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'Optimizing Women's Health Through Enhanced Skills and Best Practices'

Issue:

Controversies in Obstetrics and Gynecology

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President's Message

Dear Friends

Here's wishing all AOGD members a New Year filled with optimism, cheer, peace, good health, love, luck and warmth! The year 2017 saw us at the receiving end of unreasonable and inane allegations and accusations. Hope 2018 brings us courage, grit and unity to deal with hostile media, government, politicians and the very patients who we treat with dedication and sincerity. After all it must be understood that medicine is not a perfect science and we cannot ensure immortality! At the same time we need to continuously update ourselves and inculcate 'soft skills' in our young doctors to re-establish cordial doctor-patient relationships. The task is uphill but not impossible!

Starting the January bulletin on *'Controversies'* a number of quotes flash the mind, the best of which is that by Maya Angelou – 'Do the best you can until you know better and when you know better do better'. While some aspects of medical practice are straightforward with sufficient evidence of correct management, many issues are controversial and debatable. This is where the intellectual mind starts working and through discussion and dialogue a middle best path emerges.

Caesarean section rates have burgeoned beyond what is acceptable and one of the *'new indications'* for repeat surgery is short inter-delivery interval. This happens so frequently in practice that we as obstetricians need to ensure that women are counselled and given adequate contraception for at least 2 years. It is still controversial whether 12, 18 or 24 months is the best cut-off! Likewise incidence of fibroids is increasing and myomectomy although controversial during caesarean birth must be given a thought to avoid repeat surgery. Given the correct indication and expertise it can be safe. There are a number of management options for fibroids under 12 weeks especially in young women - conservative medical, surgical and ablative therapies must be tried. Other controversies in this issue make interesting reading so read-on!

Happy Lohri, Sankranti, Basant Panchami and Republic Day greetings! Hope you get time to bask in the warm winter sun, soak in your Vitamin D, gorge on Lohri goodies, enjoy the Republic day parade and not break your New Year resolution of keeping fit!

Cheers!

Shalini Rajaram
President, AOGD (2017-18)

Vice President's Message

Dear Friends

Goodbye 2017 and welcome 2018 – Happy New Year

Wishing you all a healthy, prosperous & peaceful new year!

It is also the time of year to spend with your family, near and dear ones. Have great fun and enjoy the season while our editorial team prepares to find solutions to controversies in the field of Obstetrics & Gynaecology

Dealing with controversial issues in Women's Health, provides the world with the opportunity to effectively debate clinical and therapeutic dilemmas and other key issues facing clinicians in their daily practice and provide an innovative, multi-disciplinary and comprehensive overview of the latest research developments in our field. Controversy promotes excellence, bridges the gaps between expansion of basic science and information, and their consolidation into clinical practice which assists practitioners reach a tangible and practical conclusions on controversial issues.

The current issue gives insight into the pressing clinical controversies, technological advances, ethical and public health issues, standards of treatment, and medical solutions being developed. I am sure.

So, please pay attention to these controversies as **Newt Gingrich** has said that *"If you get involved in a controversy, then that becomes the mesmerizing event that people remember you by".*

Cheers to the new & controversial!

Kiran Guleria
Vice President AOGD (2017-18)

From the Secretary's Desk.....

Dear AOGDians

Happy New Year & Seasons Greetings!!

Hope you are enjoying the holiday season basking in Sun, eating peanuts & gazzak. To add to this bliss, our editors have come out with the latest issue on **"Controversies in Obstetrics and Gynecology".**

In current environment of litigation and distrust between patients & doctors "To Do or not to Do" is the dilemma each doctor faces. To make informed choices easier for you we have presented evidence based approach to a wide variety of contemporary topics.

Ponder over these and along with your experience help the patient make best choice. In my experience involving the patient / husband in decision making, especially for controversial issues, is the best approach.

Happy Reading

Abha Sharma
Secretary AOGD (2017-18)

Monthly Clinical Meet

Monthly Clinical Meet will be held at Dr Ram Manohar Lohia Hospital, New Delhi on **Thursday, 25th January, 2018** from 4:00-5:00pm.

From the Editorial Board

Respected Seniors & Dear Friends,

The editorial team wishes "**A Very Happy New Year**" to all of you. A new year means new beginnings and fresh starts….the times to reflect on what has been accomplished and looking forwards to complete the unfinished tasks. With all these thoughts, we bring out this first AOGD bulletin of the year 2018 on "***Controversies in Obstetrics & Gynecology***".

In the era of evidence based medicine, one faces so many dilemmas while managing situations wherein the final word is yet to come. We have selected some interesting topics that we commonly encounter like "what is the ideal screening test for gestational diabetes?", "What is the optimum inter pregnancy interval to allow VBAC?", "To do myomectomy or not at cesarean?", "Can I leave this fibroid unremoved?", "To put in a mesh or not?", "Endometrioma…. to remove or not?" Then new developments like PGS have to pass through controversies till clear evidence is available.

Nothing interests more than a controversy as someone rightly said ***"How could anything non-controversial be of intellectual interest to grown-ups?"*** Controversy is sometimes a necessary evil. The truth is "***No great advance has ever been made in science, politics, or religion, without controversy"***. Controversies are like Bob Dylan famously described "***The answer, my friend, is blowing in the wind"*** i.e. Either the answer is so obvious it is right in your face, or the answer is as intangible as the wind. Hope you will enjoy reading about these controversies and find some answers for your dilemmas in such situations. Your feedbacks are always welcome.

With regards

The Editorial Team
AOGD (2017-18)

Current Management of Uterine Fibroids Less than 12 Weeks: Surgical or Medical

Pakhee Aggarwal
Consultant Obstetrics & Gynecology, Fortis Healthcare

Uterine fibroids are the most common benign tumors of women of reproductive age[1], with nearly a third of the women between 40-60 years having them. The management of fibroids is tailored toward symptom relief, be it abnormal bleeding, pain or pressure. It is individualized based on the patient's age, type & severity of symptoms, size, number and location of fibroids, reproductive history & desire for future fertility. This article will focus on the relevance of uterine size to the management of fibroids, and what is the current best option for treating fibroids less than 12 weeks gestation uterine size.

The options for management include:

1. Conservative
2. Medical
3. Surgical

Conservative/ Expectant Management: This remains an option for women who are asymptomatic or decline medical & surgical therapy. Confirmation that the pelvic mass is indeed a fibroid (and not an ovarian or other pelvic mass) is imperative before embarking on this line of treatment. Follow up is annually to assess for change in size or development of symptoms. As fibroids have been known to shrink after menopause and post-partum, this option is reasonable to follow in this subset of women. Several evidence based guidelines support watchful waiting in asymptomatic fibroids[2,3]. There is no role of prophylactic treatment in anticipation of future problems.

Medical Management: The therapies available are several but the evidence that any of them is beneficial for anything other than short-term symptom relief is limited. Premenopausal women with uterus less than 12 weeks and with mild symptoms can be given a trial of medical therapy for symptom relief as well as to exclude other causes of co-existing problems e.g. anovulation which may be leading to abnormal bleeding or infertility. For post-menopausal women, hormonal therapy is not recommended for symptom relief. Options for medical management of fibroids up to 12 weeks include:

(a) ***Combined oral contraceptive (COC)*:** It is useful for heavy menstrual bleeding and dysmenorrhea associated with fibroids but not for reducing bulk symptoms[4]. COCs act by causing endometrial atrophy. Therapeutic trial of 3-6 months can be tried before more invasive treatment, keeping a watch for exacerbation of bulk symptoms. The situation with use of COCs is akin to pregnancy where there are high levels of both estrogen and progesterone, which decreases risk of developing new fibroids, but may lead to increase in size of existing fibroids.

(b) ***Levonorgestrel IUS (LNG-IUS):*** Although it is FDA approved for the control of heavy menstrual bleeding, there are no RCTs evaluating its use in fibroids. It can give symptom relief in menorrhagia and adenomyosis associated with fibroids and also provide contraception. However, it cannot be used in the presence of submucous fibroids or multiple intramural fibroids distorting the uterine cavity. In uterus up to 12 weeks with a normal cavity it is 80-90% effective in reducing menorrhagia[5].

(c) ***Progesterone implants (DMPA) & POP:*** Progestogens cause endometrial atrophy and improve symptoms of menorrhagia in addition to providing contraception. However, they are useful only as short-term option, as progesterone is a growth factor for fibroids although the overall effect is complex.

(d) ***Selective Progesterone Receptor Modulators (SPRM):*** These include Ulipristal acetate and Mifepristone. Although they are not FDA approved as yet for the treatment of uterine fibroids, there have been several RCTs comparing them to placebo and GnRH analogs (PEARL I and II trials)[6,7]. A recent Cochrane review concluded that short-term use of SPRMs in symptomatic fibroids resulted in improved quality of life, reduced menstrual bleeding and higher rates of amenorrhea as compared to placebo[8]. Due to oral dosing and a favorable side effect profile (less hot flashes), with efficacy similar to GnRHa (40-50% reduction in fibroid volume and relief from menorrhagia), they are rapidly becoming first line agents of choice in the medical management of fibroids. However, the endometrial effects with continuous use are of concern and therefore they are administered as a 13-week therapy with endometrial shedding after each therapy cycle. The unique pattern of endometrial changes is called 'progesterone receptor modulator-associated endometrial changes' (PAECs) and is mainly cystic glandular dilatation, seen as endometrial thickening on ultrasound. It is not endometrial hyperplasia/ precancer as far as the current evidence goes. A combination of mifepristone and LNG-IUS could prevent the development of endometrial hyperplasia[9]. There is also a transient elevation of trans-aminases seen with high dose

regimens[10]. Ulipristal acetate is given as 5-10mg daily for 13 weeks. Upto 4 three-month treatment cycles with 5mg daily dose can be given. Mifepristone is given as 25mg/day for 3-6 months to reduce uterine volume and cause amenorrhea, thereby improving quality of life.

(e) ***GnRH analogs***: These act by creating a pseudo-menopause like state, thus are associated with hypoestrogenic symptoms (hot flushes, mood changes, vaginal dryness and bone loss with prolonged use). Another drawback is the rapid resumption of menses and increase in uterine volume after discontinuing therapy. For this reason it is FDA approved mainly as pre-operative therapy for fibroids, given 3-6 months prior to surgery along with iron supplementation. Fibroid volume reduces by 30% and total uterine volume by 35%. It is not a primary medical treatment for fibroids, except in women very close to menopause or poor surgical candidates. Add-back therapy with continuous combined HRT (not COC) is given to minimize adverse effects. The difference between using GnRH agonist and antagonist is the rapidity of onset of effect with the latter (due to lack of flare effect). A newer oral GnRH antagonist, Elagolix[11] is under study and may be more acceptable for use.

(f) ***Raloxifene*****:** It is a selective estrogen receptor modulator. Only few studies are available, which show variable results[12]. There is also the theoretical risk of venous thrombosis with raloxifene.

(g) ***Aromatase inhibitors***: Anastrazole (1mg/d), letrazole (2.5mg/d) and fadrozole have been studied in small trials and found to be efficacious in reducing fibroid volume and symptoms in women with fibroids upto 12 weeks size[13]. They have been found to be of equivalent efficacy to GnRH, without the flare effect, but are also associated with bone loss with long-term use[14].

(h) ***Danazol*****:** It is an androgenic steroid that induces amenorrhea and may thus help in treatment of anemia related to fibroids but does not reduce fibroid volume. It is also associated with undesirable effects like weight gain, breast atrophy, hirsutism and mood changes.

(i) ***Gestrinone***: It is also an androgenic steroid, but reduces fibroid volume and also has a prolonged post-treatment effect[15] that persists even at 18 months. Its downside is the androgenic side-effects like seborrhea, weight gain, acne, hirsutism & hoarseness of voice.

(j) ***NSAIDs and antifibrinolytics***: Mainly reduce bleeding and pain associated with fibroids for the duration of use.

(k) ***Others*****:** Few agents tried & under research are somatostatin analogs, Vitamin D, cabergolin and green-tea extract[16].

Thus the role of medical treatment is either stand-alone for short-term management of symptoms or as a pre-operative adjunct to reduce size of fibroids to convert a technically difficult procedure into an easier one.

Surgical management: Surgery is the mainstay of treatment for fibroids less than 12 weeks that are causing pressure symptoms (e.g. anterior wall fibroid pressing on the urinary bladder and causing urgency or posterior wall fibroid causing problems in defecation) or infertility and recurrent pregnancy loss (eg. submucous fibroid). The options for surgery are discussed below.

(a) ***Myomectomy*****:** It is a fertility sparing option that is required when fibroids interfere with fertility or cause pregnancy problems like recurrent abortions, and also prior to IVF. For uterus up to 12 weeks size, it can be done by open surgery, laparoscopic surgery or robotic surgery depending on provider expertise. Hysteroscopic myomectomy is required for type 0,1 & 2 fibroids (Table 1)[17]. Short-term complications are hemorrhage, uterine perforation and cervical laceration. A fibroid prolapsing through the cervix can be dealt with vaginal myomectomy. The advantage of myomectomy is fertility preservation, but the disadvantage is fibroid recurrence. Fibroids have a 15% recurrence rate and 10% of women undergoing a myomectomy will eventually require hysterectomy within 5 to 10 years[18]. Subserous fibroids do not interfere with fertility and while intra-mural fibroids are associated with lower pregnancy and higher miscarriage rates, there in no conclusive evidence to say that their removal improves these outcomes[19].

Table 1: FIGO classification system for leiomyomas

S-Submusosal	0	Pedunculated intracavitary
	1	< 50% intramural
	2	≥ 50% intramural
O-Other	3	Contacts endometrium; 100% intramural
	4	Intramural
	5	Subserosal ≥ 50% intramural
	6	Subserosal < 50% intramural
	7	Subserosal pedunculated
	8	Other (specify e.g. cervical, parasitic)
Hybrid leiomyomas (impact both endometrium and serosa)	Two numbers are listed separated by a hyphen. By convention, the first refers to the relationship with the endometrium while the second refers tot he relationship to the serosa. One example is below	
	2-5	Submusocal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively.

(b) ***Endometrial ablation***: In women who have completed childbearing, it can be used along with hysteroscopic myomectomy (thermal balloon ablation) or alone (microwave ablation for submucous fibroids upto 3 cm in size), mainly for the control of heavy menstrual bleeding. It causes 95% reduction in bleeding at 1 year. In one study comparing ablation and hysterectomy for fibroids < 14 weeks, no women in the TBA group had heavy menstrual bleeding at 6 months. 95% women were amenorrheic by 6 months and 5% were hypomenorrheic[20]. It will not affect intramural or subserous fibroids and is less effective if cavity is more than 9cm length[21].

(c) ***Myolysis*****:** Destroying small fibroids using laparoscopic thermal, radiofrequency or cryo-ablation is quicker and easier than myomectomy but has risks of adhesion formation and rupture during subsequent pregnancy[22]. A radio-frequency ablation device (Acessa RFVTA™) has been approved by FDA and found to be more efficacious than laparoscopic myomectomy in terms of blood loss and hospital stay[23].

(d) ***Uterine artery embolization (UAE):*** It is a minimally invasive option in women wishing to retain their uterus but not fertility. It is a good option for uterus up to 12 weeks size as failure rate increases in larger uterus. Contraindications to UAE include active genitourinary infection, genital malignancy, immune-compromise, severe vascular disease, allergy to contrast and impaired renal function. Relative contraindications include large submucous fibroids, pedunculated fibroids, recent treatment with GnRH analogs, previous iliac or uterine artery occlusion, or postmenopausal status. As a whole, it is less painful with less hospital stay compared to myomectomy and causes 30-40% reduction in fibroid size[24,25]. There is a higher risk of minor complications (vaginal discharge, post-embolisation syndrome, hematoma), readmissions and treatment failure with UAE compared to hysterectomy. A rare but significant complication is the need to undergo hysterectomy (due to sepsis) as a life-saving procedure. Though UAE is initially cost effective as compared to hysterectomy, the long term benefit is lost due to higher rates of re-intervention following UAE. There is no effect of UAE on ovarian reserve. Miscarriage, cesarean delivery and PPH rates are higher following UAE as compared to non-treated fibroid uterus in pregnancy[26].

(e) ***MRI guided Focused Ultrasound Surgery (MRgFUS; ExAblate2000™)*****:** It is a non-invasive technique using focused ultrasound beam to thermo-ablate fibroids, using MRI for localization and real-time thermal monitoring. Success depends on size, location and vascularity of fibroids. It is contraindicated for calcified fibroids, inaccessible fibroids, adenomyosis, non-enhancement with contrast, more than 5 fibroids and size >10cm; though desire for future fertility is no longer a contra-indication[27]. Advantages are outpatient procedure, rapid recovery, sustained results (2-3 years) and cost-effectiveness in terms of quality of life measures. Disadvantages are time consuming and risk of thermal damage to surrounding tissues[28].

(f) ***Hysterectomy:*** Fibroids are the most common indication for hysterectomy, but it is reserved for women who have completed child-bearing, have multiple symptomatic fibroids, do not respond to medical therapy, have failed minimally invasive procedures (like UAE or MRgFUS) and have concurrent problems like CIN, endometriosis, adenomyosis that require surgical management. The main advantage is elimination of the problem permanently and a definitive end to the symptoms. The disadvantages are morbidity associated with major surgery (bleeding, infection, thrombosis, bladder and bowel injury). Route of hysterectomy can be abdominal, vaginal (sometimes requiring pre-shrinkage with GnRH analogs), laparoscopic or robotic based on provider expertise. There is no advantage of laparoscopic hysterectomy over vaginal hysterectomy if both are feasible.

Thus, current management of fibroids up to 12 weeks needs to be individualized based on patient profile and provider experience to improve symptomatology and quality of life.

Key-points[18]

1. Effective medical treatments for women with abnormal uterine bleeding associated with uterine fibroids include LNG-IUS (Level I), GnRH analogs (Level I), SPRMs (Level I), COC's (Level II), progestins (Level II) and danazol (Level II).
2. Effective medical treatments for women with bulk symptoms associated with fibroids include SPRMs and GnRH analogs (Level I).
3. Hysterectomy is the most effective treatment for symptomatic uterine fibroids (Level III).
4. Myomectomy is an option for women who wish to preserve their uterus or enhance fertility, but carries the potential for further intervention (Level II).
5. Of the conservative interventional treatments currently available (UAE, MRgFUS, myolysis), UAE has the longest track record and has been shown to be effective in properly selected patients (Level II)

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Caesarean Myomectomy (CM): Controversies and Trends

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Myomectomy at the time of caesarean delivery is a therapeutic dilemma. With advancing maternal age, trends of late marriage and rising caesarean section (CS) rates, more and more cases of uterine fibroid during CS are expected. In pregnancy, depending upon trimester, incidence of uterine fibroids ranges between 1.6%-10.7%[1].

Caesarean Myomectomy (CM) has numerous advantages over interval myomectomy:

- Eliminates need for repeat laparotomy and its risks. In a prospective study (2006) by Liu WM et al on 48 women, repeat surgery was required in 40.9% patients with CS alone during follow-up of 6–38 months for symptomatic fibroid[2].
- Incisions on uterus are smaller.
- Easy identification of the cleavage plane.
- Elasticity of the pregnant uterus enables effortless placement of stitches.
- Chances of vaginal delivery in subsequent pregnancies.
- Puerperal uterine subinvolution can be minimized.

Bonney, pioneered myomectomy and first described about CM in 1914. He removed 6 fibroids largest being of melon-size. This patient successfully had three vaginal deliveries post CM[3].

In late 90s, obstetric textbooks strongly opposed cesarean myomectomy and the **associated concerns** were perioperative hemorrhage, drop in hemoglobin levels, need for blood transfusion, increased duration of hospital stay and duration of operation, increased post-operative morbidity, risk of hysterectomy and complications during puerperium and mortality. Incidence of intraoperative haemorrhage during CM (in reported cases) ranges from 0 - 35.3%[1,4].

Burton et al[5] in 1989 reported that 1 out of 13 patients of CM had intra-operative haemorrhage needing uterine artery ligation and blood transfusion. They concluded CM safe and feasible in selected cases. In 1991, Hassan et al[6] did a study on 60 cases with uterine fibroid in pregnancy. They all had fibroid of size >6cm. They reported 3 hysterectomies out of ten patients of CM.

Evidence For and Against CM

Kwawukume[1] (2002) recruited 24 patients in study. He reported average haemoglobin of the patients preoperatively and postoperatively to be 11.73g/dl and 9.90g/dl in CM group and 12.07g/dl and 10.34g/dl in control group. The drop in average haemoglobin, peri-operative blood loss and morbidity was not significant during CS alone and CM with tourniquet applied. Average duration of operation was longer in CM (62.08 mins) than in control group (50.83 mins), but not significant. Uterine involution was normal and there were no significant complications during puerperium.

Roman AS et al[1] (2004) did a retrospective cohort study on 111 CM patients showing no significant difference in incidence of postpartum fever and hemorrhage, operating time and length of postpartum stay.

A retrospective descriptive study done by Seffah[7] (2005) reported maternal death due to hemorrhage and disseminated intravascular coagulopathy (DIC) after CM. Three out of 17 hysterectomies were due to bleeding from myomectomy. Due to inadequate hemostasis, re-laparotomy and hysterectomy were performed but patient died after 12 hours of laparotomy. This report did not provide any data on the performed CM.

Hassiakos et al[1] (2006) studied on 47 CM patients. They reported that myomectomy added mean operating time of 15 minutes to CS. No significant difference was found in the mean hemoglobin change, length of hospital stay and puerperal complications between 2 groups. None of them received blood transfusion or had hysterectomy.

Simsek et al[1] (2012) did a retrospective study on 70 cases of CM. They reported significant difference in postoperative hemoglobin value and mean difference in hemoglobin change between 2 groups. Mean postoperative hemoglobin value was 9.6 +/- 1.5 in CM group and 10.8 +/- 1.01 in controls. Length of hospital stay was longer in CM group. Mean surgical time of the CM group was 58.1 +/- 23 minutes which was significantly increased. No post-surgical blood transfusion was given.

Machado LS et al[8] (2012) did a retrospective cohort study on 8 patients. CM added 1 day to the hospital stay and 15 minutes to mean operating time. One patient lost 900 ml, 5 patients lost 1-1.5L, 2 patients lost 1.5-2L and 1 patient with a 10 x 12 cm fibroid lost 3.2L of blood intra-operatively. Stepwise devascularisation and preoperative placement of uterine balloon catheters was done. Hysterectomy was not required.

A retrospective cohort study by Kwon et al[9] (2014) included 165 cases and divided them in 2 groups. They

further divided CM group (n=65) into 2 according to the fibroid size. Group A (n=30) with fibroid size ≤5 cm and group B (n= 35) with fibroid size >5 cm. Group B showed no statistical differences in mean hemoglobin change, operative time, post-operative transfusion incidence and hospitalized days compared to group A. There was 1 case (with myoma size of 4cm) of intractable bleeding with blood loss of 2L requiring bilateral uterine artery embolization (UAE) in group A and 6 units packed red blood cells transfusion. There was no case of UAE in group B and no peripartum hysterectomy in any group. They concluded that CM in large myomas was safe and effective.

Pattanaik et al[10] (2014) conducted a descriptive study and reported that 19 out of 23 patients had intraoperative blood loss of more than 1L, only 7 patients required transfusion. Hospital stay in all patients was on average 8 days post-operatively. There was 1 subtotal hysterectomy and one re-laparotomy. Puerperal pyrexia and sepsis was found in 8.6% cases. They concluded CM was safe in selected cases with expert hand.

Sparic et al[4] in 2015 evaluated ICU admissions following CM in 102 patients. This retrospective study was biased due to liberal ICU admission policy, a high rate of 55.88% was recorded (57 cases). Most common reason for admission to the ICU was intraoperative hemorrhage (61.40%) and the second reason was the need for intensive surveillance after surgery (28.07%). Study group showed significant increase in the rates of intraoperative transfusion (31 vs 3 units), intraoperative hemorrhage and operation time (73.68 vs 61.33 min). They suggested tailored surgical technique to lower morbidity risks.

Number, Location of Myoma and the Operatability

In 2001, descriptive study by Ehigiegba et al[11] removed 84 fibroids out of 25 patients, of which 94.8% were anterior uterine wall (size range 2-10 cm) subserosal or intramural and only 5 had anterior wall submucous fibroid.

Kwawukume[1] reported that fibroid removed ranged from one solitary nodule to 6 nodules with an average diameter of 6 cm. Eighty five percent fibroids were intramural.

Roman AS et al[1] reported no effect of size and site of fibroid on incidence of hemorrhage. Type of fibroid removed were subserosal, intramural, submucosal, pedunculated.

Machado LS et al[8], reported 7 out of 8 patients had myomas >5 cm in size and four intramural and other 4 subserous. Seven out of 8 had lower segment anterior wall fibroids at or close to the incision site and 1 patient had posterior wall fibroid projecting through uterine incision after delivery of the baby.

Pattanaik et al[10] removed 29 fibroids. Intra-operatively, Non-pedunculated fibroids (intra-mural, subserous and submucous) comprised of 51.7% and subserous pedunculated were 48.27%. Out of 29, fifteen were <5cm in size and twelve were 5-10cm while there were 2 cases with size >10cm.

Sparic et al[4] in 2015, showed that patients admitted in ICU differed significantly in terms of fibroid size and type. Out of 57 patients admitted in ICU, pedunculated type were 8, subserous in 15, intramural in 9 and multiple in 25 patients. Location of fibroid in those patients was anterior wall in 32, fundal in 5, posterior wall in 13, cornual in 3 and isthmico-cervical in 4.

Sparic R et al[12] in other study in 2015, suggested that myoma compromising fetal extraction and uterine incision or suturing should be enucleated during CS. CM is relatively safe in cases of anterior wall myomas, subserous and pedunculated myomas. Multiple myomas, deep intramural, fundal, cornual and posterior uterine wall myomas are associated with more surgical complications during CM.

Late Complications of Caesarean Myomectomy

Scar quality, adhesion formation and Abnormal placentation following CM

Assessment of scar on ultrasound and visual inspection during repeated CS suggested better scar integrity after CM than non-pregnant myomectomy[4].

Hassan et al[6] reported 2 out of 11 CM patients had dense adhesions distorting the pelvic anatomy during CS and resulted in bowel/bladder injuries.

Ehigiegba et al[11] reported 3 pregnancy post CM in 25 patients. Out of 3, two had vaginal delivery at 37–38 weeks and one had elective CS. Subsequent pregnancy in 3 women reported no placenta previa or abnormally invasive placenta.

In a prospective non-randomised study on 29 patients by Adesiyun et al[13] (2008) reported 13 patients had successful vaginal delivery out of 17 patients allowed for trial of labour after CM. Three cases of placenta previa following CM (10.3%) and one case of cesarean hysterectomy due to placenta increta were reported but it is unclear if this was solely due to previous CM.

A cross-sectional study (2015) by Turgal et al[14], divided 81 patients into 4 groups: a control group (n=19), patients who did not have CM; and three study groups. Group I - 21 patients who had myolysis by electric cauterization for fibroid <2 cm during CS; group II - 16 patients who had CM for pedunculated fibroid and group III - 23 patients with previous CM for subserous or intramural fibroid <5 cm in diameter. Incidence of adhesions were similar between the 4 groups.

Akkurt et al[15] did a retrospective study (2016) on 91 women with CM. All the 32 patients with subsequent pregnancy delivered by CS, none had uterine rupture, while 1 woman had uterine dehiscence and one had preterm delivery. One case of placenta previa was reported. They registered adhesions in 3/32 patients during subsequent CS.

Further research is needed to determine if CM itself increases the risk of these complications or if they arise because of CS.

Myoma Recurrence

Data are lacking on myoma recurrence rate after CM. Myoma recurrence rate after myomectomy on a non-pregnant uterus ranges from 4.8% up to 55.6%[4].

Sparic et al[4] reported anatomy distortion due to both adhesions and myoma recurrence in a case with posterior wall fibroid who had previous 2 myomectomies.

Myoma recurrence at the time of CS was not registered in 32 women with subsequent pregnancy after CM in a study by Akkurt et al. The remaining 59 out of 91 women had recurrence rate of 8.4% (n = 5). Mean duration of follow-up was 6.3 years. Out of 5, three (4.1%) required additional major surgery for fibroid (one abdominal myomectomy and two abdominal hysterectomies). They suggested long follow-up (mean - 8.2 years), advanced age (>45 years), history of multiple myomas and larger myoma size (>70 mm) as the risk factors for myoma recurrence[15].

Consensus

The old dictum of not doing CM should be re-assessed.

Selective CM in experienced hands is a safe procedure.

Selective CM can be safe and effective procedure in experienced hands with well-equipped setting, good anaesthesia, blood availability, blood loss minimizing techniques (uterine tourniquet, bilateral uterine artery ligation and electrocautery) and in selected patients, according to site and size of fibroid with meticulous attention to hemostasis.

Till now, there has been no consensus on the safety and feasibility of CM. There are no randomised controlled trials on CM.

A meta-analysis (2013) on 9 case – control studies including 1082 patients, identified no hysterectomies resulting from massive hemorrhage. No significant difference found in mean hemoglobin change, post-operative fever and operation time. It suggests more detailed discussion with long term risks & benefits like future pregnancy and associated risks with myoma size & location in a larger population or reliable design[1].

CM safety in patients with previous myomectomy lacks articles and the current data provide conflicting results, given that some investigations excluded women with a previous myomectomy[9]. Thus, further research and randomized controlled trials are necessary to obtain more data on fibroid management during CS.

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Use of Mesh in Pelvic Organ Prolapse: Current Consensus

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In an effort to reduce the recurrence rate of prolapse and given the success of mesh used in continence surgery and at abdominal hernias, surgeons have utilised synthetic grafts for prolapse repairs. Synthetic graft material can be permanent like polypropylene or absorbable like polyglactin mesh. Currently, there is great divergence of opinion with regard to the safe and appropriate use of mesh in pelvic organ prolapse (POP) surgery and there is still no consensus on the use of mesh in transvaginal surgical repairs for the treatment of POP.

On July 13, 2011, the United States Food and Drug Administration (FDA) issued a document entitled "**FDA Safety Communication: UPDATE on Serious Complications Associated with Transvaginal Placement of Surgical Mesh for POP**".[1] This was stated as an update of a previous document issued on October 20, 2008, entitled "A Public Health Notification and Additional Patient Information on serious complications associated with surgical mesh placed through the vagina (transvaginal placement) to treat POP and SUI (stress urinary incontinence)". Accompanying the FDA concerns was a 15-page document entitled "**Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for POP**".[2] The FDA noted mesh exposure (erosion) as the most common mesh-related complication and with mesh shrinkage (contraction), the leading cause of symptoms including bleeding, pelvic pain, dyspareunia, or apareunia.

The results of the literature review [2], summarized in the **FDA Safety Communication[1]**, were: (1) mesh used in transvaginal POP repair introduces risks not present in traditional non-mesh surgery for POP repair; (2) mesh placed abdominally for POP repair appears to result in lower rates of mesh complications compared to transvaginal POP surgery with mesh; (3) there is no evidence that transvaginal repair to support the top of the vagina (apical repair) or the back wall of the vagina (posterior repair) with mesh provides any added benefit compared to traditional surgery without mesh; and (4) while transvaginal surgical repair to correct weakened tissue between the bladder and vagina (anterior repair) with mesh augmentation may provide an anatomic benefit compared to traditional POP repair without mesh, this anatomic benefit may not result in better symptomatic results.

The FDA's key concerns are followed by 15 recommendations for health care providers including adequacy of training for each new procedure, patient information and counselling, risk/benefit analysis, and proper vigilance for the development of complications[1]. There were 17 recommendations for patients before and after surgery in terms of the questions to ask their surgeon prior to any proposed pelvic floor surgery as well as the follow-up care that is optimal following such surgery.

But the noteworthy point is limitations, which include inconsistent defining and reporting of adverse events and the paucity of studies extending beyond 2 years follow-up. Therefore, in order to contribute to a greater worldwide knowledge on this burning issue; ICS and IUGA are doing a lot in joint efforts. Already an online ICS- IUGA Complication Classification Calculator Code (CCCC) can be accessed from both society websites. From this, an online registry is being created seeking the input from individual members and different national urogynecological societies.[3]

Recently, a **Cochrane review** of results from 37 trials in 4023 women reported that women are less likely to have prolapse symptoms or measureable prolapse, and fewer require repeat prolapse surgery, after repairs with synthetic non-absorbable mesh than after a standard (native tissue) repair.[4] The evidence suggests that if 19% of women are aware of prolapse after native tissue repair, between 10% -15% will be aware of prolapse after permanent mesh repair. If the rate of recurrent prolapse on examination after a native tissue repair is assumed to be 38%, the risk would be between 11% and 20% after a repair with transvaginal permanent mesh. However, there are also problems associated with permanent transvaginal mesh. If we assume that 5% of women require repeat surgery after native tissue repair, the risk would be between 7% and 18% after permanent mesh repair. Eight per cent of women in the mesh groups require repeat surgery for mesh exposure. But not enough reliable evidence was available to suggest whether women had better quality of life.

Although, low quality evidence suggests that absorbable mesh may reduce the risk of recurrent prolapse on examination compared to native tissue repair, there is insufficient evidence on absorbable mesh to draw any conclusions for other outcomes. While permanent mesh has some advantages over native tissue, there are also disadvantages in its routine use. Many transvaginal

permanent meshes were withdrawn from use in 2011, and the newer, lightweight transvaginal permanent meshes still available have not been evaluated within a randomised study. Furthermore, few trials reported results separately for women undergoing their first or a repeat procedure.

Later on, the **PROSPECT study** showed that augmenting a primary transvaginal anterior or posterior prolapse repair with non-absorbable synthetic mesh or biological graft confers no symptomatic or anatomical benefit to women in the short term.[5] More than one in ten women had a mesh complication, but most were asymptomatic, and most of the mesh exposures measured less than 1 cm^2. Although no evidence was apparent of differences between standard, mesh, or graft repair in other adverse effects up to 2 years after surgery, mesh use did result in the need for additional surgical procedures for exposures and extrusion in the first 2 years, which might be considered to be an unnecessary risk.

So, how do we answer the question; **to mesh or not to mesh?** Information regarding the FDA's reports on the use of surgical mesh in pelvic organ prolapse repair should be made available to patients at the time of surgical planning and should be used as an adjunct in the process of obtaining informed consent. We need to have frank discussions with our patients. ***Neither approach is currently superior as they both have their pros and cons.*** Our next job as a speciality is to define which patients are at greatest risk of failing native tissue repairs and steer them towards a mesh kit repair. Conversely, we need to better define the risk factors for a mesh complication. Only then we can truly provide the best care to our patients.[6]

Discussing risks inherent to a mesh procedure, any operation carries a risk. One must also consider that mesh exposure will undoubtedly be higher with repeat surgery as the tissue is generally thinner and more scarred. The real danger looking at the research for vaginal mesh is that it does not include the "learning curve" and it is likely that the incidence will decrease as surgical expertise improves. On adopting techniques—deeper dissection, smaller incisions, two-layer closure of the vagina—the risk of vaginal mesh exposure is very low. Even if it occurs, it is usually in the midline and very small, presumably as a result of poor wound healing. It can generally be treated by vaginal estrogen application or a minor day care procedure with low morbidity.

Considering an ageing population after a substantial increase in the average life expectancy of women, we need a "one-stop" operation with life-time benefit. Mesh augmented surgeries still have a scope, provided we use it for right indication so that it has best results with least complications and can skip from any medicolegal issues.

The 2011 FDA safety communication regarding the use of surgical mesh to treat pelvic organ prolapse has led to high levels of media attention and patient search activity. But the more alarming fact is that the quality of health information on the internet remains poor.[7] Future quality assurance measures may be critical in ensuring accurate dissemination of patient-centred information.

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Diabetes in Pregnancy: Screening Strategies Over Time

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For many years, gestational diabetes mellitus (GDM) was defined as any degree of glucose intolerance that was first recognized during pregnancy, regardless of whether the condition may have existed prior to the pregnancy or persisted after the pregnancy. **Recently, the American Diabetes Association (ADA) defined it as "Diabetes diagnosed in the second or third trimester of pregnancy that is not clearly either preexisting type 1 or type 2 diabetes**". However, as per **IADPSG (International Association Of Diabetes And Pregnancy Study Groups**) criteria, women can be diagnosed to have GDM even in the first trimester, if fasting plasma glucose (FPG) is ≥5.1 mmol/L (92 mg/dL), but <7 mmol/L (126 mg/dL). The ongoing epidemic of obesity and diabetes has led to more type 2 diabetes in women of childbearing age, with an increase in the number of pregnant women with undiagnosed type 2. Women diagnosed with diabetes in the first trimester may be suspected of having preexisting pre-gestational diabetes (type 2 diabetes or, very rarely, type 1 diabetes).

It has been estimated that 16.8% of live births across the world in 2013 were in women who had some form of hyperglycemia in pregnancy. In India, gestational diabetes mellitus (GDM) has been estimated to affect over 5 million women.

GDM has been linked to adverse maternal and neonatal outcomes, including preeclampsia, operative birth, perineal trauma, macrosomia, shoulder dystocia, birth trauma, neonatal intensive care unit (NICU) admissions, neonatal respiratory distress, neonatal hypoglycaemia, hyperbilirubinaemia and perinatal mortality. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, a large-scale multinational cohort study, demonstrated that risk of adverse maternal, fetal, and neonatal outcomes continuously increased as a function of maternal hyperglycemia at 24–28 weeks, even within ranges previously considered normal for pregnancy. Treatment of hyperglycemia has been shown to reduce the above risks almost to the levels seen in women without any abnormalities in the glucose metabolism. Identifying and treating these women is important to minimize the long-term consequences both for the mother and the fetus.

However, there is no international consensus on screening methodology in terms of selective versus universal and one-step versus two-step approach.

Evolution of Screening Criteria for GDM

Historically, screening for GDM consisted of obtaining the patient's medical history, relying primarily on past obstetric outcomes and a family medical history of type 2 diabetes.

The foundation for GDM diagnosis was laid down by OSullivan and Mahan in the

early 1960s. Thresholds for diagnosis were based on 2 SD above the mean blood glucose values for 752 pregnant women. Two abnormal values were required to avoid misclassification and label as GDM. In 1973, O'Sullivan and Mahan proposed the 50-g, 1-hour oral glucose tolerance test which is widely practiced as step-1 of the two-step screening method.

Since then, the 100-g OGTT has undergone extensive modifications, to its present form, that is, Carpenter and Coustan criteria (1982). Recently, IADPSG criteria have also come into the picture. In India, the DIPSI recommended method is incorporated in the National guidelines for the screening of GDM.

In 1979, the National Diabetes Data Group criteria (NDDG) were introduced using the plasma values (approximately 14% higher as compared with the original O'Sullivan and Mahan criteria), Subsequently, glucose measurements using glucose oxidase and hexokinase methods, led to the formulation of the Carpenter and Coustan criteria in 1982.

GDM diagnosis can be accomplished with either of two strategies (Table-1):

1. "One-step" 75-g OGTT or
2. "Two-step" approach with a 50-g (non-fasting) screen followed by a 100-g OGTT for those who screen positive

In the 2011 Standards of Care, ADA for the first time recommended that all pregnant women not known to have prior diabetes undergo a 75-g OGTT at 24–28 weeks of gestation, based on a recommendation of the IADPSG. In 2013, the National Institutes of Health (NIH) convened a consensus development conference to consider diagnostic criteria for diagnosing GDM. The panel recommended a two step approach to screening that used a 1-h 50-g glucose load test (GLT) followed by a 3-h 100-g OGTT for those who screened positive

Table 1. **Screening for and Diagnosis of GDM**

One-step strategy – IADPSG Recommendation

Perform a 75-g OGTT, with plasma glucose measurement when patient is fasting and at 1 and

2 h, at 24 to 28 weeks of gestation in women not previously diagnosed with overt diabetes.

The OGTT should be performed in the morning after an overnight fast of at least 8 h.

The diagnosis of GDM is made when **any one** of the following plasma glucose values are met or

exceeded:

Fasting: 92 mg/dL (5.1 mmol/L)

1 h: 180 mg/dL (10.0 mmol/L)

2 h: 153 mg/dL (8.5 mmol/L)

Two-step strategy

Step 1: Perform a 50-g GLT (non fasting), with plasma glucose measurement at 1 h, at 24–28

weeks of gestation in women not previously diagnosed with overt diabetes.

If the plasma glucose level measured 1 h after the load is ≥130 mg/dL, 135 mg/dL, or

140 mg/dL* (7.2 mmol/L, 7.5 mmol/L, or 7.8 mmol/L), proceed to a 100-g OGTT.

Step 2: The 100-g OGTT should be performed when the patient is fasting.

The diagnosis of GDM is made if **at least two** of the following four plasma glucose levels

(measured fasting and 1 h, 2 h, 3 h after the OGTT) are met or exceeded:

Carpenter/Coustan	or	NDDG
Fasting 95 mg/dL (5.3 mmol/L)		105 mg/dL (5.8 mmol/L)
1 h 180 mg/dL (10.0 mmol/L)		190 mg/dL (10.6 mmol/L)
2 h 155 mg/dL (8.6 mmol/L)		165 mg/dL (9.2 mmol/L)
3 h 140 mg/dL (7.8 mmol/L)		145 mg/dL (8.0 mmol/L)

NDDG, National Diabetes Data Group. *The ACOG recommends either 135 mg/dL (7.5 mmol/L)

or 140 mg/dL (7.8 mmol/L). A systematic review determined that a cutoff of 130 mg/dL

(7.2 mmol/L) was more sensitive but less specific than 140 mg/dL (7.8 mmol/L).

Adapted from American Diabetic Association. Classification and diagnosis of diabetes. Diabetes Care 2017; 40(Suppl. 1): S11–S24

If the IADPSG screening criteria are used the prevalence of GDM increases by two- to three fold. There is an ongoing debate whether such an increase in prevalence allows identification of previously ignored risks, or results in over diagnosis of diabetes in healthy pregnancies.

The National Institute for Health and Care Excellence (NICE, 2015) recommends the 2-hour 75 gm oral glucose tolerance test (OGTT) to test for gestational diabetes in women with risk factors and GDM is diagnosed if

- fasting plasma glucose level of 5.6mmol/litre (100mg/dl) or above or
- 2-hour plasma glucose level of 7.8mmol/litre (140mg/dl) or above.

Indian Scenario

The Diabetes In Pregnancy Study group India (DIPSI) has given practice guidelines for GDM in the Indian scenario. They form part of the National Guidelines for Diagnosis & Management of Gestational Diabetes Mellitus- 2014. They are being followed extensively in many institutions in the country.

- Universal screening of all pregnant women is recommended as India has a very high prevalence of gestational diabetes (16.55%)
- A 2-hour 75 gm oral glucose tolerance test (OGTT) to test for gestational diabetes irrespective of the fasting status; cut off value is 140 mg/dl
- The screening is advised on the first antenatal visit
- If found negative at this time, the screening test is to be performed again around 24 – 28 weeks and finally around 32-34 weeks.

Universal Testing for Hyperglycemia in Pregnancy in First Trimester

India being a high prevalence country universal screening at the first prenatal visit is recommended. Women with poor blood sugar control early in pregnancy are at increased risk of carrying a fetus with congenital malformations. Early diagnosis of previously undiagnosed overt diabetes may allow for timely institution of appropriate treatment and minimize the risks both to the mother and the fetus

As the frequency of obesity and Type 2 DM in young adults is increasing worldwide, most guidelines now recommend screening for overt diabetes at the first prenatal visit, especially in **high-risk groups**. Universal screening for GDM has to be carried out after 24 weeks, without any doubt or controversy and the DIPSI criteria is used.

The cutoffs for tests, recommended to detect diabetes in early pregnancy are FPG: 126 mg/dL (7.0 mmol/L); random plasma glucose: 200 mg/dL (11.1 mmol/L); or HbA1c: 6.5% (47 mmol/mol), same as recommended for non pregnant population (IADPSG). However, HbA1c is not recognized for this purpose in pregnancy by the WHO.

Risk Factors for Early Screening

- BMI above 30 kg/m^2
- Previous macrosomic baby weighing 4.5 kg or above
- Previous history of gestational diabetes

- Family history of diabetes (first-degree relative with diabetes)
- Known impaired glucose metabolism
- Minority ethnic family origin with a high prevalence of diabetes.

If GDM is not diagnosed in first screening, blood glucose testing should be repeated at 24-28 weeks of pregnancy

To conclude, there are arguments both favoring and contradicting one step and two-step screening and early versus second trimester screening. But for us in India with a high prevalence of GDM, **first trimester screening using DIPSI criteria** is recommended not only to diagnose GDM but also to diagnose undiagnosed Type 2 DM as pregnancy may be the only time when a woman comes into contact with a healthcare provider. Similarly **one-step screening** is preferable as timely institution of treatment will mitigate the associated risks and also the woman may not come for the second-step testing exposing both herself and the fetus to the attendant risks of high blood sugar levels.

Suggested Reading

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Controversies in the Management of Endometrioma before IVF/ICSI Cycles – Expectant Management, Aspiration or Surgery

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Introduction

Endometriosis is a common gynecological disorder in which endometrial tissue (glandular epithelium and stroma) is found outside the uterine cavity. It affects 5–10% of fertile women and 20–40% of women with subfertility. Other symptoms include dyspareunia, severe dysmenorrhoea and chronic pelvic pain. Endometriosis mostly presents as superficial and deep pelvic peritoneal implants, adhesions and ovarian cysts. While detection of peritoneal implants and adhesions typically requires a diagnostic laparoscopy, endometriotic ovarian cysts can be reliably identified by transvaginal ultrasound. Although laparoscopic excision of ovarian endometriomas increases the chances of spontaneous conception, the value of this treatment in women selected for IVF–ICSI cycles is debated. Classical surgical management of endometriotic ovarian cysts in patients requiring IVF has been recently challenged by evidence questioning the benefits of surgery.

Impact of Endometriomas on Ovarian Reserve

Ovarian reserve can be measured by serum markers (FSH, inhibin B, antimüllerian hormone), ultrasound variables (ovarian volume, Antral Follicle Count), and by assessing ovarian response to gonadotrophin stimulation. Ovarian responsiveness to stimulation with gonadotropins is damaged both due to the presence and excision of ovarian endometriomas. In most cases, it cannot be clarified whether the damage is caused by the development of an endometrioma or by its surgical removal.

Endometrioma-mediated damage

Pathological sections of the ovarian cortex show reduced follicular numbers and activity antecedent to surgery in endometriomas when compared with teratomas or benign cystadenomas, suggesting that the disease *per se* may be detrimental to the ovary.

Surgery-mediated damage

A potential deleterious mechanism is the accidental removal of a consistent amount of healthy ovarian cortex with follicles during cystectomy. In more than 50% of the endometriomas removed, primordial follicles are found, probably due to the lack of capsule that creates strong adhesions and to technical difficulties in the removal. In fact, bilateral disease with laparoscopic removal of endometriomas from both ovaries has a 2.4% risk of premature ovarian failure.

The damage inflicted by surgery to ovarian responsiveness may be due not only to the removal of healthy tissue by laparoscopic stripping, but also to vascular compromise following electrosurgical coagulation. Bipolar coagulation should be performed with caution. The maneuver should be selective, facing the bleeding vessels and not widely grasping the entire ovarian tissue with bipolar coagulator.

Various studies have compared patients with endometriomas undergoing IVF-ICSI, who have not undergone previous ovarian surgery, to patients who have been previously operated for endometriomas (both those who are disease-free, and those with recurrence of endometriomas). Lower peak E_2 levels and higher gonadotropin requirements were documented in the operated patients. Conversely, number of oocytes retrieved, number of embryos obtained and pregnancy rate were similar in the two groups.

The harmful effect of endometriomas, and/or their excision, on ovarian responsiveness is further supported by studies focusing on women with monolateral disease and comparing responsiveness to hyperstimulation in the affected and in the contralateral intact gonad of the same patient. These studies strongly support a marked reduction in the number of developing follicles and retrieved oocytes in the previously operated ovaries.

However, the potential impact of this endometrioma-related reduced responsiveness on the success rate of IVF is less recognized. Ovarian endometriomas are mostly monolateral. Both gonads are involved only in 19–28% of cases. The contralateral intact ovary may adequately compensate for the reduced function of the affected one.

Alternative treatment options in women with endometriomas prior to IVF

Non-surgical treatment

Ovarian endometriotic cysts respond poorly to medical therapy. Medical treatment is moderately

effective in improving pain but absolutely inefficient in improving fertility in women with endometriosis. Medical treatment may prevent further growth of the cyst or reduce the size. Thus, medical therapy by itself should not be considered in infertile women with endometriomas.

In contrast, it has been suggested that pituitary suppression with the administration of GnRH analogues for a few months prior to IVF may increase the success rate in women with endometriomas. The hypothetical beneficial effects may derive from the induced amenorrhea, or to the effects of GnRH analogues on aromatase expression or on uterine NK cells. A recent meta-analysis on this subject showed that a 3–6 month treatment period with GnRH analogues prior to an IVF cycle improved the odds of clinical pregnancy in women with endometriosis by 4-fold.

Ultrasound-guided aspiration

An alternative to surgery in some cases might be ultrasound-guided aspiration of ovarian endometriomas. Whether it is just cyst aspiration or, in order to reduce recurrence, aspiration plus *in-situ* irrigation or injection with a sclerosing agent, the published evidence is still not very convincing. Sclerosing substances used vary from tetracycline to methotrexate, recombinant interleukin-2 and/or ethanol. For those patients who decline surgery, or in whom surgery is contraindicated, cyst aspiration may facilitate oocyte retrieval, although the rates of disease recurrence are high.

Dicker *et al*. documented a significant improvement in number of oocytes retrieved and embryos obtained in a cohort of women with ovarian endometriomas who failed to conceive during a previous IVF cycle and who subsequently underwent transvaginal ultrasound-guided aspiration. In a retrospective study, Suganuma *et al*. compared treatment of endometriomas before IVF either by laparotomy/laparoscopy (n = 36) or aspiration (n = 23) to no treatment at all (n = 20). A higher fertilization rate was observed in the group of patients treated with aspiration (67%) as compared to those treated with surgery (57%) or those who did not receive any treatment (56%).

Surgery

There is a general consensus that laparoscopic treatment of endometriomas increases the chances of pregnancy. Following the procedure, pregnancy rate varies from 30 to 67%. Overall, about 40–50% of young patients with endometriomas may conceive spontaneously after laparoscopic surgery.

The specific role of surgery in the management of women with endometriomas scheduled for IVF has been recently investigated in a RCT. Ovarian surgery resulted in longer stimulation, higher FSH requirements and lower oocyte numbers, but fertilization, pregnancy and implantation rates did not differ between the groups. Specifically, the pregnancy rate in the ovarian surgery group and the expectant management group was 34 and 38%, respectively.

Not all the different techniques used for surgical removal of endometrioma may have the same impact on the outcome. In particular, only opening and vaporizing or coagulating the inner surface of the cysts may prevent the inevitable removal of ovarian cortex associated with the use of the stripping technique. However, the repeatedly reported higher spontaneous pregnancy rates and lower recurrence rates associated with the stripping technique have limited the diffusion of the vaporization/coagulation approach. A better pregnancy rate and a lower rate of recurrence has been documented following laparoscopic ovarian cystectomy than after fenestration and bipolar coagulation.

Should Endometriomas be Excised before IVF–ICSI Cycles?

Garcia-Velasco *et al*. compared IVF–ICSI outcome between 133 women who previously underwent laparoscopic cystectomy for an ovarian endometrioma and 56 women with ovarian endometriomas who had never undergone ovarian surgery. Number of oocytes retrieved, number of embryos obtained and pregnancy rate (25% versus 23%) were similar. Suganuma *et al*. observed a better response to ovarian stimulation in 20 patients (30 cycles) with unoperated endometriomas undergoing IVF–ICSI cycles when compared to 36 patients (62 cycles) previously operated for endometriomas. Overall, this evidence suggests that surgery does not benefit asymptomatic women preparing to undergo IVF–ICSI who are found to have an endometrioma.

Risks of Surgery or Expectant Management

Surgery is costly and not free from complications. The rate of major and minor complications associated with laparoscopy is 1.4% and 7.5%, respectively. Though uncommon, ureteral and bowel injuries with associated sequelae may occur. Surgical treatment is also associated with higher economic costs.

On the other hand, potential risks of the expectant strategy are the following:

i. *Missing an occult early stage malignancy*.
ii. *Development of a pelvic abscess following* oocyte retrieval. The bloody content of an endometrioma may serve as an excellent culture medium and may facilitate the spread of an infection process. Though this risk is below 1.7%, prophylactic antibiotics should be routinely used and every effort should be made to avoid the puncture of the endometrioma.

iii. *Progression of endometriosis*.

iv. Rupture of the endometrioma.

v. Possible follicular fluid contamination with endometrioma content - the effects of endometriotic fluid on the oocyte quality are still debated.

vi. Difficulties during oocyte retrieval

vii. Increased obstetric complications such as preterm birth or intrauterine growth restriction. There is no evidence that surgery may significantly overcome the reported increased obstetric complications.

Conclusions

Presence of endometriomas may negatively influence ovarian function and may impose difficulties and risks during oocyte retrieval. On the other hand, there are no definite data clarifying whether the treatment of endometriomas increases (or decreases) the chances of success using IVF. Responsiveness to gonadotrophins after ovarian cystectomy is reduced. Current evidence thus recommends proceeding directly to IVF to reduce time to pregnancy, to avoid potential surgical complications and to limit patient costs. Surgeons should bear in mind that if all healthy growing follicles may be reached without damaging the endometrioma, cyst over 4-5 cm do not require surgery in asymptomatic patients; however, smaller cysts that hide growing follicles, specially when the ovary is fixed, may require intervention. Thus, some factors that need to be considered in the decision-making process to identify the best option for the couple are: age of the woman, the presence/absence of pain, the number of previous interventions, bilaterality of the endometriomas, dimension of the cysts, ovarian reserve and the possibility of occult malignancy.

Suggested Reading

1. Garcia-Velasco JA, Somigliana E. Management of endometriomas **in women requiring IVF: to touch or not to touch.** Hum Reprod. 2009;24(3):496-501.
2. Somigliana E, Benaglia L, Paffoni A, Busnelli A, Vigano P, Vercellini P. Risks of conservative management in women with ovarian endometriomas **undergoing IVF.** Hum Reprod Update 2015;21(4):486-99.
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4. Cooney LG, Mainigi MA. Surgery for endometriomas **before IVF: what are the benefits and risks?** Minerva Ginecol. 2015; 67(2):195-205.
5. Hamdan M, Dunselman G, Li TC, Cheong Y. The impact of endometrioma **on IVF/ICSI outcomes: a systematic review and meta-analysis.** Hum Reprod Update. 2015; 21(6): 809-25.
6. Dicker D, Goldman JA, Feldberg D, Ashkenazi J and Levy T. Transvaginal ultrasonic needle-guided aspiration of endometriotic cysts before ovu- lation induction for in vitro fertilization. J In Vitro Fert Embryo Transf. 1991; 8, 286–289.
7. Suganuma N, Wakahara Y, Ishida D, Asano M, Kitagawa T, Katsumata Y, Moriwaki T and Furuhashi M. Pretreatment for ovarian endometrial cyst before in vitro fertilization. Gynecol Obstet Invest 2002; 54,36–40.

Forthcoming Events

- Next **AOGD Clinical Meeting** on Thursday, 25th January, 2018 at Dr RML Hospital, Connaught Place, New Delhi.
- Skill Workshop of AOGD on **"Medico legal issues in Obstetrics & Gynaecology – Tips & Tricks"** on 10th February 2018 at GTB Hospital. Registration Free. Contact: AOGD Office (011-22692505) & Dr Richa Sharma (9868399747)
- 3rd Maternal-Fetal Medicine Workshop on **"Essentials of Fetal Medicine- Clinical Approach"** is being organized by Department of Obstetrics & Gynecology, Maulana Azad Medical College, New Delhi alongwith AOGD Fetal- Medicine Committee on 10th February 2018 at MAMC Auditorium, New Delhi. For details & registration contact Dr. Sangeeta Gupta 8447199481, Mr. Jaimohan 9811507470

Quiz Time: *Tick it, Fill it, Click it, Whatsapp/ Email it*

Bindiya Gupta
Assistant Professor, Department of Obstetrics & Gynecology, University College of Medical Sciences & Guru Teg Bahadur Hospital, Delhi

1. Write True of False
   a. In uterus up to 12 weeks with a normal cavity LNG -IUS is 80-90% effective in reducing menorrhagia
   b. Uterine Artery embolization can be performed in submucus fibroids
   c. Selective CM in experienced hands is a safe procedure.
   d. Trophectoderm biopsy of day 5/6 blastocyst-stage embryos is more popular than 3 cleavage stage embryos

2. Fill in the blanks
   a. PEARL I and PEARL II trials compare ..... and .....
   b. Dose of Mifepristone in fibroids is .....
   c. Contraindications of MRgFUS are.....
   d. Any 3 complications of cesarean myomectomy .....
   e. ESTEEM .....
   f. According to Cochrane the risk of recurrence after native tissue repair is ..... And after mesh is .....

3. Name any three methods for molecular analysis of all 24 chromosomes in PGS?
   .....
   .....
   .....

4. Which is false about lymphadenectomy in ovarian cancer
   a. Systematic lymph node dissection should be done in suspected early-stage ovarian cancer.
   b. Patients of advanced ovarian cancer with bulky nodes, benefit from removal of enlarged metastatic nodes by reducing the size of residual tumor regardless of wether intraperitoneal debulking is optimal or not.
   c. For patients of advanced ovarian cancer achieving optimal cytoreduction and no clinically suspect lymph nodes, the role of systematic lymphadenectomy remains controversial
   d. Systematic lymph node dissection in suspected early-stage ovarian cancer as provides important prognostic and staging information.

5. As per RCOG 2015, which of the following increases risk of rupture in previous cesarean section
   a. Short inter-pregnancy interval < 12 months
   b. Short Inter-delivery interval < 12 months
   c. Short Inter-pregnancy interval < 18 months
   d. Short Inter-delivery interval < 18 months

Tick the MCQs and fill in the blanks.
Click a pic and whatsapp or email to us
Whatsapp Nos.: 9810645212, 9810719002
Email: info@aogd.org

Answer Key to Quiz in December Issue

1 a) The psycho-physiological symptoms such as hot flashes, mood changes, sleep disturbances and irritability are assessed by Kuppermann score
b) pH, Rugosity, Elasticity, Vascularity **c)** Stages of Reproductive Aging Workshop
d) bazedoxifene with low dose conjugated equine estrogen **e)** *Natazia (United States) and Qlaira (United Kingdom)*

2 c; **3** d; **4 a** F, **b** F, **c** T, **d** T

5. higher BMI, higher free androgen index, insulin resistance, large ovarian volume

6. Failure to ovulate is termed as ***clomiphene resistance***. Failure to conceive despite ovulation with CC is termed as ***clomiphene failure***.

7. bazedoxifene, ospemifene, lasofoxifene **8.** Bazedoxifene **9. Tissue-selective estrogen receptor complex**

10. Leiomyoma and associated abnormal uterine bleeding and bulk symptoms, Endometriosis Contraception

11. b

Events Held in December 2017

- An adolescent health awareness programme was organised at Rukmani Devi Public School by Dr Susheela Gupta on 6th December 2017. The session covered a number of adolescent health issues including questions from enthusiastic participants.

An adolescent health awareness programme was organised at Rukmani Devi Public School by Dr Susheela Gupta

- Skill Workshop of AOGD on "Management of PPH: Practical Aspects" on 9th December 2017 at LT – 1, College Block, UCMS & GTB Hospital. Videos of different type of procedures for controlling PPH including Chhattisgarh balloon & step wise devascularisation were demonstrated

Skill Workshop of AOGD on "Management of PPH: Practical Aspects" on 9th December 2017 at LT – 1, College Block, UCMS & GTB Hospital

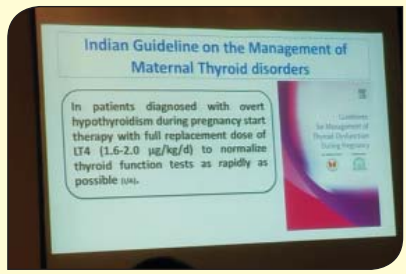
- FOGsd under the guidance of Dr Anita Sabharwal organized a CME on Infertility and X – Mas Day Celebrations under aegis of AOGD on 25th December at advanced IVF & Training Centre, Vasant Kunj


FOGsd under the guidance of Dr Anita Sabharwal organized a CME on Infertility and X – Mas Day Celebrations

- CME under the aegis of Adolescent Committee of AOGD was organised on 29th December at Hotel City Park Pitampura under the leadership of Dr Sanjivni Khanna & Dr Shakuntla Kumar

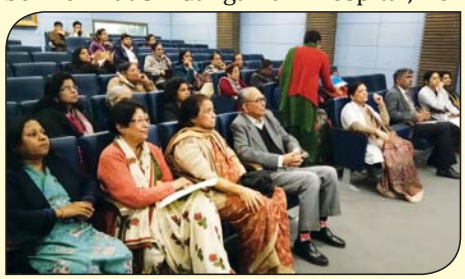




CME under the aegis of Adolescent Committee of AOGD was organised by Dr Sanjivni Khanna & Dr Shakuntla Kumar

- AOGD Monthly Clinical Meeting on Friday, 29th December 2017 at Sir Ganga Ram Hospital, New Delhi.


AOGD Monthly Clinical Meeting at Sir Ganga Ram Hospital, New Delhi

Role of Routine PGS in ART and its Impact on ART Success

Pranay Ghosh
Director, Elixir Fertility Centre, Delhi

Preimplantation genetic diagnosis (PGD), a procedure involving embryo creation by in vitro fertilization (IVF) and testing of oocytes retrieved or embryos formed for genetic defects, was initially developed as a substitute to prenatal diagnosis to decrease the risk of transmission of severe genetic diseases. Although PGD was initially introduced for pre-existing genetic conditions, its application appears to be of particular relevance for conditions such as chromosomal abnormalities that contribute significantly to pregnancy loss and infertility. At least three-quarters of all PGDs have been performed for age-related aneuploidies, resulting in the birth of thousands of healthy children. The strategy to combine screening aneuploid embryos with the routine IVF is called preimplantation genetic screening (PGS) or preimplantation genetic screening of aneuploidy (PGD-A).

Clinical assessment over many decades has established that aneuploidy is the main cause of early miscarriages and congenital birth defects, and is the most common chromosome abnormality in humans. The majority arise from errors in maternal first meiotic division. This fact on its own was important for considering how to improve outcome during an IVF cycle, but it was also believed that many of the failures of implantation were due to aneuploid embryos.

Today it bears no doubt that blastocysts found to be uniformly aneuploid in a biopsy will fail to implant, or worse, will implant and lead to a pregnancy and birth carrying a major chromosomal abnormality. However, it has been argued that a cohort of embryos cannot be improved, and that PGS is only a selection method for which efficiency has not been proven. PGS can never increase the live birth rate for that given cohort, even with a 100% efficiency rate of embryo cryopreservation. The current debate on whether PGS should be applied and to which patients it should be offered has shifted from the effect on live birth rates towards other outcomes such as the reduction of transfers and of miscarriages.

PGS is also often presented as diminishing patient anxiety and stress through decreasing unnecessary embryos transfers and miscarriages, although no data on this assertion are available. Whether this argument will show to be strong enough to add PGS as a routine part of an IVF treatment remains to be seen.

Evolution of PGS

Initially the day 3 cleavage-stage embryos were most frequently used for embryo biopsy whereas more recently the trophectoderm biopsy of day 5/6 blastocyst-stage embryos is more popular as there is evidence showing that the implantation potential of the biopsied embryos is less affected if the biopsy is taken at blastocyst stage. In few European countries (e.g. Germany) where the legal regulation of PGD/PGS is more strict, polar body biopsy remains a viable option since such biopsy does not affect the embryo integrity, though it can only diagnose the maternally inherited balanced translocation instead of the paternally inherited ones.

For more than 20 years PGS has been used with the aim of selecting human embryos with the highest developmental potential to improve the results obtained after assisted re- productive techniques (ART). However, it was demonstrated that first generation PGS was ineffective in improving IVF pregnancy rates and in reducing miscarriage rates. This disappointing result was at the time explained as being due to the three following causes: first, damage of the preimplantation embryo during cleavage stage following biopsy; second, incomplete and limited assessment of chromosomal status using fluorescence in situ hybridization (FISH); and third, mosaicism of the Day-3 embryo due to postzygotic cleavage division errors. Following these insights, a new generation of PGS has been introduced. This so-called PGS 2.0, as contrasted to PGS 1.0, is characterized by trophectoderm biopsy or polar body (PB) biopsy instead of Day-3 embryo biopsy, and aneuploidy assessments of all 23 chromosome pairs instead of FISH of a limited set of chromosomes.

Indications

The group of patients that have been suggested classically to potentially benefit from PGD-A were infertile or sub-fertile women of advanced maternal age (AMA; usually, defined as ≥ 35 years), with a history of recurrent pregnancy loss (RPL; usually at least three previous miscarriages) or with repeated implantation failure (RIF; three or more failed embryo transfers) and severe male factor. Over time, other indications have been proposed including a previous genetically abnormal pregnancy, poor embryo quality, and single embryo transfer (SET), though there is a lack of a general international consensus.

PGS is a multistep procedure involving genetic counselling of the couple; IVF; oocyte/embryo biopsy, cryopreservation of the embryo (pending the results of genetic analysis); genetic analysis of the embryo; embryo warming and embryo transfer. This requires a collaboration between an IVF unit and a molecular genetics unit.

Biopsy Strategies

Polar body (PB) biopsy involves simultaneous or sequential biopsy of first and second polar bodies. This can be done using a bevelled micropipette, three-dimensional zona dissection or use of 1.48 µm diode laser. Use of acid Tyrode for opening the zona is no longer recommended as it affects spindle development and resumption of meiosis. Being by-products of meiotic division and hence not contributing to the developing embryo, PB biopsy is considered safe. Also, PB analysis is considered ethically acceptable in countries where embryo biopsy is banned. The biopsy provides adequate time for genetic analysis before embryo transfer. However, it cannot be used for paternally derived disorders as it samples only maternal genetic material. It also fails to provide information on postzygotic mutations. Furthermore, often PBs are fragmented and this may yield ambiguous or erroneous data.

Cleavage-stage biopsy involves the removal of one or two blastomeres on third day after insemination. Zona drilling using laser is the commonest employed technique, and is quicker than chemical or mechanical drilling. The blastomeres sampled allow for detection of both maternal and paternal defects. It also provides adequate time for analysis prior to fresh embryo transfer. However, cleavage stage biopsy has the drawback of high degree of mosaicism at this stage, which may preclude the embryo from being considered for transfer. Other problems are cell lysis, multinucleation and anucleate blastomeres.

After PGS 1.0, it was clear that the cleavage stage is not the optimal stage for biopsy, especially since it was shown that cleavage-stage biopsy significantly impairs human embryonic implantation. Almost all advocates of PGS 2.0 prefer trophectoderm biopsy (TEB), since multiple cells are available after biopsy, and because this embryonic stage shows lesser chromosomal mosaicism. However, there are concerns about long-term and transgenerational effects of culture to the blastocyst stage.

Finally, a new source of embryonic genetic material can be obtained by blastocyst fluid aspiration. However, the reliability of this still needs to be demonstrated.

Methods for Comprehensive Chromosomal Screening (CCS)

Whole genome amplification (WGA), i.e. the amplification of one or two copies of the genome, can generate multiple copies in a short time and thereby result in sufficient template for comprehensive chromosome screening. The following methods can be used for molecular analysis of all 24 chromosomes: metaphase comparative genomic hybridization; array comparative genomic hybridization (aCGH); genome wide single nucleotide polymorphism analysis; PCR-based detection and next generation sequencing (NGS), or massive parallel sequencing (MPS) as it is currently called, using different platforms such as the MiSeq (Illumina) the HiSeq platform (Illumina) or the IonTorrent platform (Thermo Fischer). All these methods have been used to study the complete or partial an- euploidy for one or more of the 24 chromosomes. The lowest detection threshold for segmental abnormalities is different for the different methods, and so the minimal size taken into account for PGS 2.0 varies widely. Moreover, the different methods have different detection levels with respect to mosaicism in multicellular samples. This is important since it is a matter of debate whether the aneuploidy rates in trophectoderm are a true reflection of the rates in the inner cell mass.

PGS-CCS and ART Success

The chief goal of PGS has always been the improvement of IVF success rates. However, different authors have differently defined success such as improved implantation rates, decreased miscarriage rates, increased clinical pregnancy rates, increased live birth rates and decreased time to pregnancy. Furthermore, success rates can be expressed in different ways: as intention-to-treat, per patient, per cycle and per transfer (fresh and frozen).

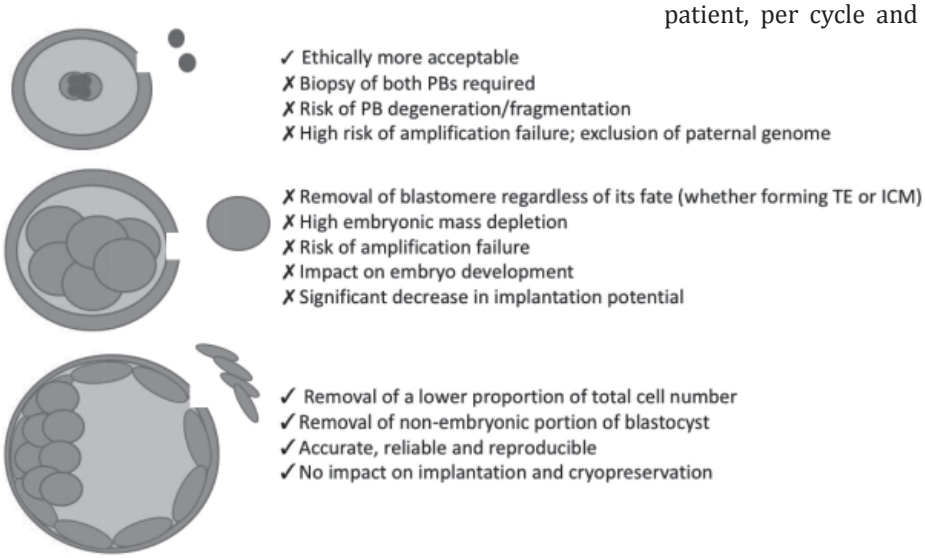


Figure 1. Comparison between different biopsy stages

This makes it difficult to compare the outcomes of various studies and; moreover, some success measures such as implantation rates and success per transfer should not be applied. Therefore, it has been suggested that pregnancy rates be calculated with cycles started rather than embryo transfers as denominator.

Several retrospective and prospective trials have reported improved clinical outcomes following PGS, utilizing trophectoderm biopsy combined with CCS for embryonic aneuploidy. These RCTs and observational studies have been recently evaluated by Dahdouh et al. in their meta-analysis, aiming to study whether PGS-CCS improves clinical implantation rates (IR) and sustained IR (beyond 20 weeks) compared with routine embryo selection in IVF cycles. Of the 29 eligible articles, only three RCTs and eight observational studies met full inclusion criteria, revealing significantly higher clinical and sustained IRs with the use of PGS-CCS in patients with normal ovarian reserve. On the contrary, a recent analysis of national U.S. PGS data for 2011–2012 have yielded different results. While more PGS than non-PGS cycles reached ET (64.2 % vs. 62.3 %), suggesting favourable patient selection bias for patients using PGS, LBRs per cycle start (25.2 % vs. 28.8 %) and per ET (39.3 % vs. 46.2 %) were significantly better in non-PGS cycles, whereas miscarriage rates were similar (13.7 % vs. 13.9 %).

The earliest RCTs which are often cited as sound evidence in favour of PGS have however been heavily criticized, the main criticisms being the small size of the study, the fact that transfer of cryopreserved embryos which could have been higher in the control group was not taken into account and could have led to additional pregnancies, the inclusion of good prognosis patients only with at least a number of analysable embryos, the difference in number of embryos transferred between the two study groups and finally the use of implantation rate as outcome measure. These trial characteristics lead to a distortion of the real a priori benefit for patients, as they do not represent those patients that for instance do not obtain blastocysts for analysis, or only have abnormal embryos and therefore do not even reach embryo transfer. Although these three RCTs were on specific patient categories, they are often cited as demonstrating PGS efficacy for all IVF patients.

In a much more robust RCT, Rubio and colleagues compared live birth rates in 105 patients of AMA receiving PGS at the cleavage stage using a-CGH with 100 patients undergoing IVF without PGS. They found no difference in cumulative live birth rates when including cryocycles: 37% in the PGS group vs 33.3% in the control group. There were however significant differences in the number of embryo transfers performed and in the miscarriage rate, which was extremely low in the PGS group (only one) versus 21 in the control group.

Another well-designed RCT is the ESTEEM (ESHRE study into the evaluation of oocyte euploidy by microarray analysis) study in an AMA population, testing a-CGH in first and second polar body biopsies. The first results of this RCT showed no differences in live birth rates (20% in the PGS group vs 22% in the control group), although the number of embryo transfers here too was lower in the study group as well as the miscarriage rate. The STAR trial is another RCT for which the results are much awaited, although as in previous RCTs, randomization of patients is only performed after the patients had obtained at least 2 analysable blastocysts.

Whether PGS can be offered routinely to a selected subgroup of patients, let alone to all patients undergoing IVF, is a matter of debate. According to few groups, the aforementioned improved outcome with PGS-CCS is based on 5 essential assumptions: (i) Most IVF cycles fail because of aneuploid embryos (ii) Their elimination prior to embryo transfer will improve IVF outcomes (iii) A single trophectoderm biopsy at blastocyst stage is representative of the whole TE (iv) TE ploidy reliably represents the inner cell mass (ICM) (v) Ploidy does not change (i.e., self-correct) downstream from blastocyst stage.

It has been argued that the significant improvement in clinical and ongoing pregnancy rates following PGS 2.0 and CCS has been demonstrated only in a select subgroup of patients i.e. the older poor prognosis patients, and is not beneficial to good or average prognosis patients. It has further been argued that the benefits in poor prognosis patients may be biased by compared the outcome of a PGS-CCS frozen thaw cycle with a previous fresh transfer.

Concerns have been raised over the accuracy of CCS as a diagnostic technique. Cases have been reported wherein patients experiencing spontaneous miscarriage following PGS-eSET (euploid single embryo transfer), upon chromosomal re-assessment were found to be aneuploidy, raising the spectre of false-negative TEBs. Of greater concern are the case reports of good prognosis patients with false positive TEBs who repeatedly underwent IVF cycles without ever reaching embryo transfers because all embryos were reported as aneuploidy.

The presence of 2 or more distinct cell lines, commonly referred to as chromosomal mosaicism, is one of the potential pitfalls when analysing embryos by CCS. The ability to detect mosaicism accurately is determined by the technology used, number of chromosomes examined, and number of cells analysed. Though some studies indicate that TE aneuploidy is an excellent predictor of ICM aneuploidy (based on TE and ICM biopsies), they are limited by the use of older methods of CCS, namely a-CGH. The incidence of mosaicism in preimplantation embryos is in fact reported to be between 4 and 90%. However, these data are in sharp contrast with what is known from clinical pregnancies, where true foetal mosaicism is observed in less than 0.5% of cases. Studies of mosaicism in blastocysts have reported much lower levels of compared to the cleavage stage. However, since all types of uniform aneuploidies can survive to the blastocyst stage, including complex aneuploidies, an alternative explanation for the observed difference between cleavage and blastocyst stage mosaicism rate can be found in the improved accuracy achieved when evaluating multiple cells instead of single cells. The rate of TE mosaicism in human embryos has been reported to be as high as 70

and 90% in cleavage- and blastocyst-stage embryos, respectively, but increasingly believed to be a normal physiological phenomenon. While Liu et al. reported that 69% of abnormal blastocysts from women of advanced age are mosaic for ICM and TE, Johnson et al. demonstrated that in younger women 20% of blastocysts are aneuploid, with a majority of the abnormal blastocysts presenting with only one or two structural chromosome abnormalities, suggesting even in young women a still critical level of mosaicism at blastocyst stage. Further evidence for a non-precise diagnoses due to TE mosaicism came from studies of multiple TEB, demonstrating up to 50% divergence between biopsies of same embryos in same laboratories, and up to approximately 80% divergence between multiple biopsies in different laboratories.

Most TEB results are either normal for all chromosomes (euploid) or abnormal, with one or more aneuploidies. However, a small proportion has intermediate copy number changes for one or more chromosomes, which may indicate possible chromosome mosaicism. In many cases, these occur in conjunction with other uniform aneuploidies. However, in some cases only mosaic aneuploidies are detected, and these may be the only embryos which are available for possible transfer. Because mosaic aneuploidies detected in TEB may theoretically have clinical implications for the pregnancy, including effects on placental function, and/or in live births clinically affected by mosaic aneuploidies, transfer of these embryos should only be considered when there is no alternative and preferably only after appropriate genetic counselling of the patient. Developments in genomic technologies for preimplantation genetic diagnosis have revolutionized our ability to detect genetic abnormalities of various kinds at the level of single or small numbers of cells. Perhaps inevitably, the increased sensitivity and resolution of these methods has allowed a spectrum of chromosome abnormalities, including chromosome mosaicism, to be detected. Available evidence currently suggests that mosaicism (at least in the trophectoderm layer) only occurs in a small minority of embryos. Nevertheless, this can present a clinical challenge in managing patients, particularly poor prognosis patients, with no normal euploid embryos available for transfer. Transfer of blastocysts in which only mosaic aneuploidies have been detected should only be considered following expert advice and appropriate genetic counselling of patients. The laboratory reporting guidelines should also be understood when advising patients of the reasoning behind any concerns regarding the transfer and the appropriateness of follow up such as amniocentesis.

Challenging the biological concept of PGS, it is also argued whether a single trophectoderm biopsy (TEB), indeed, can reliably reflect ploidy of the total TE, how accurately a TE biopsy represents the inner cell mass (ICM), from which the embryo arises, and how extensively an embryo self-corrects downstream from blastocyst stage. That embryos self-correct to highly significant degrees was strongly suggested in a recent mouse study, when early stage embryos, even when highly chimeric for euploid and aneuploid cell lineages, remarkably self-corrected downstream from blastocyst stage. Moreover, self-correction was more efficient within the ICM than within TE, from which the placenta develops. Faced with such genetic heterogeneity between early embryonic compartments, more aneuploid cells would, therefore, be expected in TE than ICM. Yet, in the current utilization of PGS (PGS 2.0), embryo biopsies are exclusively obtained from the TE. Moreover, results of embryo biopsies can significantly vary between diagnostic platforms.

Aneuploid cell lineages increase with advancing female age, likely increasing the ratio of non-constitutional to constitutional cells and, thereby, further reducing the accuracy of a single TEB. When in older women, accurate diagnosis of ploidy is needed most, PGS 2.0, therefore, appears least accurate. Considering that embryo numbers decline with advancing age, it, therefore, is not surprising that PGS, even in its earlier format (PGS 1.0) already was demonstrated to adversely affect IVF outcomes in older women and poorer prognosis patients. Recently published national U.S. data from the Centre for Disease Control and Prevention (CDC), comparing outcomes in IVF cycles with and without PGS, suggested potential negative effects from PGS. Moreover, increasing numbers of healthy offspring delivered following transfers of allegedly aneuploid/mosaic embryos have called further into doubt the longstanding policy of discarding such embryos.

In the context of evidence based medicine, the only way to ascertain whether routine PGS increases ART success rates is to conduct well-designed RCTs, some of which are currently underway. It may be presumed that in a rapidly evolving field, it is important to innovate quickly, if necessary without waiting for strong evidence, especially in private clinics depending on a sufficient patient flow to survive. However, in all fields of ART and IVF, as in other fields of medicine, RCTs are highly needed before the introduction of new technologies, the so-called add-ons in IVF, many of which are abandoned for lack of effect after having been previously applied widely in the clinical setting.

Suggested Reading

1. Preimplantation genetic screening 2.0: the theory. Geraedts J, Sermon K. Mol Hum Reprod 2016;22(8): 839-44.
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3. Preimplantation genetic testing in ART: who will benefit and what is the evidence? Vaiarelli A, Cimadomo D et al. J Assist Reprod Genet 2016;33 (10): 1273-78.
4. Chromosomal mosaicism in human preimplantation embryos: a systematic review. Hum Reprod Update 2011; 17 (5): 620-7.
5. A single trophoectoderm biopsy at blastocyst stage is mathematically unable to determine embryo ploidy accurately enough for clinical use. Gleicher N, Metzger J et al. Reprod Biol Endocrinol 2017; 15 (1): 33.

ERRATUM

Due to some error during printing, two figures in Dec issue got changed.
Pls read figure 1 on page no 13 & Figure 2 on pg 15 of Dec issues, as follows...

Figure 1: A simple plan of evaluation of precocious Breast and / or public hair development

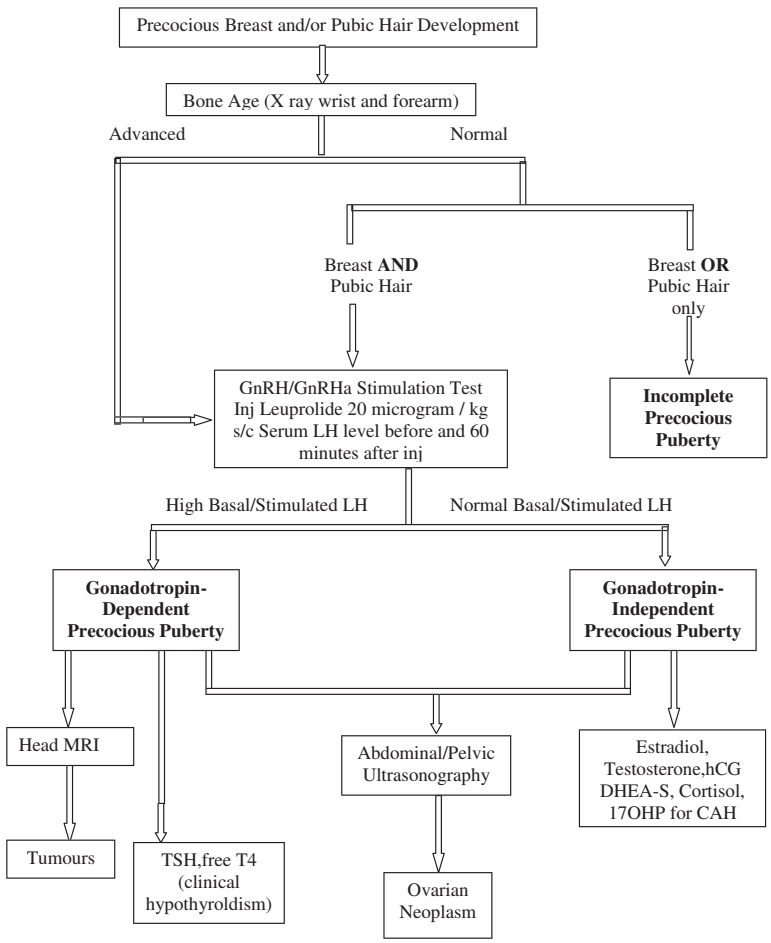
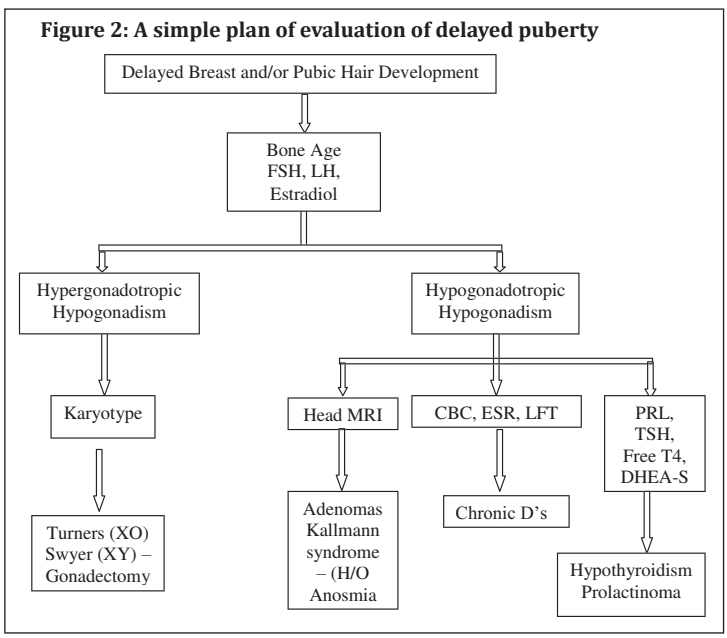


Figure 2: A simple plan of evaluation of delayed puberty



"Body, Mind and Soul"

Nadi Shodhan Pranayam: Balancing Right & Left Brain

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When the Breath wanders, the mind is unsteady, but when the Breath is still, so is the mind still."

– Hatha Yoga Pradipika

Right and left hemispheres of human brain process reality differently, affecting the way we see the world. **The right hemisphere of brain is the more creative side** and is associated with inner-strength and intuition. Those who are right-brained tend to be artistic, sensitive, nurturing and easy-going. **The left brain is the more analytical type** and is associated with aggression, physical strength, control and ego. When someone is known to be left-brained they tend to be logical, driven, analytical and fast paced.

When a balance is achieved between right and left brain tendencies, one is able to solve problems, be productive, be creative and ultimately, less stressed. In a way, this is a key to health, resilience, productivity and accessing creative genius. In his book, *How to think Like Leonardo Da Vinci*, Michael Gelb says that Leonardo Da Vinci had perfect right-left brain balance. *"So, was Leonardo a scientists who studied art, or an artist who studied science? Clearly, he was both,"* Gelb writes

There is a correlation between brain activity and the nasal breathing. Scientists have discovered that when **the right nostril is dominant, the brain activity is greater in the left cerebral hemisphere**. When the dominant nostril switches, so does the activity in the brain hemisphere. They call this "alternating dominance of cerebral hemispheric activity." So, while doing something analytical using the left brain, right nostril would be more open. And if using the creative right brain, like painting or dancing, left nostril would be more open.

So, right and left brain balance can be achieved by balancing the act of breathing. In Yoga, controlling breath is given a lot of importance in the practices of different forms of Pranayama. Yogis in India have been practicing Meditation and Pranayama for ages while scientifically we are just beginning to really recognize how important the breath is in regards to our physical, emotional and mental health.

Among the ancient yogis' most important discoveries were the *nadis.* In Sanskrit, nadi means "stream" or "flow" and is the vast network of energy channels that allow prana (cosmic energy) to move throughout the body. Out of total 75,000 nadis, three fundamental nadis are-the left, the right and the central. The *Sushumna Nadi* is the central channel, running along the spine. It is here where all 7 chakras align.

The **Ida nadi** governs the feminine, left side of the body, which in turn activates the right (visual, intuitive and creative) side of brain (Ida nadi is associated with moon). The **Pingala nadi** governs the masculine, right side of the body and activates the left (logical) side of the brain (pingala nadi is associated with sun).

Signs of poor functioning Ida nadi (femine energy) are extreme coldness, depression, low mental energy, sluggish digestion, and a blocked left nostril. Signs of a poor functioning Pingala nadi (masculine energy) are excessive body heat, quick temper, itching body, dry skin and throat, excessive appetite, excessive physical or sexual energy, blocked right nostril. When the left nostril is dominant (more airflow passing through nostril) it means the right side of the brain is more active and when the right nostril is dominant, the left side of the brain is more active. The dominance of each nostril will change throughout the day.

Ida and Pingala represent the basic duality of existence. Creating a balance between Ida and Pingala will make one more effective in the world, allowing to have a more accurate experience of reality. There are various techniques to achieve this balance including exercises, music, meditation and pranayama.

Nadi Shodhan Pranayama

"Pranayama is the link between the mental and physical disciplines. While the action is physical, the effect is to make the mind calm, lucid and steady".

To help balance masculine and feminine energy, there is an excellent breathing technique one can use called Nadi Shodhana (Alternate-nostril breathing). When practiced regularly this breathing technique helps balance the ida and pingala nadis. The *Nadi Shodhan pranayama* helps clear these blocked energy channels, thus calming the mind. This technique is also known as ***Anulom Vilom*** Pranayama.

Various Benefits of Nadi Shodhan Pranayama (Alternate Nostril Breathing Technique)

1. Excellent breathing technique to calm and center the mind.
2. *Nadi Shodhan pranayama* helps to bring the mind back to the present moment.
3. Works therapeutically for most circulatory and respiratory problems.
4. Releases accumulated **stress** in the mind and body effectively and helps relax.
5. Helps harmonize the left and right hemispheres of the brain, which correlate to the logical and emotional sides of our personality.
6. Helps purify and balance the nadis thereby ensuring smooth flow of prana (life force) through the body.
7. Maintains body temperature.

Technique

Preparatory Pose: Any Meditation posture like Lotus pose (Padmasana) or Swastikasana (Fig 1 & 2).

Focusing point: Breathing process.

Fig 1: Padmasana (The Lotus Pose)

Fig 2: Swastikasana (The Auspicious Pose)

Steps

1. Sit comfortably with spine erect and shoulders relaxed. Keep a gentle smile on face.
2. Raise the right hand. Make the Vishnu Mudra (Fig 3) by folding down the index and middle fingers.
3. Place left hand on left knee in Chin Mudra (palm facing up, index finger touching tip of the thumb) (Fig 4).

Fig 3: Vishnu Mudra

Fig 4: Chin Mudra

4. Exhale through both nostrils.
5. Now close the right nostril with the right thumb.
6. Now breathe in completely from the left nostril. This should be done to a count of "4.
7. Close the left nostril with the two end fingers so that both the nostrils are closed. Retain the breath to a count of "16".
8. Release the right nostril and exhale completely to a count of "8".
9. Now inhale through the tight nostril to a count of "4".
10. Now close both nostrils and retain breath to a count of "16".
11. Release left nostril and exhale completely to a count of "8".

This completes one round of Nadi Shodhan Pranayama (Fig 5). Practice at least 8-10 rounds daily inhaling and exhaling from alternate nostrils. After every exhalation, remember to breathe in from the same nostril thorough which just exhaled. Eyes should be kept closed throughout and breaths should be long, deep and smooth without any force or effort. Mind should be focused on breathing.

With practice, the count can be increased, but always in the ratio of 1:4:2 (inhalation: retention and exhalation). Some advocate the ratio of 1:2:2 (count of 5:10:10). The important point is that exhalation should be longer than inhalation. Initially one can start practice without retention of breath, means only inhalation and exhalation through alternate nostrils. But once comfortable, the alternate nasal breathing should be practiced with retention (Proper Nadi Shodhan Pranayam) to reap full benefits

Fig 5: Nadi Shodhan Pranayam (One round)

Lymphadenectomy in Epithelial Ovarian Cancers

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While ovarian cancer spreads into the peritoneal cavity by exfoliation and implantation, it is also known to spread through the retroperitoneal lymphatics that drain the ovary. These lymphatics follow the infundibulopelvic ligament into the lymph nodes lying along the aorta and vena cava up to the level of the renal vessels. In fact, the principal lymphatic drainage is via the paraaortic lymph nodes, and the high left infrarenal group may often harbor lymph node metastasis. The next lymph node station is the celiac trunk from where the tumor cells may travel up to the mediastinal and supraclavicular lymph nodes. Lymph channels from the ovary also pass laterally through the broad ligament and parametrium into the pelvic lymph nodes including the external iliac, obturator and hypogastric groups. Some lymphatics pass along the round ligament, resulting in spread to the inguinal lymph nodes in a few cases.

Patients with apparent stage-I epithelial ovarian cancer have a 10–24% risk of retroperitoneal nodal metastasis compared with 20–30% for patients with stage-II disease. Those with advanced disease (stage III and IV) may have involved nodes in 50–80% cases. Systematic pelvic and retroperitoneal lymphadenectomy is advocated in early stage ovarian cancers as it upstages the disease in 22–25% cases, making them appropriate candidates for adjuvant chemotherapy after surgery. Conversely, patients with low-risk disease may be spared from chemotherapy after undergoing complete staging. Another reason to advocate systematic lymphadenectomy is that involved lymph nodes may not be enlarged either on preoperative imaging or on intraoperative palpation in up to one-third of the cases, and hence only debulking of enlarged lymph nodes may miss the metastatic disease in this fraction of patients. It has also been suggested that nodal ovarian cancer metastases may be less sensitive to systemic chemotherapy because of diminished blood supply (pharmacological sanctuary), and thus lymphadenectomy may be therapeutic as a result of maximal debulking.

Systematic lymphadenectomy is associated with side-effects and complications like vascular injury and hemorrhage, thrombosis, ileus and lymphocyst formation. Lymphocele or lymphedema can occur in 7% to 22% of patients. Less frequent complications include injury to the nerves, ureters and small and large bowel. The current literature suggests that systematic pelvic and retroperitoneal lymphadenectomy must be done as part of staging in early (Stage I and II) epithelial ovarian cancers. In advanced epithelial ovarian cancers, enlarged/suspicious lymph nodes should be removed as part of tumor debulking, to achieve optimal cytoreduction. It has also been suggested that systematic lymphadenectomy may be beneficial in patients with advanced cancers where complete removal or small residual (<1cm) of intraperitoneal disease can be achieved, however its therapeutic value remains controversial.

Early Ovarian Cancers

Systematic lymphadenectomy helps in upstaging an apparent early stage ovarian cancer to stage III in up to one-fourth of the cases. This helps in directing adjuvant chemotherapy as well as the prognostication of the disease. The rate of positive lymph nodes is very low in mucinous ovarian cancer and lymph node dissection can be omitted in these cancers.

Maggioni and colleagues, in a prospective trial of 310 early (FIGO stage I and II) ovarian cancer patients, randomized cases who had undergone optimal surgical debulking to either a systematic lymph node dissection or lymph node sampling. Positive lymph nodes (which upstaged a patient to stage IIIC) were found in 9% of patients in the sampling group compared to 22% in the systematic lymph node dissection group ($p < 0.05$). The patients in the systematic lymph node dissection arm had a longer intraoperative time, more blood loss (300ml more), and received more blood transfusions (22% vs. 36%, $p < 0.05$). Both groups had similar rates of postoperative complications. There was no difference in progression-free survival (PFS) or overall survival (OS) between the two groups, but the study was not powered for the detection of a small survival benefit.

Advanced Ovarian Cancers

Though optimal cytoreduction is the cornerstone of management of advanced ovarian cancers, it is still unclear whether systematic lymphadenectomy should be part of maximal cytoreductive surgery. Despite the prognostic significance of lymph node metastasis, the effect of lymph node dissection in advanced cancers on survival is debatable. Patients in whom intraperitoneal debulking is suboptimal (residual tumor larger than 1 cm) do not benefit from lymphadenectomy. Patients with bulky nodes and optimal intraperitoneal cytoreduction benefit from removal of enlarged metastatic nodes by reducing the size of residual tumor. Systematic lymphadenectomy in patients undergoing optimal

cytoreduction but without clinically suspect lymph nodes, is controversial – it might not change the residual disease status but may reduce tumor burden that is possibly resistant to chemotherapy.

Retrospective studies have suggested a clinically significant improvement in survival after systematic lymphadenectomy, but the prospective randomized clinical trial by Panici et al reported that systematic lymphadenectomy improved the progression-free survival but not the overall survival. In this trial, 427 patients with stage IIIB-C and IV epithelial ovarian carcinoma were randomly assigned to undergo systematic pelvic and para-aortic lymphadenectomy (n = 216) or resection of bulky nodes only (n = 211). After a median follow up of 68.4 months, the median progression-free survival was 29.4 months in systematic lymphadenectomy arm vs 22.4 months in the debulking arm (difference = 7 months, 95% CI = 1.0 to 14.4 months). The sites of first recurrences were similar in both arms. There was no difference in the rate of retroperitoneal recurrences between the two arms, 2.3 versus 2.4%. The risk of death was similar in both arms (HR = 0.97, 95% CI = 0.74 to 1.29; P = .85), corresponding to median overall survival of 58.7 and 56.3 months, respectively (difference = 2.4 months, 95% CI = – 11.8 to 21.0 months). Although the number of intra-operative complications was similar in the two arms, systematic lymphadenectomy had greater perioperative and late morbidity, mainly due to lymphocysts and lymphedema. However it should be noted that that the study took more than 12 years to complete, 63% of the patients did not achieve no gross residual after cytoreduction and even the control arm underwent a lymph node debulking where the lymph nodes were enlarged.

A retrospective analysis of SEER database of 49,783 patients of ovarian cancer suggested a beneficial effect of lymphadenectomy in epithelial ovarian tumors, regardless of the stage of disease and extent of surgery. The five-year cause-specific survival rates were 37%, 62%, and 71% for the groups in which no lymph nodes were examined, in which between one and nine nodes were examined, and in which ten or more nodes were examined, respectively (P < 0.001). However, there were biases in this study due to its retrospective methodology and the possibility that thorough lymphadenectomy may have reflected the quality of cytoreductive surgery. Du Bois et al, in an analysis of three prospective randomized trials (AGO-OVAR # 3,5,7) including 1924 patients of advanced epithelial ovarian cancers, reported that in the subgroup of patients with no residual disease on cytoreduction and no enlarged lymph nodes, a systematic lymph node dissection was associated with higher survival. The median survival in patients with and without lymphadenectomy, was 103 and 84 months, respectively (P = 0.0166). Multivariate analysis confirmed a significant impact of lymphadenectomy on overall survival (OS; hazard ratio [HR] = 0.74; 95% CI, 0.59 to 0.94; P = 0.0123). In patients with small residual tumors up to 1 cm, the effect of lymphadenectomy on OS barely reached significance (HR = 0.85; 95% CI, 0.72 to 1.00; P = 0.0497). The authors concluded that lymphadenectomy in advanced ovarian cancer might offer benefit to patients with complete intraperitoneal debulking. However, the study was retrospective and the decision to perform lymphadenectomy was at the surgeon's discretion. Hence they premised that the findings should be confirmed in the context of a prospective randomized trial.

In order to explore the role of systematic pelvic and para-aortic lymphadenectomy (LNE) in patients with advanced ovarian cancer with macroscopic complete resection and clinically negative lymph nodes, the AGO study group initiated a prospective randomized study – the LION trial (Lymphadenectomy in Ovarian Neoplasms). Patients with newly diagnosed FIGO IIB-IV ovarian cancer with macroscopic complete resection and pre- and intra-operatively clinical negative lymph nodes were randomized intra-operatively to LNE versus no-LNE. Patients with non-epithelial malignancies, intraoperative clinically suspicious lymph nodes, recurrent ovarian cancer and prior neoadjuvant chemotherapy were excluded. The primary endpoint was overall survival (OS) and secondary endpoints were progression-free survival (PFS), quality of life indices and number of resected lymph nodes. The results of the trial were presented at the ASCO Meeting in 2017 - 647 patients were randomized to LNE (n=323) or no-LNE (n=324) arms. The median number of lymph nodes removed in patients randomized to LNE was 57 (pelvic 35 and para-aortic 22). Microscopic metastases were diagnosed in 56% of the patients in the LNE arm. Median OS in the no-LNE arm was 69 months and 66 months in the LNE arm (HR 1.06, 95% CI 0.83-1.34, p=0.65) and the median PFS was 26 months in both arms (HR 1.11, 95% CI 0.92-1.34 p=0.30). Surgery in the LNE arm was 64 minutes longer (means: 352 vs 288 min), resulted in a higher median blood loss (650 vs 500 ml), and a higher transfusion rate (67% vs 59%). The rate of serious post-operative complications was higher in the LNE arm (rate of re-laparotomies 12.1% vs 5.9% [p=0.006], hospital re-admittance rate 8.0% vs 3.1% [p=0.006] and deaths within 60 days after surgery 3.1 vs 0.9% [p=0.049]). The group concluded that systematic pelvic and para-aortic LNE neither improved overall nor progression-free survival despite detecting (and removing) sub-clinical retroperitoneal lymph node metastases in 56% of the patients. They suggest that systematic LNE of clinical negative lymph nodes in patients of advanced ovarian cancer achieving complete cytoreduction should be omitted.

The LION trial is a well conducted study with good survival outcomes (median OS of 67.2 months) in women

with advanced ovarian cancer. It is the only prospective randomized trial to address the question of systematic lymphadenectomy in clinically negative nodes. While the trial awaits publication, the jury is still out on this controversial issue, as the concerns that microscopically involved nodes may not be clinically suspicious and that lymph nodes respond suboptimally to chemotherapy, remain to be answered. Whether the results of the LION trial will change the heterogeneous clinical management of this subgroup of advanced epithelial ovarian cancers, remains to be seen.

Key Points

- Systematic lymph node dissection should be done in suspected early-stage ovarian cancer as it provides important prognostic and staging information which assists in decisions about adjuvant chemotherapy.
- Patients of advanced ovarian cancer with bulky nodes and optimal intraperitoneal debulking, benefit from removal of enlarged metastatic nodes by reducing the size of residual tumor.
- Patients of advanced ovarian cancer not achieving optimal intraperitoneal debulking, will not benefit from lymphadenectomy.
- For patients of advanced ovarian cancer achieving optimal cytoreduction in the peritoneal compartment and no clinically suspect lymph nodes, the role of systematic lymphadenectomy remains controversial.

Suggested Reading

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6. Du Bois A, Reuss A, Harter P, et al. Potential role of lymphadenectomy in advanced ovarian cancer: a combined exploratory analysis of three propectively randomized phase III multicenter trials. J Clin Oncol. 2010;28: 1733–1739.
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Calendar of Monthly Clinical Meetings 2017-2018

Months	Name of the Institute
25th January 2018	Dr RML Hospital
February 2018	Lady Hardinge Medical College
March 2018	UCMS & GTB Hospital
April 2018	Apollo Hospital, Sarita Vihar
May 2018	DDU Hospital

Short Interpregnancy Interval: An Indication for Elective Cesarean

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Introduction

"*Once a cesarean,always a controversy."* Flamm 1997

Trends in Cesarean Section Rates

Rates of cesarean birth are rising throughout the world. The 20th century witnessed a boom in cesarean rates. Although several guidelines, including those issued by the World Health Organization suggest that the optimal Cesarean section rate is 15%, there seems to be little effect on the current Cesarean section rate. A study in 2011 calculated that if trends continue, in 2020 cesarean rate will be 56.2% which is alarming high. According to NFHS 4 (2015-2016), present cesarean section rates in India are quite variable ranging from 6.2% (Bihar) to unacceptably high of 58% (Telangana)[1]. Due to the rise in Cesarean section rate in past few years, the number of pregnancies with previous Cesarean section has also increased.

Mode of Delivery after Previous Cesarean Section- VBAC or ERCS

The dictum "once a cesarean always a cesarean" has now changed to present dictum "the optimal management after a previous cesarean delivery." There is a consensus (National Institute for Health and Care Excellence [NICE][2], Royal College of Obstetricians and Gynaecologists [RCOG][3], American College of Obstetricians and Gynecologists [ACOG]/ National Institutes of Health [NIH][4,5]) that planned VBAC is a clinically safe choice for the majority of women with a single previous lower segment cesarean delivery.

VBAC is a good alternative to a repeat cesarean section to avoid future complication associated with multiple cesareans like morbidly adherent placenta, surgical difficulties, injuries to adjacent viscera, multiple blood transfusions etc. But this too is not 100% safe. Most feared risk while attempting trial of labour after cesarean (TOLAC) is the risk of rupture uterus. Maternal mortality after a rupture uterus in this era is very low but main insult is to the foetus with high morbidity and mortality.

And another concern is the success of TOLAC resulting in vaginal birth, as the emergency cesarean carries much higher morbidity as compared with Elective Repeat Cesarean sections (ERCS). The routine use of VBAC (Vaginal Birth after cesarean) checklists during antenatal counselling should be considered, as they would ensure informed consent and shared decision making in women undergoing VBAC. Despite many studies being conducted regarding factors affecting the outcome of VBAC like interval between previous Cesarean and current pregnancy, indication of previous cesarean, previous successful vaginal deliveries, postoperative wound sepsis etc, there are no standard guidelines for patients of previous cesarean section to attempt VBAC.

Commonest indication for elective repeat cesarean section is short interpregnancy interval and this remains the most controversial one. Many women wonder what the risks are of becoming pregnant shortly after having a cesarean. To answer the question "Is it safe to attempt a VBAC when your pregnancies are close together?" one needs to know what is optimal interpregnancy interval for TOLAC/ VBAC. In a recent retrospective study from tertiary care hospital in north India, 33% of repeat cesarean sections were performed for short interdelivery interval of < 18 months[6].

Interdelivery/ Interpregnancy Interval

Interpregnancy interval is the time interval between cesarean section and next conception (taken as LMP of current pregnancy). The timing between pregnancies has recently become an interesting predictor for a number of obstetric outcomes, VBAC success among them. It remains unclear whether the interpregnancy interval actually affects the success rate or whether it affects only the risk of uterine rupture.

Optimal time period is required after cesarean section for the healing of uterine scar. A prolonged interpregnancy interval may allow time for the previous cesarean delivery scar to reach its maximal tensile strength before the scar undergoes the mechanical stress and strain with a subsequent intrauterine pregnancy. There is little information about the healing of the lower uterine segment cesarean scar. Healing occurs mainly by fibroblast proliferation, and connective tissue proliferation becomes less obvious as scar shrinks. Pregnancies in quick succession after previous cesarean delivery may not allow complete healing of the uterine scar, causing ineffective uterine contractility, lower uterine segment thinning, and increased potential risk of uterine dehiscence or rupture. The trial of strength of scar occurs at the time of delivery, therefore more important is the interval between cesarean and next delivery, known as **Inter Delivery Interval**.

There is controversy regarding what should be ideal interpregnancy/ interdelivery interval after cesarean section. Complete uterine involution & restoration of anatomy may require atleast 6 months[7]. Studies have shown a two-to- three fold increased risk of uterine scar rupture for women with short inter-delivery interval (below 12-24 months) from their previous cesarean (RCOG 2007)[3]. In a case-control study by Esposito et al, an interpregnancy interval between cesarean delivery and a subsequent pregnancy of < 6 months was nearly 4 times as common among patients who had uterine rupture than in control subjects (17.4 vs 4.7%; OR, 3.92; 95% CI, 1.09-14.3)[8]. Shipp & colleagues (2001)[9] reported an incidence of rupture of 2.3% (7 of 311) in women with an interdelivery interval less than 18 months compared with 1.1% (22 of 2098) with a longer interdelivery interval (3 fold increased risk). Bujold and associates (2002)[10] have reported an interdelivery interval of less than 24 months to be associated with an almost three fold increased risk of uterine rupture. In this study, rate of rupture was 2.8% in women with short interval vs 0.9% in women with greater than 2 years since the prior cesarean birth. Furthermore, the combination of an interdelivery interval 24 months or less and single-layer uterine closure of the previous uterine incision increased the incidence of uterine rupture to 5.6%. This is comparable to the rate of uterine rupture for patients undergoing a TOLAC with a previous classic midline cesarean scar. In a follow-up study, the same authors examined the risk of uterine rupture between 18-24 months. After adjustment for confounding factors, they found that an interdelivery interval shorter than 18 months was associated with a significant increase of uterine rupture (odds ratio [OR], 3; 95% confidence interval [CI], 1.3–7.2), whereas an interdelivery interval of 18-24 months was not (OR, 1.1; 95% CI, 0.4–3.2). In agreement with the findings by Shipp et al, the study by Bujold et al concluded that an interdelivery interval shorter than 18 months but not between 18-24 months should be considered as a risk factor for uterine rupture[11].

Stamilio et al confirmed a similar uterine rupture rate of 2.7% in women with an interpregnancy interval of < 6 months compared with 0.9% for those having intervals of ≥6 months in a large study including > 25000 women. There was no effect on VBAC success rate, with 77% of all trials of labor ending in a successful vaginal birth. Several smaller and less recent studies report similar results[12]. Shipp et al[13] concluded that there was less than 0.25% chance of uterine rupture in women with 1 prior cesarean, more than 18 months interdelivery interval, and were either under age 30 or were under age 40 and also had one prior vaginal delivery.

On the contrary Huang and colleagues (2002)[14] found no increased risk of uterine rupture with an interdelivery interval of less than 18 months in their study on 1185 women undergoing TOLAC. Three cases of uterine rupture occurred, all in the group with interdelivery interval 19 months or more. They also concluded in their study that interdelivery interval of less than 19 months were associated with a decreased rate of VBAC success in those who had induction but not in those who went into spontaneous labour.

Similarly, a retrospective study including 3176 women who delivered following CS during the years 1988–2010 didn't find any difference in the rate of uterine rupture between the groups with different interdelivery interval including < 12 months. But short interval < 12 months was associated with increased risk of preterm delivery[15].

The RCOG guideline[16] on birth after previous cesarean birth notes that a short inter-delivery interval (less than 12 months since last delivery) potentially increases the risk of uterine rupture in women undergoing VBAC, but that further data are needed. More recently, data on uterine rupture after cesarean section from the UK Obstetric Surveillance System (Knight) showed that women who had an interpregnancy interval of < 12 months compared with ≥ 24 months had a higher odds of having a uterine rupture (aOR 3.12, 95% CI 1.62 to 6.02). There was evidence of a non-linear relationship in the association between uterine rupture and cesarean section pregnancy interval, with the odds of rupture appearing to plateau for intervals beyond 12 months (Evidence level III)[17].

Regarding the effect of interpregnancy interval on success of TOLAC, in the NICHD study, women undergoing planned VBAC whose previous cesarean birth was within 2 years of their labour had an increased risk of cesarean birth compared with women whose labour was more than 2 years from their previous cesarean (32% versus 25%, respectively)[18]. But a recently published retrospective 10-year cohort study of pregnant women with one prior cesarean, who opted for trial of labor, found VBAC success rate of 72% in the reference group (12 to 24 months). Success rates were similar in different groups with interpregnancy interval < 24 months. Longer interval had lower success rates[19].

Table 1: Relation of Interdelivery Interval (Prev LSCS) & Risk of Uterine Rupture

	Interdelivery interval	Year	Uterine rupture risk
Esposito et al[8]	< 6 months (IP interval)	2000	Four times increased risk
Shipp et al[9]	≤ 18 months	2001	Three fold increased risk
Huang et al[14]	<19 months	2002	No increased risk
Bujold et al[11]	< 18 months 18-24 months	2010	OR 3 OR 1.1
Bujold et al[10]	<24 months	2002	Threefold increased risk
Stamilio et al[12]	<6 months (interpregnancy interval)	2007	Threefold increased risk
Kessous et al[15]	<12 months	2013	No increased risk

Conclusion

The need of the hour is not only the reduction in primary cesareans but also the repeat cesareans and VBAC is a reasonably good option. Short interdelivery interval has been the most common indication of ERCS which could be reduced by a good contraceptive counseling beginning in the antenatal period itself. This indication remains debatable as available data is limited by lack of prospective, randomized trials. Also adverse maternal or perinatal outcomes are rare and large study populations are necessary to observe a significant difference in outcomes. The woman's choice to attempt a TOLAC is heavily influenced by her health-care provider and local resources - leading to selection bias in published reports.

Given that many factors contributing to uterine rupture rate cannot be modified (such as maternal age or birth history) having an optimal interdelivery interval is one way to significantly reduce uterine rupture risk. We can conclude that VBAC failure rate and uterine scar rupture rate are high with interdelivery interval < 12 months from previous cesarean delivery and should be avoided. No definitive conclusions can be drawn for interdelivery interval of 12-18 months and management for these women should be individualized. Having an interdelivery interval of less than 18 months should not prevent a mother from considering VBAC a reasonable option, and the overall risks should be considered in comparison to the risks associated with a repeat cesarean.

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HPV Vaccine Acceptance and Hesitancy: An Indian Perspective

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Cervical Cancer- A challenge for public health

Cervical cancer is a major public health challenge and the second most common cancer in women after breast cancer. India has a population of 432.20 million women aged 15 years and above, who are at risk of developing cervical cancer and accounts for an estimated 122,800 new cases and 67,500 deaths annually due to cervical cancer, which is one fourth of the global burden. The high mortality due to disease is mainly because of lack of awareness and absence of an organized screening programmes.

Preventive health has always been neglected in low middle income countries (LMICs) like India. Cervical cancer is a preventable cancer as it has a long precancerous phase, with availability of screening methods for early detection and highly efficacious treatment. The morbidity burden due to this cancer is huge and the financial burden it poses over our economy is more than any other chronic disease with an exception of cardiovascular disease. Mortality rates are high due to lack of awareness, late diagnosis and majority of women seek help only after they become symptomatic or at an advanced stage. Screening of asymptomatic patients is <5% even in the well-organized health care programs.

The causal role of persistent infection with high risk types of Human Papilloma Virus (HPV) has been documented beyond reasonable doubt and its association is shown in ~99.1% of cervical cancer cases worldwide. HPV is a very common infection and over 75% of all sexually active individuals harbor at least one HPV type during their lifetime. More than 100 types of HPV have been recognized of which about 15 types are oncogenic and HPV 16 and 18 infection are associated with approximately 82.1% of cervical cancer in India. HPV tests have been developed for screening and prophylactic HPV vaccines have been developed against the major types.

Need of HPV Vaccination in India

There has been a decline in cervical cancer incidence rates seen in different population-based cancer registries in the country which is possibly a reflection of the changing socio-demographic and reproductive profile with fewer child births and increasing age at marriage and first childbirth, improving socio-economic conditions and women's empowerment. However, several regions of India still have rates higher than other Asian countries. Moreover, the falling incidence rates seem to be reaching a plateau and are unlikely to decline further unless specific interventions are put in place. The Ministry of Health & Family Welfare has proposed a population-based screening program for oral, cervical and breast cancer but so far only pilot programs have begun, except in the State of Tamil Nadu. Screening typically requires repeated interventions at least every five years with high coverage of targeted women and involves a number of steps such as quality-assured testing, diagnosis, treatment and follow up care for it to be effective. Introducing efficiently organized population-based cervical cancer screening programmes will require substantial resources and is a challenging task.

Vaccination is well accepted by the population and an effective system is already in place for this purpose. HPV vaccination can reduce the risk of infection by the HPV types targeted by the vaccine which produces a robust immune response, as compared to the natural infection which induces a very weak response and may not lead to protection against reinfection. According to the results of a cost-effectiveness analysis by Diaz etal, 70% coverage of pre-adolescent girls (girls below age 12) with the HPV vaccine can potentially reduce the lifetime risk of cervical cancer by 44%; and is more effective than screening alone and screening three times in a lifetime reduces cervical cancer risk by 21-33%. Thus introduction of vaccination along with screening is the pragmatic way to prevent cervical cancer.

Available Vaccines

In India two HPV vaccines are available, one is a quadrivalent vaccine Gardasil™ (Merck) and second is a bivalent vaccine Cervarix™ (GlaxoSmithKline). Both vaccines target the high risk types 16 and 18 while Gardasil also protects against HPV 6 and 11 which are responsible for genital warts. A third nonavalent vaccine is likely to be marketed soon. WHO recommends the introduction of HPV vaccine in national immunization programme provided that the introduction is feasible, cost effective, sustainable and cervical cancer is a public health priority. The advisory bodies in India like Indian association of Paediatrics (IAP) and Federation of Obstetrician and Gynaecologists of India (FOGSI) have recommended HPV vaccination. Since first being licensed in 2006, more than 270 million doses have been administered with no serious adverse event linked to the HPV vaccine and till date no safety issues have been found that would alter its recommendations for the use of vaccine. The main side effects are injection site pain and redness, occasionally a mild fever. Though initially recommended to be given as 3 doses over a 6 month period, WHO now recommends 2 doses

to be administered at 0 and 6 months in healthy, immunocompetent girls prior to 15th birthday. The 2 vs 3 dose HPV vaccine trial in India supported the safety, immunogenicity and efficacy of two doses. Although the vaccines are licensed up to age 45 years, they are most effective if given before the first sexual encounter.

Issues with HPV Vaccination in India

Though the preventive vaccines are available since 2009 in India, access to these vaccines is lower and introduction of HPV vaccination into the immunization program has been strongly debated. The occurrence of deaths among girls vaccinated in a demonstration project in Andhra Pradesh and Gujarat caused great concern at the outset. However, a committee set up by ICMR found that the deaths were temporally far removed from the vaccination and could not find any evidence of cause and effect relationship. Large studies as well as postmarking surveillance globally has not found any greater risk among vaccinated populations compared to unvaccinated and it has been concluded that the vaccine is as safe as the tetanus toxoid.

Public sector spending on health in India is very low, which makes it difficult for the government to introduce an expensive vaccine in the national immunization program without external support. Gavi has included the vaccine on its priority list so the cost is substantially reduced when procured by the states and some states e.g., Punjab and Delhi have initiated the program.

Lack of awareness about cervical cancer and availability and role of the vaccine and its importance are major barriers in India. It is evident from the literature that social and cultural factors may also contribute to the low vaccination rates in developing countries with multi-religious populations. The sociocultural issues are associated with the HPV vaccine because it targets a sexually transmitted infection (STI) and primarily targets female children and adolescents. These issues significantly influences the willingness of health policy makers, health care providers, parents, adolescent and young girls to receive vaccine. In some countries, the vaccines are licensed for males and the nonavalent vaccine will also have a license for males in India. A gender neutral vaccine may find better acceptance.

The access to HPV vaccine data young women is influenced by the overall health policy and decisions of key stakeholders operating at different levels including healthcare providers, teachers, parents and the young women themselves. (Table 1)

Knowledge- has a significant impact on the success of any health programme. The limited knowledge of HPV including its prevalence, implications on health and HPV vaccine efficacy among the parents and health care providers is a significant barrier to implementation of vaccine coverage in adolescent girls. A survey in Eastern India conducted by Basu etal among educated urban men and females (n=121), with at least one girl child and belonging to middle or high socio-economic group, revealed that 72% had never heard of HPV. Only 46% of parents were in favor of vaccinating their daughters against an STI; however, after going through a brief information sheet about the HPV vaccine, 80% agreed to vaccination.

Table 1: Factors influencing the uptake of HPV vaccine in young women

Factors	Issues
Policy	Vaccine cost, its availability and delivery
Community	Socio-cultural issues
Organizational (Healthcare Providers)	Knowledge, recommendations and provision
Interpersonal (Parents)	Knowledge, decision-making and consent
Intrapersonal (Young Women)	Consent and characteristics

Vaccine safety- the parenteral concerns for the safety and fear of side effects have been cited in the literature as an important barrier, with higher concern if the child is 9–12yrs (46.3%) versus 13–18 (41.4) years of age.

Cultural barriers- includes the myths contributing to negative perceptions towards HPV vaccination and moral or religious beliefs. A key existing myth is the concern of HPV vaccination encouraging sexual promiscuity. However a large survey at Kaiser Permanente on nearly 300,000 girls found no increase in the number of partners, incidence of STI or teenage pregnancy, which were considered as markers and outcome measures in this study. Gender issues also exist, with vaccination more routinely recommended for girls (76%) as compared to boys (46%) regardless of age.

Vaccine cost- parent's out-of-pocket expenses are a concern for the providers. A key challenge for LMICs is the sustainable financing of HPV vaccine introduction. This is driven by 2 factors—vaccine price and delivery cost. Also it is primarily available in private sector (Gardasil- 3000 INR/dose and Cervarix- 2000 INR/dose). In a survey carried out at AIIMS it was seen that over 90% of parents would be willing to accept vaccination if endorsed and provided by the government.

Lack of political commitment-is identified as the most important challenge to successful implementation of HPV vaccine programmes. Expensive new public health interventions demand more cost-effectiveness and sustainability evidence in order to convince policymakers. This has been seen amply even with the latest data from Punjab.

Social structure- demands parental consent be taken for vaccinating adolescent girls and young females who are the primary targets. Parent's attitude to vaccines in turn will depend on their awareness, knowledge and perceptions regarding vaccines and their outlook towards their children's sexuality and certain personal beliefs. This will also significantly influence willingness of health policy makers, health care providers, parents, and adolescent and young girls to receive vaccination.

Major determinants of social acceptance of vaccine in India are parental awareness and attitude. A study done in college girls in Kolkata revealed that though the knowledge of girls about screening methods was low but a majority desired to have protective vaccination against cervical cancer. Another important issue are the financial constraints and so are

competing health priorities like immunization of under-5 children. However, there is abundant data illustrating the magnitude of cervical cancer problem so much so that India shares one- fifth burden of cervical cancer mortality of the world. The concern about sustainable supply of the vaccine is also one of the issue.

Increasing the chance of acceptability

In order to overcome the distrust and fear generated from years of exploitive health interventions including clinical trials, coercive population control and compulsory vaccination campaigns, public trust must be generated for HPV vaccines through the adoption of the vaccines into India's National Immunization Program (NIP). In NIP the vaccines are delivered free of cost through central / state government agencies, health workers and private practitioners. The inclusion of HPV vaccines in the program would not only improve access to the vaccine by covering the associated costs, but would also improve vaccine acceptability and delivery to the primary target who lack access to cervical cancer screening services. In addition to generating the political will to adopt HPV vaccines into the NIP, the trust of policymakers, government officials and the public must also be built by dissociating the vaccine from issues related to sexuality. Parental awareness and attitude towards the vaccine are major determinants of acceptability.

Educating the pediatrician and family physician about HPV and cervical cancer may benefit further in increasing the acceptance of vaccine among parents. Another important aspect is the importance of media, as most of the information reaches general population through television, newspapers and internet.

With the recent approval of the HPV vaccine by the Indian health system, there is a demand to survey the acceptance levels of this vaccine in India. Although considerable research regarding the acceptance of the HPV vaccine has been done in developing countries and even in parts of India, there is still a need to know the impact of religious and sociocultural aspects affecting the decision making in developing countries with diverse populations.

Current status of HPV vaccination

Globally, now it is widely accepted that vaccination against high-risk strains of HPV is a safe and effective means of primary prevention of cervical cancer. More than 80 countries have introduced HPV vaccination in their national immunization programs, of which 33 are low and middle-income countries (LMICs). Cost-effectiveness studies on HPV vaccination have shown that spending on HPV vaccinations is more cost effective than treating cervical cancer.

Delhi was the first state in India to initiate a public HPV vaccination program for school children, on the occasion of National Cancer Awareness Day (November 7, 2016). This program invited girls age 11 to 13 years to get vaccinated at the Delhi State Cancer Institutes (East and West). A total of 1,200 doses have been administered as of March 2017. The Delhi government would like to expand the program to vaccinate all class 6 students through the school health program, which will include girls from both private and public schools numbering approximately 250,000 per annum.

On November 23, 2016, the government of Punjab also initiated HPV vaccination in a campaign in the Bathinda (incidence 17.5 per 100,000 women) and Mansa (17.3 per 100,000 women) districts. In phase 1, nearly 10,000 girls studying in class 6 of government schools were covered. A total of 261 schools in Bathinda and 187 schools in Mansa were involved in the program. In total, 5,851 girls were vaccinated at Bathinda and 4,002 at Mansa, constituting 97.5% and 98.5% coverage, respectively. In the second phase, plans are afoot to include five more districts, which have the next highest incidence rates of the disease, thereby covering all districts that have a reported incidence of >10 per 100,000 women. The program will be gradually scaled up to include all girls in class 6 in both government and private schools across the state. The program is adopting both a facility-based and school-based approach to vaccination in the second phase.

These initial programs mark the first steps toward elimination of cervical cancer burden in India over the next decades. There is need to actively utilize mass media and hospitals to carry out educational and promotional programmes to be designed for parents which will increase their willingness to have their children vaccinated, eventually increasing the HPV vaccination rate of teenage children.

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Journal Scan

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1. See comment in PubMed Commons belowHum Reprod. 2017 Dec 8. doi: 10.1093/humrep/dex364.

Medical treatment or surgery for colorectal endometriosis? Results of a shared decision-making approach

Vercellini P, Frattaruolo MP, Rosati R, Dridi D, Roberto A, Mosconi P, De Giorgi O, Cribiù FM, Somigliana E

Study question
What is the degree of patient satisfaction in women with symptomatic colorectal endometriosis who choose medical or surgical treatment after a shared decision-making (SDM) process?

Summary answer
The degree of satisfaction with treatment was high both in women who chose medical treatment with a low-dose oral contraceptive (OCP) or a progestin, and in those who chose to undergo surgical resection of bowel endometriosis.

What is known already
Hormonal therapies and surgery for colorectal endometriosis have been investigated in non-comparative studies with inconsistent results.

Study design, size, duration
Parallel cohort study conducted on 87 women referring to our centre with an indication to surgery for colorectal endometriosis. A standardised SDM process was adopted, allowing women to choose their preferred treatment. Median follow-up was 40 [18-60] months in the medical therapy group and 45 [30-67] in the surgery group.

Participants/materials, setting, methods
Patients with endometriosis infiltrating the proximal rectum, the rectosigmoid junction, and the sigmoid, not causing severe sub-occlusive symptoms were enrolled. A total of 50 patients chose treatment with an OCP (n = 12) or a progestin (n = 38), whereas 37 women confirmed their previous indication to surgery. Patient satisfaction was graded according to a 5-category scale. Variations in bowel and pain symptoms were measured by means of a 0-10 numeric rating scale. Constipation was assessed with the Knowles-Eccersley-Scott Symptom Questionnaire (KESS), health-related quality of life with the Short Form-12 questionnaire (SF-12), psychological status with the Hospital Anxiety and Depression scale (HADS) and sexual functioning with the Female Sexual Function Index (FSFI).

Main results and the role of chance
Six women in the medical therapy group requested surgery because of drug inefficacy (n = 3) or intolerance (n = 3). Seven major complications were observed in the surgery group (19%). At 12-month follow-up, 39 (78%) women in the medical therapy group were satisfied with their treatment, compared with 28 (76%) in the surgery group (adjusted odds ratio (OR), 1.37; 95% confidence interval (CI), 0.45-4.15; intention-to-treat analysis). Corresponding figures at final follow-up assessment were 72% in the former group and 65% in the latter one (adjusted OR, 1.74; 95% CI, 0.62-4.85). The 60-month cumulative proportion of dissatisfaction-free participants was 71% in the medical therapy group compared with 61% in the surgery group (P = 0.61); the Hazard incidence rate ratio was 1.21 (95% CI, 0.57-2.62). Intestinal complaints were ameliorated by both treatments. Significant between-group differences in favour of medical treatment were observed at 12-month follow-up in diarrhoea, dysmenorrhoea, non-menstrual pelvic pain and SF-12 physical component scores. The total HADS score improved significantly in both groups, whereas the total FSFI score improved only in women who chose medical therapy.

Limitations
As treatments were not randomly assigned, selection bias and confounding are likely. The small sample size exposes to the risk of type II errors.

Wider implications of the findings
When adequately informed and empowered through a SDM process, most patients with non-occlusive colorectal endometriosis who had already received a surgical indication, preferred medical therapy. The possibility of choosing the preferred treatment may allow maximisation of the potential effect of the interventions.

2. J Pediatr Adolesc Gynecol. 2017 Nov 18. pii: S1083-3188(17)30511-9.

MyLARC: A theory-based interactive smartphone app to support adolescents' use of long-acting reversible contraception

Timmons SE, Shakibnia EB, Gold MA, Garbers S

Study objective

Develop and test the feasibility of a Health Belief Model theory-based interactive smartphone application (app) aimed at providing information and support to adolescents with long-acting reversible contraception (LARC).

Design, setting, participants, interventions

Using a mixed-method design, we conducted 30 in-person interviews with adolescent LARC users who were enrolled in School-Based Health Centers (SBHCs) in New York City. Interviews were conducted in two phases: during Phase 1, 12 participants viewed a pilot version of the app (MyLARC); during Phase 2, 18 additional participants interacted with an expanded version of the app. Phase 2 participants downloaded MyLARC onto their smartphone and app usage was tracked.

Main outcome measure(s)

Participants' responses to the in-person interviews and data usage of MyLARC from Phase 2 were used to determine the feasibility and acceptability of using MyLARC to support young women's satisfaction and continuation of LARC methods.

Results

Non-educational games were recommended as an approach to provide information to adolescents in an engaging way, as well as educational graphics and visually appealing content. Data tracking of MyLARC usage among Phase 2 participants revealed a total of 67 unique logins to the app with 18 average page visits per unique login. The total amount of times MyLARC was opened was 1,197. The most frequented features were 'Info about LARC' (95 unique visits) and 'Games' (80 unique plays).

Conclusion

A theory-based interactive smartphone app with LARC-specific information and support is an appropriate and appealing medium to provide information and support to adolescents using LARC. Games represented a novel opportunity to engage adolescents with health information.

3. Taiwan J Obstet Gynecol. 2017 Oct;56(5):599-605.

Amniopatch treatment for preterm premature rupture of membranes before 23 weeks' gestation and factors associated with its success

Sung JH, Kuk JY, Cha HH, Choi SJ, Oh SY, Roh CR, Kim JH

Objective

The purpose of this study is to investigate the factors associated with successful amniopatch treatment in patients with iatrogenic preterm premature rupture of membranes (iPPROM) or spontaneous PPROM (sPPROM) before 23 weeks' gestation.

Materials and methods

This cohort study included 28 women who received amniopatch treatment due to iPPROM or sPPROM at 15-23 weeks' gestation. Patients' clinical characteristics before performing the amniopatch, factors associated with the procedure, pregnancy and neonatal outcomes were compared between the iPPROM and sPPROM groups, and also between the successful and failed groups.

Results

The amniopatch was successful in 6 of 28 patients (21.4%) with a success rate of 36.4% (4/11) and 11.8% (2/17) in the iPPROM group and sPPROM group (P = 0.174), respectively. The success group had a longer PPROM-to-delivery interval, fewer cases of clinical chorioamnionitis, larger birth weight, and lower neonatal intensive care unit admission rate than the failed group. The success rate of amniopatch procedure was proportional to maximal vertical pocket prior to procedure, which showed statistically significant association (adjusted odds ratio: 3.62, 95% confidence interval: 1.16-11.31, P = 0.027).

Conclusion

The amniopatch treatment success rate was higher in the iPPROM group than the sPPROM group, but was not statistically significant. The neonatal outcome was more favorable when the amniopatch was successful. However, the only predictive factor associated with successful amniopatch was a larger amniotic fluid volume before the procedure.

4. Eur J Contracept Reprod Health Care. 2017 Dec 18:1-5. doi:10.1080/13625187.2017.1406077. [Epub ahead of print].

Moistening the new vaginal misoprostol tablets: does it increase the efficacy of cervical priming before manual vacuum aspiration in first-trimester miscarriage? A randomised clinical trial

Cruz RP, Scheffler MH, da Silva DM, Guedes Neto EP, Savaris RF

Objectives

The primary objective of our study was to ascertain whether moistening the Brazilian formulation of vaginal misoprostol tablets increases cervical dilation before manual vacuum aspiration (MVA), compared with use of dry misoprostol, in first-trimester miscarriage. The secondary objective was to ascertain whether there was any correlation between vaginal pH and the degree of cervical dilation using a moistened or dry misoprostol tablet.

Methods

In a single-centre, double-blind, randomised trial, 46 patients with first-trimester miscarriage were randomly allocated to treatment with dry or moistened (with 200 µl distilled water) 2 × 200 µg misoprostol tablets.

Results

The median (range) cervical dilation in the wet and dry groups was 8 mm (6-12 mm) and 7 mm (5-10 mm), respectively (p = .06). The median time between misoprostol insertion and carrying out the procedure did not differ between the dry (406 min, range 180-550 min) and wet (448 min, range 180-526 min) groups (p = .1). No correlation was found between vaginal pH and cervical dilation using continuous data (p = .57; r= 0.08; 95% confidence interval -0.02, 0.3) or dichotomous data (pH ≤5/>5; cervical dilation ≥8 mm or <8 mm; p = .8).

Conclusion

No difference was observed in cervical dilation between moistened and non-moistened misoprostol use prior to MVA.

Proceedings of AOGD Monthly Clinical Meet

AOGD Monthly Clinical Meeting was held at Sir Ganga Ramo Hospital on 29th December 2017 from 4:00pm- 5:00pm. Various management modalities of Endometrial carcinoma were discussed

1. Sarcoma Surprise

Puneeta bharadwaj

Introduction: Uterine adenosarcomas are rare malignant tumors. They comprise 8% of all uterine sarcomas. They can be misdiagnosed as sub mucous myomas due to their similar location. Endometrial stromal sarcomas (ESS) occur in 0.2%_1% of all uterine malignancies. They form 6-20%of uterine sarcomas. Clinical presentation is abnormal uterine bleeding in 90% cases, uterine enlargement in70%, pelvic pain, extra uterine spread in 30-50%. Diagnosis is difficult with D&C due to similarity of endometrium and ESS, so for definitive diagnosis hysterectomy specimen is required. Treatment of uterine adenosarcomas, ESS require an oncologic surgical approach.

Case Presentation: We present minimally invasive management of uterine adenosarcomas/ ESS in 28 year old, para 2 with previous two Caesarean sections. There is a definitive role of hysteroscopy in such cases.

Surgical Treatment: Exploration, pelvic cytology, total laparoscopic hysterectomy with bilateral salpingoopherectomy, omental biopsy. For younger patients, ovary sparing can be an option. Many studies showed no effect of bilateral salpingo-opherectomy on recurrence and overall survival in stage one disease. Systematic pelvic/ para aortic lymphadenectomy in clinically negative nodes not offered routinely by many as spread is hematogenous. To conclude, there is a role of hysteroscopic biopsy in cases of unknown tumor specially in young patients where conservative measures could be offered (specially when Morcellator a possibility) Oncologic correct approach could be offered if diagnosed adenosarcomas/ ESS. They are indolent tumors. Distant metastasis can occur even 20 years after first diagnosis.

2. Need of Gynae Onco-Pathologist for Evaluation of Malignancies Cases and Role of Intra Operative Frozen Sections, Whether to be done or not?

Harsha Khullar Sharmistha Garg

A 60 years old postmenopausal lady P2 L2 presented with complaint post menopausal bleeding since 12 days. She attained menopause 15 years back & her previous menstrual cycles were short. She was known case of hypothyroidism, hypertension and type II diabetes.

On examination she was obese with BMI of 32, P/A soft, P/S cervix high and on P/V uterine size could not be made out. Her routine metabolic profile was done, which was normal. CA 125 level was 21.20. ***LBC showed presence of endometrial cells without atypia.*** Bilateral mammography was BIRADS II, USG showed ET 19 mm with 35x27 mm, submucous fibroid, so patient was posted for hysteroscopy and D & C. Hysteroscopy was suggested of submucous fibroid obliterating whole of uterine cavity, no curettings could be obtained as patient started bleeding so, MRI was done which showed 43x30x46 mm hyper intensive lesions with irregularity at the junctional zone10. There was possibility of endometrial carcinoma. Patient was then taken up for total laparoscopic hysterectomy + BSO.

During hysterectomy whole specimen of uterus was sent for *frozen section which reported well differentiated endometrial adenocarcinoma grade* I. So bilateral pelvic lymph node dissection was done. *Final HPE report showed serous carcinoma endometrium* so patient was readmitted for lap omentectomy with Para aortic cystic node dissection (PACND). Now patient is doing well and has received 1 cycle of chemotherapy till now.

3. Outcome of Robotic Surgery in Ca Endometrium

Mala Srivastava

- In last 1 year 3 cases of Ca endometrium were operated robotically.
- According to various studies there is no significant difference in operation time, length of hospital stay, expected blood loss, blood transfusion and total lymph node harvesting between laparoscopy and robotic surgery.
- Similarly according to various studies comparing laparotomy and robotic surgery, they found that operation time was more in robotic than laparoscopy for ca endometrium. but the complication of length of hospital stay, expected blood loss and blood transfusion are less in robotic than laparotomy.
- Total Lymph Node Harvesting was comparable between Robotic and laparotomy.

ACOG Guidelines says that Robot-assisted gynaecologic surgery can be performed safely in centers with experienced surgeons. RCOG says Robot assisted surgery is safe for the patient.

AAGL Position Statement is Hysterectomies should be performed in as minimally invasive manner as far as possible. According to Cochrane Review robotic and laparoscopic surgery seemed comparable regarding intraoperative outcome, complications, length of hospital stay and quality of life. Robotic surgery is a feasible and promising method for the treatment of endometrial cancer compared with both laparoscopy and laparotomy.

Royal College of Obstetricians & Gynaecologists
AICC Northern Zone India

Website: **www.aiccrcognzindia.com**

RCOG UK Franchise MRCOG Final Preparation: Part II Written Course

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Registration Guidelines (Online registration available on website)

- Registration form to be downloaded from website www.aiccrcognzindia.com.
- Bank Transfer or Demand Draft must be made in favour of "RCOG NZ 2012 Plus" payable at New Delhi. (cheques not accepted).
- There will be no refunds on cancelation.
- Registration request along with Demand Draft to be posted to the Secretariat mailing address as given below:-

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