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Term Delivery Rate after Hysteroscopic Metroplasty in Patients with Recurrent Spontaneous Abortion and T-Shaped, Arcuate and Septate Uterus

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Key Words
T-shaped uterus · Arcuatus uterus · Hysteroscopic metroplasty · Delivery rate · Recurrent spontaneous abortions

Abstract
Background: To evaluate the improvement of the term delivery rate after uterine surgery in various uterine malformations. ***Methods:*** 170 patients were eligible for the present retrospective case series study. Data were weighted for the number of pregnancies observed (n = 218) after surgical intervention, stratified to the number of previous abortions (at least 2) and type of malformation. ***Results:*** Before surgery, the overall term delivery rate was 5.5%. After surgery, the overall term delivery rate was 59% (absolute benefit increase, ABI, was 54.5) and correlated with the number of previous abortions (69.7% ABI = 64.2, 56.5% ABI = 51 and 26.3% ABI = 20.8 for 2, 3–4 and >4 abortions, respectively; p = 0.0008, log-rank test). Data stratified according to uterine malformations yielded the following term delivery rate: 66.7% for T-shaped uterus, 62.8% for septum/partial septum and 55.6% for arcuate uterus (NS, log-rank test). The number of previous abortions and maternal age also affected the term delivery rate. Their effect upon the term delivery rate, expressed as an odds ratio, was 1.73 (95% CI: 1.20–2.49) and 1.11 (95% CI: 1.05–1.18), respectively. ***Conclusion:*** The term delivery rate was about 10-fold higher after surgery. T-shaped uterus surgery yielded the best term delivery rate.

Introduction

Mullerian uterine anomalies have long been recognized as major reasons for obstetric complications. They may be associated with recurrent pregnancy loss, preterm labor and infertility [1–4]. The classification of mullerian anatomic uterine defects was proposed by the American Fertility Society (AFS) [5]. The frequency of uterine malformations in recurrent pregnancy loss patients (with 2 or more consecutive abortions) has been reported as ranging from 1 to 30% [6]. Recently, Braun et al. [7] reported a 10% frequency of uterine malformations in a series of 658 infertile and sterile women: arcuate uterus (57.6%, AFS VI most common), subseptate (partial septum) uterus (18.2%; AFS V.b), uterus bicornis unicollis (10.6%), septate uterus (6.1%), bicornis bicollis (3%), unicornuate (3%) and unicornuate with double vagina (1.5%).

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From 1987 to 2004, many retrospective studies analyzed the relationship between conventional mullerian anomalies and recurrent spontaneous abortions (RSA) [20, 21, 30]. Homer et al. [8] reported the reproductive outcome in women with untreated septate uterus (in 19 studies), finding abortions in 79% of the 1,376 pregnancies. In the same study, a significant reduction in the overall abortion rate from 88 to 5.9% after uterine surgery was observed (hysteroscopic metroplasty) and the presence of a uterine septum appears to be a major indication for hysteroscopic metroplasty (table 1). However, presently there are no randomized studies on the effectiveness of hysteroscopic metroplasty in patients with recurrent abortion. Grimbizis et al. [6] asserted in 2001 that 'uterine malformations consist of a group of miscellaneous congenital anomalies of the genital system'. In their study, the arcuate uterus (the most common finding, 57.6%, among infertile/sterile women in Braun's study [7]) was detected in 20% of women with recurrent pregnancy losses due to mullerian anomalies. The literature confirms that arcuate uterus is the most frequent congenital malformation and it is unclear if it can be considered an indication for hysteroscopic metroplasty in patients with RSA or with infertility/sterility. Even though it could be separated and classified as arcuate uterus with (as in most cases) and without fibrotic tissue on the arcuate fundus, the term 'arcuate' currently includes all findings. Maneschi et al. [9] in 1995 reported a significantly lower birth rate in patients with arcuate uterus when compared with women with a normal-shaped uterus, although higher than for those affected with a septate uterus. Another unconventional type of uterine malformation is the 'T-shaped uterus or T-shaped uterine anomaly'. Muasher et al. [10] in 1984 reported 2 women with T-shaped uterine anomaly and recurrent abortions who underwent wedge metroplasty with good results.

In a series of 8 cases, Katz et al. [11] in 1996 concluded that hysteroscopic metroplasty in women with a T-shaped uterus improves the reproductive outcome, and women with this anomaly who want to improve their reproductive function should be encouraged to undergo hysteroscopic metroplasty.

The main objective of our study was to evaluate the term delivery rate after hysteroscopic metroplasty for anomalies, especially for arcuate uterus and T-shaped uterus in women with spontaneous abortion.

If hysteroscopic metroplasty has a beneficial effect particularly for women with arcuate or T-shaped uterus, it would be possible to speculate that the uterine factor is the major cause of recurrent abortions. Reproductive strategies would therefore benefit from such a finding.

Table 1. Reproductive outcome before and after hysteroscopic metroplasty for septate uterus in selected patients (with 3 or more abortions)

	Before	After
Total pregnancies	1,062	491
Abortions	933 (88%)	67 (14%)
PTD	95 (9%)	29 (6%)
TD	34 (3%)‖	395 (80%)‖

Results from 16 retrospective studies [10]. Figures in parentheses represent percentages. PTD = Preterm delivery; TD = term delivery.

Materials and Methods

352 cases were collected between 2002 and 2006. The women were admitted to hospital for spontaneous abortion and RSA. All of them had 2 or more abortions before the surgical intervention. All patients had received genetics endocrine metabolic screening and a complete screening for RSA as previously reported [2, 4].

The diagnosis of intrauterine mullerian abnormalities was performed with office diagnostic hysteroscopy. Hysteroscopy was performed in all patients by a single experienced hysteroscopist (E.G.) in the proliferative phase of the menstrual cycle. All hysteroscopies were performed using a 5-mm single diagnostic sheath on a 30° rod lens endoscope with a 4-mm optic view Olympus or Bettocchi Hysteroscope from Stortz manufacturers (Karl Stortz GmbH & Co. KG, Germany). Neither anesthesia nor analgesia was administered for pain control. An electronic hysteroflator for carbon dioxide uterine distension (Wisap GmbH, Germany) was used, with pressure not exceeding 80 mm Hg and a flow rate of 40 ml/min. The endocavitary length of the midline septum was subjectively defined by the operator (E.G.) as arcuatus (<1 cm), partial septum (involving one third of the uterine cavity), septum (involving two thirds or all of the uterine cavity) and T-shaped (hypoplasic and cavity with arched base, constriction rings around the proximal and medial uterine segment).

Out of the 352 patients who underwent surgical intervention, all had been trying to get pregnant, but only 170 resulted in at least a pregnancy and were used for statistical analysis. 170 patients and 218 pregnancies were considered in the study. The remaining women (182) are still trying to get pregnant.

The surgical intervention was hysteroscopic metroplasty performed by the same operator (E.G.) in the same hospital. The surgical technique was standard hysteroscopic metroplasty for septum/subseptum and arcuate uterus according to the literature [12].

All patients underwent resectoscopic metroplasty under general anesthesia. All the procedures were performed by a single experienced hysteroscopist (E.G.) using a speculum and a tenaculum and by dilating the cervical canal with Hegar dilatators up to size 8.5 to enable introduction of the 26-french resectoscope (Karl Stortz GmbH & Co. KG) in the uterine cavity. The septum or the fundus arcuatus was incised using the cutting 0° knife, monopolar energy (pure cat 100 W) and 1.5% sorbitol-mannitol solution as the distention medium. Dissection of the fibrotic part of the

fundus was performed on from the uterine isthmus toward the fundus until the muscular component of the uterine wall, the venous myometrial vessels, were appreciate. This is important in order to preserve adequate fundus thickness so as to avert intrauterine perforation or uterine rupture during pregnancy or labor. For the T-shaped uterus, the metroplasty was the plastic enlargement operation (to widen the cavity) with lateral and careful incision of the lateral wall of uterine cavity. The objective of this was to obtain a triangular-shaped cavity, and at the same time taking care to weaken the walls themselves.

In all patients (with arcuate, septum and T-shaped uterus), no preoperative hormonal therapy was performed, as all procedures were carried out during the early proliferative phase of the cycle, and no postoperative hormonal therapy was administered.

For T-shaped uterus, metroplasty was performed according to the description and technique of Katz et al. [11] and the uterine side walls were incised until a normal uterine cavity was achieved.

The women's gynecologic and obstetric records were compared before and after the operation. The hysteroscopic postoperative control was performed in all patients following an approved protocol previously reported [13]. In all women, surgery resulted in a satisfactory cavity.

Statistical Analysis

The statistical analyses were performed for the 170 cases which had a complete follow-up. Descriptive analysis was performed by routine test. The Kaplan-Meier and Cox analyses were used to evaluate the univariable and multivariable contributions, respectively, of the variables of interest to the term delivery rate. Data were stratified for the variables of interest and the log-rank test was used to explore differences among and between the subcategories generated. Data were weighted for the number of pregnancies observed after surgery. Cases that were not clinically pregnant and pregnancies that ended before 41 weeks (end of the follow-up) constituted the 'censor' group. The occurrence of spontaneous abortion was the 'event' of the study.

Results

According to uterine malformation, 3 subgroups of patients were generated as reported in table 2. The subgroups generated were composed of 17, 72 and 81 patients, and the relative number of pregnancies observed was 21, 89 and 108, respectively.

For the purpose of this paper, only the 170 cases who tried to get pregnant were considered. Pregnancy history for the overall series of data before uterine surgery is reported in table 3. Before surgery, the overall term delivery rate was 5.5%. As is shown, patients in group 2 were older and had a higher number of abortions (>4) than those of group 3. A stratification was performed for the number of spontaneous abortions observed before surgical intervention. The term delivery rate correlated with the number of previous abortions (2 ab. = 5.67%, 3–4 ab. = 6.26% and >4 ab. = 1.52%).

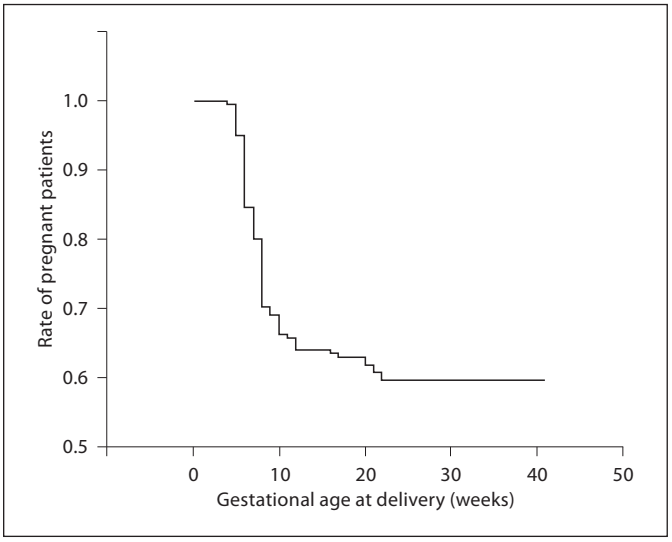

Fig. 1. Overall rate of term delivery after surgical treatment weighted for number of pregnancies (n = 218).

Table 2. Subgroups of patients (total 170) stratified according to uterine malformation

Uterine malformation	Patients, n	Pregnancies, n
Group 1		
T-shaped uterus	17	21
Group 2		
Septum	2	3
Septum partial	70	86
Group 3		
Arcuate with fibrosis	50	67
Arcuate	31	41

Eight patients had 1 ectopic pregnancy, one patient had 2 ectopic pregnancies and one patient had 4 ectopic pregnancies.

There were 53 spontaneous deliveries (24.3%) and 73 cesarean sections (33.5%). 38 patients had 1 or 2 spontaneous deliveries and 58 had 1 or 2 cesarean sections. Of these, only one patient had 1 cesarean section and 1 spontaneous delivery.

Univariable Analysis

The Kaplan-Meier algorithm yielded a crude term delivery rate of 59% as reported in figure 1.

Data stratified according to uterine malformations (T-shaped uterus, septum/partial septum and arcuate uter-

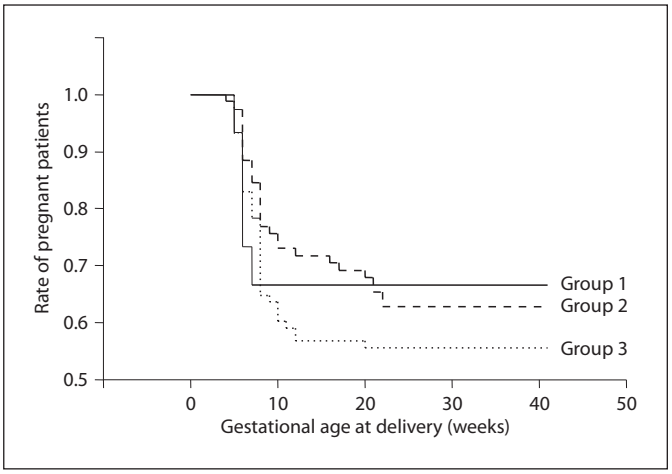

Fig. 2. Rate of term delivery after surgical treatment stratified according to uterine malformation and weighted for number of pregnancies. Group 1: n = 21; group 2: n = 89; group 3: n = 108.

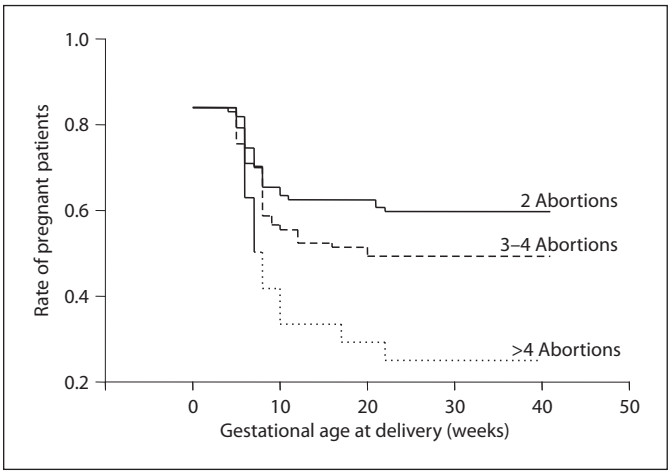

Fig. 3. Rate of term delivery after surgical treatment stratified according to number of previous abortions and weighted for number of pregnancies. Group 1 (2 abortions): n = 97; group 2 (3–4 abortions): n = 99; group 3 (>4 abortions): n = 22.

Table 3. Demographic and clinical characteristics of the series (before uterine surgery) weighted for number of pregnancies (total 218)

Variable	Group 1 (n = 21)	Group 2 (n = 89)	Group 3 (n = 108)	p value*	Post hoc test
Maternal age at surgery	39.3 ± 5.66	39.00 ± 4.41	36.6 ± 6.86	0.012	0.018**
Abortion, %					
2	52.4	38.2	48.1	NS	
3–4	42.9	42.7	48.1	NS	
>4	4.8	19.1	3.7	<0.001	<0.001**
Ectopic pregnancy, %					
0	100	94.4	93.5	NS	
1	0	4.5	3.7	NS	
2	0	1.1	0	NS	
4	0	0	2.8	NS	
Preterm delivery, %					
0	100	95.5	99.1	NS	
1	0	4.5	0.9	NS	
Term delivery, %					
0	100	87.6	88.9	NS	
1	0	12.4	10.2	NS	
2	0	0	0.9	NS	

* ANOVA and Bonferroni post hoc test or χ^2 test. ** Group 2 vs. group 3.

us) yielded the following pregnancy rate: 66.7% for T-shaped uterus, 62.8% for septum/partial septum uterus and 55.6% for arcuate (figure 2). No statistical difference was observed by the log-rank test among the 3 subgroups (p = 0.50). Excluding the patients who never had a term pregnancy before surgery, the term delivery rate was 72.7% for septum/partial septum uterus and 66.6% for arcuate. In the T-shaped uterus group, no previous term or preterm pregnancies had been observed.

A further stratification was performed for the number of spontaneous abortions observed before surgery. Three cutoff levels were generated (2, 3–4 and >4). According

to the number of abortions, by Kaplan-Meier analysis the term delivery rate was 69.7, 56.5 and 26.3% (p = 0.0008; log-rank test) as shown in figure 3. Excluding those patients who never had a term or preterm pregnancy before the surgical intervention (n = 149), the term delivery rate was 68.2, 56.9 and 17.6%, respectively (p = 0.0001; log-rank test).

Table 4 reports the term delivery rate observed before and after surgery according to the number of abortions and type of uterine malformation with and without those patients who had a previous term pregnancy.

Multivariable Analysis

Cox analysis was performed in order to calculate a pregnancy rate throughout the generated subgroups of uterine surgery. In the final model, maternal age and number of abortions before surgery were used as covariates. Table 5 reports the Cox regression output. As shown, the number of abortions, maternal age and uterine malformations were all associated with a significant odds ratio.

Table 4. Term delivery rate observed before and after surgical intervention according to number of abortion and type of uterine malformation

Stratification	Before surgery, %	After surgery, %	After surgery[1], %
Previous abortions			
2	5.67	69.7	68.2
3–4	6.26	56.5	56.9
>4	1.52	26.3	17.6
Uterine malformations			
Group 1	0	66.7	–[2]
Group 2	6.2	62.8	72.7
Group 3	6	55.6	66.6

Figures represent percentages.
[1] Only on cases that never had a term pregnancy.
[2] No cases had a previous term pregnancy.

Table 5. Outcome of the Cox regression analysis

	Odds ratio	95% CI		p value
		lower	upper	
Number of previous abortions (2 vs. 3–4 vs. >4)	1.734	1.206	2.492	0.003
Maternal age (27–48 years)	1.115	1.050	1.184	<0.001
Group (1 vs. 2 vs. 3)	1.678	1.083	2.600	0.021

Discussion

These data suggest the fundamental influence on reproductive function and dysfunction (RSA) of uterine cavity morphology in various types of anomalies, and we wanted to evaluate the term delivery rate after hysteroscopic metroplasty for anomalies, especially for arcuate uterus in women with spontaneous abortion. If hysteroscopic metroplasty has a beneficial effect, in particular for women with arcuate or T-shaped uterus, the reproductive strategies would benefit from such a finding. Investigations about RSA are extremely hard to perform because of the large amount of possible bias as recently described by Christiansen et al. [14] in 2005. In particular, case controls and cohort studies suffer from major flaws due to incorrect diagnosis of recurrent pregnancy loss (bias due to the real number of previous abortions that can be overestimated) and to estimation of RSA in the same patients before and after surgery [14].

The term delivery rate observed after surgical intervention according to the type of uterine malformation (66.7% for T-shaped uterus, 62.8% for septum/subseptum and 55.6% for arcuate uterus) was about 10-fold higher than before surgery. Particularly surgery for T-shaped uterus resulted in the best term delivery rate even though no statistical differences were found for the 3 categories of malformation. Likewise, arcuatus uterus is a finding with an uncomplicated surgery procedure and is very frequently diagnosed in patients with RSA, but often not recognized as an abnormal finding. Our data demonstrated a lower, but still acceptable term delivery after surgery (fig. 2). In fact, if our study had not considered arcuatus uterus (group 3), we would have excluded 81 patients from surgical treatment.

Above all, without T-uterus and arcuatus uterus patients (group 1 and group 3 of our study) we would have excluded 98 patients classified as idiopathic or unknown abortion from treatment (17 and 81). However, since this is a retrospective analysis, it is possible that a prospective randomized design would yield lower rates of delivery. In fact, we cannot properly demonstrate that all of the patients who did not try to get pregnant did not really have the wish of becoming pregnant.

From the results of Cox analysis, we also found a significant independent effect of the number of previous

abortions, maternal age and group (1, 2 or 3) on the term survival rate after surgery as reported in table 5. The highest odds ratio was found for the 'number of previous abortions' followed by the 'belonging to groups 1 through 3'. Such a result could be useful for counseling since one might be able to quantify the risk associated with the number of previous abortions.

The dramatic beneficial effect of hysteroscopic metroplasty on women with arcuate or T-shaped uterus inclines us to consider the uterine cavity (uterine factor) as a main factor in RSA patients. This common pathology has been analyzed for the frequency of the uterine factor by several authors [15–18] for patients with 2 or more consecutive abortions. It ranges from 1 to 30%. All of these studies consider the conventional mullerian anomalies (from the AFS classification). However, if we can also consider and include other anomalies such as T-shaped uterus and arcuate uterus, the uterine factor could become the major cause of pathology and have an incalculable percentage of incidence.

Moreover, if we consider that recently the indications for hysteroscopic treatment for congenital uterine malformation have been broadened to include not only septate/partial septate uterus related to adverse reproductive outcome, but also patients before any potential obstetric accidents, especially women with declining fertility (>35 years), and before resorting to an assisted reproductive technique (IVF), as well as women with no actual desire for pregnancy [13], we would do well to regard the uterine cavity morphology as the crucial point for all reproductive strategies. Pabuccu and Gomel [19] in 2004 demonstrated that women with unexplained infertility and septate/partial septate uterus could have great benefit from hysteroscopic metroplasty.

In conclusion, we argue that a randomized controlled trial on the effectiveness of the uterine cavity morphology is needed in patients with recurrent miscarriage.

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