

## Fertility after treatment of Asherman's syndrome stage 3 and 4

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### KEYWORDS:

Asherman's syndrome;  
Operative hysteroscopy;  
Placenta accreta;  
Reproductive outcome.

### Abstract

**STUDY OBJECTIVE:** To evaluate the efficacy of hysteroscopic adhesiolysis and subsequent fertility in patients with adhesions stage 3 and 4.

**DESIGN:** A retrospective cohort study (Canadian Task Force classification II-2).

**SETTING:** A tertiary referral center for hysteroscopic surgery.

**PATIENTS:** Seventy-one patients with intrauterine permanent adhesions.

**INTERVENTIONS:** Hysteroscopic surgery with monopolar energy (n = 31) or bipolar energy (n = 40). Uterine cavity with at least one free ostial area was restored after one (n = 31), two (n = 20), three (n = 15), or four or more (n = 5) surgical procedures

**RESULTS:** Sixty-four patients were followed. Evaluation of the uterine cavity after surgery has been performed by hysteroscopy for all the patients. All patients had resumption of menses, except for two patients with a history of uterine artery embolization. Pregnancy index rate after the procedure was 28 (43.8%) of 64, and the live birth rate was 21 (32.8%) of 64. In patients 35 years of age or younger, 20 of 30 (66.6%) conceived compared with 8 of 34 (23.5%) in patients older than 35 years (p = .01). Three patients had either hysterectomy (n = 2) or hypogastric arteries ligation for placenta accreta with uneventful postoperative course.

**CONCLUSIONS:** Hysteroscopic adhesiolysis can be performed for severe adhesions stage 3 and 4 with safety and efficacy. Age is the main predictive factors of success: the pregnancies were at risk of abnormal placentation.

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Asherman's syndrome is defined by the presence of intrauterine permanent adhesions, obliterating the uterine cavity partially or completely. The prevalence is 3.7% to 23.4% in women with a history of postpartum hemorrhage<sup>1</sup> with curettage and 5% to 39% in women with recurrent

miscarriages,<sup>2</sup> and 40% of uterine synechia are found after repeated curettage for incomplete abortion or retained placenta.<sup>3</sup> In addition, a prevalence of 2.7% has been reported in women undergoing hysterosalpingography for infertility.<sup>4,5</sup>

Women with Asherman's syndrome may have menstrual disturbance, while subfertility may be there main complaint. Hysteroscopic surgery currently is the optimal approach, which has allowed rapid improvement in the diagnosis and treatment of total or partial uterine adhesions. However, there are very few studies concerning the treatment and fertility prognosis of patients with severe adhesions.

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**Table 1** Etiology of intrauterine adhesions and symptoms at initial consultation

Etiology	No. (%)	Symptom
D&C for elective abortion	30 (42)	Subfertility
D&C for missed or incomplete abortion	18 (25.4)	Subfertility and hypomenorrhea
D&C for postpartum hemorrhage	5 (7)	Subfertility and amenorrhea
D&C for molar pregnancy	1 (1.4)	Subfertility and amenorrhea
Myomectomy	15 (21.1)	Subfertility and recurrent pregnancy loss
Uterine embolization	2 (2.8)	Subfertility and amenorrhea

D&C = dilatation and curettage.

We previously published a study of 31 patients with severe adhesions treated by hysteroscopy.<sup>6</sup> We found two factors increased subsequent fertility: the role of age (< 35 years) and the interest to repeat the procedures to restore a normal cavity. Since this first short-term study, we introduced a new surgical technique with Versapoint electrode (Versapoint Electro-Surgical System, Gynecare, Inc., Menlo Park, CA) without cervical dilatation.

The aim of this study was to evaluate the safety and efficacy of this new hysteroscopic adhesiolysis surgical technique in the treatment of 40 new patients and to evaluate the results of 71 consecutive patients with severe Asherman's syndrome by observing the complete elimination of all synechia in the uterine cavity, postoperative resumption of menses, and pregnancy rate in a retrospective case report series.

## Materials and methods

From January 1990 through December 2003, 302 patients underwent hysteroscopy treatment for intrauterine adhesions (IUA). We reviewed all operative reports and selected all patients with severe adhesions, with partial agglutination of uterine wall (stage 3) or total agglutination (stage 4) and both ostial area occluded (stage 3 and 4 according to the European Society of Hysteroscopy).<sup>7</sup> Seventy-one patients (23%) were selected according to these criteria.

Median age was 36.1 years  $\pm$  6.1 (range 26–47). Mean parity was 0.6  $\pm$  0.9 (range 0–3). Risk factors for cavity obliteration were the following: history of at least one dilatation and curettage (D&C) (range 1–5) for elective abortion in the first trimester (30 patients [42.3%]); at least one D&C (range 1–4) for missed abortion or incomplete abortion in the first trimester (18 patients [25.4%]); and D&C for postpartum hemorrhage (5 patients [7%]). One patient (1.4%) had curettage for molar pregnancy. Fifteen patients (21.1%) had myomectomy involving hysterotomy, with six of them performed in another hospital, and two patients (2.8%) underwent uterine embolization for fibroid uterus in absence of rational indication (Table 1). The interval between the causal procedure and hysteroscopy treatment of IUA unfortunately was not available.

Eight patients (11.3%) were referred to our tertiary care reproductive center after first inefficient procedure. There was no case of tuberculosis endometritis in this series.

Of the 71 patients, 31 patients (43.6%) reported amenorrhea, 19 (26.7%) profound hypomenorrhea, and 21 (29.7%) normal cycles (exclusively in cases of stage 3). Fifty patients experienced infertility (70.4%), and 21 patients (29.6%) suffered recurrent pregnancy loss. Diagnosis was made by hysterosalpingography and confirmed by hysteroscopy in all cases.

## Surgical technique

Hysteroscopy was performed under general or epidural anesthesia in the early proliferative phase of the menstrual cycle in the patients who were menstruating.

For 31 patients (43%) operated on from 1990 through 1997, a 9-mm resectoscope equipped with hysteroscopic monopolar knife (Karl Storz GmbH, Tuttlingen, Germany) was introduced into the blind reduced cavity, obtained after prudent dilatation of the cervix by Hegar's dilators. Glycine was used as distending medium. Starting in 1998, we used Versapoint bipolar electrode exclusively with normal saline solution to distend the uterine cavity (n = 40 [57%]). No cervical dilatation was needed with Versapoint 5F electrode. In both methods, fluid balance was recorded in all women.

Treatment was performed by making several myometrial incisions 4-mm deep: two or three lateral incisions from the fundus to the isthmus on both sides and two or three transversal incisions of the fundus. Procedure was stopped at that point, even if ostial areas were not visible. A simultaneous laparoscopy was performed only in three patients with a history of pelvic inflammatory disease or ectopic pregnancy, to observe the distal tubal status. In our large experience, ultrasound and laparoscopic control are not used to avoid uterine perforation with hysteroscopy, due to absence of usefulness in monitoring this surgery. Prophylactic antibiotics amoxicillin and clavulanic acid at the dose of 2 g (SmithKline Beecham, Nanterre, France) were given routinely at the induction of anesthesia. No intrauterine contraceptive device was inserted, because no significant advantages has been noted when compared with hormonal therapy alone.<sup>8</sup> Postoperative estrogen therapy (estradiol 4

**Table 2** Results according to surgical technique

	Resectoscope (n = 31)	Versapoint (n = 40)
Perforation	4	3
Normal cavity after initial procedure	16	15
After 2 procedures	7	13
After 3 procedures	7	8
After 4 or more	1	4
Lost to follow-up	3	4

mg daily; Laboratoires Cassenne, Puteaux, France) was given to all patients for 2 months to plan postoperative diagnostic hysteroscopy.

The anatomic result defined by complete elimination of synechia with restoration of normal size and shape of the uterus was checked in all patients by an outpatient hysteroscopy without anesthesia. Hysteroscopy, even if it misses small areas of adhesions, conversely to hysterosalpingography visualizes the restoration of endometrium—the cavity that appears to be the main prognostic factor—and can easily rupture filmy adhesion during this procedure. Subsequent fertility was studied by calling all patients by telephone. We considered only the first pregnancy after index surgery.

We evaluated the results between the two surgical techniques. The  $\chi^2$  test modified by Yates correction when appropriate, and Fisher's exact test were used for statistical evaluation, and  $p < .05$  was considered to be statistically significant. Where appropriate, we used means, standard deviation, and CIs for normally distributed data; and for skewed data, we used medians and ranges.

## Results

Seventy-one patients underwent a total of 136 hysteroscopic procedures. The mean operating time for the procedure was  $25.4 \pm 6.2$  minutes (95% CI 24.35–26.45). All patients were discharged from the hospital on the day of surgery. Complications were noted in seven patients (5.1%) of 136 hysteroscopies involving perforation occurring dur-

ing cervical dilatation ( $n = 4$ ) or during the procedure ( $n = 3$ ). No perforation occurred during the first surgery using Versapoint electrode. If perforation occurred, the procedure was terminated, and patients were operated on 2 months later without any difficulty, and no difference in subsequent fertility was observed.

A completed elimination of all synechia was obtained after the initial procedure by outpatient control hysteroscopy in 31 patients (43.6%), and these patients were allowed to attempt pregnancy; nevertheless in 16 of these 31 patients (51.6%), filmy adhesions easily ruptured during postoperative hysteroscopy. In the remaining 40 patients, postoperative hysteroscopy diagnosed the persistence of moderate or severe IUA and justified a second operative hysteroscopy with direct synechialysis. No difference was observed between the two surgical techniques.

Finally reconstruction of normal uterine cavity was realized after one ( $n = 31$ ), two ( $n = 20$ ), three ( $n = 15$ ), or four or more ( $n = 5$ ) surgical procedures despite the heterogeneous quality of endometrium mucosa.

Menstruation was restored in all patients with history of amenorrhea and oligomenorrhea, with the exception of two patients who underwent uterine artery embolization for uterine myomas.

Seven patients were lost to follow-up after control hysteroscopy. The median follow-up time was 41 months (range 6–86) for the remaining 64 patients. The results in accordance with surgical techniques are presented in [Table 2](#), and no difference was observed.

Twenty-eight index pregnancies were obtained in 64 patients (43.8%) with no difference between surgical techniques, and the outcomes were as follows: 3 had first trimester missed abortions, 4 had second trimester fetal losses, and 21 (32.8%) had live births. Three out of four second trimester losses occurred after resectoscope technique. All patients conceived spontaneously with the exception of three who underwent a first cycle of in vitro fertilization and embryo transfer ([Table 3](#)).

Nine (42.9%) of 21 patients with a history of pregnancy loss and 12 (24%) of 50 patients with infertility had live births. In patients aged 35 years or younger, 20 out of 30 conceived (66.6%) compared with 8 out of 34 (23.5%) in patients aged more than 35 years ( $p < .05$ ) ([Table 4](#)). In 21 patients with live births, there were 12 vaginal deliveries at

**Table 3** Obstetrical history and pregnancy outcome after synechialysis with subsequent pregnancy and live birth rate

Obstetrical history and recent obstetric outcome after synechialysis	Pregnancy rate No. (%)	Live birth rate No. (%)
Infertility	18/50 (36)	12/50 (24)
Recurrent pregnancy loss	10/21 (47.6)	9/21 (42.9)
Spontaneous pregnancy	25/28 (89.3)	20/25 (80)
Assisted pregnancy by IVF	3/28 (10.7)	1/3 (33.3)
Current pregnancy missed abortion	3/28 (10.7)	—
Current pregnancy fetal loss in second trimester	4/28 (14.3)	—

IVF = in vitro fertilization.

**Table 4** Pregnancy rate related to age

	≤ 35 years No. (%) (n = 30)	> 35 years No. (%) (n = 34)	p
No. of pregnancies	20 (66.6)	8 (23.5)	<.001
Live birth	16 (53.5)	5 (14.7)	.371

term and 9 cesarean sections (CS). Three CS were performed for breech presentation with fetal distress, and another three CS were performed for fetal distress with cephalic presentation. Caesarean sections were performed in two patients with previous one and two CS, respectively, for placenta accreta. The last CS was performed for chorioamnionitis at 30 weeks' gestation.

Severe complications occurred in 3 (14.3%) of 21 patients. Two patients had hysterectomy for placenta accreta (patients with previous one and two CS, respectively) without postoperative complications. The third patient had CS for *Candida albicans* chorioamnionitis at 30 weeks' gestation, after preterm rupture of membrane. Hemostasis was obtained by hypogastric arteries ligation with an uneventful postoperative course. The newborn required respiratory support initially. The pregnancy rate was 14 (48.4%) of 31, 10 (50%) of 20, and 4 (20%) of 20, respectively, after one, two, and three or more surgical procedures.

## Discussion

Management of uterine synechia improved progressively during the last 10 years by the widespread use of hysteroscopic surgery, which helps in diagnosis of uterine synechia and restoration of normal size and shape to the uterus, which is essential to carry a pregnancy to term. With this largest series published of patients with severe adhesions, we confirmed the role of age and the interest to repeat the procedures until restoration a normal cavity are predictive factors of subsequent fertility. Moreover, in 90% of pregnancies in our series occurred by natural means.

Various hysteroscopic adhesiolysis techniques were described and published in the last decades, either division of adhesion by hysteroscopic scissors<sup>9</sup> or by using the resectoscope.<sup>10</sup> In our study, pregnancy to term was achieved in 32.8% patients, and normal uterine cavity and menstruation were achieved in all patients with the exception of two patients with history of uterine artery embolization for uter-

ine myomas who continue to have amenorrhea. Coccia et al<sup>11</sup> achieved a 33.3% pregnancy at term rate by using pressure lavage under ultrasound guidance in adhesiolysis. The new Versapoint technique has been used in the last few years and demonstrated its efficacy in treating intrauterine pathologies.<sup>12-15</sup> We observed only 1 out of 40 second trimester fetal losses with Versapoint, whereas the rate was 3 out of 31 after resectoscope techniques. Versapoint could prevent iatrogenic cervical incompetence due to cervical dilatation realized for resectoscope techniques. This difference can be due to absence of cervical dilatation and/or less mucosa destruction by bipolar energy.

From the above studies, the rate of pregnancy at term after synechialysis was almost the same among the various techniques of hysteroscopic surgery (Table 5). All these series can be compared because, whatever the classification used in each of these series, we always considered severe adhesions.

However, the Versapoint technique has improved safety by avoiding the complication of fluid overload and cervical laceration or uterine perforation due to cervical dilatation in patients with stenosed cervix or nullipara patients,<sup>14</sup> and we observed no perforation with this technique. Moreover, the risk of excessive fluid absorbed is theoretically possible but the short time of the procedure, always less than 30 minutes, decreases the risk of this complication.

There are probably few indications left for laparotomy, even in the treatment of severe IUA. Repeated hysteroscopic procedures as described<sup>16,17</sup> and in our series allowed the re-establishment of a normal cavity in all patients, and 20% fertility after three or more procedures in spite of a higher risk of uterine perforation, whichever surgical technique was used during the repeat procedures.

Many studies fail to present their results according to the severity of the adhesion. Therefore different techniques are difficult to compare. So in our study we treated severe Asherman synechia stage 3 and 4, and we obtained a 32.8% live birth rate after adhesiolysis. The live birth rate observed demonstrates the difficulty of having a normal endometrium

**Table 5** Delivery rate after adhesiolysis using various hysteroscopic methods

Study	No. of patients	Hysteroscopic method	Pregnancy at term (%)
Valle and Sciarra <sup>9</sup>	47	Resectoscope with scissors	15 (31.9)
Chen et al <sup>10</sup>	23	Resectoscope with Laminaria (MedGyne, Lombard, IL)	8 (34.9)
Capella-Allouc et al <sup>6</sup>	28	Monopolar knife	9 (32.1)
Coccia et al <sup>11</sup>	3	Pressure lavage under ultrasound guidance	1 (33.3)
Our series (2004)	71	Versapoint and resectoscope	21 (32.8)

suitable for nidation even after restoration of a normal uterine cavity in patients with stage 4 adhesions, which corresponds to what was reported by Valle and Scierra<sup>9</sup> where the severity of adhesions affected the chance of pregnancy after adhesiolysis.

When the patient's age was considered, we found that 20 (66.6%) of 30 patients aged 35 years or younger conceived, compared with 8 (23.5%) of 34 patients older than 35 years. These results confirm that it is worthwhile repeating hysteroscopic treatments until a normal uterine cavity is restored, especially for young women age 35 years or less. For women older than 35 years, the principal aim of the treatment should be resumption of normal menses, but obstetric outcome remains disappointing.

Complications are common in subsequent pregnancy after adhesiolysis and have been described by many authors. Placenta accreta is the most common complication reported after IUA with an incidence of about 8%,<sup>9</sup> while in our study we had three patients (14.3%) with placenta accrete. Two of the three had a history of one and two CS, respectively, which ended with hysterectomy, while the third patient underwent hypogastric arteries ligation. The high rate of placenta accreta in our series is explained by defective lamina basalis after adhesiolysis especially in severe Asherman's syndrome, which allows abnormal placentation.

Other complications have been described by many authors. Deaton et al<sup>18</sup> reported a spontaneous uterine rupture during pregnancy after hysteroscopic treatment of severe Asherman's syndrome complicated by a fundal perforation. Friedman et al<sup>19</sup> described three severe complications in a series of 33 patients with mild to severe IUA: uterine sacculation, uterine dehiscence, and placenta accreta. These complications could be due to resection of the myometrium during the lysis of IUA.

Our finding that the pregnancy rate was 14 (48.4%) of 31 with one surgical procedure, 10 (50%) of 20 after two surgical procedures, and 4 (20%) of 20 after three or more surgical procedures shows that it is worthwhile to repeat lysis of IUA until a normal uterine cavity and shape are restored. Second trimester fetal losses occurred in four patients: one patient had a one-step procedure, and three had undergone four surgical procedures. Two of the four patients became pregnant again and had uneventful pregnancies after cervical cerclage at 12 weeks' gestation. Therefore, we think that cervical cerclage should be discussed with patients with multiple-stage procedures. However, the Versapoint technique avoids cervical dilatation, and this can explain the low incidence of cervical incompetence especially since we started in 1998, with one second trimester loss with this surgical technique without dilatation.

## Conclusion

Hysteroscopic adhesiolysis can be performed for severe adhesions with safety and efficacy, which offers a real

chance of parenthood in a substantial proportion of infertile couples. However, these patients with IUA undergoing adhesiolysis should be appropriately informed about the occurrence of life-threatening complications if they became pregnant and should be managed appropriately in a tertiary care center. Moreover, performance of repeat procedures is not indicated in patients older than 35 years.

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