ESHRE 2020 Virtual (5-8 July 2020)

Questions for the speakers

PCC03: The uterus revisited

A critical analysis of classifications of uterine anomalies and their impact on our clinical practice - Thierry Van den Bosch (Belgium)

Q: With T shaped uterus do you think it would be useful to resect in a case of recurrent miscarriage? (needle resection - scissors)

A: This should be investigated in a randomized trial.

The different types of T-shaped uteri should be analyzed, to see if some might benefit.

Q: Concerning adenomyosis in the case of ''outter AD'' with intact JZ do you think it would have an impact on implantation? How often do you see it

A: From a theorical point of view you expect adenomyosis of the inner myometrium (disrupting the JZ) to have an impact on implantation while outer myometrium adenomyosis can be regarded as a type of deep endometriosis, and , if isolated, does not influence implantation.

In my experience outer myometrium adenomyosis is far less frequent than inner myometrium disease.

Chapron et al. published a series demonstrating that outer myometrium adenomyosis is associated with deep endometriosis.

Q: Do you recommend the same algorithm for T-shaped uterus management in recurrent implantation failure?

A: So far yes. We really need good quality prospective, randomized data, to show whether some would benefit from surgery. Again, the different types should be strictly described in the collected data.

Q: Given the uterine contractility described, would it be useful to use uterine relaxant when scanning to evaluate uterine anomalies esp T shape or not?

A: Repeating the ultrasound scan in 15-30 minutes is often enough. Finding an effective drug, without side effects would be convenient indeed. (the same applies for transient tubal block at hysterosalpingo-foam-sonography)

How can our understanding of uterine physical chemical environment help us manage our patient? - Ying Cheong (United Kingdom)

Q: Can you comment on detrimental impacts of reactive O2?

A: Reactive oxygen species are formed as part of normal metabolism of oxygen and is important in cell signaling and maintaining homeostasis. However, in excess they can damage cellular structures. That may be why, high level of oxygen is not helpful within the reproductive tract for embryo development.

Q: How it will be ensured that the in vivo monitoring device (if placed in- utero) itself won't alter the uterine microenvironment

A: The key is to keep the device small and inert. It has already been demonstrated by the Anevivo device that gametes and later embryos can survive in an inert foreign environment. Clearly, with our device I demonstrated, we do need to continue researching and evaluating to ensure it does not detrimentally affect the uterine environment.

Q: How could help intra-uterine monitoring in assessing key points to maintain an adequate biophysical environment for oocytes in IVF lab?

A: The natural environment of the reproductive tract when properly understood can perhaps be replicated in the laboratory. This would offer the most natural way gametes and embryos can develop in vitro.

Uterine dysfunction: Fibroids and polyps - Elizabeth Stewart (U.S.A.)

Q: What about comb. oral contraceptives to control symptoms of UFs and adenomyosis. Do these medications have any significance?

A: They are typically used as a first line treatment because they are inexpensive, easily available, treat other conditions such as oligo ovulation and provide contraceptives. However, evidence reviews have suggested that there is little evidence for their benefit and comparative trials have suggested that other agents are more effective.

Q: Do you believe that performed myomectomy is effective prior IVF treatment?

A: There are clearly anecdotal cases where they appear to be benefit, but based on the Pritts review, there is only evidence supporting hysteroscopic myomectomy. [1]

1. Pritts EA, Parker WH, Olive DL. Fibroids and infertility: an updated systematic review of the evidence. Fertil Steril. 2009;91(4):1215-1223.

Q: Why do you believe that hyterectomy with bylateral ooforectomy is less effective than hysterectomy alone?

A: I don't believe that removing the ovaries provides any benefit when the indication for hysterectomy is uterine fibroids. Moreover, the risks are increased. Hysterectomy with bilateral oophorectomy is associated with **an increase in all-cause mortality** as well as increased morbidity where hysterectomy alone has just been associated with increased morbidity.

Q: What is the half-life of Elagolix? Also, what is the most common side-effect?

A: It has a short half-life, 4-6 hours, which causes twice daily dosing. When administered alone, hot flushes are the most frequent side effect. However, for fibroids, the FDA-approved formulation is formulated with low dose estrogen and progestin coadministration and studies show similar side effect profiles to placebo.[2]

2. Schlaff WD, Ackerman RT, Al-Hendy A, et al. Elagolix for Heavy Menstrual Bleeding in Women with Uterine Fibroids. *N Engl J Med.* 2020;382(4):328-340

Q: Do large intramural myoms affect fertility if they do not change the uterine cavity?

A: They can have an effect on the cavity and fertility, but it does not appear to be reversed following myomectomy. 1 It is not clear whether the consequencies of surgery such as adhesions, decreases the benefit or whether there is a more global problem with the uterus.

1. Pritts EA, Parker WH, Olive DL. Fibroids and infertility: an updated systematic review of the evidence. Fertil Steril. 2009;91(4):1215-1223.

Q: What is the advantage of using Gnrh antagonist to agonist in managing fibroids?

A: Antagonists have more rapid onset of action and avoid the flare seen with agonists. Oral GnRH agonists are now available while all agonists available now require injection.

Q: What is the risk of recurrence of symptoms/myoma growth after stopping the Elagolix therapy?

A: We don't yet know that answer since long term extension studies have not been published.

Q: How do you differently use GnRH antagonist monoTx and combination Tx? How about for bulk effect of fibroid and for pre-treatment of myomectomy?

A: Right now all we have is combination oral GnRH antagonist therapy for fibroids. There is a monotherapy that is marketed for endometriosis, but it is a different dose that that tested for fibroids. Thus, we have no data for monotherapy for fibroids.

Q: Would you remove type 2 fibroids in women with recurrent implantation failure or recurrent miscarriage if they do not affect uterine cavity?

A: I'm a little confused by the question since type 2 fibroids by definition impact the cavity. I would consider it in women with unexplained recurrent implantation failure with euploid embryos. However based on the finding from the "Right from the Start" study, I would hesitate since this well designed study suggests fibroids are not associated with miscarriage. [3]

3. Hartmann KE, Velez Edwards DR, Savitz DA, et al. Prospective Cohort Study of Uterine Fibroids and Miscarriage Risk. *Am J Epidemiol.* 2017;186(10):1140-1148

Q: Which types and which sizes of fibroid we can perform the hysteroscopic myomectomy? What is the best indication of this intervention?

A: There is some variation by surgeon, but most FIGO type 0 and 1 fibroids < 5 cms in maximal diameter can be treated with hysteroscopic myomectomy successfully. Most type 2 fibroids in this

size range can also be treated but may require two stage procedures. Heavy menstrual bleeding is the most common indication, but the COMPARE-UF registry is also showing that even some bulk symptoms may be decreased in women following hysteroscopic myomectomy.[4]

4. Laughlin-Tommaso SK, Lu D, Thomas L, et al. Short-term quality of life after myomectomy for uterine fibroids from the COMPARE-UF Fibroid Registry. *Am J Obstet Gynecol.* 2020;222(4):345 e341-345 e322.

Q: Which would be your first-choice treatment in a patient with a non cavity-distorting intramural myoma and age-related infertility, before an IVF treatment?

A: IVF without any fibroid treatment since the delay to pursue fibroid therapy will likely have more impact in women with age-related infertility.

Q: Could you elaborate how AMH dictes second line treatment for fibroids?

A: In our FIRSTT study, women with higher AMH levels were more likely to have a second intervention for fibroids than those with an AMH below the median value. [5] Just as women tend to get some relief of their fibroid symptoms as they approach menopause, less robust ovarian function may also diminish symptoms.

5. Laughlin-Tommaso S, Barnard EP, AbdElmagied AM, et al. FIRSTT study: randomized controlled trial of uterine artery embolization vs focused ultrasound surgery. *Am J Obstet Gynecol.* 2019;220(2):174 e171-174 e113.

Maintaining optimal uterine function in the management of 'gynaecological' malignancies - Frederic Amant (The Netherlands)

Q: In oncological cases, is there in your opinion good/enough collaboration between professionals of the assisted reproduct. technology and oncology fields

A: That varies among countries and centers; I believe in some this will work good, although in others there may be a lot of room for improvement.

Q: Could we consider safe the oocyte transvaginal aspiration from contraleral ovary in patients with IC1 stage low malignancy ovarian tumours?

A: I believe this could be safe provided imaging shows a normal ovary.

Q: How long would you wait after chemotherapy to use sperm? Would you still use sperm when chemotherapy was started?

A: Sperm needs something like three months to mature so I would wait for this period. I would not combine chemo and sperm prelevation.

-foam-sonography)