septum that was eventually cut with hysteroscopy scissors up to the fundus. Unfortunately, there is high morbidity associated with the procedure (17).

In the myometrial scoring technique, following cervical dilatation with Hegar's size 12-18, six to eight 4mm deep incisions are made within the uterine cavity, from the fundus to the isthmus with the aid of a Collins knife electrode (18). The aim is to enlarge the uterine cavity hoping to uncover functional endometrium. An increase in menstrual bleeding was reported in all cases. In another report, a 16-gauge type Tuohy needle was introduced alongside a 5mm hysteroscope. This was used to probe areas beyond the adhesions. A contrast medium was then injected via the needle under fluoroscopic and laparoscopic control. Hidden pockets of endometrium were divided with hysteroscopy scissors. All 55 women treated with this technique regained menstrual function, albeit there was no report on fertility outcome (19).

In a case series involving seven women, one or two laminaria tents were introduced to dilate the cervix. These were replaced after 24 hours with three or four laminaria tents pushed up to the fundus and left for another 24 hours. Hysteroscopic adhesiolysis under laparoscopic guidance was finally performed. Improvement in menses was also reported in all seven women, with three pregnancies including a miscarriage and two live births (20).

CONCOMITANT USE OF ULTRASOUND SCAN, LAPAROSCOPY AND FLUOROSCOPY

Sharma et al (21) described the measurement of myometrial thickness at the fundal, anterior, and posterior walls that guide the amount and direction of hysteroscopic adhesiolysis and lateral metroplasty. None of the 21 women reported in the study who had preoperative ultrasound scan measurement of the endometrial thickness had perforation or false passage during hysteroscopic adhesiolysis.

Intraoperative transabdominal ultrasonography guides the telescope towards the uterine cavity. Laparoscopic guidance has the advantage of preventing further trauma to pelvic organs should a perforation occur. It also has the advantage of providing an opportunity to inspect the pelvis, diagnosing, and treating concurrent pathologies. Fluoroscopy-guided adhesiolysis has the advantage of delineating free areas above or behind the adhesions. Fluoroscopy can be performed simultaneously with hysteroscopy.

There are no data to suggest that all these adjuvant interventions prevent perforation or improve surgical outcomes. However, when used appropriately in selected patients, it may minimize the consequences should perforation occur (15).

PREVENTION OF ADHESION REFORMATION

Adhesion reformation is common following hysteroscopic adhesiolysis. Hanstede et al (22) found a 27.3% recurrence rate after hysteroscopic adhesiolysis with recurrence rates much higher in patients with severe disease. It is therefore important to institute measures that would reduce the chances of adhesion recurrence.

These measures include the use of the following:

- Intrauterine device
- Intrauterine Foley catheter
- Intrauterine balloon stent
- Intrauterine gel

This topic will be dealt with in a subsequent chapter.

CONCLUSION

Asherman syndrome remains a rare disease in most parts of the world. Hysteroscopic adhesiolysis is the gold standard in the diagnosis and treatment of AS. Cold hysteroscopy scissors are less likely to damage healthy endometrial tissue. Steps should be taken following hysteroscopic adhesiolysis to prevent adhesion recurrence.

REFERENCES

1- Okohue JE. Role of assisted operative hysteroscopy in Asherman's management. In: Manchanda R (ed.). Intrauterine adhesions, diagnostic and therapeutic insights. Springer Nature Ltd. Singapore. 2021; 123 – 135.

2- Okohue JE, Okohue JO. Establishing a Low-Budget Hysteroscopy Unit in a Resource-Poor Setting. Gynecol Minim Invasive Ther. 2020; 23;9(1):18-23.

3- Fritsch H. Ein Fall von volligen Schwund der Gebarmutterhohle nach Auskratzung. Zentralbl Gynaekol. 1894; 18: 1337 – 1342

4- Schenker JG, Marglioth EJ. Intra-uterine adhesions: an updated appraisal. Fertil Steril. 1982; 37:593 – 610.

5- Okohue JE. Adhesions and Abortion. In: Tinelli A, Alonso Pacheco L, Haimovitz S (eds). Hysteroscopy; Springer, Cham, 2018. .

6- Levine RU, Neuwirth RS. Simultaneous laparoscopy and hysteroscopy for intrauterine adhesions. Obstet Gynecol. 1973;42: 441 – 445.

7- Polishuk WZ, Sadovsky E. A syndrome of recurrent intrauterine adhesions. Am J Obstet Gynecol. 1975;123: 151 – 158.

8- March CM, Israel R. Intrauterine adhesions secondary to elective abortion. Hysteroscopic diagnosis and management. Obstet Gynecol. 1976;48(4):422.

9- Sugimoto O. Diagnostic and therapeutic hysteroscopy for traumatic intrauterine adhesions. Am J Obstet Gynecol. 1978;131: 539 – 547.

10- Conforti A, Alviggi C, Mollo A, De Placido G, Magos A. The management of Asherman syndrome: A review of the literature. Reprod Biol Endocrinol 2013; 11:118.

11- Emanuel MH, Hanstede M. Hysteroscopic treatment of Asherman syndrome. In: Tinelli A, Alonso Pacheco L, Haimovich S (eds). Hysteroscopy; Springer, Cham, 2018. 709 – 718

12- Yang L, Wang L, Chen Y, et al. Cold scissors versus electrosurgery for hysteroscopic adhesiolysis: A meta-analysis. Medicine (Baltimore). 2021; 100: 177 - 91

13- Dreisler E, Kjer JJ. Asherman's syndrome: Current perspectives on diagnoses and management. Int J Women's Health 2019; 1: 191 – 198.

14- Roge P, D'Ercole C, Cravello L, Boubli L, Blanc B. Hysteroscopic management of uterine synechiae: a series of 102 observations. Eur J Obstet Gynecol Reprod Biol 65: 189 – 193.

15- AAGL Elevating Gynecologic Surgery. AAGL practise report: practice guidelines on intrauterine adhesions developed in collaboration with the European Society of Gynecological Endoscopy (ESGE). Gynecol Surg. 2017;14(1): 6 .

16- McComb PF, Wagner BL. Simplified therapy for Asherman's syndrome. Fertil Steril 1997; 11: 1047-50.

17- Munro MG, Abbott JA, Bradley LD, Howard FM, Jacobs VR, Sokol Ai et al. AAGL practise report: Practice guideline for the management of intrauterine synechiae. J.Minim invasive Gynecol 2010; 17(1):1 - 7.

18- Protopapas A, Shushan A, Magos A. Myometrial scoring: a new technique for the management of Asherman's syndrome. Fertil Steril 1998; 69: 860 – 864.

19- Broome JD, Vancaillie TG. Fluoroscopically guided hysteroscopic division of adhesions in severe Asherman syndrome. Obstet Gynecol. 1999; 93(6): 1041 – 1043.

20- Chen FP, Soong YK, Hui YL. Successful treatment of severe uterine synechiae with transcervical resectoscope combined with laminaria text. Hum Reprod. 1997;12: 943 – 947.

21- Sharma R, Manchanda R, Chandil N. Revisiting diagnostic and therapeutic challenges in Asherman's syndrome: A retrospective analysis of 5 years Int J Cur Pes 2018;10(8):72429-34.

22- Hanstede MM, Van der Meij E, Goedemans L, Emmanuel MH. Results of centralised Asherman surgery 2003-2013). Fertil Steril 2015;104(6):1561 – 1568.

The Role of Fluoroscopy in the AS Treatment

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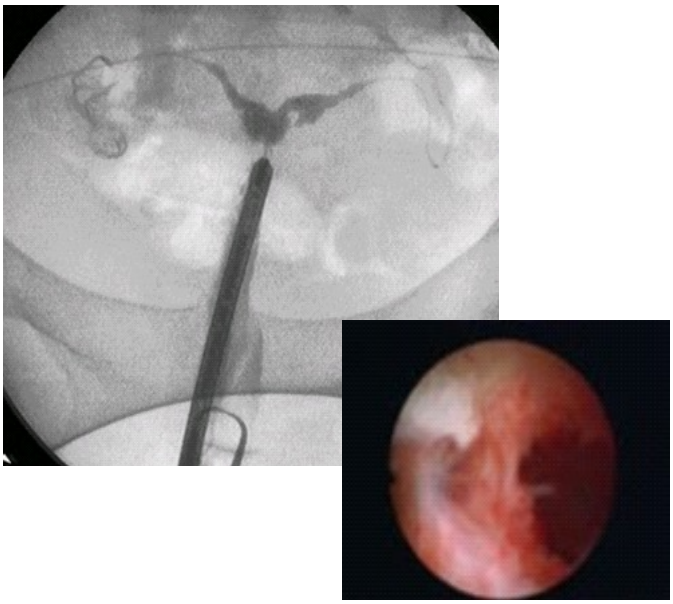
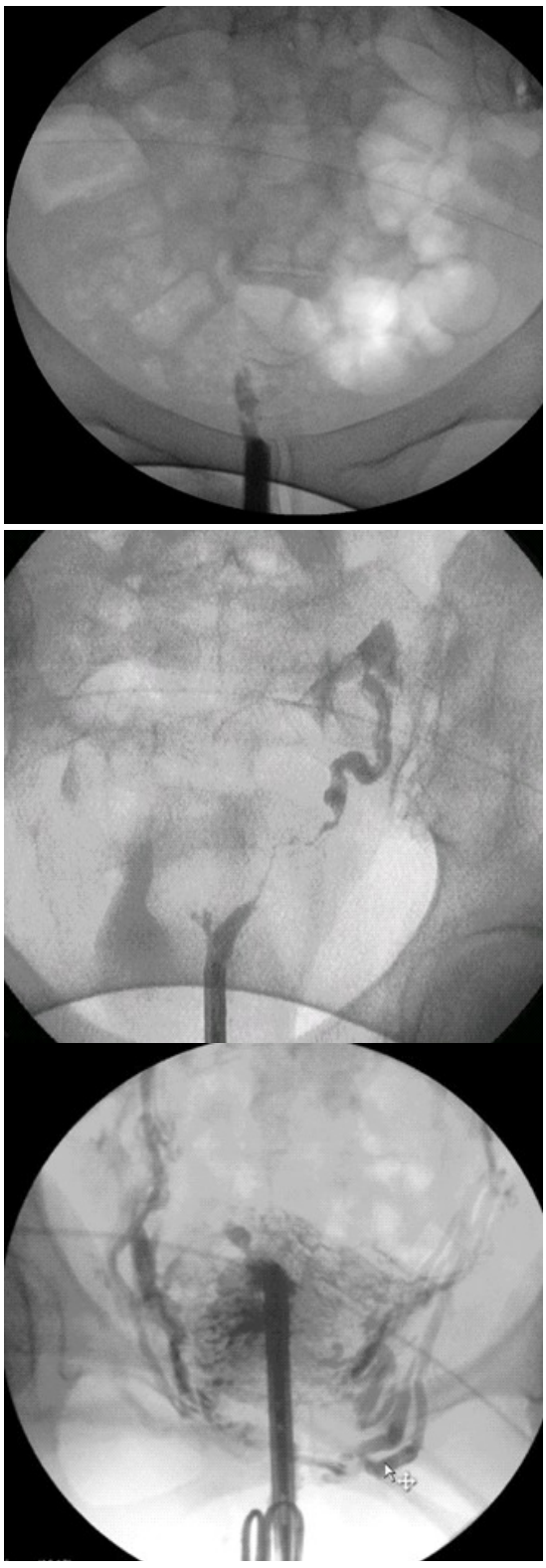
Fluoroscopy was first described by Broome and Vancaillie in 1999 (1,2). The need of guidance during hysteroscopic adhesiolysis in mild to severe cases is mandatory the repair the full intra uterine cavity. Fluoroscopic control can be used but there are also different modalities like ultrasound or laparoscopy. There is no golden standard nor is there any evidence that one method is superior to the other.

The advantage of fluoroscopy is that it can identify 'blocked' areas of original cavity and endometrium behind or above adhesions that are obscured hysteroscopically (1,2).



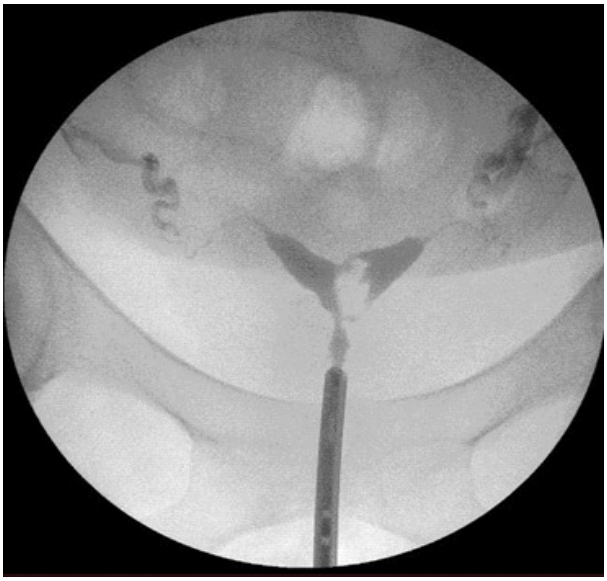
In mild or severe adhesions the areas of the uterus can be completely blocked

With a grasping forceps or scissors perforations can be made in the intra uterine adhesions. To check if this perforation leads to the upper uterine cavity, fluoroscopy can be used. The contrast medium will flow through perforated opening in the adhesions through which the hysteroscope cannot pass and will provide further information on the areas beyond.

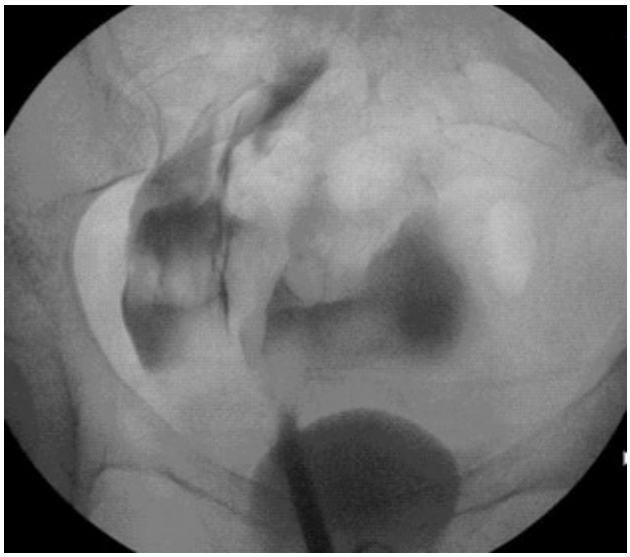


In severe cases with obliteration of the complete intra uterine cavity, intravasation of contrast dye can be used to locate the position of the hysteroscope in the uterine cavity.

Furthermore, tubal patency can be assessed during the procedure; this is of major importance as recognizing (at least one) tube(s) is a landmark of a proper anatomical restoration of the uterine cavity and it is reassuring for future fertility.



With the use of fluoroscopy, the formation of a false passage can be identified easily, which reduces the risk of perforation of the uterine wall (1,2). But when perforation occurs it is easily visualized.



REFERENCES

Wamsteker K. Intrauterine adhesions (synechiae). In: Brosens I, Wamsteker K, editors. Diagnostic imaging and endoscopy in gynecolog. London: WB Saunders; 1997:171-84

Broome JD, Vancaillie TG. Fluoroscopically guided hysteroscopic division of adhesions in severe Asherman syndrome. Obstet Gynecol 1999;93: 1041–3

Asherman Syndrome: My Personal View

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INTRODUCTION

Asherman syndrome, by definition, is characterized by both the presence of Intrauterine adhesion (IUA) and one or more symptoms arising from it. IUA can occur after trauma to the basalis layer of the endometrium with any surgery performed within the uterine cavity, especially with pregnancy. Patients with IUA may present with amenorrhoea with or without severe dysmenorrhoea, oligomenorrhoea, infertility or recurrent miscarriages. The high recurrence rate of adhesions following hysteroscopic adhesiolysis in IUA remains one of the most difficult challenges in reproductive surgery, which seriously affecting women's physical, mental, and reproductive health and worthy of clinical attention and research.

Our hysteroscopy center has been established for 31 years. The adhesiolysis for Asherman syndrome is increasing year by year. In the past 7 years, near 3 000 cases of intrauterine adhesion surgery were performed every year, many of which are difficult cases who have been operated on for several times in primary hospitals. To perform an effective operation and pay attention to postoperative management are our countermeasures.

Preoperative diagnosis should be made precisely to avoid misdiagnosis

Inadequate distension of uterine cavity, excessive uterine flexion, non-reach of the fundus by the inserted instruments (sound, Hegar, resectoscope), may misdiagnosed to the middle and lower uterine cavity adhesion. Uncornuate uterus and Robert's uterus can be misdiagnose as adhesion and one horn occlusion, endometrial hyperplasia may misdiagnose complete obstructed uterine cavity. Incorrect surgery results in damage to the endometrium, muscular and even perforation of the uterus. 3D ultrasonography is very helpful to confirm intrauterine adhesions and distinguish intrauterine adhesions from uterine malformations (Figure 1、2).

Sufficient dilatation of the cervical canal is an important step to initiate surgery

The cervical canal is the passage into the uterine cavity. Hegar is used to fully dilate the cervical canal, and the diameter of the cervical inner OS should be larger than the outer diameter of the surgical scope. The surgical scope can enter and exit cervical canal freely.

If the diameter of the cervical inner OS is equal to the outer diameter of the surgical scope, the cervical canal will be retracted after the Hegar is removed. During operation, the surgical scope needs continue to expand the cervical canal with the outer sheath to enter the uterine cavity. When the surgical scope moves up and down in the uterine cavity, there will be a sense of astringent and , which will affect the speed and accuracy of the operation.

If the uterine cavity is deeper (≥8cm) or the fundus is wider (≥2.5cm), and the adhesion is in the uterine corner, only a large enough cervical dilation, the surgical scope is not subject to the "bottle neck", smooth release/resection of the adhesive tissue. Sufficient dilatation may avoid uterine false passage and perforation, and have the effect to lysis membrane adhesion concurrently.

Does TCR dilation cause cervical insufficiency (CIC)? There is no evidence of evidence-based medicine. Among more than 1500 cases of simplified laparoscopic cervical cerclage performed by our center since 2007, only 1 case had undergone laparoscopic metroplasty for complete bicorporeal uterus, and this case had three typical CIC second trimester abortions before metraplasty [1].

We used to use a 7mm resectoscope with cervix dilated to size 9 Hegar, an 8.5mm resectoscope with cervix dilated to 10.5, and sometimes cervix dilated to size 12 with deep uterine cavity or wide uterine fundus. There are a variety of cervical pretreatment methods for soften and ripen, all can be used, to be patient and slowly according to 0.5 interval by dilation, the key is to slow dilation, to avoid cervical laceration.

B ultrasound guidance

In 1983 Baoliang Lin and Valle RF first published paper of hysteroscopic procedures monitored by B ultrasonography. Since founded at 1990, hysteroscopic diagnosis and hysteroscopic surgery in my Center was routine application abdominal ultrasound monitoring, which may improve the safety and successful rate of surgery [2、3].

During hysteroscopic examination, the distention fluid enters to the cavity above the adhesions level, which makes up for the deficiency that the hysteroscopy cannot understand the situation above the level of adhesions. B ultrasound provides visual help for the thorough removal of adhesions. Real-time guidance, indicating the direction of operation, helps to avoid complications.

From January 1, 2008 to June 30, 2016, a total of 16 983 cases of hysteroscopic examination were performed in our Center, including 2 cases complications (0.012%), 4 909 cases of hysteroscopic surgery performed and 13 cases complications encountered (0.26%), which is lower than the incidence of hysteroscopic surgery complications in abroad countries at that time (0.95%-3%). It shows that many complications of hysteroscopic surgery can be avoided by strict prevention, among which B-ultrasound monitoring is one of the important preventive measures [4].

Cold knife or electrical wire for uterine adhesiolysis

Professor T.C. Li, is Chairman of our Center. He wrote a Chapter “Hysteroscopic Management of Uterine Adhesions” for the book “Diagnostic and Operative Hysteroscopy” in which a list compares the pros and cons of cold scissors and electrical hot wire loop used to divide intrauterine adhesions as follows [5].

	Scissors (cold steel)	Electrical energy (hot wire)
Dilatation	Not required	Required[a]
Diameter of hysteroscopic system	≤5.5 mm	≤5.5 mm[b] or >7 mm[a]
Complications	Lower risk of non-target injury to pelvic structures	Higher risk of non-target injury to pelvic structures from direct or indirect thermal damage
Efficiency	Can dissect as well as cut, but scissors may sometimes blunt or break (fragile)	Always cuts well and fast
Suitability	Particularly suitable for adhesions in cervical canal or isthmic region. Avoids thermal damage to endometrium	Particularly suitable for marginal adhesions

Cold scissors are suitable for central type adhesions (Figure 2), membranous adhesions, or loose fibrous adhesions (Figure 3). Peripheral adhesions, dense fibrous adhesions, muscle adhesions, scar and connective tissue adhesions, conical uterine cavity caused by bilateral uterine corner closure, partial or total uterine cavity occlusion etc., are all performed by bipolar electrosurgical system (Figure 4). Approach to Lysis begins from the most central adhesions and moves gradually to reach the most lateral. Adhesiolysis is continued until the endometrial cavity is restored to normal and the tubal ostia are seen. It's best to do it all at once, especially for the first time of surgery.

Uterine contracture may occur after TCRA surgery due to mechanical or electrical stimulation, tissue inflammation and healing process. In order to reduce the influence of

uterine volume reduction caused by contracture, HOME-DUE (Figure 5) or Myometrial scoring can be performed with needle electrodes for patients with uterine short depth (<6cm) or bilateral wall stenosis. That's one of the reasons we do more electrosurgical procedures for Asherman Syndrome.

Effect of hysteroscopic electric resection on intrauterine adhesions

From 1990 to 2010, we used monopolar electro-resectoscopy for intrauterine adhesiolysis and excision, published a paper in 2008 (6). There were 85 cases of Asherman's syndrome who presented with a history of infertility or recurrent pregnancy loss were included in the study. The adhesions were divided hysteroscopically by electrode needle or loop under direct vision. A second look hysteroscopy was performed after 3 months. A total of 109 operative procedures were performed in 85 cases. Uterine perforation occurred on one occasion (0.9%). After hysteroscopic adhesiolysis, the chances of conception in women who remained amenorrheic (2 out of 11; 18.2%) were significantly lower than those who continued to have menses (37 out of 74; 50%). At second look hysteroscopy, the conception rate in women who had reformation of intrauterine adhesions (2 out of 17; 11.8%) was significantly lower than that of women who had a normal cavity (26 out of 44; 59.1%).

It is shown that the outcome of hysteroscopic adhesiolysis for Asherman's syndrome is significantly affected by recurrence of intrauterine adhesions

Prevention the reformation of intrauterine adhesions after surgery

In order to prevent the reformation of intrauterine adhesions after surgery, our experience is regular postoperative hysteroscopy and uterine balloon dilation which was published in 2020, There were two hundred patients with moderate to severe (European Society for Gynaecological Endoscopy Grade ≥II) intrauterine adhesions who underwent hysteroscopic adhesiolysis in my Center. All participants were randomised to a balloon group or a control group postoperatively. The balloon group received intrauterine balloon dilatation therapy at 2 weeks and 6 weeks after surgery, whereas the control group did not. All patients underwent follow-up hysteroscopy at 4 and 8 weeks postoperatively. The adhesion reformation rate and the Pictorial Blood Loss Assessment Chart scores were analysed. A total of 191 patients successfully completed the study protocol (94 cases for the balloon group and 97 cases for the control group). According to hysteroscopic evaluation at the 8th week, the overall adhesion reformation rate was significantly lower in patients in the balloon group than patients in the control group (20.2% versus 40.2%, respectively; $P < 0.05$). There was also a significant increase in menstruation flow, as assessed by the Pictorial Blood Loss Assessment Chart score (30 versus 9, respectively; $P < 0.001$). It is shown that postoperative intermittent intrauterine balloon dilatation therapy can significantly reduce postoperative adhesion reformation and significantly increase menstruation flow [7].

Post-operative Hormonal Treatments

Post-operative administration of oestrogen or progesterone is often adopted to enhance regrowth of the endometrium, stimulate re-epithelialisation of scarred surfaces and prevent recurrence. The damaged endometrium is perceived to be less responsive to hormone stimulation. For this reason, high-dose oestrogens may be used to stimulate rapid regeneration of the endometrium and, with prolonged use, to enhance continued regrowth of endometrium. Our center has conducted two studies on how many doses are appropriate. One of them published in 2017, which is prospective, randomized, controlled trial was to evaluate the efficacy of different doses of oestrogen treatment (2 mg and 6 mg daily) after hysteroscopic adhesiolysis in patients with moderate to severe adhesion according to the

American Fertility Society (AFS) classification of intrauterine adhesions. A total of 121 patients were included in the final analysis. Fifty-nine patients received 2 mg oestrogen daily (low-dose group), and 62 received 6 mg oestrogen daily (high-dose group) for three cycles after surgery. Second- and third-look outpatient hysteroscopy was performed 4 and 8 weeks after the initial surgery. There was no difference in the menstrual pattern and AFS scores before and after surgery between the two groups, and AFS scores at the second- and third-look hysteroscopy were found to be significantly lower than the scores before surgery in both groups (both P< 0.01). While this study did not address the fundamental question of whether oestrogen adjuvant therapy prevents the recurrence of intrauterine adhesions, the findings do not support the use of high-dose oestrogen therapy after hysteroscopic adhesiolysis [8].

Another one of them published in 2018, which is a retrospective cohort study to compare the clinical outcome of two doses of oestradiol valerate (4mg and 10mg daily) in the prevention of recurrence of adhesions after hysteroscopic adhesiolysis. A total of 176 women who suffered from Asherman syndrome with moderate to severe intrauterine adhesions were included: 91 subjects received a 10mg daily dose of oestradiol and 85 subjects received a 4mg daily dose of oestradiol in the postoperative period. Second look hysteroscopy was performed 4–6 weeks after the initial surgery. There was no difference in AFS scores at second look hysteroscopy between the two groups. Among 125 women who had planned to conceive, the pregnancy outcome at 18 months follow-up of the two groups are 36 (28.9%) managed to become pregnant. The conception rate in the 10mg group (29.7%) was not significantly different to that of the 4mg group (27.9%). Similarly, there was no difference in the miscarriage rate and other outcome measures between the two groups. The findings do not support the use of high-dose postoperative oestrogen therapy following hysteroscopic adhesiolysis [9]. In addition, there have been report of endometrial complex hyperplasia accompanied by atypical hyperplasia in the endometrium caused using long time as well as large amounts of oestrogen [10]. Therefore, our regimen of hormone therapy began from the day of operation, consisting of oestradiol valerate at a dose of 4 mg/day for 21 days, with the addition of dydrogesterone at a dose of 10 mg/day for the last 7 days of the oestrogen therapy. After the withdrawal bleed, the hormone therapy was repeated for a further cycle that is 8 weeks in total.

Never give up, there is hope

Some severe cases who had failed hysteroscopic surgery for many times and refused to give up had to provide some help. However, in this process, a few patients did get live babies. There were two cases of endometrial tuberculosis detected by hysteroscopy. After systematic anti-tuberculosis treatment and careful TCRA operation, both patients delivered babies, among them one patient suffered from uterine incomplete septum, endometrial tuberculosis, and adhesion atresia of the left uterine horn. After one operation, she got pregnant and delivered a child.

REFERENCES

1- Qiao-Yun Zhou, Sotirios Saravelos, Xiao-Wu Huang, Ning Ma, Tinchiu Li, En-Lan Xia. Laparoscopic metroplasty for bicorporeal uterus: surgical techniques and outcomes. Chin Med J (Engl). 2020, 134(9):1107-1109.

2- Limin Feng, Enlan Xia. Clinical analysis of 76 cases of infertility examined by hysteroscopy combined with B ultrasound. Chinese Journal of medicine. 1996, 31(2):29-35.

3- Enlan Xia, Hua Duan, Limin Feng, Huilan Duan. Experience of application on B ultrasound and laparoscopic monitoring in hysteroscopic surgery. Chinese Journal of Endoscopy. 1998,4(8):55-56.

4- Enlan Xia, Yuhuan Liu, Xiaowu Huang, et al. Analysis of complications in 21892 cases of hysteroscopy. Papers compilation of gynecological endoscopy group on the 10th National Conference of Obstetrics and Gynecology, Chinese Medical Association. 2012, P.135.

5- Mary E. Connor, T. Justin Clark. Diagnostic and Operative Hysteroscopy. In: Tin Chiu Li, Xuebing Peng and T. Justin Clark. Hysteroscopic Management of Uterine Adhesions. UK: Cambridge University Press. 2020. 180-192.

6- Dan Yu, Tin-Chiu Li, Enlan Xia, Xiaowu Huang, Yuhuan Liu, and Xuebing Peng. Factors affecting reproductive outcome of hysteroscopic adhesiolysis for Asherman's syndrome. Fertil Steril. 2008, 89(3):715-721.

7- X Shi, SH Saravelos, Q Zhou, X Huang, E Xia, TC Li. Prevention of postoperative adhesion reformation by intermittent intrauterine balloon therapy: a randomised controlled trial. BJOG. 2019, 126(10):1259-1266.

8- Jun Guo, TC Li, YuHuan Liu, EnLan Xia, Yu Xiao, FengQiong Zhou, Xue Yang. A prospective, randomized, controlled trial comparing two doses of oestrogen therapy after hysteroscopic adhesiolysis to prevent intrauterine adhesion recurrence. Reprod Biomed Online. 2017, 35(5):555-561.

9- Linlin Liu, Xiaowu Huang, Enlan Xia, Xiaoyu Zhang, Tin-Chiu Li, Yuhuan Liu A cohort study comparing 4 mg and 10 mg daily doses of postoperative oestradiol therapy to prevent adhesion reformation after hysteroscopic adhesiolysis. Hum Fertil (Camb). 2019, 22(3):191-197.

10- Ning Ma. Severe intrauterine adhesions induced endometrial atypical hyperplasia by repeated high-dose estrogen: a case report. Shandong Medical Journal. 2012,52(12):41-42.

The Importance of Asherman in IVF Unit

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INTRODUCTION

Intrauterine adhesions, intrauterine synechie or Asherman's syndrome are defined as lesions on endometrial tissue characterised by partial or complete obliteration of uterine cavity. It has detrimental effect on normal menstruation and reproduction and can cause subfertility.

The true incidence of Asherman's syndrome is not identified as many cases are asymptomatic, however it is said to be found in 1.5% cases on hysterosalpingography, in 5-39% patients with recurrent pregnancy loss and in upto 40% cases following curettage (1).

ETIOPATHOGENESIS

It is known that gestational complications such as missed or incomplete abortion and post partum haemorrhage are responsible for approximately 90% of the cases of Asherman's syndrome where surgical curettage causes disruption of the basalis layer leading to endometrial sclerosis and adhesion formation (2). Previous instrumentation of the uterus like in a hysterotomy, submucous myoma resection and endometrial ablation can also cause synechie which increase in severity depending on the number of procedures. Nonetheless in developing countries even in absence of previous curettage, Asherman's is on the rise due to genital infections especially tuberculosis and chronic endometritis which remain important causes of subfertility having recurrence even after treatment (3).

ROLE OF ASHERMAN IN INFERTILITY

It is imperative to understand that implantation requires a normal uterine cavity where a complex interplay can happen between a healthy embryo and endometrium. Electron microscopic assessment shows that in women with Asherman's the glandular cells have severe alterations in ribosome metabolism which result in ATP depletion and subsequent tissue hypoxia. There is an abnormal expression of different growth factors leading to activation of cytokines related to the adhesion and a proinflammatory cascade (4). The presence of these adhesions in the uterine wall interferes with embryo implantation hampering the embryo cellular fixation on the endometrial luminal layer. Prevalence of 8.5% of intrauterine synechiae in women with embryo implantation failure was found in a study by Demirol and Gurgan, which confirms the importance of a clinical investigation (5).

Whether mild intrauterine adhesions have an adverse effect on fertility remains unclear but moderate to severe adhesions definitely affect implantation as seen by various studies showing improved pregnancy rates following adhesiolysis. Also scarring of tubal ostia, more likely following untreated Kochs and scarring of endocervical canal lead to subfertility.

DIAGNOSIS

Transvaginal ultrasound aided with doppler flow study and followed by hysterosalpingography help

to identify intrauterine adhesions but the advent of hysteroscopy has revolutionized the whole scenario. It allows direct visualization of the uterine cavity and enables treatment, hence is the gold standard for diagnosing Asherman and its management in the same sitting (6). It is recommended to proceed with hysteroscopy to confirm intrauterine adhesions, especially in the setting of recurrent pregnancy loss or infertility (Fig: 1) . A recent study demonstrated use of office hysteroscopy in 421 patients with recurrent IVF failure where treatment of IUA and other uterine pathologies increased the clinical pregnancy rates compared to that in those with normal hysteroscopic finding (5).

TABLE 3 American Fertility Society/ASRM classification of Asherman's syndrome[16]

	0	1	2	3	4
Cavity involved	None	< 1/3	1/3-2/3	> 2/3	N/A
Type	N/A	Filmy	Mixed	Dense	N/A
Menstrual pattern	Normal		Hypomenorrhea		Amenorrhea

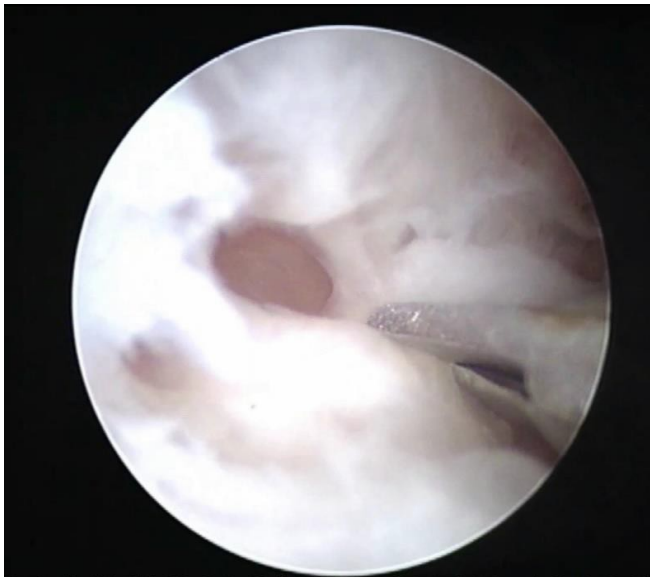
Mild 2-4. Moderate 5-8. Severe 9+

Accurate classification of Asherman is important not only for treatment but also to determine prognosis. ASRM has suggested a classification system depending on extent of cavity obliteration, appearance of adhesions as well as degree of menstrual disturbance and is seen to have better prognostic value for reproductive outcome (7).

TREATMENT

Before hysteroscopy, cervical dilation and curettage associated with estrogen therapy and use of IUD ensured 84% success rate in the treatment of Asherman's syndrome. But now hysteroscopy is the most important tool for resection of the adhesions to restore normal uterine cavity. It enables amplification and general observation of adhesions allowing to view all structures, which decreases the risk of uterine perforation (8). Hysteroscopic adhesiolysis is done in an infertile couple whenever found on routine workup and also in women with recurrent implantation failure undergoing IVF where no other cause of reproductive failure could be identified.

Flimsy adhesions may many a times be removed by hysteroscope alone. But adhesiolysis of dense adhesions should always be done layer by layer by sharp dissection with scissors (Fig:2) or electrosurgery wherein no difference in outcome has been noted between use of monopolar or bipolar (9). Identification of the correct plane of dissection and adequate postoperative hormonal treatment with estrogen and progesterone or use of Intrauterine device to prevent adhesion reformation remains the key for successful outcome following adhesiolysis.It is important to explain to patients that in presence of dense extensive adhesions, multiple procedures may be required to obtain a near normal cavity in size and shape.



The biggest challenge for the treatment of Asherman's syndrome is to prevent the recurrence of adhesions after the early treatment, which reaches 66% (10). There are studies comparing the use of intrauterine device (IUD) with intrauterine balloon catheter, Foley's catheter, hormonal treatment and amniotic membranes/ hyaluronic gel membranes with conflicting results.

Platelet-rich plasma (PRP) is a form of treatment for intrauterine adhesions after operative hysteroscopy and may be a substitute for the intrauterine balloon. In a study by Tandulwadkar et al. on 68 women with suboptimal endometrial growth in frozen embryo transfer cycles, a significant increase in vascularity was seen with autologous PRP instillation with a 60.93% Bhcg

positivity rate (11). However, randomized controlled trials with large sample sizes are required to further compare the efficacy of intrauterine infusions of PRP with intrauterine balloons applied immediate postoperatively.

RECENT ADVANCES

The stem cell therapy approach is much more efficient due to the potential for multiplication of a single cell and its transformation into undifferentiated forms (self-renovation) and into mature cells. Cervello et al. in their study on 11 patients with Asherman's syndrome treated with autologous bone marrow derived CD133+ cells observed successful outcomes (12).

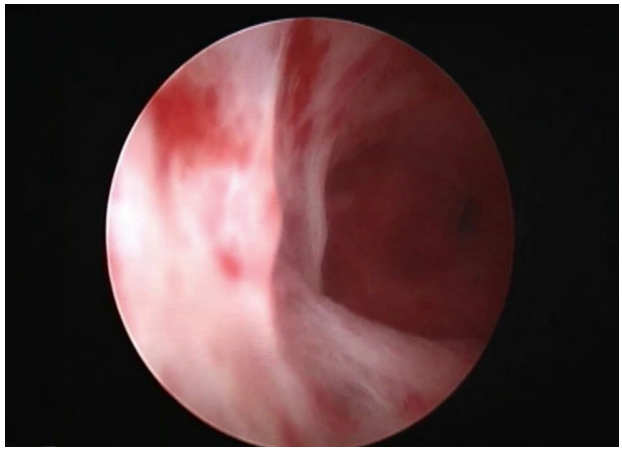
In 2016, Tan et al. investigated mesenchymal stem cells derived from bone marrow and stromal cells coming from the menstrual bleeding through transmiometral administration in the subendothelial area, direct installation of stromal cells in the uterine cavity and infusion of cells in spiral arteries through a catheter (13). Five out of six women with Asherman's syndrome recovered their menstrual periods. Others reached adequate endometrial thickness and regular menstruation cycles and were able to get pregnant right after that.

Thus, stem cell therapy is a new modality for regenerative medicine more specifically for the regeneration of endometrial diseases with Asherman's syndrome and thin endometrium. However, stem cell transplantation for Asherman's syndrome is far from being common.

Inspite of normal size and shape restored following adhesiolysis, vascular perfusion deficit may persist which adversely affects delivery of sex steroids to endometrium. Therefore investigators have also used low dose aspirin, Nitroglycerine and sildenafil citrate to improve subendothelial blood flow to obtain a minimal endometrial thickness of 7-8 mm required for successful embryo implantation (14).

PROGNOSIS

Surgical treatment of IUA offers promising results overall, with the caveat that the severity of the adhesions adversely affect the outcome in terms of recurrence as well as symptom resolution. Improvement in menstruation is seen in 80-96.8% cases post adhesiolysis followed by reproductive



VIDEO:
https://www.youtube.com/watch?v=xCLyMTJhkNs

success. Pregnancy rates after final adhesiolysis for Ashermans may be 53%-63%.Some have reported pregnancy rates of 93%,78% and 57% after treatment of mild, moderate, and severe adhesions with live birth rates of 81%,66% and 32%, respectively (15). According to Siegler and Valle's detailed review involving 800 women with Asherman's syndrome, the overall pregnancy rate after adhesiolysis was 60% and the live birth rate was 38.9% (16). With respect to recurrent abortions, a significant decrease in pregnancy loss from 86.5 to 42.85% has been seen. Age of the patient also plays an important role. It is seen that younger women (<35 years) have fertility rates of 66% post adhesiolysis compared to that in older women where only about 16%-23% success rates are seen (17).

Pregnant patients after Ashermans treatment do present more 1st and 2nd trimester miscarriages hence cerclage should be considered. Also such pregnancies are high risk as they may be associated with placenta accreta, premature delivery and abnormal placentation

CONCLUSION

Asherman's syndrome is identified as intrauterine adhesions caused by aggressive curettage or other intrauterine procedures and infections that destroy the endometrium. It has inimical effects on normal menstruation and fertility. Stunted endometrial development due to impaired uterine perfusion in Asherman's presents as implantation failure. Hysteroscopy is the most valuable tool for diagnosis and management of intrauterine synechie. Though hysteroscopic adhesiolysis can

cure infertility in mild, moderate and severe IUA in around 90, 70 and 30%, respectively, maximum care should be taken when using hysteroscopic scissors and electrosurgical energy and the biggest challenge is to prevent recurrence of adhesions after the early treatment. Stem cell therapy is emerging as a promising therapy for rejuvenation of endometrium. It is important to make the patient understand that normal size and shape of endometrial cavity is necessary, but not always sufficient to obtain a good outcome in terms of pregnancy or live birth. Gestational surrogacy remains an alternative for those patients with intrauterine adhesions that stay infertile (18).

REFERENCES

1- Ventolini G, Zhang M, Gruber J. Hysteroscopy in the evaluation of patients with recurrent pregnancy loss: a cohort study in a primary care population. Surg Endosc 2004; 18:1782 – 1784.

2- Hur C, Rehmer J, Flyckt R, Falcone T. Uterine Factor Infertility: A Clinical Review. Clin Obstet Gynecol. 2019 Jun;62(2):257-270

3- Bukulmez O, Yarali H, Gurgan T. Total corporal synechiae due to tuberculosis carry a very poor prognosis following hysteroscopic synechialysis. Hum Reprod 1999; 14:1960–1961.

4- Tao Z, Duan H. [Expression of adhesion-related cytokines in theuterine fluid after transcervical resection of adhesion]. Zhonghua Fu Chan Ke Za Zhi. 2012 Oct;47(10):734-7.

5- Demirol A, Gurgan T. Effect of treatment of intrauterine pathologies with office hysteroscopy in patients with recurrent IVF failure. Reprod Biomed Online. 2004 May;8(5):590-4.

6- Yu D, Wong YM, Cheong Y, Xia E, Li TC. Asherman syndrome--one century later. Fertil Steril. 2008 Apr;89(4):759-79.

7- Khan Z, Goldberg JM. Hysteroscopic Management of Asherman's Syndrome. J Minim Invasive Gynecol. 2018 Feb;25(2):218-228.

8- Doroftei B, Dabuleanu AM, Ilie OD, Maftei R, Anton E, Simionescu G, Matei T, Armeanu T. Mini-Review of the New Therapeutic Possibilities in Asherman Syndrome-Where Are We after One Hundred and Twenty-Six Years? Diagnostics (Basel). 2020 Sep 17;10(9):706.

9- Zikopoulos KA, Kolibianakis EM, Platteau P, et al. Live delivery rates in subfertile women with Asherman's syndrome after hysteroscopic adhesiolysis using the resectoscope or the Versapoint system. RBM Online 2004; 8:720– 725.

10- Benor A, Gay S, DeCherney A. An update on stem cell therapy for Asherman syndrome. J Assist Reprod Genet. 2020 Jul;37(7):1511-1529.

11- Sunita R. Tandulwadkar, Manasi V. Naralkar, Akash D. Surana,M. Selvakarthick, Avinash H. Kharat. Autologous Intrauterine Platelet-Rich Plasma Instillation for Suboptimal Endometrium in Frozen Embryo Transfer Cycles: A Pilot Study.J Hum Reprod Sci. 2017 Jul-Sep; 10(3): 208–212.

12- Santamaria X, Cabanillas S, Cervelló I, Arbona C, Raga F, Ferro J, Palmero J, Remohí J, Pellicer A, Simón C. Autologous cell therapy with CD133+ bone marrow-derived stem cells for refractory Asherman's syndrome and endometrial atrophy: a pilot cohort study. Hum Reprod. 2016 May;31(5):1087-96.

13- Tan J, Li P, Wang Q, Li Y, Li X, Zhao D, Xu X, Kong L. Autologous menstrual blood-derived stromal cells transplantation for severe Asherman's syndrome. Hum Reprod. 2016 Dec;31(12):2723-2729.

14- Zinger M, Liu JH, Thomas MA. Successful use of vaginal sildenafil citrate in two infertility patients with Asherman's syndrome. J Women's Health 2006; 15:442 – 444.

15- Goldenberg M, Sivan E, Sharabi Z, et al. Reproductive outcome following hysteroscopic management of intrauterine septum and adhesions. Hum Reprod 1995; 10:2663–2665.

16- Siegler AM, Valle RF. Therapeutic hysteroscopic procedures. Fertil Steril 1988; 50:685 – 701.

17- Fernandez H, Al-Najjar F, Chauveaud-Lambling A, et al. Fertility after treatment of Asherman's syndrome stage 3 and 4. J Minim Invasive Gynecol 2006;13:398 – 402.

18- Brinsden PR. Gestational surrogacy. Hum Reprod Update. 2003 Sep- Oct;9(5):483-91.

Pregnancy after Asherman's Syndrome treatment

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We have already read how the treatment of the patient with Asherman's Syndrome (AS) is aimed at achieving an adequate uterine structure, with restitution and / or improvement of menstrual volume, however for the patient who wants to conceive, her goal is to take a healthy child home, which as we will see, it can be difficult.

The chance of pregnancy after the diagnosis of AS, has changed after the incorporation of hysteroscopy as a standard of care for its treatment. Before the use of the hysteroscope, the chance of pregnancy in treated those who did not receive treatment was practically the same, 51 vs 46% (1). Yu in 2008 reported a pregnancy rate after hysteroscopic treatment of AS, of 74%. Deans in 2018, reports a pregnancy rate of 79%, with a live birth rate of 63.7% (2). Jun Guo et al, in 2019, carried out a systematic review on the reproductive outcomes after treatment of AS, reporting a pregnancy rate after hysteroscopic treatment between 10.5 and 100%, with an average of 50.7% and curiously, they showed a slight increase when the treatments before 1985 and after 1986 were compared (44 vs more than 51%), this probably related to the incorporation of the Versapoint® into the hysteroscopic arsenal (3). In 2021, Hanstede et al, reported a live birth rate of 67.4%, with more than 80% of cases achieving pregnancy in the first year after treatment. (4) Fernandez, when he studied patients with grade 3 and 4 AS, reported a live birth rate, after treatment, of 32.8% (5). Hooker reports a post-treatment pregnancy rate of 54%, significantly lower than that of patients without a history of AS (76%), with a live birth rate of 50% vs 71%, respectively (6).

How the success range of hysteroscopic treatment can be appreciated, when a pregnancy is the goal, is very wide and is due to the fact that there are many variables at stake, as we will analyze shortly.

Achieving a pregnancy, in the first place, depends on several factors that can act individually and collectively. There are factors directly related to fertility, regardless of AS or its treatment, and others that are inherent to the pathology and its treatment. In general, we can break them down as follows: age of the patient, degree of injury, time of injury, hysteroscopic technique (dilation or not), endometrial thickness and tubal patency (ostiums and tubes).

PATIENT'S AGE

Among the complications of Asherman's post-treatment pregnancies are abortions, which are reported with higher rates than in the general population (33% vs 8-20%), however, when broken down by age groups we see that in the group of women under the age of 25 the rate is only 1.4%, while in those over 35 it rises to 41.9%. When they performed a multivariate analysis, age, the cause of the injury, and abortions after the procedure were included as strong predictors of live birth in this group of patients (4). Age would act as an independent risk factor related to fertility, since the quality of the ovum decreases at an older age.

TUBAL PERMEABILITY

The fact that a patient is diagnosed with Asherman's syndrome does not necessarily mean that this is her only cause of infertility. Bhandari, in a series of cases, reported that those patients treated by hysteroscopy and those who underwent concomitant laparoscopy, presented multiple obstructions in the tubes (38.1%) and obstruction of the fimbriae (21.4%). It is difficult to explain this, since patients with AS have already conceived in most cases. However, these findings would justify infertility, and not necessarily a history of AS (7). The factors that can cause tubal injury can be present before or after AS. Among the main causes of tubal injury in infertile patients the infectious causes due to Chlamydia trachomatis were the most common followed by Endometriosis.

INJURY SEVERITY

A retrospective study indicates that 58.1% of patients with grade I and II lesions (according to the classification of the European Society of Hysteroscopy ESH) achieved pregnancy, compared to only 13.3% with grade IV lesions (2). In Jun's systematic review in 2019 (3), the mean pregnancy rates were 69.1% in mild cases, 61.3% for moderate cases, and 44.3% in severe cases (classification performed through a grouping of the classifications reported: March 1978, American Fertility Society AFS 1988, SEH 1989 and European Society of Gynecological Hysteroscopy ESGE 1995), observing a significant difference between mild and severe cases. Hanstede et al, reported that patients with mild injuries (grade 1 and 2 of the ESGE classification) achieved at least one pregnancy in 80.6% of the treated cases, while severe cases (grade 5 ESGE) the chances decreased to 41.4%. Fernandez and Valle, conclude that in cases of adhesions grade 4 of the ESH, despite achieving a restitution of the anatomy of the uterus, it is not possible to generate an adequate endometrium for the nesting of a pregnancy, which reinforces the idea that the severity of adhesions negatively affects the chance of pregnancy after lysis of adhesions. (5.8)

TIME OF INJURY

Hanstede, reports that those women in whom the procedure causing the injury was performed in the first trimester of pregnancy are more likely to achieve pregnancy than those in whom the procedure was performed postpartum (OR, 0.43; CI 0.29-0.63) (4)

TECHNIQUE FOR HYSTEROSCOPY

It is important to note that the treatment itself can have negative effects on a subsequent pregnancy. This is the case of the need for cervical dilation to perform hysteroscopy. For example, Fernandez reported that in the cases in which Versapoint was used, patients with gestational losses in the second trimester were due to iatrogenic cervical incompetence in 1/40 cases, while with the receptoscope technique in 3/31 cases, given by the need to perform cervical dilation. Obviously, the technology is evolving and with it, decreasing the size of the equipment with which these iatrogenic cases would be avoided. (5). The use of scissors, bipolar electrode or laser, has not demonstrated having an impact on subsequent pregnancy rate.

TECHNIQUE TO ACHIEVE PREGNANCY

After AS treatment, pregnancy can be achieved spontaneously or through the use of advanced reproductive techniques such as In Vitro Fertilization (IVF). Deans reports that 62.9% of the patients diagnosed with AS achieved pregnancy spontaneously without treatment, while 32.3% required treatment to achieve it (2). The need for the use of assisted reproductive therapy has been reported among pregnant women, in approximately 28% (3). In a recent series, they found that most of the patients who achieved pregnancy did so naturally, while 80 of 373 patients required assisted reproductive techniques (4). Due to the multifactorial nature of fertility, it is difficult to define the exclusive impact of hysteroscopic treatment of AS and it would only be limited to cases where the visualization of the ostiums was not achieved during the anatomical restoration of the uterus.

OBSTETRICAL COMPLICATIONS

Common obstetric practice and in human reproduction, the notion that achieving a pregnancy is just the beginning of the journey to bring a healthy child home. Women who manage to conceive after treatment of AS, have higher obstetrics risks, which are related to problems of the patient, the pathology itself, as well as the treatment carried out. Among the most frequent complications that can occur are spontaneous abortion, preterm delivery, abnormal placentation (both placenta accreta (9) and placenta increta (10)), retention of placenta (10), and uterine sacculation over the insertion area of the placenta (11), intrauterine growth restriction and uterine rupture during pregnancy (12,13) or delivery (14,15). In turn, we also have the consequences of these complications such as postpartum hemorrhage and hysterectomy.

Pregnancy losses in the first trimester

Deans, presents a gestational loss rate of 23.4% (2). In 2019, a prevalence of preterm births of 14.5% was reported in 1,370 pregnancies and early pregnancy losses in the order of 17.7% in 1705 pregnancies (15). Hooker reports a 42% pregnancy loss rate in patients treated with AS, compared to 26% in those without a history (6). More recently, in 2021, an abortion rate of 33% was reported (4)

Ectopic pregnancies

Studies report an increase in the rate of ectopic pregnancies in patients treated for AS, among them Hooker publishes a rate of 8%, compared to his control group with 0% incidence (6). Yu, in his systematic review of the literature, found an ectopic pregnancy rate of 4.2% in 589 pregnancies (15).

Second trimester pregnancy losses

Patients with AS, who have required repeated dilations can develop cervical insufficiency with pregnancy loss in the second trimester or very early pre-term deliveries (16). Hooker reports a 6% rate of cervical insufficiency in patients treated for AS compared to 1% in those without (6). Cervical insufficiency was evidenced in 12.5% of 55 pregnancies in Yu's review (15).

Intrauterine growth restriction

In a systematic review published in 2019, uterine growth restriction was presented in 8.7% of 403 pregnancies (15), perhaps associated with distortion of the architecture of the uterine wall, which would generate placentation failures.

Neonatal deaths

Neonatal deaths were reported in 10.3% in 58 pregnancies (15).

Placenta previa

An increase in placenta previa is observed in patients treated for AS (11.6%), compared to those without (3.1%) (17). Yu, reports the presence of placenta previa of 2.8% among 832 pregnancies (15)

Placental retention

42.5% of the patients treated for AS had retention of the placenta at the time of delivery, which is much higher than the group of patients without AS (8.6%) (17). In another study, the presence of 6 % vs. 1% of patients without treatment for AS, requiring manual removal of the placenta in 19% of cases compared to 9%, respectively (6)

Abnormal placentation

Feng reported in his study that 49 patients treated for AS were diagnosed with placental accrete spectrum. Of these, 26 cases of placenta accreta, 21 cases of placenta increta, and 2 cases of placenta percreta. This is substantially more frequent when compared with patients without a history of AS, in whom only 8 cases of placental accreta were observed in a large number of cases (17). Meanwhile, Yu reported placental accreta in 10.1% of 1415 pregnancies (15)

Postpartum hemorrhage

Postpartum hemorrhage is more frequent in this group of patients (8.9% vs 1%) and a higher percentage requiring blood transfusion (14.4% vs 0.3%) (14). Situation associated with other complications such as placenta previa, and placental retention.

Chorioamnionitis and preterm rupture of membranes

Fernandez in his series, reports that delivering by cesarean section due to premature rupture of membranes due to chorioamnionitis caused by Candida albincas at 30 weeks of gestation (5) and Yu 5.7% of premature rupture of membranes in 371 pregnancies (15)

Placental abruption

In Yu's 2019 review, he found a placental abruption rate of 2.3% out of 300 pregnancies (15)

OBSTETRICAL CARE AND ROUTE OF DELIVERY

When the patients treated for AS are compared with those without it, an increase in the rate of cesarean section is observed (71.2% vs 45.2%) (17). In other studies, such as Hooker's, no statistically significant difference was found in the delivery route between patients with a history of AS and those without, however, a vaginal delivery rate of 88% versus 13% was observed (6).

RECOMMENDATIONS FOR CARE

Due to the obstetric complications that can occur in pregnancies after Asherman's Syndrome treatment, these pregnancies should be considered high risk.

In the prenatal care, an early ultrasound should be performed to verify fetal viability and location of the pregnancy. The evaluation should be repeated between 8 and 10 weeks to confirm fetal cardiac activity, due to the high risk of pregnancy loss. In the second trimester, cervical length and presence of funnelling, and the need for a timely cerclage should be evaluated and monitored (15,16). In the third trimester, evaluate the fetal growth pattern and the placenta to rule out accreta, including MRI in suspected cases (15,16).

For obstetric care, as such, plan it electively, in the morning hours, on weekdays, where all the personnel and resources necessary for adequate care are available. In cases in which a cesarean section is indicated, schedule it and make provisions so that labor does not start before it.

Immediately after the delivery, a thorough evaluation of the placenta should be made, verifying that it is complete and that no portion will be retained. Also, be very attentive to the possibility of postpartum hemorrhage. (16)

CONCLUSIONS

For patients with history of Asherman's Syndrome, a live birth rate is estimated, in general, of around 63.7% (2). If a pregnancy is achieved, it should be considered high risk, taking into account the high incidence of obstetric complications in this group of patients. We must avoid all unnecessary intrauterine instrumentation at the time of an abortion, incomplete abortion and other situations that can trigger the formation of intrauterine adhesions.

REFERENCES

1. Schenker JG, Margalioth EJ. Intrauterine adhesions: an updated appraisal. Fertil Steril 1982;37:593-610.
2. Deans R, Vancaillie T, Ledger W, Liu J, Abbott J. Live with rate and obstetric complications following the hysteroscopic management of intrauterine adhesions including Asherman syndrome. Hum Reprod 2018;10:1847-1853
3. Jun Guo E, Piu J, Chiu L, Chiu T. Reproductive outcomes after surgical treatment of Asherman syndrome: a systematic review. B Pract Res Cl obstet gynecol 2019;59:114-9
4. Hanstede M, Van der Meij E, Veersema S, Emanuel M. Live births after Asherman syndrome treatment. Fertil Steril 2021. Preview online access.
5. Fernandez H, Al-Najjar F, Chauveaud-Lambling A, Frydman R, Gervaise A. Fertility after treatment of Asherman´s syndrome stage 3 y 4. J Min Inv Gynecol 2006;13:398-402
6. Hooker A, de Leeuw R, Twisk J, Brölmann H, Huirne J. Reproductive performance of women with and without intrauterine adhesion following recurrent dilatation and curettage for miscarriage: long-term follow-up of a randomized controlled trial. Hum Reprod 2020; :1-12.
7. Bhandari S, Bhave P, Ganguly I, Baxi A, Agarwal P. Reproductive outcome of patients with Asherman´s syndrome : A SAIMS experience. J Reprod Infertil 2015;16(4):229-235.
8. Valle RF, Sciarra JJ. Intrauterine adhesions: Histeroscopic diagnosis, classification, treatment and reproductive outcome. Am j Obstet Gynecol 1988;158:1459-1470
9. March CM. Intrauterine adhesions. Obstet Gynecol Clin North Am 1995;22:491-505
10. Feng ZC, Yang B, Shao J, Liu S. Diagnostic and therapeutic hysteroscopy for traumatic intrauterine adhesions after induced abortions: clinical analysis of 365 cases. Gynaecol Endoc 1999;8:95-8
11. Friedman A, DeFazio J, DeCherney A. Severe obstetric complications after aggressive treatment of Asherman Syndrome. Obstet Gynecol 1986;67:864-7
12. Deaton JL, Maier D, Andreoli J Jr. Spontaneous uterine rupture during pregnancy after treatment of Asherman´s Syndrome. Am J Obstet Gynecol 1989;160:1053-4
13. Hulka JF. Uterine rupture after treatment of Asherman´s syndrome. Am J Obstet Gynecol 1990;162:1352-3.
14. Shia CS, Hsieh CC, Chiang CH, Hsieh TT, Chang MY. Intrapartum spontaneous uterine rupture following uncomplicated resectoscopic treatment of Asherman´s syndrome. Chang Hung Med J 2005;28:123-7
15. Yu D, Wong YM, Cheong Y, Xia E, Li TCh. Asherman syndrome - one century later. Fertil Steril 2008;89(4):759-779
16. March Ch. Asherman´s Syndrome. Semin Repor Med 2011;29:83-94
17. Feng Q, Gao B, Huang H, Je-Chuen J, Zou L, Zhao X, Cheng C, Xu D. Obstetrical outcome in the third trimester after hysteroscopic adhesiolysis. Ann Transl Med 2020;8(4):51-61

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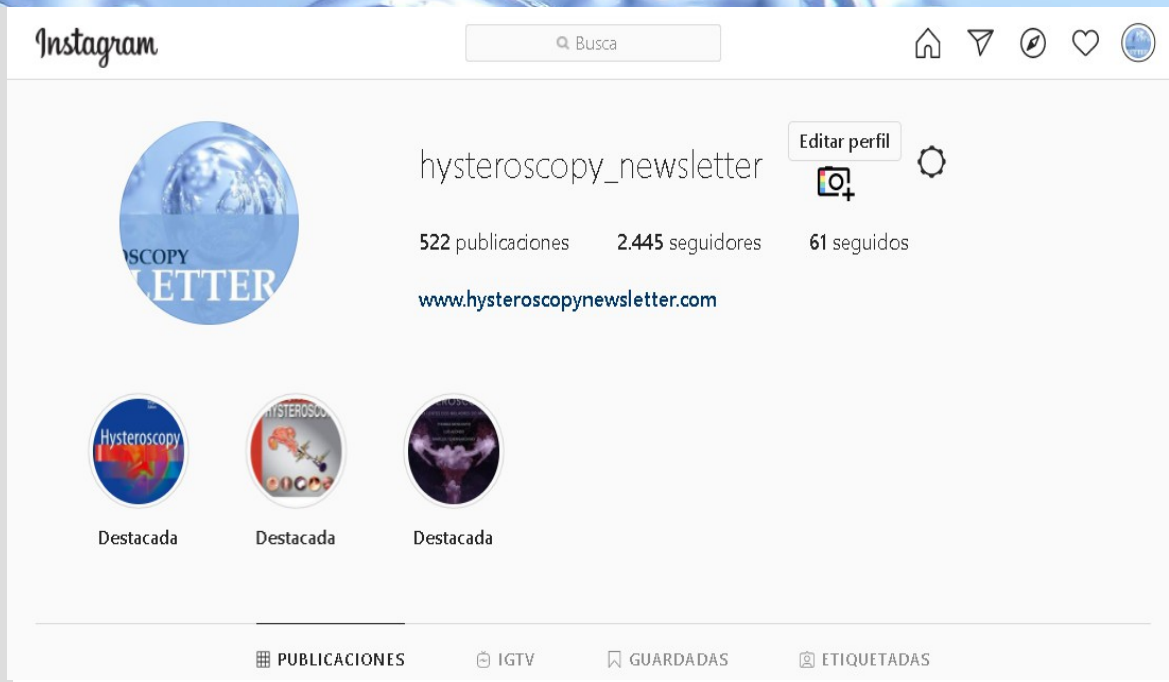

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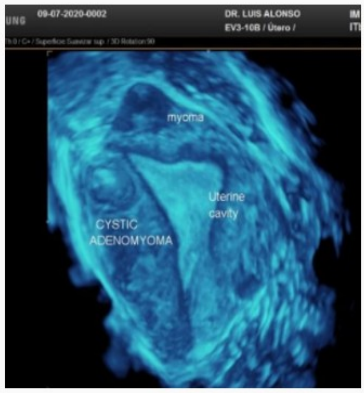

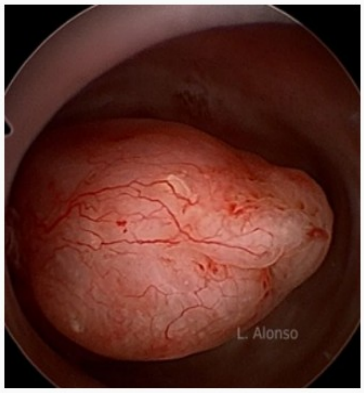

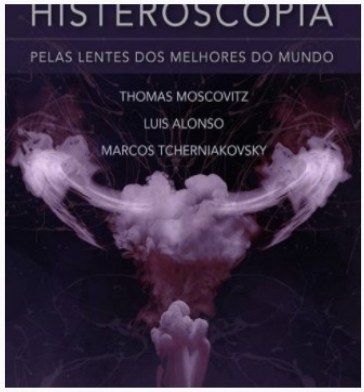

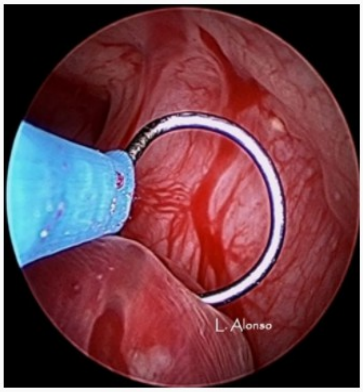

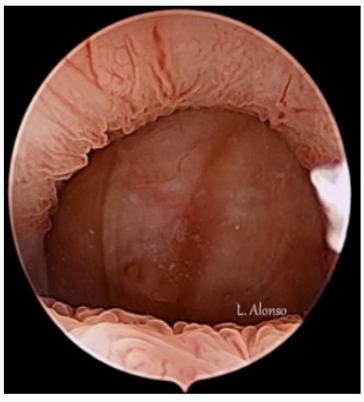

HYSTEROSCOPY NEWSLETTER