Removal of a residual portion of a uterine septum in women of advanced reproductive age: obstetric outcome

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BACKGROUND: To learn more about the obstetric outcome after initial septum resection and remnant septum (≥1 cm) resection. METHODS: In 94 patients with septate uteri who underwent uterine septum resection, the reproductive efficiency was analysed in a prospective observational study. The reproductive outcome was analysed after initial resection and (if required) consecutive procedures. RESULTS: A total of 94 women were enrolled in the study; all had had two or more miscarriages. The septum was completely removed during the first hysteroscopy in 58 (62%) cases. A residual septum was observed in 36 (38%) patients. Subsequent operative hysteroscopy was performed in the cases (29/36; 80.5%) involving repeated miscarriage and unsuccessful conception. The minimum observation time was 24 months. The difference in delivery rate after the first hysteroscopy between those with a normalized uterine cavity (26/58; 44.8%) and those with remnants (7/36; 19.4%) was statistically significant (P < 0.05). In fact, following the normalization of the uterine cavity, 62.1% (18/29) of the patients delivered, as compared with 19.4% of those (7/36) with a residue and Kaplan–Meyer curves revealed a statistically significant difference (P < 0.05). CONCLUSIONS: Women with a remnant uterine septum have an increased chance of successful pregnancy with an improved obstetric outcome after normalization of the uterine cavity.

Key words: hysteroscopy/infertility/metroplasty/miscarriage/remnant septum

Introduction

In the USA and Western Europe, there has recently been a major shift in reproductive behaviour towards delayed childbearing. In many instances, couples are postponing childbearing; hence, infertility specialists have witnessed a dramatic shift in the age of infertile women undergoing examination during the past decade. Among couples of advanced reproductive age, there is a strong trend towards uterine factor infertility becoming more common (Menken et al., 1986; Hollander and Breen, 1990; Death et al., 1999).

Congenital uterine anomalies have been estimated to affect 0.06 to 10% of women, depending on the method of patient selection, the criteria for diagnosis and the types of diagnostic tests used (Buttram, 1983; Rock and Schlaff, 1985; Acién, 1997; Campo et al., 1999). A septate uterus accounts for approximately 80 to 90% of these abnormalities (Fayez, 1986; Simon et al., 1991).

Most Müllerian defects are never diagnosed because they do not cause complications. The ones that do come to medical attention are those that cause a gynaecological or obstetric dysfunction. Many such anomalies are therefore recognized among women in their thirties (Golan et al., 1989).

Congenital uterine malformations have been associated with a poor reproductive outcome. The pregnancy loss in patients with uterine septa has been reported to be as high as 90% after other causes for miscarriage have been excluded (Daly et al., 1989; Acién, 1993; Goldenberg et al., 1995; Acién, 1996).

After initial hysteroscopic metroplasty, a residual septum or adhesions are more frequent than normally anticipated (Fedele et al., 1991; Fedele et al., 1993; Parsanezhad and Alborzi, 2000; Porcu et al., 2000; Saygili-Yilmaz et al., 2002).

In contrast with the numerous studies on the outcome of initial hysteroscopic metroplasties (Homer et al., 2000), there has been only one report (Fedele et al., 1996b) on the reproductive performance after hysteroscopic remnant uterine septum resection in women of advanced reproductive age.

There is still insufficient evidence that a remnant intrauterine abnormality definitely has an effect on the reproductive outcome. It is reasonable to suppose that a septal endometrium is unsuitable for implantation of the blastocyst, independent of the extent of the uterine abnormality (Fedele et al., 1996b). The aim of this study was to evaluate the influence of the elimination of a residual septum on the reproductive performance of women of advanced reproductive age with recurrent miscarriage.
Materials and methods

The reproductive efficiency in patients with septate uteri who underwent uterine septum resection in our Department of Obstetrics and Gynaecology between July 1997 and June 2002 was analysed in a prospective observational study.

We enrolled patients with a subseptate uterus who had had two or more spontaneous miscarriages. Before surgery, all patients underwent a standardized examination. Women with associated genital or pelvic diseases (myomas, endometriosis, adhesions and sequelae of pelvic inflammatory disease) were excluded, and other causes of infertility were eliminated by work-up procedures such as sperm analysis, hormonal profiles that included thyroid, LH, FSH and midluteal progesterone assay, karyotyping, transvaginal ultrasound scan and hysterosalpingography. Traditionally, hysterosalpingography has been used to screen for anatomic abnormalities and tubal patency in patients with a history of infertility. Laparoscopy was used for a clear differentiation of a bicorneate from a septate uterus. The septum length was measured by ultrasound (Combison C530, Kretztechnik AG, Austria). The measurement was accepted if the hysteroscopic verification was <5 mm. The structural points of the resectoscope were applied to consider the length of the septum in the uterine cavity. The intrauterine anomalies were classified according to the American Society for Reproductive Medicine guidelines (The American Fertility Society, 1988). The exclusion criteria included a bicorneate and a complete septate uterus. Surgery was scheduled early in the follicular phase to optimize the hysteroscopic visibility. The surgical procedure was performed under general anaesthesia by one author (B.G.M.) after dilatation of the cervix up to Hegar size 10, with a 10 mm passive resectoscope fitted with a monopolar knife electrode and with a 30-degree fore-oblique hystroscope. The uterine cavity was distended with 4% sorbitol as medium for dilatation. The measurement was performed under general anaesthesia by one author (B.G.M.) after dilatation of the cervix up to Hegar size 10, with a 10 mm passive resectoscope fitted with a monopolar knife electrode and with a 30-degree fore-oblique hystroscope. The uterine cavity was distended with 4% sorbitol as medium for dilatation irrigation. A Hamou Hysteromat was used to ensure an intrauterine pressure of 100–120 mmHg with a flow rate of 150 ml/min. (All equipment was manufactured by Karl Storz GmbH, Tuttingen, Germany.)

After visualization of the tubal ostia, the section was carried cephalad with progressive horizontal cuts equidistant from the anterior and the posterior walls extended up to the fundus. The incision was considered complete when the uterine architecture had been normalized and vertically running blood vessels of the myometrium appeared.

The same author performed all of the hysteroscopies, including the initial and (if required) the consecutive procedures. All enrolled patients were found to have normal external uterine fusion by laparoscopy within a month. (Not all of the patients underwent laparoscopy in our department.)

All patients were scheduled for follow-up ultrasound and diagnostic hysteroscopy 2 months after the initial resection in order to assess the uterine cavity. If the resection was judged to be adequate (no residual septum, or a residual septum ≤1 cm), patients were allowed to attempt to conceive in subsequent cycles.

After the first operative hysteroscopy, we examined the outcome of pregnancy without regard to the residual septum (≤1 cm). However, if there was no successful pregnancy during the next 24-month follow-up period, the remnant (≤1 cm) was removed during a second hysteroscopy with the aim of increasing the frequency of term pregnancy. The reproductive outcome was monitored in the 24 months after the first hysteroscopy and in the 24 months after removal of the remnant.

Preoperatively, all patients received a detailed explanation of the operative hysteroscopic and laparoscopic procedures, including the risks and benefits involved. They also signed a general surgical informed consent for the procedure. This is part of our routine surgical protocol; special approval from the Human Investigational Board was therefore not needed. Patient confidentiality was maintained at all times.

No preoperative hormonal treatment was applied to thin the endometrium. All patients received postoperative combined oestrogen–progestogen hormonal therapy (30 μg of ethinylestradiol and 150 μg levonorgestrel; Richter Gmbh, Budapest, Hungary) over 1 month.

The results relating to the septum resections were compared statistically with the Statistical Package for the Social Sciences for Windows program (SPSS 11.0, Chicago, IL, USA). The Kolmogorov–Smirnov test for statistical normality was used. Because of the low numbers of patients in the study groups and the lack of statistical normality of the samples, non-parametric statistical tests were applied for comparisons with the Wilcoxon test for continuous variables. Univariate comparisons for categorical variables were assessed by means of Fisher’s exact test. Statistical significance was defined at the two-sided P < 0.05 level. The cumulative delivery rate was assessed after the initial (with and without remnant groups) and the second (septum ≤1 cm) hysteroscopy with Kaplan–Meyer analysis. All data are presented as mean ± SD.

Results

After the exclusion of 52 patients in whom there were other reasons for the infertility, the remaining 94 women were enrolled in the study. Their mean age ± SD was 33.2 ± 4.9 years. The mean follow-up time was 26.4 ± 2.2 months. The mean septum length was 1.85 ± 0.9 cm. All of the remaining uteri were classified as American Society class Vb (partial septate uterus).

No hysteroscopic, laparoscopic (uterine perforation, fluid overload, haemorrhage or postoperative fever) or anaesthetic complication occurred. It was not necessary to interrupt the procedure because of intraoperative sequelae or technical problems.

The mean duration of infertility was 51.5 ± 27.5 months. After the first operative hysteroscopy, the results were similar to those reported in the literature: the follow-up diagnostic tools revealed a normal uterine architecture (complete removal of the septum) in 58 patients (62%), a residual fundal septum >1 cm in 1 patient (1%) and a residual fundal septum ≤1 cm in 35 patients (37%).

The 94 patients undergoing hysteroscopy were subsequently divided into two groups: those in whom complete septum resection was achieved (n = 58) and those in whom there was a residual septum (n = 36). All 94 patients were followed-up for a minimum of 24 months postoperatively. During the 24-month postoperative period after the first operation, 48 of the 94 patients (51.1%) became pregnant, 32 of the 58 (55.2%) in the complete resection group and 16 of the 36 (44.4%) in the residual septum group. Of these pregnancies, a total of 15 (15.9%) (6 and 9, respectively) ended in miscarriage, 5 (5.3%) (2 and 3, respectively) ended in pre-term delivery and 28 (29.7%) (24 and 4, respectively) ended in term delivery. The average length of gestation at the end of the pregnancy after the initial metroplasty was 33 ± 11 weeks, as compared with 18.1 ± 12.5 weeks prior to surgery. After an observation time of 24 months, 29 of the 36 patients with a residual septum and a history of pregnancy loss or continued infertility were re-operated. Because of these successful pregnancies, seven patients were not scheduled for the remnant severing strategy. During the second follow-up period of 24 months after severing of the remnant, 23 patients (79.3%) achieved pregnancy: 5 (17.2%) of these pregnancies ended in miscarriage, 5 (17.2%) in pre-term delivery; and 13 (44.8%) in term delivery (Table I). The average length of gestation at the end of pregnancy after the second operation was 33.7 ± 9.4 weeks.

Normal vaginal delivery was planned for all these patients, and the need for caesarean section was based on obstetric
indications rather than on the history of the metroplasty. Cae-
sarean sections were more prevalent amongst the patients who
underwent one hysteroscopy procedure (17/33: 51.5% versus 8/
18: 44.4%). The delivery in the group after the initial metro-
plasty where a remnant was observed ended with caesarean
section in a considerable proportion (71.4%). No systematic
cervical cerclage was instituted in patients who underwent rem-
nant severing.

The rates of pregnancies and deliveries were increased by the
strategy of remnant severing, though not to significant extents
(Table I). The overall viable pregnancy rate (33/94; 35.1%) after
the initial metroplasty improved to 54.2% of the total (51/94)
after extirpation of the residue. Although premature labour was
more frequent as compared with the total number of deliveries
after the remnant severing strategy (5/18, 27.8% versus 5/33,
15.2%), the prematurity was associated with a longer gestation
period (data not presented), reflected by a trend towards higher
birth weight of the new-borns in the second hysteroscopy group.

Significantly higher delivery (44.8 versus 19.4%; \( P < 0.05 \))
and term pregnancy frequencies (41.4 versus 11.1%; \( P < 0.05 \))
characterized the successful initial hysteroscopy group relative
to those with a remnant. No significant difference was
observed between the two groups as regards the pregnancy rate
(55.2 versus 44.4%). A trend towards a higher frequency of
pre-term birth (8.3 versus 3.4%; not significant) and an increased
rate of miscarriage (25.0 versus 10.3%; not significant)
was found in the remnant group.

Severing of the remnant resulted in improvements in pregnancy
rate (79.3%), delivery rate (62.1%) and term pregnancy rate
(44.8%). The rates of caesarean section and abortion (44.4 and
17.2%, respectively) were lower after the second metroplasty.
The differences were not significantly different.

Figure 1 illustrates the distribution of the first viable preg-
nancies in time after the first and second hysteroscopies. The

**Table 1.** General characteristics of the patients in the study groups and characteristics of the patients after the first hysteroscopy and after the remnant severing strategy.

<table>
<thead>
<tr>
<th>Total number of patients undergoing first hysteroscopy (n = 94)</th>
<th>Number of cases where the first hysteroscopy left no remnant (n = 58)</th>
<th>Number of cases where the first hysteroscopy left a remnant (n = 36)</th>
<th>Number of cases requiring remnant severing strategy (n = 29)</th>
<th>P-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (mean ± SD) (years)</td>
<td>33.2 ± 4.9</td>
<td>33.9 ± 5.1</td>
<td>32.7 ± 4.8</td>
<td>34.3 ± 5.0</td>
</tr>
<tr>
<td>Initial length of septum (mean ± SD) (cm)</td>
<td>1.85 ± 0.9</td>
<td>2.7 ± 0.9</td>
<td>1.7 ± 0.9</td>
<td>0.76 ± 0.3</td>
</tr>
<tr>
<td>Number of patients who become pregnant [n (%)]</td>
<td>48 (51.1)</td>
<td>32 (55.2)</td>
<td>16 (44.4)</td>
<td>23 (79.3)</td>
</tr>
<tr>
<td>Number of patients who delivered [n (%)]</td>
<td>33 (35.1)</td>
<td>26 (44.8)</td>
<td>7 (19.4)</td>
<td>18 (62.1)</td>
</tr>
<tr>
<td>Number of patients undergoing caesarean section [n (%)]</td>
<td>17 (51.5)</td>
<td>12 (46.2)</td>
<td>5 (71.4)</td>
<td>8 (44.4)</td>
</tr>
<tr>
<td>Number of patients achieving term pregnancies [n (%)]</td>
<td>28 (29.7)</td>
<td>24 (41.4)</td>
<td>4 (11.1)</td>
<td>13 (44.8)</td>
</tr>
<tr>
<td>Number of pre-term pregnancies [n (%)]</td>
<td>5 (5.3)</td>
<td>2 (3.4)</td>
<td>3 (8.3)</td>
<td>5 (17.2)</td>
</tr>
<tr>
<td>Number of miscarriages [n (%)]</td>
<td>15 (15.9)</td>
<td>6 (10.3)</td>
<td>9 (25)</td>
<td>5 (17.2)</td>
</tr>
<tr>
<td>Birth weight (mean ± SD) (g)</td>
<td>2952 ± 785.8</td>
<td>3138 ± 369.1</td>
<td>2937 ± 726.5</td>
<td>3136.0 ± 421.1</td>
</tr>
</tbody>
</table>

NS, not significant.

*Statistical analysis was not performed.

**Statistical comparison was performed between the data after the first hysteroscopy without a remnant (n = 58) and the data after first hysteroscopy with a remnant (n = 36).

The number of caesarean sections is compared with the total number of deliveries.

The percentage values relating to pregnancy (i.e. term, pre-term and miscarriages) were calculated with respect to those who became pregnant.

**Discussion**

The aetiology of reproductive failure in patients with uterine
anomalies remains unclear. The mechanisms by which septate
uteri cause early pregnancy loss and infertility have not been established. We do not know the minimal uterine cavity extent needed for a normal pregnancy. It has been demonstrated that the endometrial mucosa covering the septum is poorly responsive to oestrogen. The alterations indicate irregular differentiation and maturation of the septal endometrial mucosa. Accordingly, removal of the septum not only eliminates an unsuitable site for implantation but also results in a better endometrial function, probably through re-vascularization of the connective tissue of the uterine fundus (Fedele et al., 1996b).

The septum was discovered during infertility evaluation. All of our patients were referred with a diagnosis of septate or bicornuate uterus on hysterosalpingography. At the beginning of the study, diagnostic hysteroscopy was not widely used in the referral hospitals. We confirmed the diagnosis by using diagnostic hysteroscopy combined with diagnostic laparoscopy in one session. Only when the diagnosis in our department confirmed the presence of septum did we treat septate uterus in infertile patients at the time of diagnostic hysteroscopy without laparoscopic guidance. In our experience, laparoscopic guidance during hysteroscopic septum resection does not furnish any advantage. The septate uterus has been widely reported to be associated with miscarriage and other obstetrical complications (Goldenberg et al., 1995). As opposed to many previous studies, our investigation included only infertile women in whom no other cause of infertility was identified. In recurrent miscarriage, foetal chromosomal aberrations had not been excluded, although both parental karyotypes were normal. Accordingly, we concluded that the septum was the cause of pregnancy loss.

From the beginning, we have applied exclusively the same method for resection of the septum. Previous studies agreed that the method of incision did not influence the reproductive outcome (Fedele et al., 1993).

Fedele et al. concluded that the preoperative endometrial thickness influences the operating conditions (Fedele et al., 1996a). Thus, it is important to emphasize that in our study no preoperative hormonal treatment was used to thin the endometrium. The only method used was to time the operation within a 2-week period after menstrual bleeding.

Very similar prevalences of residual septum occurrence were observed in previous publications (Fedele et al., 1991; Fedele et al., 1993; Parsanezhad et al., 2000; Porcu et al., 2000; Saygili-Yilmaz et al., 2002; Pabuccu and Gomel, 2004). The differences are probably due to the differences in the samples of women between the individual working groups and to the hysteroscopic confirmation of the adequacy of the initial resection. The most crucial part of the operation is the complete division of the septum, without causing uterine perforation or leaving a residual septum. The occurrence of a remnant is greatly influenced by the location of the surgeon on his or her learning curve. In 2002, we observed a residual septum in only two cases, as opposed to 20 cases in the first 3 years.

On the second hysteroscopy, both the remnant and the myofibrous adhesions could be verified as whitish in colour and resistant to the touch. Some investigators claim that the adhesive process can be progressive and therefore advise early intervention. They postulate that adhesions limit the uterine muscular activity, thereby reducing the perfusion of sex steroids to the endometrium, with atrophy as a consequence (Edstrom, 1974). After 2 months, the uterine cavity is almost normal, with a minimal tendency to central fundal adhesion (Candiani et al., 1990a,b). The control procedures to determine the adequacy of the metroplasty were therefore performed in that period.

Postoperative uterine rupture, one of the most serious life-threatening complications, did not occur in our series. It has been suggested that a residual septum may result in weakness during uterine enlargement in pregnancy (Angell et al., 2002).

Although the average gestation period is longer and the perinatal outcome is improved post-metroplasty, it remains unknown how much of this can be attributed to the metroplasty and how much to increased prenatal observation and intervention. Some authors have found that not all patients with unexplained infertility seem to be cured by hysteroscopic metroplasty, but it may prevent subsequent miscarriage or labour complications in patients considering conception and may improve the perinatal outcome (Daly et al., 1989;). As opposed to previous investigations of patients with a ≤1 cm remnant septum, which tended only to consider the reproductive outcome in cases with this residual uterine anomaly (Fedele et al., 1996c; Pabuccu and Gomel, 2004), our study demonstrates the advantageous possibility of obstetric achievement after the remnant severing strategy. After the initial metroplasty, the pregnancy rate was 51.1%. This result is similar to a previous finding (Pabuccu et al., 2004).

Our Kaplan–Meyer analysis indicated a significantly favourable delivery rate after both the first and the second normalization of the uterine cavity as compared with the remnant group.

Subsequent to the achievement of a normal uterine cavity, the pregnancy rate was relevantly, but not significantly higher (79.3%) than in the event of a remnant (44.4%). Our results point to prematurity not being significantly frequent after hysteroscopic septum resections (2/26 versus 5/18). On the other hand, the birth weight was more favourable after full normalization of the uterine cavity, reflecting that the gestational age in prematurity was higher and more deliveries occurred close to the term. The birth weight was lower and the prevalence of malposition as an indication of caesarean section was higher after only one hysteroscopy when there was a remnant, highlighting the need for full normalization of the uterine cavity.

Like every other report on this topic, this one is limited by its design. It compares a group of women examined because of failed reproduction with the same women after treatment. No clinical trial on uterine septa has been published in which the pregnancy rate is compared in a treated and an untreated group. A randomized prospective multicentre study should be undertaken, but it would not be ethical not to treat patients with infertility.

Our findings may fuel the controversy concerning the appropriate treatment of women with a remnant septum. There seems to be a general consensus, based on only a few reports, that a remnant septum ≤1 cm is supportable and there is no need for any further intervention to remove it. However, our data reveal that women with such a remnant have an increased and reasonable chance of successful pregnancy after normalization of the uterine cavity without serious sequelae. These results
encourage a widening of the indications of hysteroscopic metroplasty in patients of advanced reproductive age with a residual septum to improve the ability for term childbearing.

References