Is surgical management of uterine septum necessary prior to IVF?

Professor T C Li
Professor of Reproductive Medicine & Surgery
Sheffield
Should septum be removed prior to IVF?

Should septum be left alone prior to IVF?
I remove septum prior to IVF because .... there is good enough evidence that it will improve outcome

I do not remove septum prior to IVF because .... there is no good evidence that it will improve outcome
The evidence
Prevalence of Septate uterus

High Accuracy studies (n=13110)
# Sheffield RM Data

<table>
<thead>
<tr>
<th>Patient group</th>
<th>1(^{st}) Trimester</th>
<th>2(^{nd}) Trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unexplained RM((n=630))</td>
<td>68%</td>
<td>3%</td>
</tr>
<tr>
<td>Septate ((n=106))</td>
<td>73%</td>
<td>13% **</td>
</tr>
</tbody>
</table>

**p<0.001

*Adapted from:* Saravelos et al. *RBM Online*. In press
# Sheffield RM Data: 1st Trimester Loss

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Biochemical</th>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unexplained RM</td>
<td>30%</td>
<td>49%</td>
<td>21%</td>
</tr>
<tr>
<td>(n=263)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septate (n=45)</td>
<td>11% **</td>
<td>58%</td>
<td>31% *</td>
</tr>
</tbody>
</table>

* p<0.05  
** p<0.01  

Adapted from: Saravelos et al. *RBM Online*. In press
REPRODUCTIVE OUTCOME BEFORE AND AFTER HYSTEROSCOPIC METROPLASTY FOR SEPTATE UTERUS

A meta analysis of 16 published series

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>1062</td>
<td>491</td>
</tr>
<tr>
<td>Miscarriage</td>
<td>933 (88%)</td>
<td>67 (14%)</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>95 (9%)</td>
<td>29 (6%)</td>
</tr>
<tr>
<td>Term delivery</td>
<td>34 (3%)</td>
<td>395 (80%)</td>
</tr>
</tbody>
</table>

Homer, Li and Cooke Fertil and Steril, 2000
KEEPER’S RESPONSE

• Evidence is rather weak, as historical control data only, therefore subject to bias

• Data primarily on miscarriage and pregnancy outcome, not on infertility (fecundability)
Case Series 1

Reproductive outcome after hysteroscopic metroplasty in women with septate uterus and otherwise unexplained infertility

Pabuccu & Gomel Fertil Steril 2004

- 61 women
- 25 (41%) conceived within 8-14 months
- 18/25 (72%) live birth
- 5/18 (27.8%) preterm delivery
Case Series 1

Reproductive outcome after hysteroscopic metroplasty in women with septate uterus and otherwise unexplained infertility

Pabuccu & Gomel Fertil Steril 2004

• Conclusion : Women with uterine septum and otherwise unexplained infertility might benefit from hysteroscopic metroplasty
Hysteroscopic resection of the septum improves the pregnancy rate of women with unexplained infertility: a prospective controlled trial
Mollo et al, Fertil Steril 2009

• 44 women with septate uterus and unexplained infertility underwent hysteroscopic metroplasty
• 132 women with unexplained infertility as control subjects
Prospective Controlled Trial

Hysteroscopic resection of the septum improves the pregnancy rate of women with unexplained infertility: a prospective controlled trial

Mollo et al, Fertil Steril 2009

<table>
<thead>
<tr>
<th></th>
<th>Pregnancy rate</th>
<th>Live birth rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>unexplained infertility &amp; septum removed</td>
<td>38.6%</td>
<td>34.1%</td>
</tr>
<tr>
<td>Unexplained infertility</td>
<td>20.4%</td>
<td>18.9%</td>
</tr>
</tbody>
</table>
• Although data is more related to infertility, it is not specifically on IVF
• Although data is more related to infertility, it is not specifically on IVF

Should septum be removed prior to IVF?
Is hysteroscopic correction of an incomplete uterine septum justified prior to IVF?

Ozgur et al Reprod Biomed Online 2004

• 119 women with incomplete uterine septum
• 119 age-matched control patients

<table>
<thead>
<tr>
<th></th>
<th>Septum removed</th>
<th>control</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of miscarriage</td>
<td>14.2%</td>
<td>6.0%</td>
</tr>
<tr>
<td>Previous IVF failure</td>
<td>32.7%</td>
<td>20.6%</td>
</tr>
<tr>
<td>Clinical pregnancy</td>
<td>47.8%</td>
<td>46.5%</td>
</tr>
<tr>
<td>Miscarriage rate</td>
<td>10.5%</td>
<td>20.3%</td>
</tr>
</tbody>
</table>
Retrospective Control Study

The outcome of singleton pregnancies after IVF/ICSI in women before and after hysteroscopic resection of a uterine septum compared to normal controls


- 31 women who conceived following IVF or ICSI before hysteroscopic resection of large (12) or small (19) uterine septum; and 106 women who conceived following IVF or ICSI after hysteroscopic resection of large (49) or small (57) uterine septum.

- For each pregnancy in the study group, 2 pregnant matched, control women identified from IVF/ICSI registry
Retrospective Control Study

The outcome of singleton pregnancies after IVF/ICSI in women before and after hysteroscopic resection of a uterine septum compared to normal controls


<table>
<thead>
<tr>
<th>Septum Type</th>
<th>Miscarriage rate</th>
<th>Miscarriage rate in matched controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large septum, not removed</td>
<td>83.3%</td>
<td>16.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Small septum, not removed</td>
<td>78.9%</td>
<td>23.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Large septum removed</td>
<td>30.6%</td>
<td>20.4%</td>
<td>NS</td>
</tr>
<tr>
<td>Small septum removed</td>
<td>28.1%</td>
<td>19.3%</td>
<td>NS</td>
</tr>
</tbody>
</table>
KEEPER’S RESPONSE

• The evidence is somewhat better, but I am not sure if you can call it Grade B+, I would call it Grade B- or Grade C

• The finding is contrary to my experience because I know some patients with a septate uterus have no problems conceiving

• I like to see the results confirmed by a properly conducted RCT before changing my practice
There is **no RCT** on the surgical removal of septum prior to IVF treatment

So what do we do?
TRUST

The Randomised Uterine Septum Transection Trial
TRUST

• Mutli-centred, Dutch study
• 68 women with 2 or more miscarriage before 20 weeks with a septate uterus
• septum length at least ¼ of cavity
• Hypothesis : Live birth rate increases from 35% to 70%
2014.... RCT finally published...

Removal of septum produced better outcome.

Keeper’s responses

• It is about miscarriage population, not about IVF population ....

• I do not do this type of operation anyway. I do not think I will do a good job, I am never a good surgeon and I may make it worse.
2014......RCT finally published...

Removal of septum did **not** produce better outcome.

Cutter’s responses

- The study was underpowered
- Some surgeons did not do it properly - they are rather inexperienced. They did not remove all the septum and leave a bit behind. They did not use anti-adhesion gels......
So the debate continues....
What does that mean to you (now)...

Two good news

• You can carry on doing what you believe – no one can really say that what you do is wrong.
• There is no absolute right or wrong, there is no need for confrontation, the keepers and cutters could continue to be friends.
My Opinion

• The currently available evidence does suggest that septum should be removed prior to IVF
• The quality of currently available evidence is reasonable, Grade B-
• Properly conducted and powered RCT should be welcome to provide more robust, Grade A evidence
The future

1. Better diagnosis
## Classification of congenital uterine anomalies

<table>
<thead>
<tr>
<th>Classification</th>
<th>Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Hypoplasia/agenesis</td>
<td>(a) Vaginal, (b) Cervical, (c) Fundal, (d) Tubal, (e) Combined</td>
</tr>
<tr>
<td>II Unicornuate</td>
<td>(a) Communicating, (b) Non Communicating, (c) No cavity, (d) No horn</td>
</tr>
<tr>
<td>III Didelphus</td>
<td></td>
</tr>
<tr>
<td>IV Bicornuate</td>
<td>(a) Complete, (b) Partial</td>
</tr>
<tr>
<td>V Septate</td>
<td>(a) Complete, (b) Partial</td>
</tr>
<tr>
<td>VI Arcuate</td>
<td></td>
</tr>
<tr>
<td>VII DES drug related</td>
<td></td>
</tr>
</tbody>
</table>

How to differentiate between a small uterine septum and an arcuate uterus?
2. Better selection
PATIENT SELECTION

Everything in surgery is patient selection – the chief determinant of results, mortality and morbidity
What type of septum should be removed prior to IVF?

Does size matter?

Is reproductive history important?

Does vascularity affect outcome?
3. Proper surgical techniques
ULTRASOUND CONTROL
HYSTEROSCOPIC REMOVAL OF SEPTUM

- resectoscope - diathermy needle
- hysteroscopic scissors
- laser
Prevention of adhesion

- Hormone treatment
- Intrauterine contraceptive device (IUD) ± Balloon?
- Antibiotics
- HyalobARRIER
4. Better counselling
What is the best time to perform ICSI/ET after hysteroscopic surgery for an incomplete uterine septum?

Berkkanoglu et al Fertil Steril 2008

- 282 women who underwent ICSI/ET after removal of uterine septum

<table>
<thead>
<tr>
<th></th>
<th>&lt; 9 weeks</th>
<th>10-16 weeks</th>
<th>&gt; 17 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>133</td>
<td>93</td>
<td>56</td>
</tr>
<tr>
<td>Clinical pregnancy rate</td>
<td>45.8%</td>
<td>43.1%</td>
<td>41.1%</td>
</tr>
<tr>
<td>Miscarriage rate</td>
<td>6.4%</td>
<td>7.9%</td>
<td>5.1%</td>
</tr>
</tbody>
</table>
Obstetric outcome

- Premature labour
- Abnormal presentation
- Cervical weakness
- Rupture of uterus
5. Proper RCT
Conclusions
Should septum be removed prior to IVF?

Probably Yes
Should septum be removed prior to IVF?

Probably Yes

RCT awaited

Case selection

Proper surgical techniques
Thank You