Strategy for Myomas Associated with Infertility: Surgery Versus ART?

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Conflict of interest

I declare I have no conflict of interest in this presentation.
Items Addressed

1- Myomas and fertility.
   1.1. Natural conception.
   1.2. ART.

2- Strategy for Myomas, associated with infertility.
   2.1. Myomectomy.
   2.2. Myomectomy followed by ART.
   2.3. ART.
   2.4. ART followed by Myomectomy.

3- Conclusion.
Mean age of women at the birth of the first child (2008)
UN Statistics, July 2011
This recent trends of women to delay childbirth to their 30\textsuperscript{th} and 40\textsuperscript{th}, when the incidence of fibroids is significantly increased, resulted in an increasing number of infertile patients seeking treatment and have myomas; not uncommonly multiple and large myomas.

Pundir J et al 2015
J Obstet and Gynecol, 35:37-41
Other Main Risk Factors for Development of Myomas

• African- American ethnicity (almost three times as likely as white women).

• Nulliparity.

• Obesity.

• Cigarette smoking.

Though uterine fibroids occur in up to 77% of women in reproductive age*, yet as a sole cause of infertility they may be responsible for only 2-3% of infertility cases**.

How Fibroids cause Infertility?

1. Physical location impending egg or sperm transport.
2. Impaired uterine peristalsis.
3. Vascular changes.
4. Chronic inflammatory response by the endometrium to underlying fibroid.
5. Disruption of the uterine intracavitary biochemical milieu.

Several studies had shown that infertility could be attributed to submucosal fibroids and intramural fibroids distorting the endometrial cavity and impeding sperm transportation or normal implantation.

Leiomyomas that distort the uterine cavity (submucosal or intramural with an intracavitary component) result in difficulty conceiving a pregnancy and an increased risk of miscarriage.

- Pritts, EA, Parker, WH, Olive, DL. 2009Fertil Steril; 91:1215.
Women with cavity-distorting fibroids who did versus did not undergo myomectomy had a significant increase in conception rate (RR 2.03, 95% CI 1.08–3.83).

Updated Systematic Review of the Evidence had shown that by removing SM fibroids women had comparable pregnancy rates to controls with no fibroids (RR: 1.545 nonsignificant).

Patients undergoing IVF have a decreased pregnancy rate and an increased miscarriage rate if they have submucosal or intramural fibroids distorting the endometrial cavity.

In contrast, subserosal fibroids do not impair fertility. The role of non-cavitary distorting intramural fibroids in infertility is controversial.

Women with non-cavitary distorting intramural myomas/ Natural conception

Less likely to become pregnant  RR 0.81, 95% CI 0.70–0.94
More likely to have a spontaneous abortion  RR 1.7, 95% CI 1.2–2.5

Pitts EA 2009. Fertil & Steril. 91:1215
Non-Cavitary distorting Intramural myomas & ART

In a prospective study by our group of 406 infertile patients including 39 patients with non-cavitary distorting myomas undergoing ART it was found that uterine myomas <7cm and not encroaching on the cavity did not affect implantation or miscarriage rates.

More recently Oliveira et al (2004) and Vimercati et al (2007) indicated that interstitial myoma <4cm, not distorting the uterine cavity, do not pause threat to the pregnancy and live birth rates following IVF.

However, Khalaf et al (2006) found that even the small myomas significantly reduced the ongoing pregnancy rate at each IVF/ICSI cycle by 40% and the Live birth rate at each IVF/ICSI cycle by 45%.

A recent systematic review and meta-analysis compiling >6000 patients reported a significant reduction in the clinical pregnancy and live-birth rates following IVF treatment in women with non-cavitary distorting intramural fibroids, compared with controls.

### Negative Effect of Non-Cavitary Distorting Intamural Fibroids/ Patient without Fibroids Meta-analysis

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<th>Observational studies</th>
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<td>19</td>
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<tr>
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<th>6,087 IVF cycles</th>
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<th>LBR</th>
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<td>RR=0.79; 95% CI=0.7-0.88; P&lt;0.0001</td>
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<th>CPR</th>
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<tr>
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<td>RR=0.85; 95% CI=0.77-0.94; P=0.002</td>
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A recent meta-analysis has highlighted a number of study design issues with suboptimal localization of fibroid position being a common problem in interpreting the exact role of intramural fibroids. Since fibroid location was determined by imaging methods, less reliable than hysteroscopic documentation, thus biasing the results.

Myomas associated with other confounding factors of infertility
More commonly myomas are associated with other confounding factors of infertility as:

- Tubal or ♂ factor infertility,
- Advanced maternal age
- Long duration of infertility
- Failure of previous management (IVF/ART).

All these must be taken into consideration when outlining strategy for myomas associated infertility.
What is the strategy for Myomas?

- Mymectomy
- Myomectomy followed by ART
- ART
- ART followed by myomectomy
Before counselling the couple the RM physician should ask his/herself:

1- Is myoma/s the sole possible cause of infertility?
2- What is site, size and number of myoma/s?
3- Is myoma/s associated with other confounding factors of infertility?
4- Age of the patient.
5- duration of infertility
If Myoma/s is/are the sole possible cause of infertility, the Answer is Surgery.
Although myomectomy remains the preferred treatment method for women who wish to preserve fertility, sufficient evidence that myomectomy improves fertility is lacking due to absence of well designed randomised trials.

The only prospective controlled trial on 181 women had shown that in women with IM myomas there was no significant difference in pregnancy rates between those who had myomectomy (56.5%) and those who did not (41%).

In a review of 27 studies by Vercellini et al 1998, prospective data revealed a pregnancy rate of 57% after abdominal myomectomy.

Existing literature suggests that the pregnancy rates after abdominal myomectomy ranges between 24-72%.

The live-birth rate after abdominal myomectomy for a large fibroid uterus or a greater number and deeper localization of myomas is likely to be low.

In a recent retrospective study of abdominal myomectomy for subfertile women with a large fibroid uterus of $\geq$ 16 weeks in size, LBR was 20% and miscarriage rate was 32% after 3-7 years follow up.

The most important factor that influences the odds of achieving a live birth after abdominal myomectomy is the age of the woman at the time of surgery.
Significantly higher chances of successful pregnancy were reported in women younger than 30 years of age and a very low chance of pregnancy in women > 38 years at the time of surgery.

Surgical modalities for Myomectomy

- Hysteroscopic myomectomy (HM)
- Abdominal myomectomy (AM)
- Laparoscopic myomectomy (LM)
Choice of type of surgery

Depends upon:

- The location of the myoma/s.
- Number and size of myomas.
- Size of the uterus.
- The expertise of the surgeon and supportive endoscopic equipment.
Current evidence from two randomized controlled trials suggests there is no evidence for a significant effect of AM or LM on:

- The live birth rate (OR 0.80, 95% CI 0.42 to 1.50),
- Clinical pregnancy rate (OR 0.96, 95% CI 0.52 to 1.78),
- Ongoing pregnancy rate (OR 1.61, 95% CI 0.26 to 10.04) or
- Miscarriage rate (OR 1.31, 95% CI 0.40 to 4.27)

Cochrane review, 2012.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Total Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>M.H., Fixed, 95% CI</th>
<th>M.H., Fixed, 95% CI</th>
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<tr>
<td>Palomba 2007</td>
<td>32</td>
<td>20.6%</td>
<td>1.32</td>
<td>[0.39, 4.30]</td>
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<td>Seracchioli 2000</td>
<td>59</td>
<td>79.2%</td>
<td>0.66</td>
<td>[0.31, 1.39]</td>
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<td><strong>Total (95% CI)</strong></td>
<td><strong>91</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>0.80</strong></td>
<td><strong>[0.42, 1.50]</strong></td>
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Heterogeneity: Chi² = 0.90, df = 1 (P = 0.34); I² = 0%
Test for overall effect: Z = 0.70 (P = 0.48)

Forest plot of comparison: 2 Open versus laparoscopic myomectomy, outcome: 2.1 Live birth rate.

Cochrane review, 2012.
Cochrane review, 2014 concluded LM compared with all types of AM is a procedure associated with:
- less subjectively reported postoperative pain,
- lower post operative fever and
- shorter hospital stay.
More studies are needed to assess rates of uterine rupture, occurrence of thrombo-embolism, need for repeat myomectomy.

Bhave Chittawar P et al http://www.thecochranelibrary.com
However, uterine size, number, size, and sites of fibroids to be removed, and the level of expertise of the surgeon are limiting factors for LM.
Myectomy followed by ART.
Indications

- Associated infertility factors as male or tubal factor infertility.
- Failure to get pregnant after myomectomy particularly in elderly women.
- Young women with long duration of infertility and previously subjected to myomectomy.
A high clinical pregnancy rate (52%) was reported in women undergoing IVF following abdominal myomectomy for different sizes of fibroid uteri.

When ART is a first choice for infertile couples with myomas?
ART first choice.

- Subserous myomas.
- Some interstitial myomas (<4 cm) not distorting the uterine cavity.
- Other confounding factors as tubal or male factor infertility in the absence of distortion of uterine cavity.
- Advanced maternal age with small myomas.
ART followed by myomectomy

A woman in her late thirties with a small fibroid (<4cm) not distorting the uterine cavity deserves a trial of ART to get pregnant without myomectomy
If this trial fails or ends in a miscarriage, she may be counselled for sugary before repeat trial.
Conclusion

In women with myoma/s associated infertility myomectomy or ART can be an appropriate first line of treatment or complimentary to each other depending upon site, size and number of myomas, other confounding factors, age of the woman, duration of infertility and outcome of previous treatment whether myomectomy or ART.
THANK YOU