Preservation of fertility in women with fibroids: UAE, HIFU & Myomectomy

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Conflict of interest - NONE
The past 20 years has witnessed an unprecedented expansion in treatment options for fibroids – ?? spoilt for choice

SURGICAL?
Hysterectomy
Myomectomy –
  Abdominal
  Laparoscopic
  Robotic
Hysteroscopic
Vaginal

MEDICAL THERAPY?
GnRHa+/- add-back therapy
SERMS
Aromatase Inhibitors
Antiprogestins
Androgens
SPRMs - UP

Less invasive
Radiological Interventions?
UAE
MRgFUS
The imperative to optimize the care of women with fibroids

- Not just because fibroids are the commonest tumour in women of reproductive age

- Nor because fibroids impact negatively on women’s QoL

- And not just because they have major health and economic implications

But perhaps more importantly because of the changing demography of childbirth
Women are delaying pregnancy until later in life when fibroids are more prevalent & symptomatic.

Source: ONS
The old adage:

babies, then fibroids, then hysterectomy no longer works for an increasing number of women!
Women would like to preserve the uterus for fertility and personal reasons.

Borah et al reported that 79% of all respondents would like a treatment for their fibroids that did not involve invasive surgery (2013).
My Talk 20.03.2017

• UAE & fertility - all safe and sound
• HIFU & fertility – what do we know?
• Myomectomy – approaches to optimizing outcomes
  - banish pre-myomectomy GnRHa
  - minimizing blood loss at complex myoma surgery
  - minimization of adhesions – pelvic & intrauterine
  - Neither age, number of fibroids nor size or location should be barrier to complex myomectomy

Concluding remarks
Radiological Management of fibroids

Do they enhance or compromise fertility?
Radiological treatments for fibroids

UAE

MRgFUS

LEVEL EVIDENCE
Efficacy of UAE for symptom relief and improvement in quality of life is well-established.
UAE & Pregnancy - Concerns

• Hypothesis that embolization of BOTH uterine arteries leads to placental insufficiency

• Hypothesis that embolization impairs ovarian function

• Migration of fibroids towards the uterine cavity following UAE could compromise receptivity and normal placentation
UAE & Pregnancy – debunking a myth

Hypothesis that embolization of BOTH uterine arteries leads to placental insufficiency??

- Not supported by doppler studies
- Markers of tissue ischaemia absent 48hrs post UAE
- By 6 months post-UAE, when pregnancy is advised, the majority of uterine arteries have re-canalized!

(Piccone et al J Mat Fetal Neonatal Med 2003)
UAE & Pregnancy – debunking another myth

**Hypothesis that embolization impairs ovarian function**

1. Arterial flow to the ovary is likely to be transiently occluded during UAE. Despite this the incidence of clinically apparent injury to ovarian reserve is low.

1. Results of 10 studies on hormonal assessment of ovarian reserve showed no observable effect on ovary in women <45yr.

1. Further studies using AMH before definitive conclusions can be reached.

*(Kaump & Spies JVIR 2013)*
UAE & Pregnancy

Migration of fibroids towards the uterine cavity following UAE could compromise receptivity and normal placentation

- Mara et al, 2012:
Observation of negative impact of UAE

Meta-analysis & Review (Horner & Saridogan Fertil Steril 2010)

- 227 completed pregnancies post UAE
- Spontaneous abortion rate 35% vs 16.5% for non-UAE fibroid controls
- PPH 14% vs 2.5%
- Pre-term delivery, IUGR & malpresentation not increased
UAE & Pregnancy

• Systematic review (2013) of 21 studies of UAE
  – Pregnancy rates following UAE are comparable to the age-adjusted rates in general population

  – Pooled analysis
    • Cumulative pregnancy rate 58.6%
    • Miscarriage rate 28%
    • Cumulative live birth rate was 65.2%
    • Mean age of patients was 36 years

Overall this is comparable to the age-adjusted pregnancy rate in the general population

Recommendations from RCOG / RCR

“The evidence for the beneficial effect of myomectomy or UAE on fertility and pregnancy outcomes is weak .......

“Women who desire pregnancy but experience subfertility or recurrent miscarriage due to fibroids can be offered UAE with counselling and review by an assisted reproduction and fertility specialist....”
Magnetic Resonance-Guided Focused Ultrasound Surgery of Uterine Fibroids

Focused Ultrasound generates heat by focusing ultrasound waves, ablating tissue only at the focal point... an effect similar to a magnifying glass used to focus the sun’s energy on a single point.

Efficacy of MRgFUS for symptom relief and improvement in quality of life is well-established.
**MRgFUS**

- Approved by FDA in 2004
- NICE – Audit & Research setting only

**Advantages**
- Non-invasive uterus sparing procedure
- No hospitalization
- No general anesthesia
- Faster recovery, next day return to normal activity
- Low rate of complications
- No ionizing radiation
- Treatment can be repeated
- Decreased risk of infections
- Absence of post-treatment scarring and adhesion formation

**Disadvantages**
- MRgFUS is a complex technology and initial set-up is expensive (requiring MR and Focused Ultrasound machines)
- Only small volumes of fibroid can be treated at a time: 2-4h per treatment.
- Not suitable for massive fibroids
- Minimal head-to-head comparative data with other uterus sparing procedures

**IMPACT ON FERTILITY UNCERTAIN ! !**
Myomectomy

Does it enhance or compromise fertility?
Myomectomy could compromise the very same fertility it is intended to preserve / enhance

- By the use of GnRHa
- Failure to pay meticulous attention to blood loss
- Failure to prevent intrauterine and pelvic adhesions
- Failure to remove ALL the fibroids at myomectomy
- Surgical inexperience

Also, denying women a myomectomy because of their age, or size, number or location of their fibroids should be considered poor practice in contemporary practice
The use of GnRHa in fibroid disease

87% of UK gynaecologists use GnRHa pre-treatment in fibroid disease ostensibly to:

• reduce blood loss at myomectomy
• correct anaemia prior to surgery
• Reduce fibroid mass to convert a vertical to a transverse incision at abdo hysterectomy; or an abdo hysterectomy to a vaginal hysterectomy
A role for GnRHa in fibroid disease..............???

? Reduce blood loss at myomectomy:

- In fact they destroy tissue planes - render fibroid enucleation difficult: longer operation, potentially greater blood loss!

? Correct anaemia prior to surgery

- humble norethisterone: simple, vastly cheaper and just as effective, without the side effects of GnRH analogues
A role for GnRHa in fibroid disease ......???

? Reduce fibroid mass to convert a vertical to a transverse incision at abdominal hysterectomy; or an abdominal hysterectomy to a vaginal hysterectomy.

• The perceived need for vertical incisions for massive fibroids is a product of habit & upbringing.

• We very rarely ever use vertical incisions: very occasional for repeat open myomectomy.

-> transverse suprapubic with high sheath incision (the boat incision)

Remember that you perform term caesarean deliveries via a Pfannestiel incision!
Towards an evidence-based practice:
- BANISH GnRHa in fibroid disease!

- Expensive & NOT cost-effective

Kongnyuy EJ, Wiysonge CS. Interventions to reduce haemorrhage during myomectomy for fibroids. Cochrane Database of Syst Rev 2007: CD005355

- Triple tourniquets are better than GnRHa at reducing blood loss during myomectomy.

Towards an evidence-based practice:
- BANISH GnRHa in fibroid disease!

• They delay surgery
• Considerable, well-described side effects
• Minimal, if any, efficacy for very large fibroids
• Progestogens are cheaper & just as effective to facilitate correction of anaemia

They mask smaller fibroids
(increase apparent rates of recurrence)
Evidence-based practice:
- BANISH GnRHa in fibroid disease!

A detailed rehearsal of the arguments

“GnRH Agonists: Do They Have a Place in the Modern Management of Fibroid Disease?”
A Protocol for minimizing blood loss (at complex myoma surgery)

Pre-op measures

Peri-operative techniques to minimize blood loss

Post-operative measures
Pre-operative measures to minimizing blood loss (at complex myoma surgery)

Optimization of Hb levels:
• Oral iron supplementation
• Intravenous iron supplementation
  (convenience of ferric carboxymaltose!)
• - Blood transfusion – emergency only

Optimal minimum Hb – ?? minimum 120g/L
(The special case of JW’s - ?? minimum Hb 140g/L

Historical measure – pre-myomectomy UAE
• In JW patients
• For repeat myomectomy
Peri-operative techniques to minimize blood loss

- Availability of cell salvage facilities
- Tranexamic Acid – 1g slow iv with induction of GA
- Liberal use of VASOPRESSIN
- Minimal number of uterine incisions to enucleate fibroids
- Insertion of surgicell in subserous layer
Post-operative measures to minimizing blood loss (at complex myoma surgery)

3 further doses of Tranexamic Acid 1g 6 hourly

Fragmin following morning
The evidence base for our Protocol for minimizing blood loss

Extensive / significant literature of the following:

- Ferric carboxymaltose
- Pre-myomectomy UAE
- Tranexamic Acid
- Vasopressin
- Use of cell salvage
- Tourniquets

Evidence awaiting publication
- Use of sub serosal surgicell
- Optimal Hb levels
Outcomes of measures to minimize blood loss (at complex myoma surgery)

• Blood transfusion rates 5-8% in complex myoma surgery cp 20-24% in literature

• Average blood loss 200 – 500 despite massive fibroids

• Largely dry operative field allows removal of all visible and /or palpable fibroids

• Rare use of drains
Optimizing outcomes from myomectomy

Myomectomy can compromise the very same fertility that it is intended to preserve by the formation of BOTH pelvic and intra-uterine adhesions

Solution:

Optimizing outcomes from myomectomy

Many women are offered ONLY hysterectomy as the treatment option for their fibroids, being told that either they are too old for child-bearing anyway, or their fibroids are too large, too many or in the wrong place!

Our view:

At myomectomy, some surgeons advocate the removal of only the large fibroids and/or those that are deemed to be symptomatic.

Questions:
- How does one know which ones are symptomatic?
- Surely those left behind will just continue to grow!

Wijisekera NT, Mauri G, Gupta S, Belli AM, Manyonda IT
“MR imaging evaluation of fibroid clearance following open myomectomy for massive/multiple symptomatic fibroids”
Arch Gynecol Obstet 2012, 286; 1165-71
Impact of current surgical, radiological & medical treatments for uterine fibroids.

Improve quality of life & clinical symptoms

Manyonda IT, Bratby M, Horst JS, Banu N, Gorti M, Belli A-M.


BUT impact on human reproduction is uncertain
Concluding Remarks

Radiological treatments UAE & HIFU:
- Case series of successful pregnancy following treatments abound
- No rigorous research evidence for enhancement of fertility
- Some sequale of UAE (fibroid migration) give cause for concern
- Continued research is vital

Myomectomy:
- The operation itself could compromise fertility
- Meticulous attention to detail and consider the following:
  - Do not use pre-operative GnRHa
  - Take measures to minimize operative blood loss
  - Take measures to reduce BOTH pelvic & intrauterine adhesions
  - Are you the right person to perform the operation?
Thank you