# FOGSI
# ONCOLOGY COMMITTEE

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NEWS LETTER

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## Message

**Dr. Anita Singh**
Vice President, FOGSI
2020

It is a pleasure to send my good wishes for the next news letter of Oncology committee. Dr Bhagyalakshmi Nayak the Chair Person of this committee deserves a lot of credit for her continued efforts to organize webinars and release news letters on all the upcoming new topics in the field of Gynaecological Oncology.In this news letter again, two very important topics -Hysteroscopy in PMB and BRCA testing has been contributed by the two eminent Gynaecological oncologists.I hope ,it will be of great value to the readers.

Jai Hind! Long live FOGSI !

**Dr. Anita Singh**
Vice President, FOGSI, 2020

| Date | Links of FOGSI Oncology Committee Webinars for those who have missed |
|---|---|
| 9th Aug | https://astrazeneca.zoom.us/rec/share/Cyci5oNX76ktjhl4WXOjYG03eAj2_i0pm7w1L4BLH4bxq2ObZf4SZFVbjRs77t7C.r1LTgbS9iwCyb3dg |
| 2nd Sep | https://astrazeneca.zoom.us/rec/share/DsYuOGYwCwJ1hfdvi-yGkXvUEV-p2YqXC3exyDH2kjlpGJds0TINm8wyL17fU833.V_On9wo2RMbDHByr |
| 13th Sep | https://astrazeneca.zoom.us/rec/share/Z-MFBKEn83s92E3NNGTRzFXkvQVFcGm80YDZRjDc7V1nn3hsxFzU521EhtcfWBbm.BrvJNRiqzKeIpk2G |
| 26th Sep | https://astrazeneca.zoom.us/rec/share/30rtlC1EgjdXp1q1kGs9AaIYk_EwXzKqpD8SxdAE0AO3afLd0W9iN_DKLWGj7usb.Qx2pV1feOdXyKYLZ |
| 3rd Oct | https://astrazeneca.zoom.us/rec/share/TZDzCCIYxnD3aaVvkpb1YRoMAGnrUl1coAbdkXMaToNsUlfSEk0hT0_tdfZ4fGPD.MN9fe1_JHo9O_QtJ |
| 11th Oct | https://astrazeneca.zoom.us/rec/share/IN14E3hwGJ_CeKKL3b7CR-ZDCRX7xhi1LdtUtxH3nE4nEgYfZKitCAmaYVKNDfAU.VykDEa02E8SGDl0- |
| 17th Oct | https://astrazeneca.zoom.us/rec/share/dhrOFJXpawks_CBVza_8Mf5AxE9Myl7kRjpdTPRpER6qIugTJX3fBOl1jOgvmjsT.6QDo0TB8qp8NcSAC |

# BRCA TESTING IN OVARIAN CANCER

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**Introduction: "Ovarian cancer is a silent killer"**[1]

It is easy to overlook the early symptoms of ovarian cancer because they are nonspecific, although recurrent. The early symptoms include abdominal bloating and pain, abnormal fullness after eating, difficulty in eating, an increased urge to urinate, fatigue, indigestion, and constipation, among others. The symptoms are often persistent if they are due to ovarian cancer. Symptoms usually become more severe as the disease progresses. By then, the cancer is advanced and usually spread outside of the ovaries and pelvis,making treatment difficult. As ovaries are situated deep within the pelvic cavity, it is unlikely for the woman to appreciate the mass until it spreads to the abdominal cavity. There is no routine diagnostic screening test available for ovarian cancer. Hence, it is important to counsel women to report unusual or persistent symptoms to their health care providers, as the disease whispers by way of above symptoms and health care providers are to listen carefully for early diagnosis[1].

The exact cause of ovarian cancer is yet unknown.[2] Certain factors can increase the risk of a woman having ovarian cancer, one of them being genetic mutations of genes associated with ovarian cancer, such as breast cancer gene 1 (BRCA1) or breast cancer gene 2 (BRCA2).[3,4] Knowing about BRCA mutation could determine treatment eligibility for targeted therapies. Some types of targeted therapy, especially poly(ADP)-ribose polymerase (PARP) inhibitors can target BRCA-mutated cancer cells, which means that women with a ovarian cancer having BRCA mutation do have better response to this type of treatment.[5]

**What are the BRCA genes?**

BRCA stands for Breast CAncer susceptibility gene.[6] Everyone is born with BRCA genes. These are tumor suppressor genes that work to suppress carcinogenesis. Healthy BRCA genes produce tumour suppression proteins which help repair damaged DNA [3,4] and cell stability, thereby preventing tumour development. When these genes are mutated, their normal function is altered, they may not be able to fix DNA damage nor suppress tumour development, leading to an increased risk of cancer.[3,4]

**Relevance of testing for the BRCA gene mutation**

Having a mutation in the BRCA genes means that there is an increased chance of developing cancer during his or her lifetime. BRCA mutations put them at an increased risk of developing breast, ovarian, prostate, and pancreatic cancer. With this knowledge, it may be possible to consider scheduling regular screenings for cancer detection in this population.[7] If she already has cancer, knowing that she has a BRCA mutation can help determine whether or not she can receive treatment specifically meant for BRCA mutants.[5]

If there is a BRCA1 mutation, she has an estimated 72% chance of developing breast cancer by age 80 and an estimated 39% chance of developing ovarian cancer by age 70.[8]

If there is a BRCA2 mutation, she has an estimated 69% chance of developing breast cancer by age 80 and an estimated 11% chance of developing ovarian cancer by age 70.[8]

After having been diagnosed with ovarian cancer, knowing BRCA status can help the health care team plan potential treatment options, such as targeted therapy[5] Knowing BRCA status empowers the patient and the physician to approach treatment differently. Some therapies work differently depending on whether or not there is BRCA mutation. This is why finding out BRCA mutation earlier can help the physician determine what treatment options are right for the patient. It can also help inform others in the family about their own cancer risk.[3,4]

Patients with ovarian cancer who carry a BRCA pathogenic mutation have longer survival rates, a favourable response to platinum-based chemotherapy and may demonstrate sensitivity to novel treatments such as PARP inhibitors, which target the DNA repair pathway that is defective in the tumour cells of carriers.

**When to get tested**

The sooner they get tested for a BRCA mutation, the sooner we know more about her cancer and decide on treatment options.[3] Early testing would mean an earlier treatment plan. For women with ovarian cancer, testing could happen as early as diagnosis or during surgery. If she tests positive for a BRCA mutation, we can make treatment decisions earlier to help stop cancer from progressing or recurring.

On the other hand, it is never too late to get BRCA tested. You can test for an inherited BRCA mutation at any time with a germline test.[3] Even if the cancer has already been diagnosed or has recurred, she can still get tested.

**Who should get tested**

Several guidelines recommend that patients with breast or ovarian cancer get BRCA tested:

- Society of Gynecologic Oncology :All women diagnosed with ovarian cancer, regardless of age or family history, should receive genetic counseling and be offered genetic testing.[9]
- National Comprehensive Cancer Network : Patients with ovarian cancer, fallopian tube cancer or primary peritoneal cancer should have genetic risk evaluation and BRCA1/2 testing[10]
- American Society of Clinical Oncology :All women diagnosed with epithelial ovarian cancer should have germline genetic testing for BRCA1/2 and other ovarian cancer susceptibility genes[11]
- The United States Preventive Services Task Force recommends that women who have family members with breast, ovarian, fallopian tube, or peritoneal cancer be evaluated for BRCA mutations.. The recommendation was to test for BRCA in following situations[12]:
- Breast cancer diagnosed before age 50 years
- Cancer in both breasts in the same woman
- Both breast and ovarian cancers in either the same woman or the same family
- Multiple breast cancers in the family
- Two or more primary types of BRCA1- or BRCA2-related cancers in a single family member

- Cases of male breast cancer
- Ashkenazi Jewish ethnicity

**Family history:**

BRCA testing guidelines vary considerably between countries, but there is an evolving trend to look beyond family cancer history.13-16BRCA mutations may be present in 15-44% of individuals with no family history of ovarian or breast cancer. Genetic testing should be expanded to all women with ovarian cancer regardless of family history. Testing should be done not only for germline BRCA mutations but also for somatic BRCA mutations

Although it's true that men cannot get ovarian cancer, they are at risk for the other cancers related to BRCA mutations. If they test positive for a BRCA mutation, they are still at risk of (male) breast, prostate, and pancreatic cancer.[3,4] Men can also pass this genetic mutation on to their children, so finding out about a BRCA mutation can help inform the rest of their family about their own cancer risk.

**Getting tested in the laboratory:**

**Types of mutation:**

**Germline mutations**

These are inherited mutations found in all body cells. Everyone carries 2 copies of BRCA genes inherited from his or her mother and father. If 1 parent has a BRCA mutation, all of his or her children have a 50% chance of inheriting that mutation. Even if a child inherits only 1 mutated BRCA gene, that person's risk of developing cancer increases.

**Testing for a germline mutation:** is done either by a blood (or saliva) sample.[17]

**Tumor mutation testing :**

This type of testing is comprehensive and can be done as early as during surgery. It finds both inherited and acquired BRCA mutations. This makes it an important step to determine which treatments are available.

Testing for a tumor mutation: is done by a tumor tissue sample.[17]

**Genetic counselling:**

A genetic counselling session will help to understand genetic information.[18] A genetic counsellor will discuss the benefits and risks of testing. A typical visit with a genetic counsellor might include questions about her family history, discussion of treatment options if a mutation is found, or referrals to other resources for help. These visits can be useful when deciding whether or not she should be tested, which genetic test is right for her, and what your results mean. Together, with the counsellor,she can decide if it is appropriate for her or family members to be tested.

**During a Pre test counselling session, the genetic counsellor will :**

- Introduce themselves to the patient
- Speak about the process of diagnosis & understand reason for referral
- Explain to the patient about testing process & set expectations regarding the test & outcomes
- Take personal details and draw a pedigree based for 3 generations based on family history

- Collect detailed medical & surgical history
- Explain the advantages & disadvantages of genetic testing
- Suggest clinical management options available

**During a Post test counselling session, the genetic counsellor, along with the oncologist, will :**

- Reveal the test results to the patients, preferably along with family/spouse/parent/kin
- Will help the patient interpret their results
- Assist in disease management
- Offer psychological support
- Discuss family dynamics & ethical, social and legal implications if any
- Schedule a follow up session for review
- Discuss genetic counselling & mutation testing for first degree family members

**Conclusion :**

BRCA1 and BRCA 2 gene mutations are associated with increased risk of breast and ovarian cancers in women. Testing for BRCA gene mutation is recommended in all women with non-mucinous epithelial ovarian cancers, regardless of family history. This helps risk stratification, guide treatments and predict response to treatment. Laboratory testing of both germline mutation and tumor mutation are done. Combined counselling with a genetic counsellor both pre and post testing is helpful.

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Inauguration of Cervical Cancer screening programme by DG Police at Cuttack on 8th March, 2020

Inauguration of Cervical Cancer screening programme by Commissionarate of Police at Bhubaneswar on 8th March, 2020


Breast & Cervical Cancer awerness programme

# HYSTEROSCOPY IN POSTMENOPAUSAL BLEEDING-A REVIEW

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**Abstract:**

**Background:** This study was conducted to assess the accuracy and feasibility of hysteroscopy in the evaluation of postmenopausal bleeding in the various studies.

**Search strategy:** Electronic databases were searched from 31 January 1991 to 1 January 2016 without language selection. The medical subject heading (MeSH) and textwords for the following terms were used: hysteroscopy, diagnosis, histology, histopathology, hysterectomy, biopsy.

**Selection criteria:** The inclusion criteria were studies which reported on accuracy of hysteroscopy in women with postmenopausal bleeding

**Data collection and analysis:** Electronic databases were searched for relevant studies and references were cross-checked.

**Main results:** Hysteroscopy not only can clearly and accurately display the appearance of endometrial cancer but also demonstrates any possible involvement of the lower uterine segment and cervix. Clark et al in a systematic review conducted in 2002 concluded that diagnostic accuracy of hysteroscopy is high for endometrial cancer but only moderate for endometrial disease defined as cancer and/or hyperplasia.(8) Moawad et al reported that almost 60% of women who underwent diagnostic office hysteroscopy for AUB were able to avoid the need for intervention in the operative suite, saving almost $1500 per patient.(9) Rebeiro et al, reported the sensitivity and specificity of hysteroscopy to be 92.6% and 65.8% for polyps, 52.6% and 95.9% for fibroids, 94.4% and 97% for cancer or hyperplasia and 35.3% and 99.6% for normal endometrium.(10)

**Conclusion:** This non-systematic review shows that Hysteroscopy has added a new dimension in the work up of patients with postmenopausal bleeding. It has improved our diagnostic capabilities over blind procedures. The entire uterine cavity can be visualized directly and any abnormal areas identified precisely and the same taken for histopathological examination. It has been a lifesaving procedure as combined use of hysteroscopy and endometrial biopsy leads to almost 100% accuracy in the diagnosis of endometrial neoplasia and its precursors.

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## Introduction:

Hysteroscopy is a day care procedure which can be done by a gynaecologist under local anaesthesia or sedation.

Postmenopausal bleeding (PMB) is defined as bleeding that occurs from the genital tract after one year

of amenorrhoea, in a woman who is not receiving hormone replacement therapy (HRT).(1) The average age of menopause in Asian women is 46 years.

With increasing life expectancy, a healthy 50-year-old woman today spends as much as 40% of her life in postmenopausal state. During this prolonged period, women are vulnerable to various conditions, of which one of prime importance and sincere concern is postmenopausal bleeding (PMB). Vaginal bleeding in postmenopausal women is an alarming symptom. Patients with PMB have 10%-15% chance of having endometrial carcinoma and therefore the diagnostic workup is aimed at excluding malignancy. Patient characteristics can alter the probability of having endometrial carcinoma in patients with PMB; in certain groups of patients the incidence has been reported to be as high as 29%. (2)

Unlike other malignancies, endometrial cancer often presents at an early stage when there is a possibility of curative treatment by hysterectomy. Survival decreases with increased staging and poorer histological differentiation, thus accurate and timely diagnosis is important and should preferably be carried out by a safe, simple and minimally invasive method.

The causes of postmenopausal bleeding includes endometrial atrophy, hyperplasia ,polyps, submucosal myoma, and cancer.(3) The increasing burden of endometrial cancer requires early diagnosis and treatment. Ultrasound evaluation has very low specificity in the differentiation of the type of endometrial hyperplasia as compared to directed biopsy.(4) A thickened endometrium on TVUS of ?4 mm in a postmenopausal woman with PMB warrants additional evaluation with endometrial sampling.

**Methods :**

This review was focused on studies in which studied the results of hysteroscopy in the evaluation of the uterine cavity in postmenopausal bleeding. The population of interest was postmenopausal women with symptoms of abnormal uterine bleeding.

Dilatation and curettage (D and C) was the only option available in the past for evaluating a case of PMB. However focal lesions may be missed on D and C.(1) Reports in the literature indicate that curettage alone with endometrial biopsy techniques carry false negative rates between 2 and 6% as curettage is a blind procedure and in approximately 60% of curettage procedures, only half of the uterine cavity is curetted. (5)With Hysteroscopy, entire uterine cavity can be examined and an additional advantage is the fact that a great number of benign pathological changes may be treated in the same sitting by using the office hysteroscope or resectoscope.

The goal of evaluation of PMB is to reach at the diagnosis with greatest accuracy, with least risk and expense for the patient. With the advent of hysteroscopy in the last two decades, focus has shifted from endometrial biopsy to hysteroscopic-guided biopsy as a "gold standard" diagnostic tool in the evaluation of PMB.(6) Other methods, less invasive, for evaluating the female reproductive tract with a prevalent use are the transvaginal ultrasonography (TVS) with saline infusion sonography or without saline infusion into the endometrial cavity, hysterosalpingography (HSG), and the blind endometrial sampling with pipelle. The main advantage of hysteroscopy is that it combines a more reliable method with greater diagnostic accuracy because of direct visualization. The only disadvantage of hysteroscopy is that it acquires specific teaching and training and has a longer learning curve.(4)

**Search strategy:** Electronic databases were searched from 31 January 1991 to 1 January 2018 without language selection. The medical subject heading (MeSH) and textwords for the following terms were used: hysteroscopy, diagnosis, histology, histopathology, hysterectomy, biopsy.

Selection criteria: The inclusion criteria were report on accuracy of hysteroscopy in women with postmenopausal bleeding

Data collection and analysis: Electronic databases were searched for relevant studies and references were cross-checked.

**Results:**

In a study by Liang lee et al vaginoscopic no touch hysteroscopy is found to be faster, safer and gold standard for assessment of endometrium. This is called as office hysteroscopy,in which no anesthesia is used.

**Core competencies required for hysteroscopy are as follows:**

1) Patient positioning and cervical exposure - modified dorsal lithotomy position is preferred.
2) Cervical dilation - in office hysteroscopy, there is no need of dilatation as a thin tube less than 4 mm is used. If necessary, oral or vaginal misoprostol may be used 3-8 hours before the procedure.
3) Uterine distension - distension is necessary to create a viewing space. Choices for distension include - CO2 gas, 32% dextran 70, 1.6% glycine, 3% sorbitol, 5% mannitol and 0.9% normal saline. For diagnostic hysteroscopy normal saline is useful and a safe medium and does not cause electrolyte imbalance.
5) Visualization and imaging -rigid or flexible hysteroscopes are used commonly of 4 mm outside diameter and 0 ,15 or 30 degree versions.
6) Intrauterine cutting and hemostasis -biopsy forceps are used to sample targeted lesions.

Hysteroscopic studies have shown pale endometrium with absence of glands with histopathologic correlation of atrophic endometrium in 35-42% cases. Thin endometrium with bleeding vascular patches suggestive of proliferative, secretory or mixed phase endometrium in 30-32% cases, endometrial polyp in 8-11% of cases. Focal endometrial thickening suggestive of simple hyperplasia in 8-10% cases. Submucosal myoma with blood vessels are seen in leiomyoma is 4-5% cases . Extensive endometrial growths and polypoid area with bleeding vessels are seen in carcinoma in 2-5% cases.(3)

Hysteroscopy not only can clearly and accurately display the appearance of endometrial cancer but also demonstrates any possible involvement of the lower uterine segment and cervix. (4)

Compared with other, more invasive procedures, hysteroscopy may provide the following advantages:

- Avoidance of hysterectomy
- Possible avoidance of "open" abdominal surgery (7)

**Discussion:**

Clark et al in a systematic review conducted in 2002 concluded that diagnostic accuracy of hysteroscopy is high for endometrial cancer but only moderate for endometrial disease defined as cancer and/or hyperplasia.(8)

Moawad et al reported that almost 60% of women who underwent diagnostic office hysteroscopy for AUB were able to avoid the need for intervention in the operative suite, saving almost $1500 per patient.(9)

Rebeiro et al, reported the sensitivity and specificity of hysteroscopy to be 92.6% and 65.8% for polyps, 52.6% and 95.9% for fibroids, 94.4% and 97% for cancer or hyperplasia and 35.3% and 99.6% for normal endometrium.(10)

Hysteroscopic appearance is not always confirmatory of endometrial carcinoma. Hence, hysteroscopy should always be accompanied by biopsy of the endometrium. Concern has been raised regarding the dissemination of carcinoma into the peritoneum by the spill over of the distension medium into the peritoneal cavity but in practice it does not occur because the superficial cells of the tumour are not viable. It is further substantiated by the fact that malignant cells are not recovered from the peritoneal cavity in women undergoing hysterectomy immediately after hysteroscopy. Some investigators have proposed that distention of the endometrial cavity with saline solution or $CO_2$ during the hysteroscopic procedure can, under certain circumstances, disseminate endometrial cancer cells to the abdominal cavity and change both the prognosis and the course of treatment. There are several conflicting arguments and concerns about this hypothesis. On the one hand, it is well-known that all examination methods (bimanual examination, D&C, and even hysterectomy) may lead to migration of endometrial cancer cells through the fallopian tubes to systemic circulation and peritoneal cavity without increasing the incidence of metastasis.(4) Tanizawa et al. in 1,040 women with endometrial cancer examined by hysteroscopy, found no significant differences in the presence of intraperitoneal tumor cells compared to patients evaluated by a different method. (11)Taddei et al. demonstrated that hysteroscopy evaluation of the extent of endometrial carcinoma could lead to an individualized therapeutic program and have a beneficial effect on survival rates.(12) Nagele et al. in a prospective randomized self-controlled study showed that there was no significant difference in the spreading of endometrial cells after hysteroscopy either by the use of natural solution or by the use of $CO_2$ for uterine distention. Only transtubal dissemination has occurred in about 25% of the patients.(13) Finally, de Sousa Damiao et al., after they have diagnosed endometrial cancer in 72 women, concluded that the hysteroscopic evaluation of endometrial cancer, if it is performed under low pressure of $CO_2$, does not cause spread of malignant endometrial cells into the peritoneal cavity.(14) On the other hand, Takac et al., after a retrospective study on 146 patients with endometrial cancer, emphasized that hysteroscopy significantly increases the risk of positive peritoneal cytology in women with endometrial cancer in comparison with D&C.(15) Revel et al. only a few years earlier have mentioned an increased risk of peritoneal contamination by malignant cells after hysteroscopy but with no evidence for these women to face worse prognosis comparing to patients who have undergone other diagnostic procedures.(16) Polyzos and his colleagues very recently analyzed nine clinical trials with 1,015 women with histologically proven endometrial carcinoma who either underwent or did not undergo preoperative hysteroscopy evaluation. Hysteroscopy resulted in a significantly higher rate of malignant peritoneal cytology compared to no hysteroscopy, especially if the distention medium was isotonic sodium chloride and if the inflated media pressure reached or exceeded 100 mmHg.(17)

**Conclusion:**

Hysteroscopy has added a new dimension in the work up of patients with postmenopausal bleeding. It has improved our diagnostic capabilities over blind procedures. The entire uterine cavity can be visualized directly and any abnormal areas identified precisely and the same taken for histopathological examination. It has been a lifesaving procedure as combined use of hysteroscopy and endometrial biopsy leads to almost 100% accuracy in the diagnosis of endometrial neoplasia and its precursors.(18)

Hysteroscopy represents the ideal technique for the examination of women over the age of 45 years who complain of abnormal uterine bleeding. Thus hysteroscopy combined with endometrial biopsy should be considered the method of choice for identifying intrauterine pathology.

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## Glimpses of some Webinar



Dr. A.K. Vaid
AskIT
Dr Sonali
Bhavana


Dr Archana dwivedi
Neharika Malhotra
Swapnil Sonar
Ashok Mehta
tibrewala
Dr. Sneha Bhuyar
Sudeep Mukherjee
Ragini
Bhagyalaxmi Nayak
Dr. Kirtan Vyas
Pramesh CS
Mitra Saxena
Charulata Bapaye
Alpesh- Arihant Hospital, Ah...
SHARVARI PURANIK
Jaydeep Tank
P 03 Sarita Bhalerao
Dr. T. Ramani Devi
Swapnil Sonar


Dr Adarsh Dharmarajan
Dr Priya Ganeshkumar
POGS
Puneet Chandna
Dr K Ambujam
Dr Fessy Louis
20th September at 11.00am
Dr Shalini Rajaram
Dr Aswath Kumar
Dr Abdul Vahab
Dr Manish Chandra
Dr Santosh Kuriakose
Dr Sandeep Mathur