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AOGD BULLETIN

Holistic Approach to Women's Health

AOGD 2023

Gynaecology Oncology and Cancer in Pregnancy

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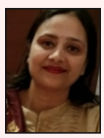

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From the AOGD Office


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Dear Friends

Warm greetings!

It has been a busy year for us so far. After a successful conference in August, we had a very memorable September. Most importantly, WE WON THE BID TO HOST AICOG 2026 at Delhi!

We were confident and well prepared to present our case to the Managing Committee Meeting at Mumbai (22nd September) after intensive brainstorming and planning by the team AOGD and the bidding committee.We were joined by other senior members of AOGD including the incumbent office bearers in visiting the two possible venues, IICC, Dwarka and IECC, Pragati Maidan. Our gratitude goes out to the Patrons and Advisors for their benevolent guidance. We acknowledge the young members of the bidding committee for their assistance in designing the slides and videos.. Our presentation was well received. AOGD has been unanimously elected as to host AICOG 2026.The physical presence of many senior members of AOGD viz Dr Alka Kriplani, Dr Neerja Bhatla, Dr Achla Batra, Dr J B Sharma, Dr Ashok Kumar, Dr Reena Yadav, Dr Mala Srivastava , Dr Ratna Biswas , Dr Anita Sabharwal, Dr Richa Sharma along with the positive vibes and good wishes from other members from Delhi, demonstrated the unity and strength of the organization. We are especially thankful for the inspiring presence of Dr Alka Kripalani.

September calendar was also dotted by CMEactivities conducted by AOGD members. There has been a great deal of change in the way we diagnose and treat gynecological malignancies, especially when there is the challenge of associated pregnancy. With articles contributed by experts in the field, this issue of the bulletin highlights important updates related toCancer in Pregnancy and Gynecology Oncology. Hope you find this issue useful.

The festivals are round the corner. Admittedly, this is one of the best times of the year.

With Warm Season's Greetings

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From the Editor's Desk


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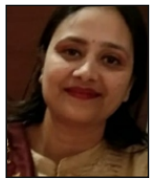
Dr Anupama

Co-Editor

Respected seniors and dear friends

As we begin with the festive month of October, this issue brings to you recent advances in Gynae Oncology and Cancer in pregnancy.

With advancing maternal age and increasing incidence, cancer in pregnancy is becoming an important issue; We have discussed two most common cancers in pregnancy i.e. breast and cervical cancer, hereditary cancers especially HBOC have gained a new dimension and we have included information on setting up of hereditary cancer clinic.

Oncology is a team effort and multidisciplinary team approach is now the backbone of decision making which has been aptly discussed. Do not forget to click on the the video in the Snap shot section on sentinal node mapping. Articles on surgical management of ovarian cancer, HPV vaccination and many more make this issue a must read.

Thank you so much for your constant encouragement and appreciation of the previous issues and we hope that we continue to live up to your expectations.

Last but not the least, let us all pray for the world peace

सर्वे भवन्तु सुखिनः ।

सर्वे सन्तु निरामयाः ।
सर्वे भद्राणि पश्यन्तु ।
मा कश्चित् दुःख भाग्भवेत्
शान्तिः शान्तिः शान्तिः

Editorial Team AOGD (2023-24)

Managing breast cancer during pregnancy

Navneet Kaur

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Pregnancy-associated breast cancer (PABC) is commonly defined as a breast cancer occurring during pregnancy, throughout 1 year postpartum, or during lactation. The reported incidence of pregnancy associated breast cancer is 1.3 – 3.7 per 10,000 deliveries. Despite being a rare circumstance, PABC is one of the most common types of malignancies occurring during pregnancy and lactation. Its incidence is increasing due to decreasing age of the onset of breast cancer, and to increasing maternal age. Women with PABC often present with more advanced disease with axillary nodal metastasis. A delay in diagnosis is thought to play an important role in the late stage at presentation, leading to poorer outcome in PABC.

Clinical Presentation and Diagnostic Evaluation

The most common presentation of breast cancer during pregnancy is as a painless lump, as in non-pregnant women. Any lump that is persistent in a pregnant patient beyond 2 to 4 weeks needs thorough evaluation. The ideal time for examination of the breasts is during the first trimester of pregnancy as it is easy to detect any lump if present. As pregnancy advances examination becomes difficult due to physiologic hypertrophy and proliferation during pregnancy. Occasionally, the refusal by an infant to nurse from a lactating breast may be a sign of an underlying occult carcinoma and is described as the "Milk rejection sign". Usually the failure on the part of the patient to report a lump, or reluctance of the clinician to biopsy a lesion for fear of complications, is responsible for the often late presentations of PABC.

Imaging Studies during Pregnancy

Ultrasonography of the breast and axilla is the investigation of choice for evaluation of a breast lump in pregnancy, as well as lactation. Mammograms are typically not obtained during pregnancy, even though radiation exposure from a standard mammographic examination is relatively low (0.0004 Gy) and can be further reduced by abdominal lead shielding. It is because the increased parenchymal density of the breasts in pregnancy limits the information obtained from a mammogram. Role of MRI in evaluation of the breast in pregnancy is also limited as hormonal changes and lactation likely increase the vascular permeability resulting in the increased enhancement making interpretation difficult and also data on use and safety of gadolinium in pregnancy is limited. In recent years, novel unenhanced functional techniques such as diffusion-weighted imaging (DWI) have shown promising results.

For staging evaluation, Chest x-rays are considered to be safe during pregnancy, particularly if abdominal lead shielding is used. Computed tomography scanning is generally avoided because of the associated high radiation doses. Bone is the most common site of breast cancer metastasis. Since during pregnancy levels of Alkaline phosphatase rise, it can't be relied upon as an indicator of bone involvement. Bone scintigraphy is reported as safe, as it causes a minimal radiation exposure of .02cGy to the foetus. Adequate maternal hydration should be ensured to reduce this exposure further. Alternatively to assess the skeletal metastasis during pregnancy, thoracic and lumbar spine MRI without contrast is recommended. Data on the use of PET in pregnancy is very limited. However in nursing mothers it can be used with the caution, that mother should avoid contact with the baby for at least 12 hours after the test.

Breast Biopsy during Pregnancy

As in non-pregnant women, ductal invasive

carcinoma is the most common histological type of PABC and usually shows more aggressive features such as high nuclear grade and higher rates of lymphovascular invasion, often in association with large size of the breast primary and axillary nodal metastasis. Additionally, pregnancy-associated breast cancers are more likely to be estrogen receptor (ER) and progesterone receptor (PR) negative. The prevalence of Her2 over expression in PABC is slightly higher, with rates reported between 28% and 58%. Ki-67, which is a nuclear protein and a biomarker of cellular proliferation is also found to exhibit a higher expression. In addition, incidence of aggressive inflammatory breast cancers is higher among women with PABC, with 2.5 times higher chances of distant metastatic disease at the time of diagnosis.

Fine needle aspiration cytology (FNAC) can be used for the diagnostic evaluation of a breast lump in pregnancy. However, because of the increased cellularity and frequent mitosis that are present in the breast, it is important for the cytopathologist to be aware of the patient's pregnant state to avoid a false positive report. A core biopsy provides a more accurate diagnosis than FNAC. However, it can give rise to the development of a milk fistula. There is also an increased risk of bleeding and infection. These risks can be minimized by the cessation of breast-feeding prior to the biopsy if the patient is postpartum, prophylactic antibiotics, and by ensuring adequate haemostasis.

Treatment of breast cancer during pregnancy

A diagnosis of PABC complicates the management of pregnancy, as well as the cancer. The primary aim of treatment of PABC is to maximize the potential for cure of the cancer, while minimizing the risk of cancer treatment to the foetus. This requires management of the patient by a multidisciplinary team of experts involving medical and surgical oncologists, high-risk obstetric care specialist, genetic counsellors, radiation oncologists, and the neonatologist

Surgery

Surgery is considered the safest treatment at any stage of pregnancy. Mastectomy is generally the procedure of choice during the first and second trimesters of pregnancy. Breast conservation treatment can be offered to women diagnosed in the third trimester of pregnancy, with scheduling of radiation therapy in the postpartum period. Administration of general anaesthesia in the first and early second trimesters of pregnancy is associated with relatively higher risk.

As regards management of axilla, Sentinel lymph node biopsy (SLNB) which is the standard of care in patients with clinically negative axilla can also be safely performed for PABC. Use of 99m-Technetium is safe and accurate while Isosulfan blue dye and Methylene Blue are not recommended due to risk of anaphylaxis and teratogenicity respectively.

Systemic Chemotherapy

Systemic chemotherapy for primary breast cancer is typically recommended in premenopausal women with node-positive breast cancer, or when the tumor size is more than 1 cm. Undue delays in starting chemotherapy should be avoided, especially for the patient with locally advanced or poor-prognosis breast cancer as delays in receiving treatment are associated with significantly worse survival outcomes.

The use of chemotherapy is strictly contraindicated in the first trimester of pregnancy, and should not be given before 14 weeks due to critical period of organogenesis. Chemotherapy during second and third trimester has relatively lower chances of malformation, but still can give rise to intrauterine growth retardation, prematurity and low birth weight. For those patients with early-stage breast cancer diagnosed in the third trimester with a clinical indication for adjuvant chemotherapy, delaying chemotherapy until the postpartum period should be considered.

The most commonly used drug combinations are alkylating agents and anthracyclines.

Patients can receive doxorubicin and cyclophosphamide (FC) or 5-fluorouracil, doxorubicin and cyclophosphamide (FAC) combination chemotherapy. Methotrexate should be strictly avoided in all stages of pregnancy, as it possesses abortifacient effect and has teratogenic potential. Use of Taxanes during the second and third trimester can be considered with limited risk for the mother and foetus. Carboplatin may also be considered. Dose dense chemotherapeutic regimens have also been found to improve DFS and overall survival in high-risk patients without increasing the risk of maternal or foetal complications.

As regards targeted therapies, the use of tamoxifen or other selective oestrogen receptor modulators for patients with ER-positive and/or PR-positive tumors, should be avoided during pregnancy and delayed until after delivery because of the risk of associated vaginal bleeding, spontaneous abortion, birth defects, and foetal death. International guidelines also recommend against the use of Trastuzumab, used for treatment of HER2 positive tumors due to the possibility of serious adverse effects during pregnancy.

Radiation Therapy

Radiation therapy is not an option while the patient is pregnant. In view of the possible adverse effects, it is reasonable to delay locoregional radiotherapy until the postpartum period. Delays in radiotherapy for up to 6 months to accommodate adjuvant chemotherapy, or up to 4 months when no adjuvant systemic therapy is planned, do not seem to compromise local control. Pregnant women with early-stage breast cancer who are diagnosed in the late second or early third trimester can undergo breast-conserving surgery followed by adjuvant chemotherapy. In case no adjuvant systemic therapy is planned, surgery can be performed in the third trimester, with radiation therapy deferred until after delivery.

Irradiation of the breast also has a bearing on lactation, as it causes lobular atrophy, periductal and perilobular fibrosis with ductal shrinking, and cytoplasmic loss. Women are also advised against breast-feeding from the irradiated breast for fear that mastitis, if it develops would be more difficult to resolve, especially if they have undergone an axillary lymph node dissection

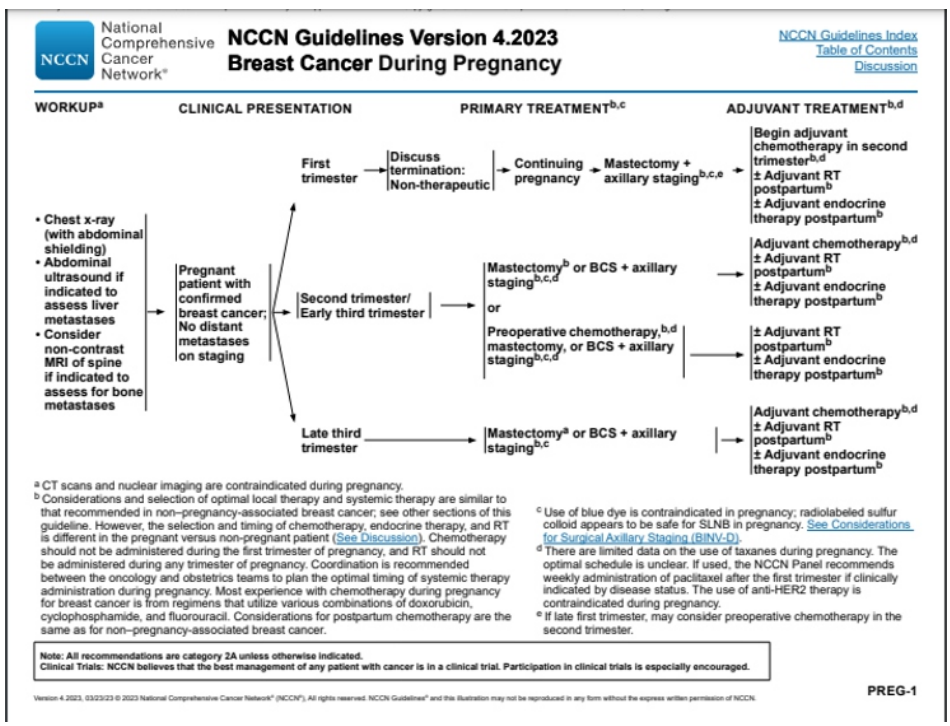

Figure 1: NCCN guidelines for management of breast cancer in pregnancy

Monitoring of Pregnancy and Delivery

Optimum time for the delivery of PABC is after 34 weeks of gestation to minimize the morbidity of prematurity. As far as possible, the foetus should be delivered once lung maturity has been established. Patients should be called for obstetric review every third week during pregnancy to have an ultrasound assessment of the foetus, umbilical artery flow and amniotic fluid. If an anthracycline-based chemotherapy regimen is being given, an imaging study like echocardiogram of the heart to assess the cardiac function is recommended. It is also preferable to allow at least 2 weeks between the last cycle of chemotherapy and delivery to avoid the risk of infectious complications and excess bleeding from the hematologic effects of chemotherapy and to minimize the risk of delivering a neutropenic infant. Many cytotoxic drugs are excreted in breast milk. Therefore, patients should be cautioned against breastfeeding while receiving chemotherapy

Therapeutic abortion and genetic counselling

Recommendations for therapeutic abortion are usually considered in cases where a diagnosis of advanced or metastatic disease is made in early pregnancy and the treatment of the disease will likely endanger foetal development. Given the younger age of the women with PABC, the risk of carrying a mutation in a gene (such as BRCA1 or BRCA2) responsible for a hereditary cancer syndrome is higher and genetic counselling and testing should be offered to all these women.

An algorithm about the approach to diagnosis and management of PABC is provided in Figure1.

Suggested Reading

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Setting up a Hereditary Cancer Clinic in Gynae-Oncology

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Max Healthcare

Launching and maintaining a hereditary cancer clinic in gynecologic oncology is a complex and dynamic endeavor that requires ongoing dedication and a commitment to providing the best care possible to patients and their families. Collaboration with other healthcare providers and organizations is key to success in this important field of medicine.

A multidisciplinary team is essential for the successful operation of a hereditary cancer clinic in gynecologic oncology. This team brings together professionals from various specialties to provide comprehensive care to patients at risk of hereditary gynecologic cancers.

Here are some key members of the multidisciplinary team associated with such a clinic:

1) **Gynecologic Oncologists:** These are specialized surgeons and physicians who diagnose and treat gynecologic cancers, including those that have a hereditary component.
2) **Medical/Clinical Geneticists:** Collaborate with genetic counselors to provide additional expertise in the interpretation of complex genetic information.
3) **Genetic Counselor/Genetic counseling:** These are specialized healthcare professionals with extensive training in medical/clinical genetics and psychology. Genetic counseling in a hereditary cancer clinic in gynecologic oncology is a vital component of patient care. It empowers individuals to make informed decisions about their health and helps them navigate the complexities of hereditary cancer risk. Effective communication, compassion, and up-to-date knowledge are essential for providing high-quality genetic counseling services.
4) **Nurse Practitioners/Physicians assistants:** Advanced practice nurses or physician assistants can assist in patient assessments, follow-ups, and coordinating care plans.
5) **Radiologists:** Radiologists are responsible for interpreting imaging studies (e.g., ultrasounds, CT scans, MRIs) and guiding interventional procedures, such as biopsies.
6) **Pathologists:** Pathologists analyze tissue samples from biopsies and surgeries to diagnose cancer and provide insights into its genetic characteristics.
7) **Oncology Nurses:** Oncology nurses provide patient education, administer treatments, and offer ongoing support throughout the patient's journey.
8) **Social workers:** Social workers assist patients and their families with emotional, practical, and financial aspects of cancer care, including connecting them with support services.
9) **Onco-psychologists:** Mental health professionals (sub-specialized in cancer care) help patients cope with the emotional and psychological challenges associated with hereditary cancer risk and diagnosis.
10) **Nutritionists/Dieticians:** These professionals offer dietary guidance to patients, especially those undergoing treatment, to maintain their overall health and well-being.
11) **Research Scientists:** Researchers may be involved in clinical trials, studies, and genetic research related to hereditary gynecologic cancers, contributing to advancements in knowledge and treatment.
12) **Administrative staff:** Administrative professionals manage patient

appointments, medical records, billing, and clinic operations.

As the name suggests, "Hereditary" Cancer Clinic, Genetic counselors and Genetic counseling plays a crucial role in a hereditary cancer clinic in gynecologic oncology. It helps individuals and families understand their genetic risk factors, make informed decisions about testing and screening, and develop personalized risk management plans.

Here are key components and considerations for genetic counseling in such a clinic:

1) **Multidisciplinary team:** Collaboration and communication among the team members listed above is crucial to ensure that patients receive comprehensive, well -coordinated care. Regular multidisciplinary meetings or tumor boards can be organized to discuss complex cases, treatment strategies, and individualized care plans. Additionally, ongoing education and training are essential to keep the team updated on the latest developments in hereditary gynecologic oncology.
2) **Patient referral and assessment:** Identify individuals at risk through referrals from primary care physicians, gynecologists, or family history assessments. Conduct thorough risk assessments, considering family history, personal medical history, and other relevant factors.
3) **Informed consent:** Obtain informed consent from patients before initiating genetic testing, ensuring they understand the implications, benefits, and limitations of testing.
4) **Genetic testing:** Determine the appropriate genetic tests based on the patient's risk factors and family history. Explain the genetic testing process, including sample collection, laboratory analysis, and result interpretation.
5) **Result disclosure:** Provide clear and empathetic communication of genetic test results, whether positive, negative, or inconclusive. Offer emotional support and counseling to help patients and families cope with the results.
6) **Risk assessment and management:** Assess the patient's risk of developing hereditary gynecologic cancers based on genetic test results and other factors. Develop personalized risk management plans, which may include increased surveillance, preventive surgeries, or lifestyle modifications.
7) **Family communication:** Assist patients in communicating their genetic risk to family members and encourage them to seek testing and counseling as appropriate.
8) **Psychosocial support:** Provide emotional support and counseling to address the psychological and emotional impact of genetic risk and cancer diagnoses. Offer resources for support groups or therapy if needed.
9) **Education and Informed Decision making:** Educate patients about the genetics of cancer, inheritance patterns, and the significance of their test results. Help patients make informed decisions regarding their healthcare, including options for risk reduction and screening.
10) **Privacy and Confidentiality:** Maintain strict patient confidentiality and adhere to all legal and ethical standards. Explain privacy policies and procedures to patients.
11) **Cultural Sensitivity:** Be culturally sensitive and aware of potential cultural differences in how patients perceive and approach genetic testing and counseling.
12) **Documentation:** Maintain detailed records of genetic counseling sessions, including patient assessments, test results, and counseling plans. Ensure compliance with privacy laws and record-keeping standards.
13) **Quality Assurance:** Implement quality assurance measures to monitor and improve the effectiveness and quality of genetic counseling services.
14) **Research and Clinical Trials:** Participate in research and clinical trials related to

hereditary gynecologic cancers to advance knowledge and treatment options.

Now, that we have our members and the key considerations for genetic counselling here are the *key steps to setting up the Hereditary Cancer clinic:*

1) **Needs assessment:** Conduct a comprehensive needs assessment to determine the demand for a hereditary cancer clinic in your region. Identify the types of hereditary gynecologic cancers that are prevalent in your area.
2) **Team building:** Assemble a multidisciplinary team of healthcare professionals, including gynecologic oncologists, genetic counselors, nurses, and administrative staff. Ensure that team members have expertise in hereditary cancers and genetic counseling.
3) **Facility and equipment:** Secure a suitable physical location for the clinic with adequate space for patient consultations, counseling sessions, and administrative work. Equip the clinic with necessary tools and technology for genetic testing, counseling, and patient education.
4) **Ethical considerations:** Ensure strict adherence to patient confidentiality and ethical guidelines.
5) **Genetic testing services:** Establish partnerships with reputable genetic testing laboratories to perform DNA testing for hereditary cancer syndromes. Develop clear protocols for ordering, conducting, and interpreting genetic tests.
6) **Patient education and counseling:** Develop educational materials and resources to inform patients about hereditary gynecologic cancers and the importance of genetic testing. Provide genetic counseling services to patients and their families to help them understand test results and make informed decisions.
7) **Referral Network:** Collaborate with primary care physicians, gynecologists, and other healthcare providers to establish a referral network for patients at risk of hereditary gynecologic cancers.
8) **Data management and patient records:** Implement a secure and efficient system for managing patient data and test results. Ensure compliance with patient data privacy laws (e.g., HIPAA).
9) **Treatment and surveillance:** Develop guidelines for the management and surveillance of patients with hereditary gynecologic cancers.
10) **Community outreach and education:** Organize awareness campaigns and community events to educate the public about hereditary gynecologic cancers and the services offered by your clinic.
11) **Research and Clinical trials:** Consider engaging in research related to hereditary gynecologic cancers and participate in clinical trials to advance knowledge and treatment options.
12) **Funding and sustainability:** Secure funding through grants, partnerships, or healthcare institutions to ensure the long-term sustainability of your clinic.
13) **Documentation and reporting:** Maintain detailed records of patient consultations, genetic test results, and treatment plans. Prepare regular reports for internal use and external stakeholders.
14) **Patient support groups:** Establish support groups for patients and families dealing with hereditary gynecologic cancers to provide emotional and informational support.

Launching a hereditary cancer clinic in gynecologic oncology is a complex endeavor, but it can significantly improve the care and outcomes for individuals at risk of these types of cancers. Collaboration, ongoing education, and a patient-centered approach are key to its success.

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Heartiest congratulations

Dr Neerja Bhatla

for receiving the 2023 award of
WHO-IARC for
Women in Cancer Research

Vulvar Intraepithelial Neoplasia: Case Snippets

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The spectrum of vulvar lesions varies from infections, dermatoses, effects of hormonal, and systemic disturbances to vulvar intraepithelial neoplasia (VIN) and invasive cancer. The incidence of VIN is on rise particularly among women in their 40s.[1] Although spontaneous regression has been reported, VINs should be considered a premalignant condition and thus requires treatment and surveillance.

In this article two interesting cases of VIN are being discussed.

CASE 1

History: 29 years old P2L2 presented with complaints of vulvar itching and burning for 6 months not responding to multiple courses of local and systemic medication.

Investigations: Wet smear- normal

Pap's- NIELM

Vulvoscopy and directed biopsy-HPV like changes with moderate dysplasia (VIN2)

Colposcopy and directed biopsy-HPV related changes with moderate dysplasia (CIN 2)

Treatment: Thermal ablation for CIN 2 and Imiquimod for VIN 2

Question: What is Vulvoscopy and why was Vulvoscopy done in this case?

Answer: Vulvoscopy is a useful diagnostic tool involving careful naked-eye and low-power (5-10X) magnified examination of the vulva under illumination. All parts of the vulva are examined: labia majora and minora, vestibule, clitoris, terminal urethra, perineum, and perianal area.

Visual examination

The examination of the vulva should start by visual examination (without magnification) of the entire vulvar region. If needed, the lowest magnification is used followed by higher magnification, especially to examine for smaller satellite lesions.

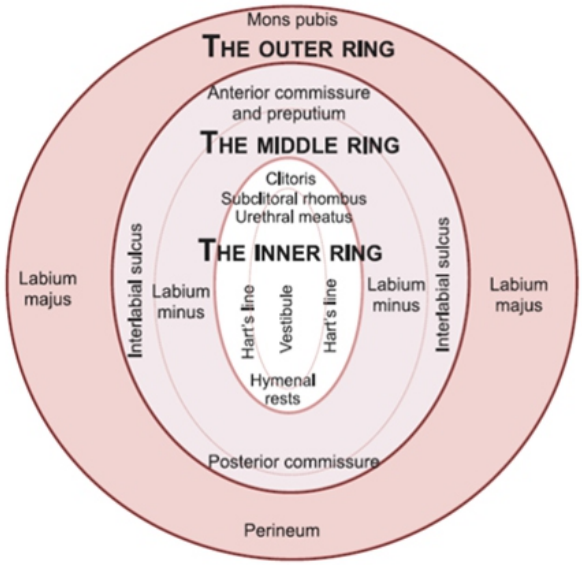

Figure 1: The concept of three rings in Three Rings Vulvoscopy (courtesy Harni V et al).

Application of acetic acid

To make the examination of the keratinized skin more efficient, acetic acid should be more concentrated (5%) and applied liberally for a longer period of time (3-5 minutes) using soaked gauze piece. Aceto-whitening of the vulva has high sensitivity (97%) but low specificity (40%) as a predictor of high-grade vulvar intraepithelial neoplasia.

Harni V et al [2] introduced the concept of Three Rings Vulvoscopy considering vulva as a complex organ, both histologically and embryologically to ensure a more accurate and systematic mapping of vulvar lesions (figure 1)

Vulvoscopy is indicated in patients with:

- Visible abnormalities of the vulva
- No abnormalities of the cervix or vagina that can account for the abnormal cervical cytology
- Focal vulvar itch, pain, or burning, without a clear etiology

In the case discussed above, Vulvoscopy was

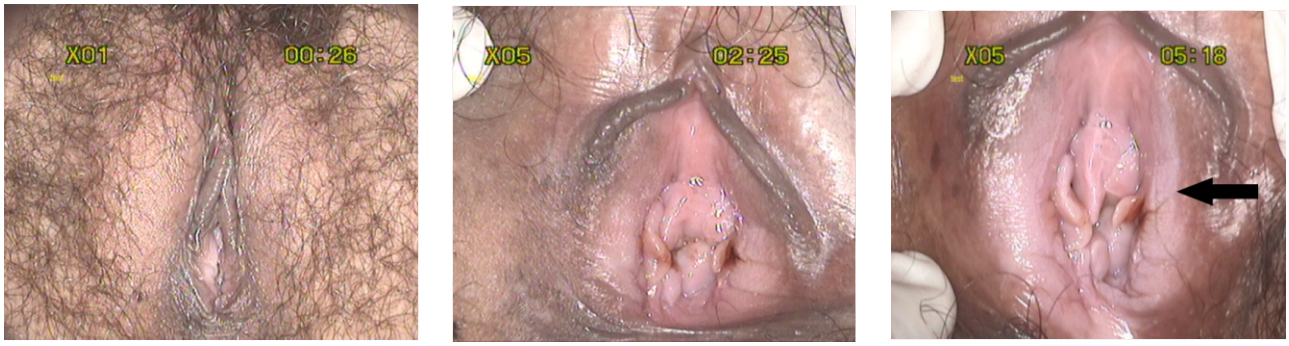

Figure 2: Vulvoscopy with and without magnification. The arrow points towards aceto-whitening after application of acetic acid.

done to diagnose the possible pathology causing persistent vulvar symptoms in the absence of any visible abnormality, not responding to treatment. (Figure 2)

Colposcopy was also done in the same patient despite a normal Pap's because HPV related intraepithelial lesions can be multifocal and multicentric warranting a thorough examination of the entire genital tract, anus, and anal canal if required.

Question: How were the findings of Vulvoscopy interpreted in this case?

Answer: 2011 IFCPC colposcopic terminology of the vulva[3] defines normal and abnormal findings on vulvoscopy and helps to take a decision for vulvar biopsy. In this case, acetowhite epithelium is the abnormal finding and hence biopsy was taken.

Question: How was the site and technique of vulvar biopsy chosen in this case?

Answer: Vulvoscopy helps to localize the best site for biopsy especially if lesions are not visible or not clearly demarcated. Biopsy should be targeted to the area of most prominent changes (acetowhitening on inner aspect of labia minora in this case) Sometimes multiple biopsies are taken if the abnormal area is large or multifocal. The choice of biopsy technique depends on the amount of tissue to be removed.

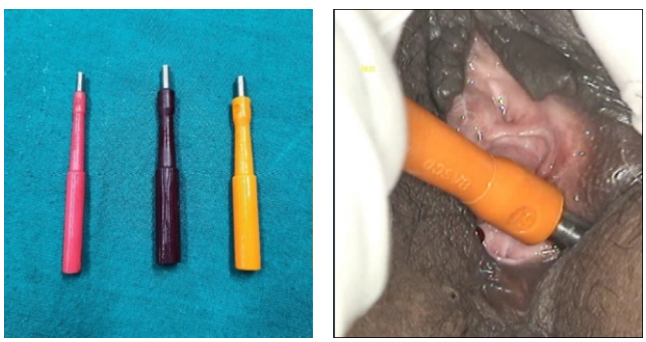

Figure 3: Keyes punch biopsy

Keyes Punch Biopsy was chosen for this case. (Figure 3) A punch biopsy removes a small (2 to 6 mm) circular piece of skin and is used when all skin layers need to be examined. Rotatory and gentle downward pressure is used to cut through the skin surface and into the dermis. The recommendation for tissue sampling of suspected precursor lesions is to obtain optimal specimens with a minimum 4 mm width with 5 mm depth for hair-bearing skin and 3 mm depth for hairless skin and mucosal sites.[4]

Question: Is the HPE report of VIN 2 consistent with the latest classification of vulvar intraepithelial neoplasia?

Answer: According to latest terminology, diagnosis in this case is Vulvar High Grade Squamous Epithelial Lesion (VHSIL) which is equivalent to usual VIN or VIN2/VIN3 of previous classifications.

The evolution of terminology and classification of vulvar Squamous Intraepithelial neoplasia has been depicted in Table 1.

Question: What was the rationale for treating VIN 2 in this case, and choosing Imiquimod for her?

Answer: Studies suggest that an underlying early invasive squamous cancer may be present in up to 20% of VHSIL patients . Moreover, in a long-term follow-up study, median progression time to cancer ranged from 0.3 to 24.2 years after VIN diagnosis: Because of these risks

Table 1: Evolution of terminology and classification of vulvar Squamous Intraepithelial neoplasia

YEAR OF PUBLICATION AND EXPERT GROUP.	1986 ISSVD	2004 ISSVD	2012 LAST (Lower Anogenital Squamous Terminology)	2015 ISSVD	2020 WHO
HPV ASSOCIATED	VIN 1	Condyloma (HPV effect)	LSIL	LSIL (vulvar LSIL, flat condyloma or HPV effect)	LSIL
	VIN 2 VIN 3	VIN usual type • Warty • Basaloid • Mixed	HSIL	HSIL (vulvar HSIL, VIN usual type)	HSIL
HPV INDEPENDENT	Differentiated VIN (dVIN)	Differentiated VIN (dVIN)	N/A	Differentiated VIN (dVIN)	Differentiated VIN (dVIN); Differentiated exophytic vulvar intraepithelial lesion (DEVIL); Vulvar acanthosis with altered differentiation (VAAD)

associated with VHSIL, counselling, treatment, and surveillance becomes an integral part of management.

Management options for vulvar HSIL include excision, ablative therapy, and topical treatment.

Decision to choose either of the therapies must be individualised for each patient depending upon examination, biopsy result, prior treatment history, location and focality of lesion. Table 2 summarises the same.

Ablation and Medical therapy must be preceded by several representative biopsies to exclude malignancy.

In this case, local medical therapy (Imiquimod) was chosen as she did not have any focal lesion suitable for excision, was compliant for treatment and follow up. Such type of patients can also be taken up for ablative therapy if the facilities are available.

Table 2: Modality of treatment with indications

Modality	Indications
Excision	• Lesion is doubtful for invasion irrespective of biopsy/colposcopy • Lesion in setting of high-risk factors for invasive disease (e.g., previous vulvar HSIL, differentiated VIN, vulvar carcinoma, immunosuppression, and lichen sclerosus) • For single lesions (in the absence of above features)
Ablation	• Multifocal disease • Lesion involve clitoris, urethra, anus or vaginal introitus
Medical Therapy	• WHO prefer to avoid excision and ablation (clitoral lesion) • Compliant to long term course (4-6 months)

Ablative therapy

- CO2 laser vaporization (most used).
- Argon beam ablation.
- Cavitational ultrasonic surgical aspiration.

The goal of ablative therapy is to treat the entire area of intraepithelial abnormality. Colposcopy is used to control the depth of tissue destruction to less than 1 mm (for hair-free epithelium), which will ablate the intraepithelial lesion and allow for rapid healing. Ablation to 3 mm of depth is required in hairy areas of the vulva because the hair root extends as deep as 2.5 mm and is at significant risk for harbouring HSIL.

Topical medical therapy

Imiquimod 5% cream is a topical immune response modifier, stimulates secretion of pro-inflammatory cytokines, thereby eliciting strong immune infiltration. It is applied topically to individual lesions, three times per week (alternating days) for a total duration of 16 weeks. Side effects of imiquimod are common and consist mostly of inflammation at the application site, including mild to moderate erythema or erosions.

Cidofovir 1% (cream, gel) has also been tested in clinical trials with comparable efficacy and lower recurrence rates when compared to Imiquimod.

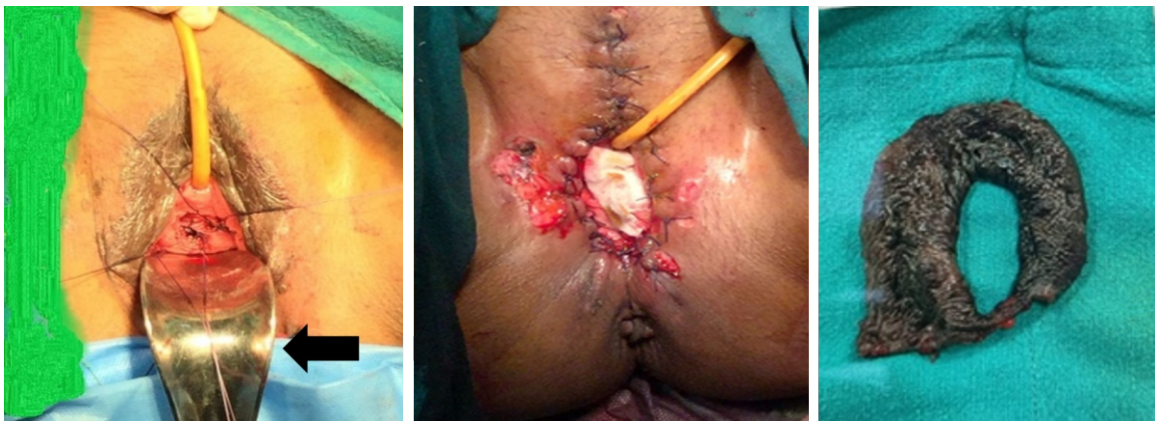

Figure 4a: Cervical conisation. Arrow points towards lichen sclerosus; **4b:** Simple vulvectomy; **4c:** Simple Vulvectomy specimen

Question: Is there any role of adjuvant HPV vaccination in this case?

Answer: Published studies show reduced VHSIL recurrence when HPV quadrivalent vaccines are administered before or after treatment. A reduction of 78.5% in incident/reactivated HPV infections was demonstrated. However, large multicentre randomised trials would be needed to build up strong evidence.

Question: How is follow up of vulvar SIL cases done?

Answer: Evidence suggests approximately one-third of patients develop recurrent vulvar SIL regardless of the treatment modality employed. Women treated surgically for VIN still have a residual risk of developing invasive cancer in the order of 2–4%. At least 4% (up to 25%) of women diagnosed with VIN will have intraepithelial neoplasia at other lower genital tract sites.

After treatment has been completed, long-term surveillance of the entire genital tract is mandatory. Follow-up with a gynaecologic examination (including visual inspection of the vulva) every six months for five years and then annually lifelong is done. Further evaluation with colposcopy and biopsies is warranted if required.

CASE 2

History: P3, 56 years old. Known case of Lichen Sclerosus for 2 years, presented with increased vulvar burning and itching.

Investigations: Pap's - HSIL

Colposcopy –T2 TZ, No obvious lesion

Vulvar biopsy – dVIN

Treatment: Conisation and simple vulvectomy. (Figure 4)

Cervical cone HPE – normal

Simple vulvectomy HPE – dVIN, margins clear.

Satellite area wide local excision – dVIN with positive margin.

Question: How is the clinical presentation of dVIN different from Vulvar SIL?

Answer: Differentiated VIN is usually

- Unifocal
- Unicentric
- Associated with lichen sclerosus
- Found adjacent to 80% of vulvar squamous cell carcinoma
- Shows rapid progression to squamous cell carcinoma
- Generally, does not react to acetic acid
- seen primarily in older women.

Question: What are the differentiating features on HPE?

Answer: The histologic features of dVIN can be subtle, and the histological diagnosis may be further complicated by coexisting conditions such as lichen sclerosus. dVIN shows basal atypia with abrupt (premature) maturation (hypereosinophylic keratinocytes), basal spongiosis, absence of granular layer, and parakeratosis. (Figure 5)[5]

P53 often shows an aberrant staining pattern in the dysplastic cells of dVIN.

Question: How does immunohistochemistry helps to differentiate vulvar SIL and dVIN?

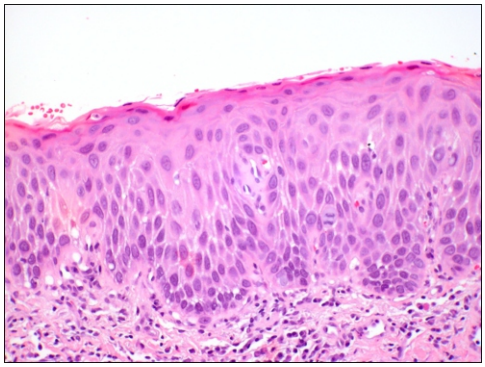

Figure 5: HPE dVIN (courtesy Mario Preti et al).

Answer: Experienced histopathologist with knowledge of immunohistochemistry can differentiate between vulvar SIL and dVIN. Table 3 summarises the role of immunohistochemistry in diagnosing pre-invasive vulvar lesions.[4]

Question: Why was vulvectomy chosen as the treatment modality in this case?

Answer: Surgical excision is the treatment of choice in dVIN as it is associated with risk of progression to squamous cell carcinoma with a short interval. There is no role of ablative or medical therapy. Wide local excision or simple vulvectomy can be chosen as per the patient's presentation.

Choosing the type of excision

- Wide local excision- Focal or small lesions.
- Simple vulvectomy- Lesions that are extensive or multifocal and highly symptomatic, particularly when prior treatments (smaller excisions) have failed.

Question: How to deal with positive margins of satellite nodule? Does it require re-excision?

Answer: Positive epithelial margins are risk factor for recurrent disease. If there is gross visible residual lesion, it should be treated. If margin is positive microscopically, but there is no visible residual disease, the patient may be followed by close clinical observation and Vulvoscopy. Retreatment is provided if another visible lesion occurs.[4]

Question: Is there any role of corticosteroids post excision in this case?

Answer: After dVIN excision, treatment of associated Lichen sclerosus and Lichen Planus with topical high potency corticosteroids is recommended to reduce the risk of recurrence/progression to vulvar carcinoma.[6]

Question: How is the follow up done?

Answer: Data suggest that dVIN carries a higher risk of progression to malignancy (as high as 50%) and recurrence. Thus, closer follow-up is recommended after dVIN treatment.

Thorough examination including vulvoscopy and directed biopsy, if indicated is the norm every six months till five years followed by annual visits lifelong.

Table 3: Role of immunohistochemistry in diagnosing pre-invasive vulvar lesions

Lesion	Immunohistochemistry	Comment
VHSIL (VIN2/3)	P16 block positivity, Ki-67 extends above basal layers through entire epithelium	Ki-67 will stain above the basal layers in LSIL as well and cannot be used to distinguish LSIL from VHSIL. P16 is more useful in this distinction and can be occasionally positive in LSIL
dVIN	Aberrant p53 staining patterns. P16 not block positive. Ki-67 confined to basal layers	A panel of p53, p16, and ki-67 helpful in distinguishing VHSIL from dVIN

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ALGORITHM

Cervical Cancer in Pregnancy

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INTRODUCTION

Cervical cancer has emerged as the fourth most common cancer worldwide and the second most common cancer in India. According to Globocan 2020, each year 604,127 cases of cervical cancer occur worldwide resulting in 341,831 deaths. Amongst these 123,907 new cases were diagnosed in India resulting in death of 77,348 women. It is also one of the most common malignancies in pregnancy mostly and can present both in early and advanced stage.

Around 1-3% of women diagnosed with cervical cancer were pregnant or postpartum at the time of diagnosis. Approximately one half of the cases were diagnosed prenatally and the other half were diagnosed within 12 months after delivery.

CLINICAL PRESENTATION

- Asymptomatic
  - Gross cervical lesion (on per speculum examination)
- Symptom

  Early stages
  - Abnormal vaginal bleeding
  - Vaginal Discharge

  Advanced stages
  - Pelvic pain
  - Sciatica type leg pain
  - Chronic Anemia

DIAGNOSTIC EVALUATION:

Ability to detect early neoplasia by physical examination may be limited by normal pregnancy associated cervical changes like ectropion, stromal edema and hypertrophy, decidual changes, increased vascularity and extra mucus.

Challenges in Colposcopy during Pregnancy:

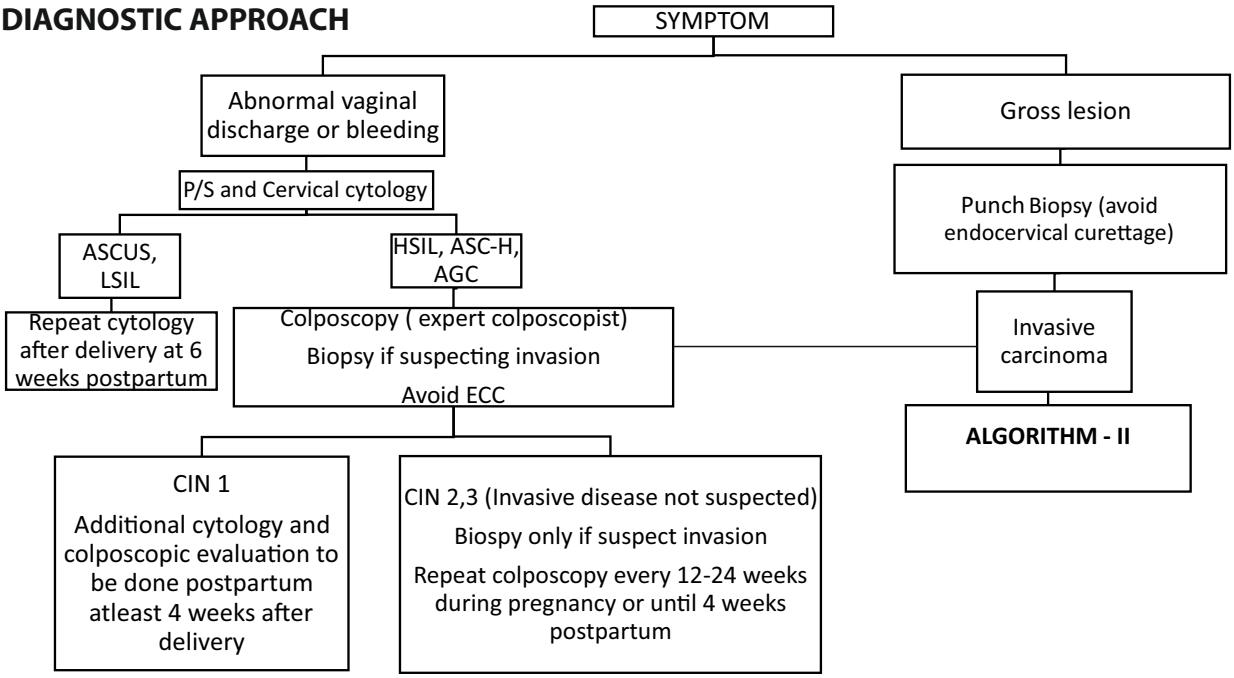
- Transformation zone: Satisfactory examination after 20 weeks of gestation, because of migration of transformation zone to the ectocervix
- Cervical biopsies: can be done during pregnancy without an Increased risk of excessive bleeding
- ECC not performed -may disrupt pregnancy
- Reliability of Colposcopy & Biopsy : Increased vascularity of gestational cervix exaggerates the reaction of metaplastic epithelium to acetic mimicking a dysplastic growth
- Normal Pregnancy associated cervical changes (mentioned previously)

Cervical cancer in pregnancy: Special considerations

1. Lymph nodes assessment-
- Depending on the stage and if suspicious nodes are present on imaging
  - <14-16 weeks: Minimally invasive surgery
  - 16-24 weeks: Laparotomy
- Role of sentinel nodes experimental

2. Platinum based chemotherapy can be considered after 14 weeks of pregnancy and can be combined with taxanes
3. Bevacizumab and Immune check point inhibitors are contraindicated
4. Before starting each cycle of chemotherapy, an assessment of clinical response should be made by clinical examination, transvaginal or transrectal USG. If no response is achieved after 2 cycles of chemotherapy during pregnancy, treatment strategy should be re-evaluated. At least a 2 week interval is recommended between

ALGORITHM – I
DIAGNOSTIC APPROACH

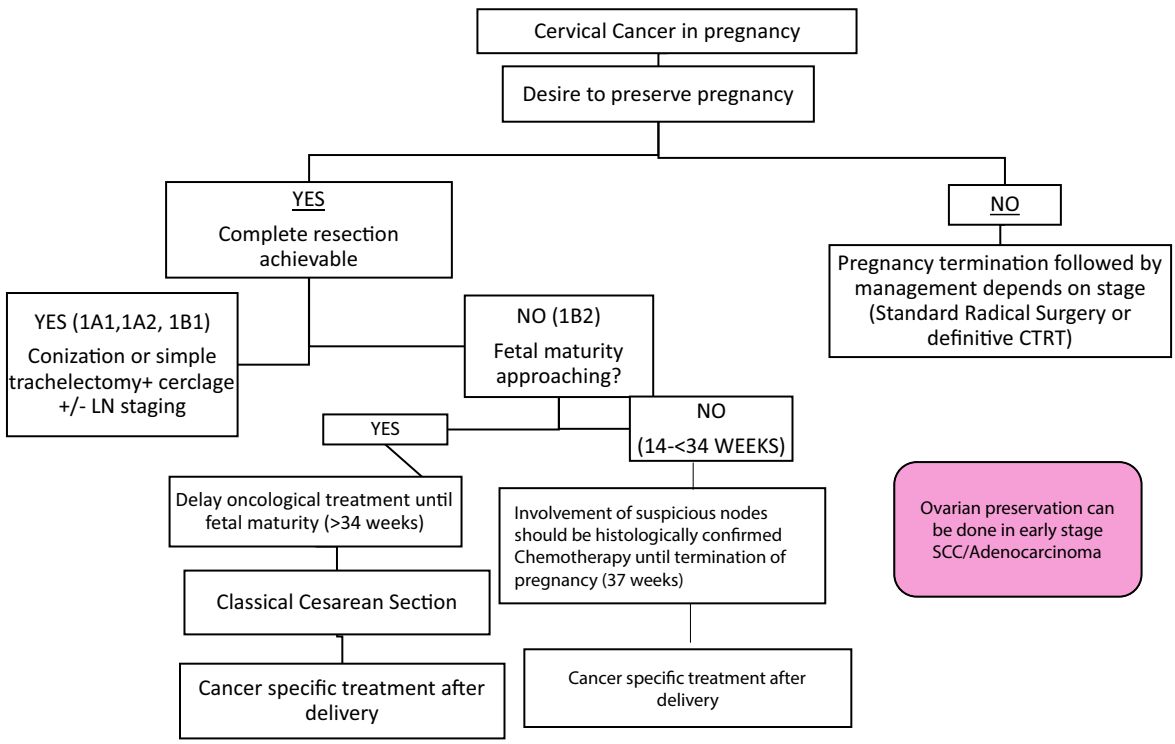


ALGORITHM-II: Management of cervical cancer in pregnancy

AIM: Oncological safety of pregnant woman with fetal survival without additional morbidity.

-Multidisciplinary approach (gynae oncology, neonatology, anaesthesia, pathology, radiation oncology, psychoncology)

-Depends on gestational age and stage of the lesion



Preferred imaging modalities for staging includes Diffusion weighted MRI abdomen and pelvis or expert USG. Gadolinium based contrasts should be avoided. CECT is contraindicated.
If not available chest CT with abdominal shielding is an alternative. PET-CT should be avoided during pregnancy.

Breastfeeding after Chemotherapy

Platinum Compounds:

Due to the potential for toxicity in the breastfed infant, it is recommended to discontinue breastfeeding during carboplatin and cisplatin treatment and if breastfeeding is desired, platinum levels in breast milk should be monitored.

Monitoring parameters:

- CBC (with TLC, DLC)
- Serum Electrolytes
- Serum Creatinine & Blood urea nitrogen
- Liver Function Test

- Breastfeeding is generally considered acceptable when the relative infant dose (RID) of is <5% to 10%
- Discarding breast milk for 24 hours after the dose would decrease the cumulative exposure to a breast feeding infant.

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Medico Legal Corner

Multidisciplinary team meetings: Evidence and challenges

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I. Introduction

a. Definition:

An MDT, or Multidisciplinary Team, is a group of healthcare professionals with diverse backgrounds and expertise who collaborate to provide comprehensive and coordinated care to patients with complex medical conditions, such as cancer.[1] The primary objective of an MDT is to ensure that patients receive personalized care that is tailored to their specific needs and preferences.[2]

Research has shown that MDT meetings improve patient outcomes in cancer care.[3,4]The team comprises healthcare professionals from different disciplines, such as medical oncologists, radiation oncologists, surgeons, pathologists, radiologists, nurses, and other specialists, who work together to develop a personalized treatment plan for each patient. Regular MDT meetings facilitate information exchange and communication flow between all those involved in the treatment of the patient. The team members can monitor adherence to evidence-based guidelines and can streamline resources for improved management strategies, lower waiting times, and enhanced cost-effectiveness. The MDT meeting provides an opportunity for education and learning to its members and trainee doctors. Cancer MDT meetings are also viewed as an important opportunity to identify patients who are eligible for research trials.

b. **Importance** - In the specific domain of gynecologic oncology, as outlined by reputable organizations like the European Society of Gynecological Oncology (ESGO), the European Society for Radiotherapy & Oncology (ESTRO), and the European Society of Pathology (ESP), the foundational principle underscores that cancer treatment planning should primarily take place within a multidisciplinary framework.[2]

To ensure the highest standard of care, the treatment process necessitates centralization and the active involvement of a diverse multi-disciplinary team. This team typically comprises essential specialists, including a gynecologic oncologist or a surgeon with dedicated expertise in managing gynecological cancers (as stipulated in quality indicator 2), a radiologist, a radiation oncologist, a medical or clinical oncologist, and a pathologist. (Fig 1) The multidisciplinary approach mandates a structured program encompassing diagnostic investigations, treatment planning, and ongoing patient follow-up.

c. Current Utility and Benefits

In contemporary oncology practice, MDT meeting have evolved into an indispensable tool, playing a pivotal role in shaping the landscape of cancer care. The current utility of MDT meetings can be illuminated by examining their multifaceted contributions to the care

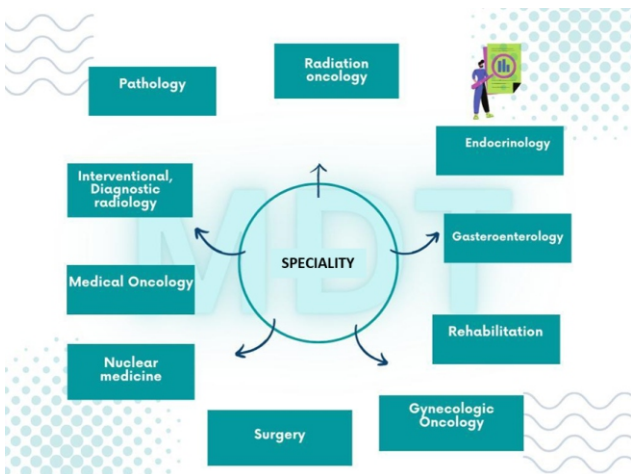

Figure 1: Multidisciplinary approach in managing gynaecological cancers

continuum:

Enhanced Treatment Decision-Making:

By harnessing the collective wisdom of specialists, MDT meetings ensure that the most suitable therapeutic modalities are selected, minimizing the risk of suboptimal or inappropriate treatments.

Individualized Patient Care:

MDT meetings facilitate the personalization of treatment strategies, accounting for factors such as the patient's overall health, preferences, and unique disease characteristics. This patient-centred approach is a hallmark of contemporary cancer care, and MDTs play a central role in its implementation.

Improved Patient Outcomes: The collaborative nature of MDT meetings consistently results in enhanced patient outcomes, including improved survival rates, reduced recurrence, and enhanced quality of life.[1,2]

Quality Assurance:

MDT meetings serve as a quality assurance mechanism by promoting adherence to evidence-based guidelines and best practices. Through rigorous case discussions and peer review, these meetings foster a culture of continuous improvement, minimizing errors and optimizing patient outcomes.[4]

Comprehensive Care Coordination:

MDT meetings facilitate seamless coordination among various healthcare providers, ensuring that all aspects of a patient's care are integrated and synchronized and also reduces the potential for fragmented or disjointed services.

Education and Training:

- MDT meetings offer invaluable educational opportunities for healthcare professionals. They provide a platform for knowledge sharing, mentoring, and the dissemination of the latest advancements in the field.
- Work Satisfaction: The sense of shared responsibility and the opportunity to collaborate with peers from different specialties contribute to increased job satisfaction among team members. This, in turn, promotes a more positive and productive work environment.
- Resource Optimization: Regular MDT meetings promote efficient resource allocation by ensuring that diagnostic tests, treatments, and interventions are judiciously administered based on the patient's specific needs. This approach leads to streamlined management strategies, reduced waiting times, and improved cost-effectiveness.

Research and Innovation:

MDT meetings often serve as fertile ground for clinical research and innovation. They provide a forum for discussing novel treatment modalities, experimental therapies, and emerging technologies. They serve as a vital conduit for identifying eligible patients for clinical research trials [5]

II. **Evidence for MDT meetings –**

a. Studies supporting the effectiveness of MDT meetings

b. Examples of successful MDT models

MDT have evolved into a cornerstone of oncology practice, recognized as the pivotal decision-making forum for patient management

Studies Supporting the Effectiveness of MDT Meetings:

While the body of evidence supporting MDT meetings is growing, it's essential to note that the absence of extensive high-quality evidence should not be interpreted as evidence of ineffectiveness. Notably, a randomized controlled trial stands out, demonstrating the benefits of MDT meetings. In this trial, patients in the intervention arm, which featured a centralized diagnostic pathway followed by MDT review, exhibited superior outcomes compared to those in the control arm, which followed a conventional pathway without MDT review.[6]

Examples of Successful MDT Models:

One prominent example of a successful MDT model is the breast cancer MDT. This model has demonstrated improved patient outcomes and reduced treatment waiting times. It brings together a collaborative team of healthcare professionals, including surgeons, medical oncologists, radiation oncologists, pathologists, radiologists, and nurses. These experts collaborate closely to craft personalized

treatment plans that account for each patient's unique circumstances.

While the body of supporting evidence is evolving, the success of models like the Breast Cancer MDT underscores their efficacy in contemporary cancer care.

III. Challenges of Multidisciplinary Team Meetings (MDT) in Cancer Care

Despite the undeniable benefits of Multidisciplinary Team Meetings (MDT) in cancer care, several challenges must be acknowledged and addressed to ensure their effectiveness.

a. Barriers to Effective MDT Meetings

One of the foremost challenges to effective MDT meetings lies in the absence of clearly defined roles and responsibilities among team members. This ambiguity can lead to confusion and conflicts within the team, ultimately jeopardizing the quality of patient care. Additionally, barriers often include insufficient resources, both in terms of time and funding, as well as a lack of support from senior management. These factors can impede the smooth functioning of MDT meetings and hinder their ability to optimize patient care.

b. Communication Challenges:

The complexity of cancer care, coupled with the involvement of multiple healthcare professionals with distinct specialties, can create communication challenges within MDT meetings. Poor communication can result in misunderstandings, treatment delays, and even errors in patient care. To mitigate these challenges, it is crucial to establish clear communication channels and protocols, fostering effective information exchange among team members.

c. Time Constraints and Workload:

MDT meetings, while essential, can be time-consuming and add to the already demanding workloads of healthcare professionals. This heightened workload can lead to burnout and diminished job satisfaction among team members. It is imperative to ensure that MDT meetings are efficient and effective, and that healthcare professionals receive the necessary resources and support to manage their workloads effectively.

d. Resistance to Change:

Resistance to change represents a significant barrier to the implementation and success of MDT meetings. Healthcare professionals may exhibit reluctance due to a variety of factors, including a lack of understanding regarding the benefits of MDT meetings, concerns about losing professional autonomy, or apprehensions about increased workloads. To overcome this resistance, it is imperative to address these concerns directly, offer education and training, and cultivate a culture that emphasizes the value of MDT collaboration.

IV. Role of clinical decision support technology in MDT meetings

Clinical Decision Support Technology (CDST) plays a pivotal role in modern healthcare by providing healthcare professionals with patient-specific assessments and recommendations, facilitating clinical decision-making.

a. Definition of Clinical Decision Support Technology:

Clinical Decision Support Technology (CDST) is a computerized system designed to assist healthcare professionals in making clinical decisions. This technology leverages patient-specific data and matches it with a comprehensive clinical knowledge base. Subsequently, it offers tailored assessments and recommendations to clinicians, facilitating informed decision-making.

b. Benefits of Using Clinical Decision Support Technology in MDT Meetings:

The integration of CDST into MDT meetings yields a range of benefits, including:

- Enhanced Decision Quality: CDST empowers MDT members with real-time access to patient-specific data, evidence-based guidelines, and treatment options.
- Improved Consistency: CDST standardizes the decision process by providing a common framework for assessment and recommendations, reducing the risk of variability in care.
- Reduced Errors: CDST helps minimize errors and ensures that the chosen treatment aligns with best practices.

- Enhanced Communication: CDST provides a centralized platform where team members can collaborate, share insights, and jointly make decisions, enhancing the overall communication flow.
- Real-time Monitoring: CDST allows for real-time monitoring of patient progress and the evaluation of treatment plan to optimize patient care.

c. Examples of Clinical Decision Support Technology in MDT Meetings:

Several examples of CDST have been developed for use in MDT meetings:

- Breast Cancer MDT Tool: This tool offers a summary screen for the patient, prognostication tools, and a decision panel that highlights system recommendations and eligible clinical trials.
- Lung Cancer MDT Tool: The lung cancer CDST tool offers a dashboard view of patient data, including imaging, pathology, and treatment history.

V. Future Directions for Multidisciplinary Team (MDT) Meetings

As technology continues to advance and the healthcare landscape evolves, several key aspects should be considered when envisioning the future of MDT meetings:

a. Potential for Technology to Improve MDT Meetings:

The rapid acceptance of health information technology has paved the way for leveraging advanced Clinical Decision Support (CDS) systems to unlock the full potential of cancer MDT meetings.

b. Need for Further Research on MDT Meetings:

Despite the growing acceptance of MDT meetings, there remains a pressing need for robust research initiatives to comprehensively evaluate their impact. Future research endeavours should focus on several critical areas like patient outcomes, quality of decision making and cost-effectiveness

c. Importance of Addressing Challenges to Improve MDT Meetings:

To unlock the full potential of MDT meetings, concerted efforts are needed to address the challenges that may impede their effectiveness. Collaborative initiatives involving healthcare professionals, senior management, and policymakers are essential to:

VI. Conclusion

In conclusion, Multidisciplinary Team (MDT) meetings have not only become a standard practice but have ascended to the status of a pivotal decision-making forum in the realm of oncology. Despite the numerous benefits they offer, challenges persist that warrant our attention to ensure their continued effectiveness. These challenges encompass barriers to effective meetings, communication complexities, time constraints, workload burdens, and resistance to change.

The integration of Clinical Decision Support Technology (CDST) into MDT meetings holds immense promise for the future. It offers the potential to enhance the quality and consistency of decision-making, reduce errors, and foster more robust communication among team members.

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HPV Vaccination Update

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Introduction

Cervical cancer is a leading cause of mortality among women. India contributes to almost one-fourth of the global burden of cervical cancers with 1,23,907 new cases in 2020 and 77,348 deaths.

Human papillomavirus (HPV) types 16 and 18 are responsible for the majority of cervical cancers worldwide, accounting for 80 to 85% of cervical cancers in India. Most HPV infections (70–90%) are asymptomatic and resolve spontaneously within 1–2 years. Persistent infection with high-risk types may progress to precancerous lesions which, if not detected and treated appropriately, can progress to invasive carcinoma at the site of infection. Vaccines are the primary prevention for cervical cancer and other conditions. It is one of the most beneficial, most important and cost effective disease prevention measures that can be provided for adolescents.

About the HPV Vaccine

All vaccines are prepared, using recombinant DNA and cell-culture technology, from the purified L1 structural protein. HPV vaccines do not contain live biological products or viral DNA and are therefore non-infectious. All HPV vaccines contain VLPs against high-risk HPV types 16 and 18; the nonavalent vaccine also contains VLPs against high-risk HPV types 31, 33, 45, 52 and 58; and the quadrivalent and nonavalent vaccines contain VLPs to protect against anogenital warts causally related to HPV types 6 and 11. HPV vaccines are available as a prefilled syringe or in single or 2-dose vials.

All HPV vaccines should be maintained at 2–8 °C, not frozen and protected from light. They should be administered as soon as possible after being removed from the refrigerator.

The vaccines should be administered intramuscularly in the deltoid region. The dose is 0.5 ml. To prevent syncope, clients should be seated and observed for 15 minutes following vaccination.

Safety

HPV vaccines are safe and well tolerated and can be used in persons who are immunocompromised or HIV infected. Mild systemic adverse events including headache, dizziness, myalgia, arthralgia and gastrointestinal symptoms (nausea, vomiting, abdominal pain) are rare. No serious safety issues to date except rare reports of anaphylaxis.

Primary and secondary target groups

- Primary target group: HPV vaccination in girls aged 9–14 years before they become sexually active. Achieving over 80% coverage in girls also reduces the risk of HPV infection for boys due to herd immunity.
- Vaccination of secondary target populations, e.g. females aged ≥15 years, boys, older males or MSM, is recommended only if this is feasible and affordable.

WHO Vaccination schedule

- A 2-dose schedule can be used in the primary target group from 9 years of age and for all older age groups for which HPV vaccines are licensed. In the 2-dose schedule, the second dose to be given 6–12 months after the first dose The three dose regime should be used in immunocompromised conditions.

All vaccines except Cervavac have been licensed for 9-45 years while for the latter the upper age limit is 26 years.

- Alternative single-dose schedule. As an off-label option, a single-dose schedule can be used in girls and boys aged 9–20 years for all

vaccines except Cervavac. The use of a single dose schedule can offer substantial benefits that outweigh the potential risk of a lower level of protection if efficacy wanes over time, although there is no current evidence of this

WHO position paper with SAGE recommendation can be adopted so that girls can be vaccinated on a large scale.

- One or two dose for 9-14 years
- One or two dose for 15 -20 years
- Two doses for 21 years and above

HPV vaccines available in India

- Bivalent(CERVARIX by GSK) licensed for girls 10-45 years.
- Quadrivalent (Gardasil by MERCK) licensed for girls 9-45 years.
- Nonavalent (Gardasil by MERCK) licensed for girls 9-45 years.
- Quadrivalent (Cervavac by SIL) licensed for girls and boys 9-26 years.

Points to Note

- HPV vaccine can be safely co administered with other age appropriate vaccines and with other routine vaccines containing diphtheria (d), tetanus (T) and acellular pertussis (pa), with no clinically relevant interference with antibody response to any of the components of either vaccine. The same vaccine for all doses should be used when using a multidose schedule
- However, if the vaccine used for the prior dose(s) is unknown or unavailable, any HPV vaccine can be administered to complete the recommended schedule.
- Lactating women can receive HPV vaccine
- Sexual assault survivors should be given age appropriate HPV vaccination, with the first dose at the time of initial examination.
- Women with abnormal Pap/Positive HPV test/ previous HPV lesions can be vaccinated if they desire. But they have to understand that the efficacy may be lower in preventing the pre-invasive and invasive cancer of cervix.

Conclusion

In order to put each nation on the path of eradicating cervical cancer within the next century, they must reach the 90-70-90 targets by 2030 set by WHO. The HPV vaccine is our strongest line of protection against malignancies caused by HPV. It is possible to effectively combat the threat of cervical cancer by raising awareness and dispelling misinformation. Although immediate improvements in screening, diagnosis, and treatment are required, the most significant contribution to the disease's eradication will come from widespread immunization against the human papillomavirus.

Suggested reading

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SNAPSHOT

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Introduction

AS per GLOBOCON 2020, Endometrial Cancer is the fourth commonest malignancy in women in India. The estimated number of uterine corpus cancer cases in India for the year 2022 were 27,922, making a cumulative risk of 1 in 190 women 0-74 years

Surgical Staging of EC was introduced in 1988 and since then the prognostic role of pelvic and para-aortic lymphadenectomy is well established. However, the therapeutic role of lymphadenectomy is disputed after the publication of RCT by Kitchener et al and Panici et al. Evidence has also suggested that complete retroperitoneal lymphadenectomy in early, low risk cases is an overtreatment and is associated with significant morbidity.

With this background, sentinel node mapping was first introduced in endometrial cancer in 1996 and gradually it has evolved as an alternative to systematic lymph node dissection.

SLN Node concept and Indication in EC

SLN is the first lymph node that drains the lymphatic vessel from the primary malignant tumour. Theoretically, if SLN is negative then, the regional lymphatic basin is taken to be uninvolved.

SLN mapping can be considered for patients with endometroid cancers with apparent uterus confined disease. Evidence on SLN biopsy in low grade endometrial cancer is adequate and is favoured with consensus. There is limited data on the suitability of SLN biopsy in high grade Endometrial Cancer. SGO suggests that SLN mapping with SLN algorithm and add on completion pelvic lymphadenectomy with para-aortic assessment is an acceptable approach in high grade cancer until more data is available.[1] NCCN and ESGO states that SLN mapping can be considered in high intermediate and high-risk disease also.

Injected Substance and Site

ICG dye is preferred dye and cervix is the most preferrable location of injection. ICG dye comes as 25 mg powder vial. As per MSKCC method, the vial is reconstituted in 20 ml of sterile water making a concentration of 1.25 mg/ml. Syringe is attached to 22 gauze spinal needle. 4 ml of of ICG dye is injected in 2 quadrants the cervix, both superficial (1-3mm) and deep (1-2cm) injection (1 ml each). The pneumoperitoneum is created before injection. The para vesical and para rectal spaces are opened gently within 5-15 minutes of cervical injection. The firefly mode is activated and the fluorescent lower para cervical lymphatics are identified, and followed to first lymph node. That node is dissected, excised and florescence checked ex vivo also. The para-aortic nodes are also inspected for any fluorescence. The nodes are properly labelled and sent for ultra staging.

SLN Algorithm

All societies highlight the importance of systematically mapping the SLN and using an algorithm that recommends side specific lymphadenectomy for patients with unmapped nodes and removal of suspicious looking nodes.[2]

Detection Rate, Failed SLN Mapping

FIRES trial, a multicentre prospective trial, has demonstrated a combined overall detection rate of 86% and bilateral detection rate of 52%. The sensitivity, NPV and FNR was 97.2%, 99.65 and 2.8%[3]

Reasons of Failed mapping

Surgeon's experience, non-endometroid histology, type of injected substance, obesity,

lymphatic obstruction by bulky tumour are reasons for failed SLN mapping. The tracer can be re injected if SLN detection fails after first attempt.

Ultra staging

Subjecting the SLN to serial sectioning and review of multiple haematoxylin and eosin-stained slides by pathologist with or without IHC is called ultra staging. Ultra staging gives us the advantage of examining selected nodes in detail and identify low volume disease with better accuracy. SLN mapping with ultra staging increases the detection of metastases and upstages EC patients in 5-15% of cases. All guidelines advocate ultra staging but no uniform protocol of ultra staging is advised.

The protocol proposed by MSKCC is initial evaluation by routine H and E, and if negative, two adjacent 50 µm sections (one H and E and one cytokeratin AE1/AE3) cut from each paraffin block at each of two levels 50 pm apart.

False Negative rate

False negative rate is the percentage of patients who have positive non SLN and negative SLN. FNR close to 5% is considered acceptable diagnostic accuracy for patients with endometrial cancer and most of the prospective and retrospective studies on low, intermediate and high risk histologies have demonstrated a FNR < 5%. FNR can be improved by using the right technique, surgeon experience and SLN algorithm.

SLN Mapping Reduced Intra operative and Post operative Complications.

Many studies have compared the post operative outcome of staging with lymphadenectomy and staging with SLN mapping. The lymphadenectomy group had extended OT time, more lower limb edema, increased blood loss and lymphocyst formation.

Oncologic Outcomes

The oncologic outcome of SLN staging vs systematic lymphadenectomy staging has not been investigated in prospective randomized trials for any histologic subtype and our knowledge is limited to retrospective observational studies.

Multiple retrospective studies have compared the oncologic outcome between two nodal assessment approaches with non-endometroid and endometroid histologies. No difference in short term DFS and OS was seen in between two approaches.

Conclusion

SLN Biopsy is well accepted diagnostic technique to determine nodal metastases in Endometrial cancer, however the focus of attention is prospective trial on oncologic outcome.

Link to video

https://drive.google.com/file/d/10WsMAGexu_2efQsKR2A--bvbDAG_F_V9/view

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Endometrial cancer: Recent update

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Introduction

The incidence of endometrial cancer is rapidly increasing and IARC estimates more than 50% increase in incidence of endometrial cancer worldwide by 2040.

We are well aware of the risk factors of endometrial cancer and their relative risk, with atypical endometrial hyperplasia having the highest RR (8-29), followed by unopposed estrogen therapy (RR 4-8), obesity (RR 3-10), and others like nulliparity, late menopause, diabetes and tamoxifen having RR 2-3.

This article will focus on the recent advances in diagnosis, staging, surgical management and adjuvant therapy in this ever-changing field. In addition, there is emerging a role of fertility preservation in young women with well differentiated tumors who have yet to complete their family. In a nutshell, diagnosis is becoming more molecular based, surgical staging more minimally invasive and adjuvant therapy more immunological in nature. These are elaborated below:

1. Recent advances in diagnosis

Diagnosis of endometrial cancer is on biopsy, which should at the very least be able to comment on histological type (endometrioid or non-endometrioid-mucinous, serous, clear cell, undifferentiated) and grade of tumor (grade 1,2,or 3). Grade 3, serous and clear cell carcinomas are high grade by definition. With advances in molecular medicine, molecular subtyping of the tumor using IHC is recommended. The Cancer Genome Atlas (TGCA) classifies endometrial cancer into four distinct molecular subgroups using using IHC for p53 and MMR proteins (MSH6 and PMS2), and mutation analysis to detect POLE mutation as follows:

- POLE mutation (POLEmut group) / ultramutated
- Microsatellite instability-high/hypermutated (mismatch repair deficient [MMRd] group)
- High somatic copy-number alterations (serous-like group, driven by TP53 mutation, also called p53abn group)
- Low somatic copy-number group without a specific driver mutation (NSMP group), here estrogen receptor status and grading is more relevant.

This surrogate marker approach helps to predict the tumor behavior and prognosis and guide targeted therapy in advanced and recurrent cancers. Tumors with POLEmut are good prognosis, MMRd and NSMP are intermediate prognosis, and p53abn are poor prognosis. The clinical correlates of this profiling (prognosis, recurrence, survival) are being evaluated in clinical trials, and soon we may have modifications in adjuvant treatments (either de-escalation or intensification) based on these criteria.

In addition, molecular testing for Lynch syndrome (germline mutation in mismatch repair genes -MLH1, MLH2, MSH6 and PMS2) in those with family history of breast, ovarian and colorectal cancer is recommended, as Lynch syndrome is seen in 3-6% of the endometrial cancers, and endometrial cancer is the most common cancer in these women.

Office endometrial biopsy has become the first line investigation, along with transvaginal sonography to look for endometrial thickness. D&C, with or without hysteroscopy is reserved for patients who have suspicion of polyps or submucous myomas, or a negative biopsy in the presence of persistent symptoms.

2. Recent advances in surgical staging: The traditional protocol for surgico-pathological staging of endometrial cancer involved a vertical midline incision, peritoneal washings

from abdomen & pelvis, inspection and palpation of omentum, liver, cul-de-sac, adnexa and lymph nodes in pelvic & para-aortic locations followed by extrafascial total abdominal hysterectomy and bilateral salpingo-oopherectomy. The changes which have occurred over the ages in this protocol are outlined below:

(a) Route of surgery – minimally invasive robot-assisted hysterectomy has become the standard of care, giving similar oncological outcomes as open surgery, with benefits of minimal invasive procedure like faster recovery, less blood loss, less post-operative pain.

(b) In premenopausal women with low-grade, early-stage disease, ovarian preservation may be considered, after appropriate counselling

(c) Where cervical stromal involvement has been demonstrated pre-operatively, a Type II modified radical hysterectomy has been historically performed, but emerging consensus suggests that a simple hysterectomy with free margins together with pelvic and para-aortic lymphadenectomy may be sufficient.

(d) Staging infra-colic omentectomy is performed in Stage I serous carcinoma, carcinosarcoma and undifferentiated carcinoma due to high risk of microscopic omental metastasis; it can be omitted in clear cell & endometrioid carcinoma.

(e) Role of lymphadenectomy – it does not have any therapeutic value, but has an important role in prognosis and guiding adjuvant therapy. If pelvic nodes are positive, systemic pelvic lymphadenectomy is not required, as it does not add to OS and PFS, but debulking of enlarged lymph nodes and para-aortic staging can be considered. The utility of pelvic & para-aortic lymphadenectomy is disputed, although it is part of current staging system. Any deeply invasive tumor (based on intra-operative assessment of myometrial invasion) or radiological suggestion of positive nodes requires assessment & removal of enlarged or suspicious nodes.

(f) Sentinel node mapping – a technique which is slowly becoming the gold standard in detection of pelvic nodes which are most likely to be involved by tumor. Accurate documentation of negative node potentially reduces the need for EBRT, specially in patients who would have received EBRT based on uterine factors. Sentinel node is the first draining lymph node from the tumor bed. Three lymphatic pathways in endometrial cancer are - along the uterine artery to obturator & internal iliac (85%), along meso-ureter to presacral & common iliac (10%) and gonadal vessels to para-aortic (5%). Sentinel node mapping using indocyanine green, methylene blue or Tc99m is becoming the preferred method of lymph node sampling in all grades of endometrial cancer, with complete lymphadenectomy being reserved for those where no sentinel node is detected. The site to inject the dye is at 3 & 9 o'clock, superficially and deep into the cervical stroma, followed by identification of the sentinel pathways. In early-stage endometrial cancer, an SLN mapping and excision is an adequate alternative to systematic lymphadenectomy, even in high-intermediate and high-risk cases. It is being routinely done for low and low-intermediate risk to rule out occult lymph node metastasis.

3. Update in the FIGO staging (2023): The FIGO staging has been updated in 2023 to incorporate the molecular profiling, type of cancer and LVSI. This is depicted in Table 1. Grade 1 & 2 endometrioid adenocarcinomas are considered low-grade non-aggressive histological types, while grade 3 endometrioid, serous carcinoma, clear cell carcinoma, mixed carcinoma, undifferentiated carcinoma, carcinosarcoma, mesonephric-like and gastrointestinal type mucinous carcinomas are aggressive histological types. In addition, grade 3 endometrioid is a molecularly heterogenous

Table 1: 2023 FIGO staging of cancer of the endometrium

Stage	Subtype	Description
I - Confined to the uterine corpus and ovary	IA	Disease limited to the endometrium OR non-aggressive histological type, i.e. low-grade endometroid, with invasion of less than half of myometrium with no or focal lymphovascular space involvement (LVSI) OR good prognosis disease IA1 Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium IA2 Non-aggressive histological types involving less than half of the myometrium with no or focal LVSI IA3 Low-grade endometrioid carcinomas limited to the uterus and ovary
	IB	Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSI
	IC	Aggressive histological types limited to a polyp or confined to the endometrium
II - Invasion of cervical stroma without extrauterine extension OR with substantial LVSI OR aggressive histological types with myometrial invasion	IIA	Invasion of the cervical stroma of non-aggressive histological types
	IIB	Substantial LVSI of non-aggressive histological types
	IIC	Aggressive histological types with any myometrial involvement
Stage III - Local and/or regional spread of the tumor of any histological subtype	IIIA	Invasion of uterine serosa, adnexa, or both by direct extension or metastasis IIIA1 Spread to ovary or fallopian tube (except when meeting stage IA3 criteria) IIIA2 Involvement of uterine subserosa or spread through the uterine serosa
	IIIB	Metastasis or direct spread to the vagina and/or to the parametria or pelvic peritoneum IIIB1 Metastasis or direct spread to the vagina and/or the parametria IIIB2 Metastasis to the pelvic peritoneum
	IIIC	Metastasis to the pelvic or para-aorticlymph nodes or both IIIC1 Metastasis to the pelvic lymph nodes IIIC1i Micrometastasis IIIC1ii Macrometastasis IIIC2 Metastasis to para-aortic lymph nodes up to the renal vessels, with or without metastasis to the pelvic lymph nodes IIIC2i Micrometastasis IIIC2ii Macrometastasis
Stage IV - Spread to the bladder mucosa and/or intestinal mucosa and/or distance metastasis	IVA	Invasion of the bladder mucosa and/or the intestinal/bowel mucosa
	IVB	Abdominal peritoneal metastasis beyond the pelvis
	IVC	Distant metastasis, including metastasis to any extra-or intra-abdominal lymph nodes above the renal vessels, lungs, liver, brain, or bone

group where profiling can distinguish the good prognosis group (POLEmut) from the bad prognosis group (p53 abn). Molecular classification is more relevant for Stage I & II tumors, where POLE or p53 abn can modify the FIGO stage of disease (down-staged or upstaged respectively). MMRd and NSMP are intermediate prognosis and should also be recorded if available. Molecular profiling is less relevant for Stage III & IV, as it will not change the stage of disease, but should be recorded nevertheless if available.

4. Recent advances in adjuvant therapy: Molecular profiling of tumors, in addition to the traditional risk factor evaluation guides adjuvant therapy. For primary advanced and recurrent endometrial cancer, previously

paclitaxel and carboplatin were the first line drugs. However, two landmark phase III trials (RUBY and Keynote-868) have shown significant advantages in PFS with addition of immune-checkpoint inhibitors (pembrolizumab and dostarlimab) as maintenance therapy, to standard pacli-carbo chemotherapy, in MMRd subtype endometrial cancer patients. RAINBO program includes four ongoing multicenter trials evaluating the role of molecular typing. For guiding adjuvant treatment in endometrial cancer. The landscape of endometrial cancer therapy is evolving over the last decade. Advances in radiotherapy utilizing volume modulated, intensity modulated or image-guided adaptive radiotherapy techniques, which spare normal tissue are becoming the preferred modality to give radiation.

5. Recent advances in fertility preservation: In patients with concurrent ovarian and endometrioid adenocarcinoma of endometrium, it is important to distinguish true synchronous tumors (St IA3), from spread of endometrial cancer to ovary (St IIIA1) using the following criteria: superficial myometrial invasion (<50%), no other metastasis, no significant LVSI, unilateral involvement of ovary without invasion of capsule. These are thought to have a common-clonal origin.

Women who have grade 1 endometrioid adenocarcinoma (confirmed on hysteroscopy D&C – not office biopsy), confined to endometrium, with no contra-indications to progesterone therapy, highly motivated for fertility, willing for regular follow-up and understanding the risks of this non-standard nature of treatment in terms of persistence / recurrence of cancer are candidates for fertility preservation. Hysteroscopic resection of the tumor and/or LNG-IUS with high dose oral progesterone are given, and office biopsy done every three months. When two consecutive biopsies are negative, pregnancy planning is pursued. If the cancer persists in three biopsies, despite increasing dose of progesterone (9-12months). Patient should be counselled that this approach is not the definitive treatment and hysterectomy is required after completion of child-bearing.

Thus, several advances have occurred in the field of endometrial cancer in the past decade, due to advances in molecular medicine and immunotherapy. With constant evolutions in the medical realm, this is a rapidly changing arena.

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Surgical Management for Ovarian Cancer

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Introduction

Ovarian cancer presents in the third or fourth stage in 75-80% of patients. According to WHO Classification 2020, ovarian tumours are divided into- epithelial tumours, mesenchymal tumours, mixed epithelial and mesenchymal tumours, sex cord stromal tumours, germ cell tumours, miscellaneous tumours and tumour-like lesions. Epithelial ovarian cancer (EOC) is the most common type of ovarian malignancy and includes serous (70%) , mucinous, endometroid, and clear cell cancer. Early-stage cancers have traditionally included both stage I and stage II tumours.

A detailed pre-operative workup includes imaging and tumour markers. Serum CA125 should be done in all cases, CA 19.9 and CEA are advised to rule out hepatobiliary or gastrointestinal tract metastasis, when suspected. Serum B-HCG, AFP, LDH are recommended in all women less than 40 years of age to rule out germ cell tumours. In females with irregular bleeding or postmenopausal bleeding serum inhibin- B levels should be done to rule out granulosa cell tumour. Any of the available radiological imaging studies like ultrasound of the whole abdomen, CE- MRI abdomen, abdominal contrast-enhanced computed tomographic scan (CECT) and positron emission tomography (PET)- CT scans, can be done to define the extent of the disease. Patients with bilateral solid ovarian masses raising a suspicion of Krukenberg tumour, suspected primary peritoneal cancer or with CA125:CEA ratio more than equal to 25, should undergo additional upper GI endoscopy and colonoscopy to rule out primary G.I. malignancy (Figure 1). Mammography to rule out breast primary must also be done. Comprehensive surgical staging or Primary debulking surgery (PDS) is the preferred primary treatment in all cases except patients with stages III and IV where optimal cytoreduction is not achievable and or patient is too frail to undergo surgery. Neo-adjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) should be considered in these patients. Major randomized trials have shown that, progression-free survival (PFS) and overall survival (OS) rates in patients given NACT-IDS were not inferior from those of patients undergoing PDS with significantly lower adverse effects and mortality rates after IDS than patients undergoing PDS.[1] However PFS and OS in these trials were much lower than primary cytoreductive trials. In view of many limitations of these trials consider neoadjuvant chemotherapy in all advanced cases is questionable. Results from TRUST trial might throw some light on the exact timings for surgery for advanced cases.

Borderline tumours are difficult to detect clinically and radiologically. Pelvic & abdominal ultrasound helps in identifying the ovarian mass and ascites. Serum CA125 may not be raised in 53.8% of patients with borderline tumours while serum CA-19-9 may be raised in patients with mucinous BOTs. Borderline ovarian tumours are not PET-avid and hence are interpreted as "benign" tumours on PET. Ovarian masses that

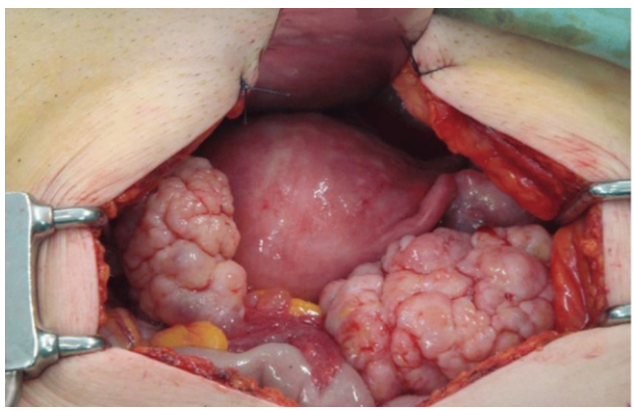

Figure 1 Bilaateral ovarian masses – likely Krukenberg tumour

show complex features on MRI that are concerning for malignancy but appear as "benign" on PET are said to be characteristic of borderline ovarian tumours.

Surgical staging of ovarian cancer

Surgical staging should be performed because subsequent treatment will be determined by the stage of the disease. Our aim is to achieve optimal cytoreduction of the disease in CRS i.e. <1 cm of residual disease (preferably no grossly visible tumour), as the extent residual disease directly affects the prognosis in advanced EOC.[2]

This involves the following steps:-

1. A midline vertical incision should be used for laparotomy for debulking surgery. Minimal invasive procedures like diagnostic laparoscopy may be used in select cases.
2. Any free fluid, especially in the pelvic cul-de-sac, should be submitted for cytologic evaluation. If no free fluid is present, peritoneal "washings" should be performed by instilling and recovering 50 to 100 ml of saline from the pelvic cul-de-sac, each paracolic gutter, and from beneath each hemidiaphragm.
3. A systematic exploration of all the intra-abdominal surfaces and viscera should be performed. This should proceed in a clockwise fashion from the caecum cephalad along the paracolic gutter and the ascending colon to the right kidney, the liver and gallbladder, the right hemidiaphragm, the entrance to the lesser sac at the para-aortic area, across the transverse colon to the left hemidiaphragm, and down the left gutter and the descending colon to the rectosigmoid colon. The small intestine and its mesentery from the ligament of Treitz to the cecum should be inspected.
4. Any suspicious areas or adhesions on the peritoneal surfaces should be biopsied. If there is no evidence of disease, multiple intraperitoneal biopsies should be performed. The peritoneum of the pelvic cul-de-sac, both paracolic gutters, the peritoneum over the bladder, and the intestinal mesenteries should be biopsied.
5. The diaphragm should be sampled either by biopsy or by scraping with a tongue depressor and making a cytologic smear.
6. Total hysterectomy and bilateral salpingo-oophorectomy should be performed, with an effort to remove the encapsulated mass intact to avoid abdominal cavity spillage.
7. The omentum should be resected from the transverse colon, a procedure called an infra-colic omentectomy. All involved omentum, preferably also including the supra-colic omentum should be removed in involved cases.
8. Nodal dissection is an important part of gynaecological oncology surgeries. They provide information regarding the staging, prognosis and tailoring of adjuvant therapy in these cases. Bilateral pelvic lymphadenectomy should be performed with the removal of lymph nodes overlying common iliac and external iliac vessels, overlying and medial to hypogastric vessels, and from the obturator fossa anterior to obturator nerve (Figure 2). Para-aortic lymph node dissection should be performed by removing nodal tissue overlying the vena cava and aorta, preferably to the level of renal vessels (Figure 3). In early-stage EOC, complete systemic lymphadenectomy is recommended in all high grade histologies for appropriate staging and tailoring adjuvant chemotherapy. The frequency of pelvic and paraaortic metastases were 30% (82 of 276) and 40% (122 of 276), respectively. In a study by Morice et al of 276 patients, the frequency of lymph node metastases in patients with stage IA, IB, and IC disease, were 13%, 33%, and 38%, respectively.[3] None of with stage IA grade 1 and mucinous tumours confined to the ovary had nodal involvement. Lymphadenectomy can be omitted in low grade or expansile mucinous tumours. In advanced stages, patients need not undergo systematic pelvic and para-aortic lymphadenectomy, as this does not improve progression-free survival or overall survival and only enlarged lymph nodes should be removed.[4]

9. In advanced cases, procedures like bowel resection, with or without colostomy, appendectomy, peritonectomy, diaphragmatic stripping, splenectomy, partial cystectomy, partial hepatectomy, cholecystectomy, partial gastrectomy or distal pancreatectomy, may be done to achieve optimal cytoreduction (Figure 4). An appendectomy may be performed in all mucinous tumours, either early, advanced or borderline. But, it should be emphasized that progressively complex upper abdominal surgeries and bowel resections should be undertaken only if the surgeon is able to achieve a complete surgical debulking with no gross residual disease. Incomplete, but complicated, resections should be avoided as this may delay the chemotherapy and have a poorer prognosis.

Borderline Tumours

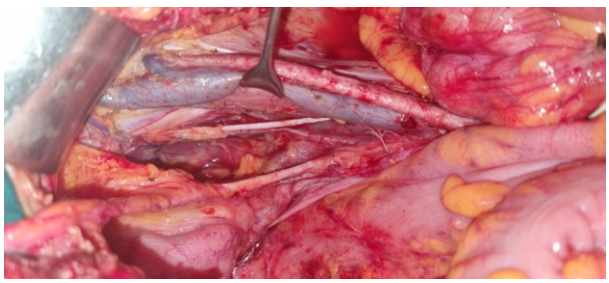

Figure 2: Pelvic lymphadenectomy - obturator nerve*

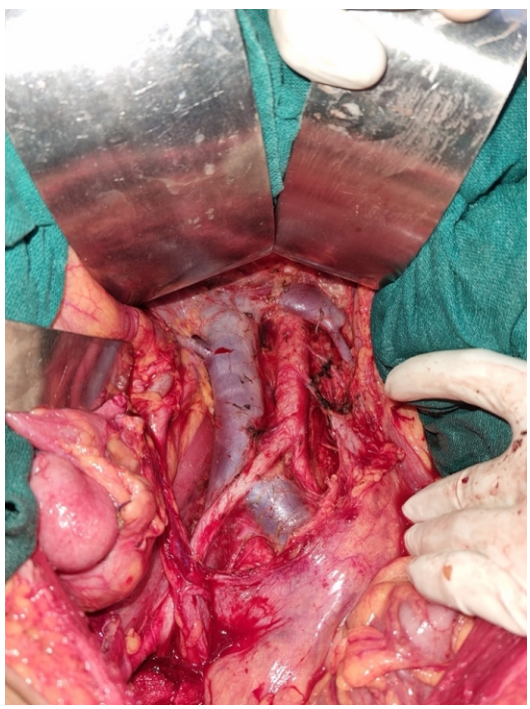

Figure 3: Para-aortic lymphadenectomy until renal vessels

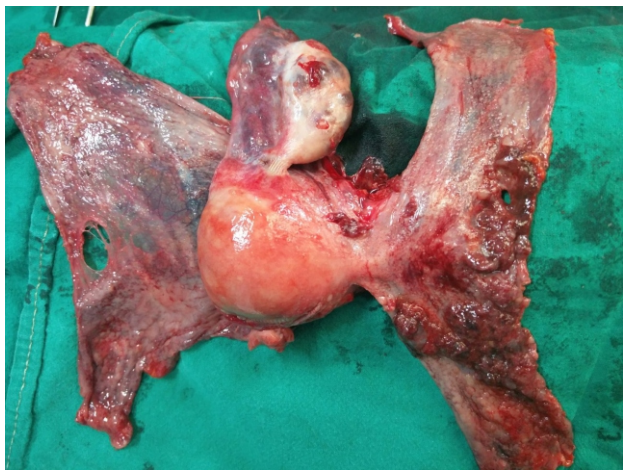

Figure 4: TAH BSO + PERITONECTOMY done in advanced cases

In postmenopausal women or in women who do not wish to preserve fertility, type I hysterectomy with bilateral salpingo-oophorectomy and complete surgical staging is done as mentioned above. Routine retroperitoneal node dissection as part of surgical staging in clinically ovarian-confined disease is not recommended as it does not have any survival benefit. Fertility-sparing surgery BOTs are usually diagnosed in younger women where preservation of fertility is an important issue. In patients with tumours confined to one ovary, unilateral salpingo-oophorectomy can be done with complete surgical staging. Biopsy from the normal-looking contralateral ovary is not required as it may interfere with the ovarian reserve and also can form peritoneal adhesions. In case of bilateral ovarian involvement, the option of unilateral or bilateral ovarian cystectomy / a unilateral salpingo-oophorectomy with contralateral cystectomy may be considered with an increased risk of recurrence. The relapse rate varies between 12 and 58% for cystectomy and between 2.5 and 5.7% for radical surgery.[5] Thus, the gynaecologic oncologist has to adequately weigh the pros and cons of a fertility-preserving approach in selected patients of borderline ovarian tumours with proper counselling of the advantages and disadvantages and the advice of a regular and long-term follow-up.

Fertility Preservation in Early-Stage Ovarian Cancer

In patients who have undergone a comprehensive surgical staging and in whom there is no evidence of spread beyond the ovary, the uterus and the contralateral ovary can be retained in women who wish to preserve fertility An ovarian biopsy of the contralateral ovary is not required if it is grossly normal. Women who have undergone fertility-sparing surgery for low-stage, low-grade epithelial ovarian cancer should be followed carefully with routine transvaginal ultrasonography and estimation of serum CA125 levels. Generally, the other ovary and the uterus should be removed at the completion of childbearing. An endometrial curettage must be carried out to rule out concomitant uterine cancer in patients with granulosa cell tumours if fertility-sparing surgery is planned for them.

Role of neoadjuvant chemotherapy

The surgical management of all patients with advanced-stage disease is approached in a similar manner, with modifications made based on ECOG status of the patient.

If the patient is medically fit for surgery, she should undergo an initial exploratory procedure with removal of as much disease as possible with the objective being to have no residual disease at completion of surgery. The operation to remove the primary tumour as well as the associated metastatic disease is referred to as debulking or cytoreductive surgery. Most patients subsequently receive six cycles of combination intravenous chemotherapy with platinum and paclitaxel. In selected patients who are not candidates for initial cytoreductive surgery, three to four cycles of platinum-based neoadjuvant chemotherapy(NACT) are administered followed by interval debulking surgery. Confirmation of clinical diagnosis of ovarian cancer is required by biopsy preferably with IHC. NACT-IDS has gained credibility as a valid therapeutic strategy for patients with advanced disease and poor general condition, massive pleural effusion, compromised nutritional status and unresectable bulky tumours. Absolute indications for NACT based on imaging include :

- Diffuse deep infiltration of the root of small bowel mesentery (Figure 5)
- Diffuse carcinomatosis of the small bowel involving such large parts that resection would lead to a short bowel syndrome (remaining bowel < 1.5 m)
- Diffuse involvement/deep infiltration of
  - stomach/duodenum
  - head or middle part of pancreas
- Involvement of truncus coeliacus , hepatic arteries, left gastric artery
- Central or multisegmental parenchymal liver metastases
- Multiple parenchymal lung metastases (preferably histologically proven)
- Non-resectable lymph nodes
- Brain metastases

The accuracy of preoperative assessment of the feasibility of complete resection with no residual macroscopic disease after upfront surgery remains contentious. CT and MRI scans have been used to try to predict suboptimal resection. The peritoneal cancer index (PCI) scoring system can also be used.

Non-Epithelial Ovarian Cancer

In contrast to epithelial tumours, other ovarian malignancies like germ-cell or sex-cord stromal tumours usually present at an early stage. As many of these patients may be of younger age,

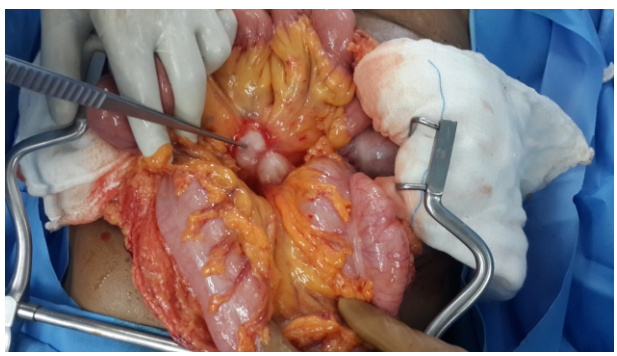

Figure 5: Deep infilteration of root of mesentry- criteria for inoperability

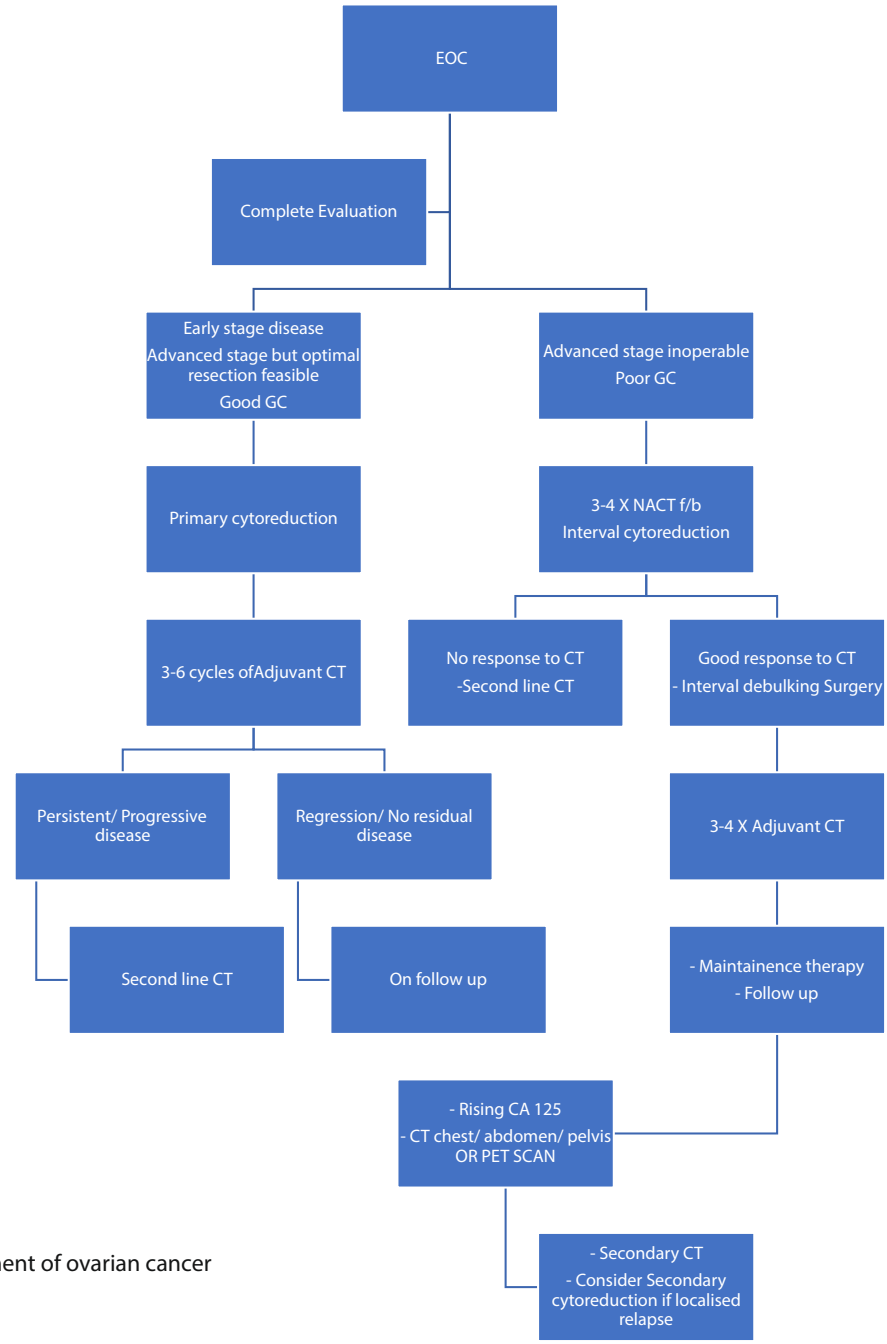

Figure 6: Management of ovarian cancer

fertility-sparing surgery must be done in these patients. However, if the disease is advanced or if the patient does not desire fertility, then they should undergo comprehensive surgical staging just like epithelial tumours. Node dissection should be carried out in cases with suspicion of nodal involvement. An endometrial curettage must be carried out to rule out concomitant uterine cancer in patients with granulosa cell tumours.

Role of Minimal Invasive Surgery

Minimal-invasive surgery is performed currently to stage and treat ovarian cancer at different stages of disease. Major concerns of minimal-invasive surgery are related to minimizing tumour disruption and dissemination, removing the adnexal mass intact, and adequate retro-peritoneal staging. Minimal-invasive surgery may be used in ovarian malignancy in the following situations:-

- For BOT and early stage ovarian cancer laparoscopic surgery should be reserved for experienced centres where oncological principles are strictly followed to reduce the

risk of intra-abdominal tumour/ cyst rupture and thus reduce the recurrence rate.

- In advanced cases, laparoscopic assessment may be done to assess if complete cytoreduction is possible. The peritoneal cancer index (PCI) scoring system (Figure 7) is a diagnostic and prognostic tool that is a sum of scores in thirteen abdominal regions. Each receives a score of 0-3 based on the largest tumour size in each region. Scores range from 0 to 39. Higher scores indicate more widespread and/or larger tumours in the peritoneal cavity. Neoadjuvant chemotherapy could be considered if the PCI is higher than 24.[6]
- Minimal invasive surgical methods may also be used to resect localized recurrences.

Role of HIPEC AND NIPEC

Hyperthermic Intra-Peritoneal Chemotherapy (HIPEC) is a single dose of heated chemotherapy in the intraoperative period. Randomized trial of HIPEC in cases of interval cytoreduction showed significant improvement in DFS and OS with no increased morbidity. There are other studies which have not proven the advantage of HIPEC. Due to limitations of these studies HIPEC is still considered experimental and should be used in research settings only.[7] Recent studies have shown emerging role of NIPEC (Normothermic intraperitoneal chemotherapy), which is non–heated intraperitoneal chemotherapy with prognostic advantages similar to HIPEC. It is a feasible procedure with a role in both primary and interval cytoreduction. It is user-friendly combining the prognostic benefits of IP chemotherapy with the assurance of early timely administration of chemotherapy in advanced EOC. NIPEC may be turn out to be a safer and cost effective alternative to HIPEC, with minimal toxicity rate and more tolerability.

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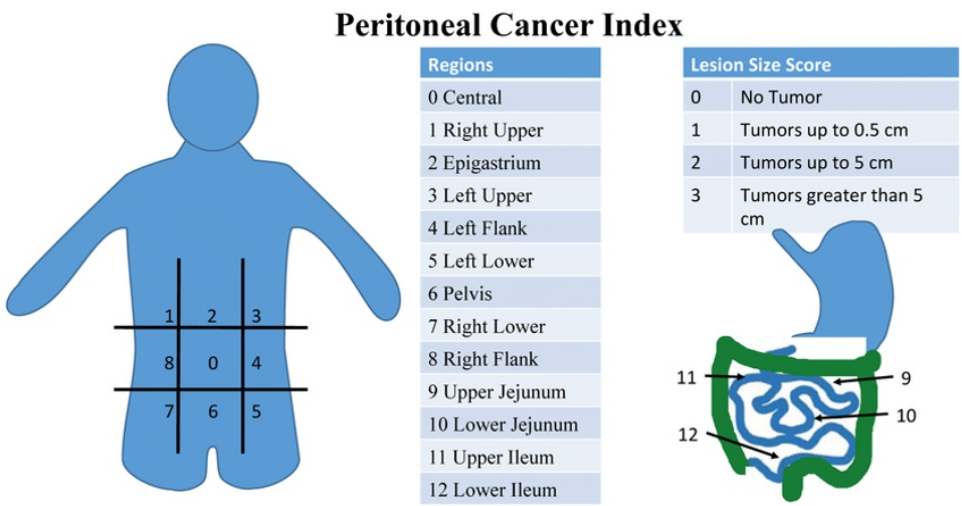

Figure 7: PCI INDEX

Perioperative Music Therapy: A Tool to Soothe

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"The role of music lies in helping the consciousness uplifts itself toward the spiritual heights."

Music therapy is one of the expressive therapies, consisting of a process wherein music is used to create an effect on all planes of one's being–physical, emotional, mental, social, aesthetic, and spiritual–to help the patients attain health at all levels. Historically, music is even older than language; healing sounds have always been considered as an important aid in the medical practice. Described as an alternative medicine and allied health profession, its growth as therapeutic science is a well researched phenomenon of a fact known since times immemorial. There is evidence that music helps with a variety of chronic disorders, including cardiac conditions, depression, autism, substance abuse and Alzheimer's disease. It can help with memory, lower blood pressure, improve coping, reduce stress, improve self-esteem.

There is lot of evidence that music therapy helps in oncology patients by reducing stress, anxiety and improving depression and fatigue and thus improving over all well being and hope.

Recently lot of interest has been generated in using music therapy perioperatively. As surgeries involve lot of stress, anxiety and pain, growing need to provide integral care for pain, anxiety, and psychological well being in perioperative periods has led researchers to scientifically study the effects of music therapy in these clinical situations.

How can Music Help

Exposure to music produces certain neuro endocrinal and psychoneuroimmunological

changes in the body which can contribute to its healing effect. Listening to music has been shown to reduce anxiety levels by lowering the levels of various stress hormones and biochemical markers, such as cortisol, epinephrine and norepinephrine. This is due to the neural connections between the auditory pathway and the hypothalamus, hippocampus and reticular activating system. In addition, music provides mental distraction and masks unpleasant noises, contributing to its calming effect. Different genres of music can also affect cortisol levels and boost immune system components such as IgA and natural killer cells

Music therapy functions to control pain via the spinal pain gate control theory. Furthermore, it is hypothesized that music therapy activates the anterior pituitary gland to release endorphins which relieve pain. Music can also act as a distraction from pain.

Listening to slow and repetitive music can help reduce anxiety by inducing relaxation and altering the consciousness. Music occupies attention channels in the brain, ultimately reducing anxiety by diverting attention from stressful environmental stimuli.

Acceptance and results of music therapy is influenced by multitude of factors such as cultural beliefs and preferences, cognitive level, and awareness about music, personal aptitudes, emotional requirements/susceptibilities, type of music, and musical instruments used.

Different types of Music Therapy

MT can be utilized in numerous forms—a patient may listen to selected recordings or a live performance by a musical therapist. In addition to passive listening, patients may also actively participate within this setting and join in creating music Music therapy can be any one of these three types: Receptive, Resonance and Active Participative

Receptive music therapy

In this form patient is not active herself but outwardly passive as she listens to the music.

The focus is placed entirely on the listening process. Calmness, stillness and undivided attention can arise. Once the anxious brooding has quietened due to attentive listening, tension and discomfort gradually ease.

Goals of receptive music therapy are:

- Relaxation
- Calmness and serenity
- Being able to listen attentively
- Release from brooding thoughts
- Trust

Resonance therapy

Patients can hear the music on the one hand while also feeling its vibration at the same time. The instruments are placed on different parts of the body, played in a calm flowing rhythm and supported with the voice as needed.

Goals of resonance therapy are:

- Release of physical and mental tension
- Antispasmodic and muscle relaxing effect
- Stimulation of the vegetative metabolic processes
- Regulation of the respiratory process
- Improving body awareness

Active music therapy

In active music therapy, the patient herself plays

Goals of active music therapy are:

- Release from worrying thoughts and feelings
- Strengthening bonding
- Creating trust and confidence in this life situation
- Stimulating self-efficacy and creative processes

While all types of music therapies and useful and effective in pregnancy, chronic conditions, malignancies etc., in perioperative scenario, only receptive music therapy can be used.

Evidence of Role of Perioperative Music Therapy in OBGYN

Number of studies have documented positive effects of Music therapy in various clinical conditions, yet there is a dearth of studies of its effect during gynecological operations (eg hysterectomies and obstetric surgeries (Cesarean sections). Although psychological care is important in both these surgeries, it often takes a back seat due to priority of physical care over the one's emotional, spiritual, and psychological needs.

Vaishnav et al performed a Randomized controlled trial in a tertiary hospital in Gujrat involving patients undergoing elective caesareans and hysterectomies. Pre recorded classical ragas based instrumental music was used peri operatively. They found that as compared to the control group, the experimental group had significantly lower level of anxiety and a higher level of satisfaction in both the surgical interventions perioperatively. Patients also reported a reduced sense of insecurity and suspense at the commencement of operation, increased confidence, reduced discomfort after waking up from the operation, reduced postoperative pain, nausea, and vomiting.

Similarly Shukla et al also found in women undergoing hysterectomy, perioperative music therapy reduced post operative anxiety and improved satisfaction. Javan Casarin et al found significant reduction in pathological stress pre operatively and in early post op periods by perioperative music therapy in women undergoing laparoscopic hysterectomy in a randomized controlled trial.

The analgesic and anxiolytic effect makes music particularly useful for obstetricians. Randomized controlled trials have shown consistently that it has a strong impact on vaginal birth (VB) by significantly reducing the amount of stress and anxiety perceived by the parturient measured by visual analogue scales during all stages of labour and post partum upto 24 hours , significantly reducing blood pressure and heart rate. Parturients who listen to music are also more likely to deliver spontaneously.

Similarly there is increasing evidence about the advantageous effects of music in the setting of caesarean section (CS). Several studies have shown a reduction in stress and anxiety

perceived by the mother during and while preparing for CS with an effect lasting even hours after the music intervention ended. A meta-analysis of 18 concluded that women in the intervention group had lower intraoperative anxiety levels than the controls. The same relationship persisted when the cesarean delivery was unscheduled and when the music was selected by the patient or by the study team.

Effect on Health care Professionals

In the above mentioned studies even the health care professionals (operating surgeons, anaesthetists, and nurses) reported increase in enthusiasm, reduced fatigue, and stress of surgery as an effect of listening to music played during the surgery. They observed that it was helpful in focussing on surgical work and improved efficiency while making working

in operation theatre more comfortable and enjoyable. It also helped in reducing the autonomic reactivity of theatre personnel in stressful surgeries. One needs to be careful about the type of music and volume as music can interfere with communication within medical teams and thus causing detrimental effects on the patient's treatment and well-being.

To conclude, for patients undergoing gynaecological surgeries like hysterectomy and caesarean section, a especially composed receptive music therapy can act as a powerful nonpharmacologic tool to enhance psychological well being. It is likely to reduce pre and post operative anxiety, stress, pain and improve well being. It also helps in creating an

environment that stimulates and maintains relaxation, well being, and comfort of health care providers in the midst of prolonged, stressful working hours. Implementation in clinical

routine therefore seems advisable. There is a need to create a "culture of care" founded on integral understanding of human beings for including multimodal interventions in care.

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Writing a Research Paper

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You have done the Herculean task of painstakingly designing a study protocol, diligently carrying out data collection over many months or sometimes even years, crunching the numbers to make some meaningful interpretation out of the data, and now the masterpiece is ready to be unveiled in front of the whole wide world. But alas, there is one more step left before bringing out the showpiece research, and it is writing the research paper! A good research can be marred or made by the way it is wrapped up into those word-limited and page-bound research paper and how well it gets presented in the paper.

Splice and slice.. into neat sections!

By and large, each research paper that is written to convey the findings of an original research consists of well defined sections to make the presentation more systematic. The pneumonic 'IMRaD' well serves to remind oneself of the bare basics – the paper should have an I – Introduction, M – Methodology, R – Results a-and, D – Discussion sections. This often and quite commonly represent the sections that a good peer reviewed journal will expect your research work to be sprucely sectioned in. Of course, the exact division or segments of the paper may not be universally same across all journals. Some may choose to label the first section as 'Background' instead of Introduction, and some prefer the authors to begin the paper by telling about 'What is already known' about the particular topic. The section on Methodology may be labeled as 'Materials and Methods', while the Results and Discussion may be combined as one segment in some journal layouts. There sometimes are additional sections or sub-sections like Conclusion, Summary, Strengths, Limitations, 'What this study adds', or 'Key take-aways' as per particular journal guidelines.

Make the trailer good, for the movie the viewer shall be hooked!

Well yes, most certainly a scientific research paper is not meant to compete with a movie running in a cinema in terms of popularity, but some of the rules apply the same anyway! Just like a good trailer can draw the crowd to the see the movie, a well constructed abstract helps!

Each journal issue carries a multitude of original articles, and then there are multiple issues in a year, and then multiple journals. It is unfortunately easy for your top-notch paper to get lost in the sheer quantum of scientific output it is present within. You may help your cause a lot by drafting a compact yet powerful abstract or summary. This can go a long way in attracting the fickle borderline readers into being interested enough to go onto read the whole paper. The abstract is usually the last part of the paper you will be writing, and suffice it to say that spend some time constructing it. It is arduous to be reflecting the same details about your whole research as the full paper, but that is what it is meant to do – convey succinctly to the readers that what the study was all about.

It can possibly help to create multiple variants of the abstract, fitting each within the stipulated word limit, choosing variations of text from the main text to present in the abstract. A colleague or more than one, can then be requested to read the abstract options, read the full paper thereafter and suggest to you which abstract they found better represents the gist of the research work.

Well begun is half the job done!

The Introduction is many a times often considered and given as much importance as the poor cousin who has come from a remote far-away small town to attend the wedding in

your family, and whom you have not seen for a long time and do not expect to be seeing anytime soon again. Well, the Introduction if well written, can turn out to be the hero for you!

Make the reader understand the importance of the topic, and why you needed to do it. Back up with evidence from the literature that what were the findings so far, some topics or angles of looking at the topic that got missed or deserved to be studied in the Indian context. Findings closer home (e.g. Delhi then North zone, then India, then world), or closer in time (e.g. this year, then last five years, then this decade, then earlier) may help the cause better, importance of the findings itself being the same. Sentences or a paragraph on 'rationale for the study' and the 'aims and objectives' are a nice way to wrap up the Introduction section without specifying these sub-sections, unless otherwise indicated by the journal guidelines.

Be Methodical about the Methods section!

Do not gloss over the vital importance of this section for your research. A learned reader will read the methodology you present, read your results (and interpretations) and then go back to go through your methods section again to see if your research ways were competent to catch the truth as it actually is, and whether the conclusions you have drawn are justified in view of the research methodology you adopted.

Try to make it as detailed as possible, to convey how the research work was done. The thoughts that can and should be covered in this section are the basics of enquiry – who, what, when, where and how. The things to cover include describing the study area, study population, study period, study design, study tools in detail, operational definitions, sampling method, data collection technique and methodology, inclusion and exclusion criteria, specifications of tools/devices used if any, among other things. The section actually becomes quite exhaustive if everything is presented in all the detail. The cause can be helped if there is a provision of shifting some of the detailed presentation to online-only additional supplements, if the option is offered by the specific journal.

The golden mantra can be that once you have finished writing your Methods section, read it patiently and carefully and just evaluate that whether a reader can re-create your entire research work process (process, not necessarily the same findings!) based solely upon the Methodology you have presented to her.

Systematic presentations.. Results away!

Often regarded the meatiest among the sections of the paper, the king among the equals or the 'pièce de résistance', the results of your hard work would be what readers will be interested in the most. Begin by sharing the details of the 'who' – the study population. Their socio-demographic characteristics, differences between the cases and the controls, differences of the characteristics of your sampled population from that of the underlying study universe in case you feel that has important bearing on the results. Anything that describes the population, and that may have a bearing on the understanding of the later results regarding the stated study objectives, should go in the initial paragraph(s) here. It is good practice to arrange the presentation of the main results in a logical flow. It should ideally be from descriptive (the means and proportions) to the analytical results (all the statistical tests), and also as per the study objectives sequence. A mistake sometimes made and to be kept in mind is that do not spring a surprise on the readers by bringing in a study variable for the first time in the analytical results, it should get a mention in the descriptive results part first.

Many of the results are amenable to graphical presentation by way of tables and figures. The diagrams definitely aid the reader's understanding, but make sure to anchor all the diagrams at relevant places in the Results section. This means that give a reference to the particular table/figure within the flow of text and discuss only the major findings, there being no need to repeat in the text all that is presented in the diagram.

All's well that ends well!

The analysis of what your findings mean, and what you want to convey to the readers that they mean, is contained here. Unlike a thesis

work that all the MD/MS postgraduates among the readers would have done, there is usually no 'review of literature' (ROL) section in an article presenting an original research. All the comparison and reading current findings in context of the wide literature, is to be done in this section only. Again, being systematic here would mean mentioning and discussing each of your main results one by one, with each main result's discussion taking a separate paragraph for clarity. The number of studies and previous findings available for context may vary widely depending on the topic (or particular finding) at hand. Be thorough in your ROL to either convey confidently that there is no previous literature to compare your novel findings with, or to present the context with the most important studies only in case multitude are available.

The tiny finishing touches!

Polish off your well crafted research paper by detailing the strengths and limitations of your study, particularly the methodology. This can either be a separate section (if the journal demands so), or a paragraph towards the end of the Discussion. Carefully evaluate what you feel could have been done better, or how you would like others to do the same work better when they read your paper. Mentioning the limitations honestly and the ways you took to overcome them or the ways to overcome in future, is more and more being appreciated by the journals to be an important part of writing a good paper. And surely it is much better than a reviewer or a reader pointing out the deficiency later! In a similar vein, also list the possible strengths of the study for the reader and the future researcher.

It's a matter of evidences, have good references!

That splendid introduction you did, the wholesome discussion you wrote must be backed up by a list of references at the end of the article. It is sometimes a waterloo for an otherwise very well construed research paper. Take some time to read the specific journal requirements regarding styling, format your references accordingly. Most of the reference systems are straightforward in what they want the styling to be, and the journals many a times offer examples of how they wish the reference pattern to be. Consult the previous works, do not plagiarize from them.

Clathrate.. Formulate.. Liberate!

Well, that is borrowed from chemistry! Journal specific instructions are actually a lattice that may trap (Clathrate!). While targeting submission to a particular journal, read the instructions or author guidelines meticulously for journal specific requirements. It may be old-fashioned but many actually find it handy to take a printout of the instructions, and discuss it in-person with the co-authors regarding what needs to be done to make your manuscript in line with the journal requirements. To each her own, and many journal offices do have their subtle variations of the preferences as to how a manuscript should be framed for their consideration. Do follow it and try to make the paper accordingly (Formulate!). Browsing the original research section of the latest issues of the journal to understand the formatting can also be advantageous.

And finally (Liberate!) can mean two different things. Either the paper gets accepted for publication, where it is liberated out of your hands and onto the world through the journal, or you are politely (always politely) liberated from the journal submission process with a 'better luck next time' note. Do not be disheartened by rejection.. It is always handy to learn from the editor and reviewer comments shared back, if any, and going back to formulate and edit the paper accordingly. If the research work is good, and you trust your hard work, it will always find a good publication home. Writing the research paper well makes the process smoother for sure!

Dear readers, the entire short paper has been written in a somewhat lighter vein deliberately to keep the basically tough process light. It always seems that there are some who just have a 'knack for writing' while others seem to struggle with it. Let us not forget that ultimately there is a science to the scientific process, as well as to the scientific writing to present it. It is hoped that at least some of the tips may be useful reading or revision for the esteemed readers. Happy writing!

JOURNAL SCAN

Bhanupriya

Professor

Department of OBGY, UCMS & GTBH

Change of Fagotti score is associated with outcome after neoadjuvant chemotherapy for ovarian cancer

Saner FAM, Ruggeri G, Siegenthaler F, et al. *International Journal of Gynecologic Cancer 2023;33:1595-1601.*

Abstract

Objective To investigate whether a change in the Fagotti score (ΔFagotti) following neoadjuvant chemotherapy is predictive of resection to no residual disease (R0) and survival in women diagnosed with ovarian cancer.

Methods Women treated with neoadjuvant chemotherapy for newly diagnosed ovarian cancer between January 2012 and June 2021 at the Bern University Hospital were included in this retrospective cohort study. Fagotti scores before and after neoadjuvant chemotherapy treatment were assessed for a potential association with resection status at interval debulking surgery defined as no residual disease (R0), macroscopic residual disease with a diameter of 0.1–1 cm (R1) or >1 cm (R2), and survival.

Results During the study period, 130 patients received neoadjuvant chemotherapy, mainly in response to advanced ovarian cancer International Federation of Gynecology and Obstetrics (FIGO) stages IIIC (68.5%) or IV (20.8%). 91 patients (70%) experienced a relapse and 81 (62%) died due to their disease. Median overall survival was 40 months (95% CI 30.6 to 49.4). Fagotti scores dropped from a mean of 7.8 (95% CI 7.14 to 8.42) at diagnosis to 3.9 (95% CI 3.34 to 4.46, p<0.001) after neoadjuvant therapy. This decrease was associated with resection status during interval debulking surgery (mean ΔFagotti "4.9 in R0, "2.2 in R1, "0.6 in R2, p<0.001). Women whose Fagotti score declined more than 2 points after neoadjuvant chemotherapy (n=51/88, 58%) survived significantly longer (median overall survival of 42 vs 32 months, p=0.048).

Conclusion Fagotti scores and ΔFagotti scores are associated with complete cytoreduction at interval debulking surgery and longer overall survival in women treated with neoadjuvant chemotherapy for ovarian cancer. These markers are valuable for individualized patient treatment planning and should always be performed after neoadjuvant therapy.

Author's Comments

Approximately 75% of patients are diagnosed at an advanced stage of ovarian malignancy as per FIGO staging. The main cornerstone of treatment remains neoadjuvant chemotherapy and interval debulking surgery where complete tumour resection seems not achievable. In 2006, Fagotti et al proposed a laparoscopic index predictive of optimal cytoreduction based on peritoneal carcinomatosis, omental cake, diaphragmatic involvement, bowel or gastric infiltration, mesenteric retraction and liver metastasis. The Fagotti score after neoadjuvant treatment strongly correlates with resection status, and progression-free and overall survival. Fagotti scores are valuable for individualized patient treatment planning and should be routinely assessed at time of interval debulking surgery. This study evaluated the prognostic value of the change of the score (ΔFagotti) during neoadjuvant chemotherapy. It highlighted that change in Fagotti score is a novel measure for response to chemotherapy at the time of interval debulking surgery for ovarian cancer. It was observed that >90% of women with either a Fagotti score d"6 after neoadjuvant treatment, or with a ΔFagotti > "2 had an R0 resection at interval debulking surgery. The main limitation of the study lays in the retrospective evaluation of the Fagotti score. The lack of some video or photo documentation may result in an underestimation of Fagotti. The long follow-up

period—from 2012 to 2022—and the consistency in surgical and oncological treatment provided in a single tertiary referral hospital were additional strengths.

Proof-of-concept randomized phase II non-inferiority trial of simple versus type B2 hysterectomy in early-stage cervical cancer ≤ cm (LESSER)

Carneiro VCG, Batista TP, Andrade MR, Barros AV, Câmara LHLD, Ramalho NM, Lucena MA, Fontão DFS, Tancredi R, Silva Júnior TC, Bezerra ALR, Baiocchi G.

Int J Gynecol Cancer. 2023 Apr 3;33(4):498-503. doi: 10.1136/ijgc-2022-004092.

Abstract

Objective: To evaluate the non-inferiority and safety of simple hysterectomy in early stage (<2 cm) cervical cancer.

Methods: This proof-of-concept randomized phase II non-inferiority trial was performed between May 2015 and April 2018 in three oncological centers in Northeast Brazil. Patients with International Federation of Gynecology and Obstetrics (FIGO) 2009 stages IA2-IB1 cervical cancer and tumors ≤ 2 cm were treated with either simple or modified radical hysterectomy (Querleu-Morrow type B2). Intention-to-treat analysis was carried out. The primary endpoint was 3-year disease-free survival and secondary endpoints were overall survival, operative outcomes, adjuvant therapy, and patient's health-related quality of life (QoL).

Results: A total of 40 patients underwent either simple hysterectomy (n=20) or modified radical hysterectomy (n=20). All patients except three underwent open procedures (n=37/40, 92.5%). At a median follow-up of 52.1 months (IQR 43.9-60.1), 3-year disease-free survival was 95% (95% CI 68% to 99%) after simple hysterectomy and 100% (95% CI 100% to 100%) after modified radical hysterectomy (log-rank p=0.30). The corresponding 5-year overall survival rates were 90% (95% CI 64% to 97%) and 91% (95% CI 50% to 98%), respectively (log-rank p=0.46). The operative time was shorter after simple hysterectomy than after modified radical hysterectomy (150 min (IQR 137.5-180) vs 199.5 min (IQR 140-230); p=0.003), with a trend towards a longer time for vesical catheterization removal (1 day (IQR 1-1) vs 1 day (IQR 1-2); p=0.043). There was no post-operative mortality and the rates of post-operative complications were not statistically different between arms (15% and 25%; p=0.69). QoL questionnaires were received from only 17 patients (42.5%), with no major differences observed over time between the surgical arms.

Conclusions: Simple hysterectomy is safe and potentially non-inferior to the radical surgery in patients with early-stage cervical cancer d"2 cm.

Author's Comments

The standard treatment for early stage carcinoma cervix is radical hysterectomy with pelvic node dissection which eventually leads to surgical morbidity and complications related to autonomic plexus. In these settings, less radical approaches have therefore been considered a treatment option to reduce morbidity of surgery without affecting the oncological safety in early-stage cervical cancers. The risk of parametrial invasion has been reported to be less than 1%, which supports a role for sparing parametrial resection in women with cervical cancers with a tumor size of ≤ 2 cm. Hence, conservative surgery has emerged as a safe and feasible alternative to radical surgery especially to women who want fertility preservation. The only published prospective trial is the ConCerv study and results from a large randomized controlled trial, the SHAPE trial, are still awaited.

This study shows that simple hysterectomy is safe and potentially non inferior to radical surgery in terms of disease-free survival, with similar 5-year overall survival rates and no major differences in terms of patients' health-related QoL and it may provide peri-operative advantages like shorter operative time, urinary catheter for lesser time and no surgical morbidity associated with non radical approach.

A main point of interest for non-radical surgery

in cervical cancer is to accurately identify patients at risk of parametrial involvement before hysterectomy. In this study, parametrial invasion occurred in 5% of patients and even though the inaccuracy of the clinical methods for estimating tumor size resulted in 20% of patients having tumor >2 cm on the final pathological examination, only one patient in the entire cohort had cervical cancer relapse, which mainly resulted from a missed detection of parametrial involvement in the former report from pathology. The discrepancy in the tumour size estimation was observed as it was based on clinical examinations without the systematic use of magnetic resonance imaging. This was also possibly the main reason for the high use of adjuvant therapy. Other lacunae was small sample size, lack of pathologic evaluation of surgical specimens to assure compliance with the assigned arm of the study, the deviation from standard of care given that no magnetic resonance imaging was performed prior to surgery to evaluate tumor size, the non-strict criteria for administration of adjuvant treatment, the lack of information on sentinel lymph node evaluation and ultrastaging.

Forthcoming Events

1. **Webinar on "Endometriosis In Adolescents: Concerns & Consensus"Organized By : Endometriosis Sub committee of AOGD & Dept. Of Obstetrics & Gynecology Lady Hardinge Medical College & Smt. Sucheta Kriplani Hospital**

   Chairperson Endometriosis subcommittee : Dr Reena

   Vice-Chairperson Endometriosis subcommittee : Dr Ratna Biswas

   Date : 7/10/2023 , Saturday Time 5:00PM -7:00PM

2. **AOGD and Delhi PG Forum will be organising a Case discussion on "Jaundice in pregnancy" on 16.10.23 at 7:00 -8:30 pm. Coordinator Delhi PG Forum: Dr. Sunita Malik, Dr Shivani Agarwal**

3. **Next AOGD monthly clinical meeting will be held online on 27th October 2023, 4-5pm and will be organised by All India Institute of Medical Sciences, New Delhi.**

4. **Online webinar "Breast cancer- gynecologists concerns" under aegis of AOGD oncology committee on 28th October 3-5 pm, organized by UCMS and GTB Hospital**

   Conveners: Dr Amita Suneja, Dr Bindiya Gupta

Events Held

1. A webinar on Gynae Oncology was organized on 31st August by Institute of Obstetrics and Gynecology, Sir Ganga Ram Hospital under the aegis of ISOPARB Delhi Chapter, Rural committee of ISOPARB, and Oncology committee of AOGD.

2. DELHI PG FORUM conducted an online class: case discussion on "AMENORRHEA" on 18.09.23.

3. 24th Gynae Update was organised by IMA Janakpuri under Aegis of AOGD on 24th September 2023, at Hotel Hyatt Centric, Janakpuri ,New Delhi.

4. Pre Conference Public Awareness Forum was held under the aegis of RCOG, FOGSI, NARCHI, AOGD and FOGsd. Awareness talks on issues like anemia, cancer prevention, fertility along with health checkups were done at auditorium of ISKCON temple, East Of Kailash, Delhi on 27th September.

Calendar of Virtual Monthly Clinical Meetings 2023-24

Date	Name of Institution
27th October, 2023	All India Institute of Medical Sciences
24th November, 2023	MAMC & LNJP Hospital
29th December, 2023	Sir Ganga Ram Hospital
30th January, 2024	Dr RML Hospital
23th February, 2024	VMMC & Safdarjung Hospital
28th, March, 2024	UCMS & Guru Teg Bahadur Hospital
19th April, 2024	LHMC & Smt. Sucheta Kriplani Hospital
31st May, 2024	B L Kapoor Hospital

AOGD Risk Management Support [ARMS] Group

One of the ways to ensure stress-free work environment and optimal patient care is mutual support among professional colleagues. An advisory group was set up last year so that they can be contacted if any of us is caught in a complex clinical dilemma / dealing with aggressive clients or is apprehensive about how to document or effectively troubleshoot a potential problem. The same group will continue to provide timely advice and is led by

Convener- Dr. Vijay Zutshi- 9818319110

Co convener- Dr. Aruna Nigam- 9868656051

We invite suggestions from all members regarding functioning of this cell which will guide us forming the SOPs. Pl mail to **aogd.ucmsgtbh2023@gmail.com**

PROCEEDINGS OF AOGD MONTHLY CLINIC MEETING- SEPTEMBER

AOGD Clinical Meeting held at ESI-PGIMSR Basai Darapur, New Delhi on 29/09/2023

PREPUBERTAL YOLK SAC TUMOR: "A GYNAECOLOGIST'S PERPLEXITY'

Bhanvi Pandey, Anamika Das, Taru Gupta, Disha Rajput

Yolk Sac Tumor are derived from the primitive yolk sac. They are the third most frequent malignant germ cell tumors of the ovary. Yolk Sac Tumor occur in patients with a median age of 16 to 18 years. About one-third of the patients are premenarcheal at the time of diagnosis. Abdominal or pelvic pain is the most frequent initial symptom, occurring in about 75% of patients, whereas an asymptomatic pelvic mass is documented in 10% of patients. Management includes surgical exploration, unilateral salpingo-oophorectomy, and Chemotherapy.

A 10-year-old presented with ~15cm solid mass palpated till umbilicus. Mass had restricted mobility and non-tender with regular borders. This mass was first noticed 4 months back and rapidly grew since. There was also a history of lower abdominal pain and significant weight loss. Tumour Markers for this patient showed AFP >30, 000, CEA 1000, LDH 345.12. MRI Pelvis suggested large, well marginated, pelvico-abdominal complex solid cystic mass lesion, arising from left adnexa (8.7*12.3*15.6cm). This was associated with left hydroureter. No peritoneal or omental deposits. CECT Abdomen suggested left ovarian origin with absence of ascites. Therefore, based on tumour markes and radiology a diagnosis of Germ Cell Tumour was made. On Surgical Staging: a ~12*15 cm left ovarian solid cyst seen with prominent vessels and evidence of rupture of ~3 cm. Left salpingo-oophorectomy was done. Right tubes and ovaries were normal and uterus was infantile. Surgical Staging was Stage 1C2. HPE confirmed the diagnosis of Yolk Sac Tumour. Biopsies taken from Peritoneum and Omentum were negative for cancer. Patient received 3 cycles of BEP regime. Patient had normal AFP 4 weeks post op and after 3 cycles of Chemotherapy the young girl is still in remission.

A RARE CASE OF LOW GRADE ENDOMETRIAL STROMAL SARCOMA

Deepshika Jaiswal , Rageshwari Sharma, Pratiksha Gupta , Nupur Gupta

Endometrial stromal sarcomas are rare malignant tumours of the uterus. In general, endometrial stromal sarcomas (formerly called low-grade) are thought to be the most frequently encountered stromal tumour variant and are twice as common as high-grade undifferentiated sarcomas. In most cases, diagnosis is made postoperatively. A 32yrs old female presented with complains of heavy menstrual bleeding, difficulty in micturition, pain lower abdomen for 5 months. On clinical examination and investigation suggested of bulky uterus , firm , freely mobile, irregular margins likely Fibroid uterus. Patient was planned for Myomectomy/ Total abdominal hysterectomy in view of multiple fibroids. Intraoperatively, uterus was enlarged irregularly with multiple fibroids. Histopathology report came as low grade Endometrial Stromal sarcoma (LG-ESS) with unusual immunohistochemistry profile.

A RARE CASE OF PLACENTA ACCRETA SPECTRUM (PAS) IN EARLY PREGNANCY

Priyanka Singh, Akriti Sah, Leena Wadhwa

Placenta accreta spectrum is a potentially life-threatening condition that may complicate first-trimester abortion on rare occasions and is difficult to be recognized preoperatively. A high

index of clinical suspicion based on early recognition of the risk factors and anticipation of placenta accreta is highly essential in early pregnancy. Mrs. X, a 23 yr old female G3P2L2 with previous 2 LSCS with POG of 8wks on USG, conceived in lactational amenorrhea presented with bleeding per vaginum in compensatory shock in our emergency. She had history of self MTP pill intake followed by D&E 10days back. She was severely pale and dyspneic on examination with tachycardia. Clinical examination, investigations and ultrasound was suggestive of uterine perforation. Pt was taken in OT suspecting uterine perforation and with consent for hysterectomy. Intra op findings included a ballooned up lower uterine segment (LUS) and placenta was seen popping out of serosa of LUS suggestive of placenta percreta. Hysterectomy done. Histopathology was suggestive of placenta percreta at such an early gestational age.

AOGD Sub - Committee Chairpersons 2023-25			
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Endoscopy Sub-Committee	Dr Swati Agrawal	9810181964/ 9953938995	drswatilhmc@gmail.com
Fetal Medicine & Genetics Sub-Committee	Dr Sangeeta Gupta	8368199481/ 9968604349	drsangeetamamc@gmail.com
Oncology Sub-Committee	Dr Saritha Shamsunder	9313826748	shamsundersaritha@gmail.com
QI Obst & Gynae Practice Sub-Committee	Dr Kiran Aggarwal	9312277346	dr_kiranaggarwal@hotmail.com
Urogynaecology Sub-Committee	Dr Monika Gupta	9312796171	drmonikagupta@hotmail.com
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Infertility & Reproductive Endocrinology sub-committee	Dr Manju Khemani	9810611598	dr.manjukhemani@gmail.com
Community Health & Public Awareness sub-committee	Dr Shivani Agarwal	9868249464	dragarwal.shivani@gmail.com
Safe Motherhood sub-Committee	Dr Kiran Guleria	9811142329	kiranguleria@yahoo.co.in

Dil Se ....

Surbhi Joshi
Senior Resident

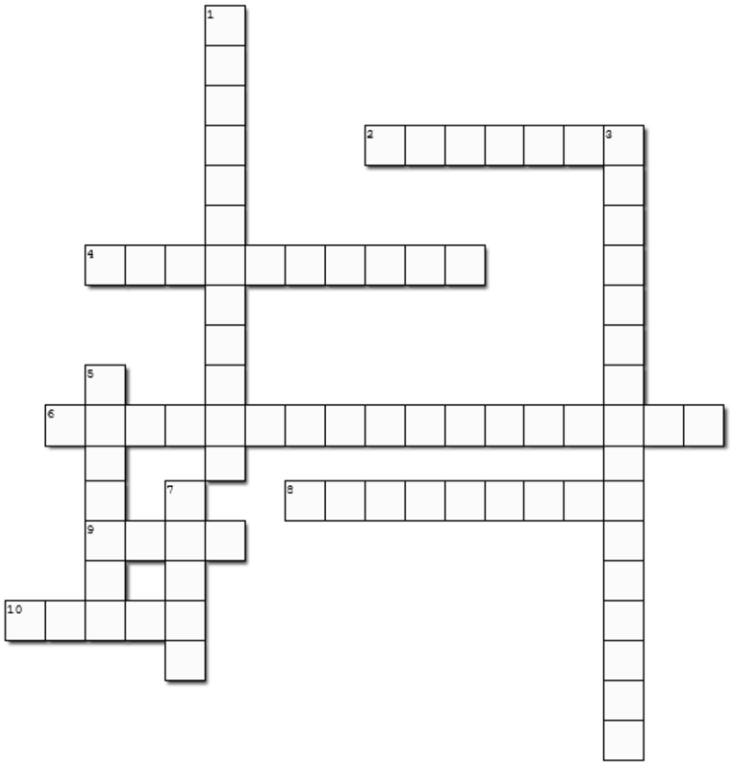
An Ode to my Patient
(The Change in Perspective)

One day we wake up with same old faces but a new life inside
Pleasantly surprised, its a moment of joy and pride
Along with a new set of concerns and emotional tides
When we reflect into those years of treating mothers and delivering babies
And ourselves going through it
Something gets changed, our perception
Now its more real and raw
The pain ,the distress, the pukes and bloating become equally perceptible
just like those pearls of excitement and joy
It gives birth to a new feeling, we enjoy
And makes us more woman alike
Belonging to the same coven
And only another woman can feel how its all woven
The change is not only physical as we sometimes think
Its a rollercoaster ride of highs and lows, all in a single blink
Those crying spells in OPD now starts making more sense
And we make these mothers believe, that their pain is being heard
and understood with the same motherly lens.
A divine constructive principle forms a bond
between us and our patients
which is utterly unique and lies beyond.

CROSSWORD PUZZLE

Bhanupriya

Complete the crossword puzzle below



Across

2. Which laparoscopic score is used for completeness of cytoreduction at primary debulking surgery in women with advanced cancer
4. Which type of hpv vaccine has best coverage against cervical cancer
6. The landmark for Level 4 lymph node dissection
8. Which drug when used during pregnancy as chemotherapy causes Goldenhar syndrome.
9. What is the name of minimally invasive technique to perform inguino femoral Lymphadenectomy(abbreviation)
10. Colposcopic score for prediction of pre invasive cervical lesion

Down

1. Which node is likely to be left when tracer is injected at the cervix.
3. Which dye is detected under Near infra red imaging during sentinel lymph nodes biopsy
5. Most commonly used contrast agent in Contrast enhanced ultrasound
7. Method of chemotherapy delivery immediately after surgery (abbreviation)

Paraaortic, fagotti, HIPEC, nonavalent, swede, VEIL, aorticinfrarenal, indocyaninegreen, sonovue, tamoxifen

Associaton of Obstetricians & Gynaecologists of Delhi

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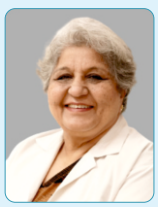

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