Reproductive Outcomes of Patients with Septate Uterus after Hysteroscopic Metroplasty: A Retrospective Clinical Study

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Abstract

Background: A retrospective clinical study was performed in a University-affiliated hospital to investigate the reproductive outcomes of patients with septate uterus after hysteroscopic metroplasty.

Methods: Fifty-eight patients with septate uterus and concomitant infertility/miscarriage were admitted in the First Affiliated Hospital of Sun Yat-sen University to undergo hysteroscopic metroplasty between February 2010 and December 2011. Hysteroscopic metroplasty was performed.

Results: The duration of post-operative follow-up ranged between 15 and 37 months. Among these 58 patients, 42 became pregnant after the surgery. The post-operative pregnancy rate of infertility was 66.6% (14/21) and 35 patients became pregnant within 12 months after surgery, accounting for 83.3% (35/42) of the pregnant patients. The average duration between the surgery and pregnancy was 8.0 ± 4.59 months. The post-operative overall live birth rate was 51.7% (30/58). There were no cases of uterine rupture. After surgery, the pregnancy rates of patients with complete and partial septate uterus increased from 29.4% and 34.1% to 64.7% and 73.2%, respectively (both P < 0.05) while the spontaneous abortion rates decreased from 100.0% and 88.5% (pre-operation) to 9.1% and 3.3% (post-operation), respectively (both P < 0.05). The full-term live birth rates of patients with complete and partial septate uterus increased from 0% and 7.7% (pre-operation) to 62.5% and 95.8% (post-operation), respectively (both P < 0.05).

Conclusions: In patients with septate uterus and concomitant infertility/miscarriage, hysteroscopic metroplasty demonstrated an increase in the pregnancy rate and full-term live birth rate, and decrease the miscarriage rate, as well as improves the patients’ reproductive prognosis. Hysteroscopic metroplasty is an effective, safe and simple procedure.

Keywords: Septate uterus; Hysteroscopy; Miscarriage; Live birth

Background

Septate uterus, a type of uterine malformation resulting from incomplete absorption of the septum after fusion of the bilateral mullerian ducts during embryogenesis, accounts for 1/3 of the malformation cases caused by mullerian duct anomalies [1]. Uterine septa are classified by whether the septum is complete or partial. The malformation is often associated with miscarriage, premature birth and malpresentation, if the placenta is anchored to the uterine septum, the patient is exposed to high risk of postpartum retained placenta. Clinically, septate uterus is mainly diagnosed with the aids of hysterosalpingography (HSG), 3-D transvaginal sonohysterography and hysteroscopy [2]. Being characterized by less intra-operative bleeding, lower trauma, rapid recovery and lower risk of postoperative pelvic adhesions, hysteroscopic metroplasty is the most preferable option at the moment for the treatment of septate uterus. In order to evaluate the effects of hysteroscopic electrotomy on the reproductive prognosis of septate uterus, a retrospective review was conducted herein.

Methods

General Data

From February 2010 to December 2011, a total of 58 patients with septate uterus and concomitant infertility/miscarriage were admitted in the First Affiliated Hospital of Sun Yat-sen University to undergo hysteroscopic electrotomy for the treatment of septate uterus.

The 3-D ultrasonographic findings of all patients suggested the presence of septum in the uterus, which was subsequently confirmed at hysteroscopy exams.

Eligibility criteria

• The subject was defined as infertility/miscarriage;
• The female's sex hormonal test result was normal;
• The male had normal semen quality;
• Both (male and female) acquired normal results at chromosome examinations; and
• Written informed consents should be obtained from the patient for participating in follow up and the post-operative laparoscopic examinations.

Exclusion criteria

• The female subject had concomitant immunological infertility;
• The female subject had concomitant uterine neoplasm;
• Occurrence of bilateral proximal tubal obstruction.

Surgical Procedure

Apparatus: The procedures were performed by using KARL STORZ resectoscopes equipped with a monopolar knife (diameter 5mm or 9mm), an imaging monitor system and continuous-perfusion uterus expansion machine, a needle-like metallic electrode and a cold light source. All infertility patients had received concomitant laparoscopic procedures and three patients underwent vaginal septum incision. Laparoscopic surgeries were performed by using an OLYMPUS laparoscope.

Surgical Preparations: Pre-operative examinations were identical to those of the conventional hysteroscopic gynaecological procedures, while routine preoperative vaginal preparations were conducted. Surgeries were performed on Day 3-7 after the end of menstruation cycle. Endotracheal general anesthesia was adopted.
The fluid used to expand uterus was 1.5% mannitol. The pressure was from 100 to 110 mmHg, while the flow rate was 130 – 150 ml/min. The power of incision was 75-85 W, while coagulation 50-60W.

**Surgical procedures:** Patients were retained in a lithotomy position, with pre-operative routine disinfection of the vulva, vagina and cervix. For the patients with vaginal septum, the septa were removed by electrical knife (electrode). After cervical dilation with Hegars to a width of 10 mm, a hysteroscope was inserted to get a clear view of the types of septate uterus, the width of basement, the endpoint of the terminal, the locations of bilateral oviducts opening and the general conditions of bilateral uterine cavity. Along the midline of septum, a needle-like electrode was used to cut off the septum in the direction from the inferior margin to the fundus of uterus. The incision was made in an alternative manner; and the electrocision needle was moved inside-out from the most distal viewpoint, until the septum basement was reached. The septum basement was incised to the largest extent. When the incision was preceded to the bilateral uterine horns, the septum basement was shaved off in a concave manner; so that the basement could be at the same level as the openings of bilateral fallopian tubes, resuming the normal morphology of the uterine cavity, i.e. an inverted-triangular and symmetrical cavity. For the patients with complete septate uterus, the electrode was inserted into one of the cavity compartments at first to make a small incision at 0.5-1 cm above the inner opening of the uterine cavity, so as to transform the complete septate uterus into a partial septate uterus. The rest of the procedures were the same as those during partial septum surgery. Any septum in the cervical canal was retained.

**Post-Operative Management and Follow Up**

Among these 58 patients, an intrauterine device (IUD) was placed immediately after the surgery; and progynova 2 mg per day was administered for a total of 21 days. During the last 7 days of the 21-day treatment period, medroxyprogesterone acetate 4 mg BID was concomitantly administered. These management measures were repeated for 2-3 cycles. On Month 2-3 post operation, hysteroscopic review was conducted and the IUD was placed immediately after the surgery; and progynova 2 mg per 21-day treatment period, medroxyprogesterone acetate 4 mg BID was concomitantly administered. These management measures were repeated for 2-3 cycles. On Month 2-3 post operation, hysteroscopic review was conducted and the IUD was placed immediately after the surgery; and progynova 2 mg per

<table>
<thead>
<tr>
<th>Types of Uterine Septum</th>
<th>Complete Uterine Septum</th>
<th>Partial Uterine Septum</th>
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<tr>
<td>Grouping</td>
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<td>Post-operative</td>
</tr>
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<td>Total no of cases</td>
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<td>17</td>
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<tr>
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<td>11</td>
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<tr>
<td>Total number of miscarriage</td>
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<td>1</td>
</tr>
<tr>
<td>Rate of miscarriage (%)</td>
<td>100.0(7/7)</td>
<td>9.1(1/11)</td>
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<td>Number of premature birth cases</td>
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<tr>
<td>Number of full-term live birth cases</td>
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<td>5</td>
</tr>
<tr>
<td>Rate of full-term live birth (%)</td>
<td>0(0/7)</td>
<td>62.5(5/8)</td>
</tr>
</tbody>
</table>

*Table 1:* The variations of the reproductive status between pre- and post-operative periods

**Notes:** Pregnancy rate = number of pregnant cases / total number of cases; rate of miscarriage = total number of miscarriage / total number of pregnancies. Rate of full-term live birth = number of full-term live birth / total number of pregnancy.

From the table above: 1) after surgery, the pregnancy rates of the patients with complete and partial uterine septum increased from 29.4% (5/17) and 34.1% (14/41) to 64.7% (11/17) and 73.2% (30/41), respectively. The differences were statistically significant (both P < 0.05). 2) The spontaneous abortion rates of the patients with complete and incomplete uterine septum decreased from 100.0% and 88.5% (pre operation) to 9.1% and 3.3% (post operation), respectively; and the differences were statistically significant (both P < 0.05). 3) The full-term live birth rates of the patients with complete and partial uterine septum increased from 0% and 7.7% (pre operation) to 62.5% and 95.8% (post operation), respectively; and the differences were statistically significant (both P < 0.05).

All of the 58 patients returned for the follow up examinations, i.e. a follow-up rate of 100%. The duration of follow up ranged from 15 to 37 months, with a mean of 22.4 ± 3.94 months. Both telephone survey and outpatient diagnosis were conducted to collect the patients’ clinical data, including the results of review by hysteroscopy, whether attempted pregnancy, number of gravida and the outcomes (miscarriage, premature delivery, uterostegation full-term live birth and delivery outcomes), as well as the adoption of other assisted reproductive technologies in any form.

**Statistics**

The data were analyzed using SPSS17.0 software. The variables were expressed in the forms of frequency and mean ± standard deviation. The inter-group variations were assessed by non-parametric test. \( P < 0.05 \) was considered statistically significant (two-sided).

**Results**

**General Conditions of the Surgery**

All infertility patients were evaluated by both hysteroscopic and laparoscopic examination. Eighteen patients were diagnosed with pelvic disorders, which were treated with concomitant procedures, such as laparoscopy-guided surgical lysis of pelvic adhesions in seven cases, endometriosis electrofulguration in seven cases, ovarian teratoma resection in two cases, ovarian cystectomy in two cases and mesosalpinx cystectomy in one case. In addition, three patients also received concomitant vaginal septum removal. The 21 patients with concomitant infertility also underwent hysteroscopic hydrodistilation, of which the results showed no obstruction in the oviducts. The other 37 patients (without concomitant) only received single hysteroscopic electrotyotomy.

The duration of the surgery ranged from 15 to 80 minutes, with a mean of 37.5 ± 14.1 min; the amount of blood loss ranged from 5 to 50 ml, with a mean of 21.8 ± 12.4 ml. No intra-operative complications (e.g. perforation of the uterus, water intoxication and etc.) occurred during the surgeries. The course of hospitalization ranged from 1 to 4 days, with a mean of 2.9 ± 0.8 days. Three patients had slight fever on the second day after operation; and they were all cured and discharged after receiving anti-inflammatory therapies.
The Post-Operative Reproductive Outcomes

Among these 58 patients, 17 were diagnosed as complete septate uterus and 41 had partial septum. 21 patients had septate uterus and concomitant infertility; 37 patients claimed normal sexual activities without taking any contraception measures for more than one year, during which one or more pregnancies had occurred but terminated due to spontaneous abortion. Fifty eight enrolled patients ranged from 20 to 38 years, with a mean of 28.40 ± 3.94 years. The average gravidity was 0.983 ± 0.982 times, while the average number of abortion was 0.517 ± 0.863. The difference of the reproductive status between pre- and post-operative periods is shown in Table 1.

After hysteroscopic metroplasty, 30 of the 58 patients were successfully pregnant and gave birth to live infants, i.e. an overall live birth rate of 51.7% (30/58). Two of these 30 patients experienced premature labor and both of them gave birth vaginally with a gestation of 35 (1 case) and 36 (1 case) weeks respectively. The two premature babies survived and were healthy. Twenty eight of the patients had full-term births, i.e. a full-term live birth rate of 48.3% (28/58). Among these 28 patients, 18 of them received cesarean delivery, with a cesarean delivery rate of 64.3% (18/28). The reasons for cesarean delivery included patient’s self-requirement without any obvious signs (7 cases), macrosomia (6 cases), oligohydramnios (2 cases), uterine inertia (2 cases) and malposition (1 case). There were no cases of uterine rupture.

Among the 21 infertile patients (11 primary infertility and 10 secondary infertility), 14 of them (6 primary infertility and 8 secondary infertility) were successfully pregnant after undergoing the procedure, i.e. the post-operative pregnancy rate of the originally infertile patients was 66.7% (14/21). 12 of these 14 patients were pregnant naturally, while the remaining two were only pregnant after undergoing artificial reproductive techniques.

Duration Between the Surgery and Pregnancy

Among the 58 patients with septate uterus and concomitant infertility/miscarriage, 42 of them were successfully pregnant after the operation, implying an overall pregnancy rate of 72.4%. The duration between the surgery and pregnancy ranged from 2.5 to 22 months. Thirty five of these patients were pregnant within 1 year, accounting for 83.3% (35/42) of total number of pregnant subjects. Seven patients were pregnant at a time > 12months, accounting for 16.7% (7/42) of the total number of pregnant patients. The average duration between the surgery and the pregnancy was 8.0 ± 4.6 months.

Discussion

It has been reported that the incidence of uterine malformation (a polygenic disease) is up to 3-4% in normal women [3], while septate uterus is the most common uterine malformation. Septate uterus gained much attention, because it has an incidence of up to 6% - 8% in patients with recurrent abortion [4], and it is one of the important diseases affecting the reproductive outcomes of the women currently.

Effects of Septate Uterus on The Reproductive Outcomes and the Necessity of Metroplasty

The spontaneous abortion rate in normal women of childbearing age is 4.23% [6]. However, it was reported by the related summaries [5] that 79% of pregnancies would end in abortion in women with septate uterus and the majority (2/3) occurs in early pregnancy, suggesting that septate uterus may cause abortion and infertility. The reason is possibly considered to be related to decrease uterine receptivity due to uterine abnormalities.

Septate uterus is caused by the impeded fusion of the bilateral mullerian ducts during embryogenesis. By inducing the changes in the symmetrical morphology of the uterus, septate uterus is associated with a disturbance in normal reproductive functions, making the patient prone to primary or refractory infertility. The septum is a convex structure in the uterine cavity; it is composed of the residual tissues left after fusion. The zygotes tend to be implanted into the convex septum. However, when compared with the myometrium, the septum has less arterioles in its apex and central portion. Also, the amount of endometrial glands located in the septum is much less than those in the endometrium and the glands in the septum are not proliferated synchronously with those in the endometrium. Besides the disarranged glandular epithelium cells, the sparse cilia, absence of apocrine secretion, and lower expression levels of estradiol/progesterone receptor [7] all contribute to the lowered estrogen sensitivity and differentiation ability in the septum, resulting in dysmaturity. The asynchronous growth cycle would cause undesirable decidualization and the formation of placenta, influencing embryonic implantation and development. Furthermore, the septum has larger and intermingled fibre contents, which may cause the disorder uterine contraction, as well as recurrent miscarriage and premature delivery [9]. Septum may alter the symmetrical morphology of the uterine cavity, increase the intrauterine pressure or cause the concomitant cervical incompetence, and thus resulting in the embryo implantation dysfunction and ecysis. It also poses great risks of premature delivery, abnormal presentation and intrauterine growth retardation. All of these factors are proved to disturb the normal reproductive function, inducing refractory infertility. The incidence of reproductive failure caused by septate uterus in the paramesonephric duct abnormalities was the highest. The majority of septate uterus patients without infertility did not come to a hospital for acquiring treatment, therefore, the pregnancy data of all the patients with septate uterus were not obtained in this study. However, from the clinical statistics obtained from patients with septate uterus and concomitant infertility in our center, the pregnancy rates of the patients with complete and partial septate uterus increased from 29.4% and 34.1% to 64.7% and 73.2%, respectively; the differences were statistically significant (both P < 0.05). The spontaneous abortion rates of the patients with complete and incomplete septate uterus decreased from 100.0% and 88.5% (pre-operation) to 9.1% and 3.3% (post-operation), respectively; and the differences were statistically significant (both P < 0.05); and the full-term live birth rates of the patients with complete and partial septate uterus increased from 0% and 7.7% (pre-operation) to 62.5% and 95.8% (post-operation), respectively; and the differences were statistically significant (both P < 0.05), suggesting that hysteroscopic metroplasty was able to increase the post-operative pregnancy rate and the live birth rate, as well as to decrease the miscarriage rate, for the patients with septate uterus and concomitant infertility. The probable explanation may be: metroplasty eliminated the inappropriate sites for embryonic implantation; and it was also able to facilitate the angiogenesis within the tissues in the uterine basement, to improve/restore the endometrial function, to resume the normal morphology for uterine, to expand the space of cavity and to increase the receptivity of uterine, and thus favouring embryonic implantation and development.

Therefore, it is thought that hysteroscopy should be performed routinely in patients with infertility or those with the history of spontaneous abortion. The women who were diagnosed as septate uterus should receive the treatment timely to improve the pregnancy rate, prevent potential abortion and the complications after pregnancy and improve the reproductive prognosis.
Advantages and Experience of Hysteroscopy in the Treatment of Septate Uterus

Before the wide application of hysteroscopy, the orthopedic methods for the treatment of septate uterus include laparotomy method by Jones and Tompkins. These surgeries are required to incise the abdomen and uterine with the disadvantages of severe trauma and slow recovery, and the patients after such surgeries must take contraception methods for more than six months and are often required to receive cesarean section when they reaches full-term pregnancy to prevent uterine rupture. Meanwhile, such surgeries may cause uterine scar, intrauterine adhesions, and even infertility. In the present study, the average duration of the surgical procedures was 30 minutes, while the average blood loss was 22.2ml. No intra-operative complications (e.g. perforation of the uterus, water intoxication and etc.) occurred. The average course of hospitalization was 2.9 days. The findings of hysteroscopic reviews confirmed the success of the primary surgeries; and the endometrial wounds were healed steadily. None of the patient had post-operative intrauterine adhesion. The minimal duration between the first pregnancy and the surgery was 2.5 month, while the mean duration was eight months. After surgery, the rate of spontaneous abortion (miscarriage) decreased significantly, while the live birth rate improved. None of the patients who had given birth by the end of follow up underwent cesarean delivery due to hysteroscopic incision. No placental adhesion or implantation was found. It is suggested that hysteroscopic incision of septate uterus featured the advantages of minimally-invasive, less intra-operative bleeding, rapid recovery, shorter duration between the surgery and the pregnancy and etc. Besides, the procedures did not increase the risks of delivery complications and the rate of cesarean delivery, and thus being an effective and safe procedure for the restoration of the normal morphology and functions of the uterus. These results were very close to those reported in the foreign literatures [9].

In the present study, hysteroscopic metroplasty was conducted on 58 patients with septate uterus and concomitant infertility/recurrent miscarriage; and all of the 58 patients had their primary surgeries succeeded. No post-operative complications, such as intrauterine adhesion, reduced menstruation, residual septum and etc. The overall pregnancy rate of 58 patients was 72.4% and the overall live birth rate was 51.7%; these two results were very close to those (33-66%) reported by previous studies [10-12]. The following precautions should be taken into consideration during the hysteroscopic metroplasty.

First, Pre-operative evaluation of the length and width of septate uterus by using 3-D B-ultrasonographic technique was able to improve the safety profile for this procedure, as well as to provide guidance for the complete incision.

Second, Needle-like electrode was applied to make incision along the midline of the septum. It was unnecessary to use a loop-like electrode to trim the convex wound surface. Loop-like electrode was also unsuitable for the incision of septate uterus. Such selection of electric knife could maximally protect the peripheral normal endometrium, so as to minimize the wound and prevent post-operative adhesions.

Third, In order to ensure the safety of the procedures, the incision was made in an alternative manner; and the electrocision needle was moved inside-out from the most distal viewpoint.

Fourth, In order to avoid septum retention, the basement of septum should be shaved off by a needle-like electrode so that the basement could be at the same level as the openings of bilateral fallopian tubes. 5%, any septum in cervical canal was retained, so as to prevent postoperative cervical incompetence.

Conclusions

From the above findings, we believe that hysteroscopic metroplasty should be highly recommended for patients with septate uterus and concomitant infertility. This procedure was proved to increase the patients’ pregnancy rate, full-term live birth rate, as well as to decrease the rate of spontaneous abortion so as to improve patients' reproductive prognosis. After all, Hysteroscopic metroplasty is an effective, safe and simple procedure.

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

Yu-Qing Chen participated in the conception and design of the study, analysis and interpretation of data.

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Reference


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