INTRODUCTION

Ovarian cancer is the seventh cause of cancer deaths among women globally[1.] . According to population based cancer registries in India, ovarian cancer is the third common site of cancer among women, after cervix and breast cancer. Incidence rate is between 5.4 to 8 per 100,000 populations across the country[2].

It accounts for 2.5% of female cancer patients, but leads to 5% of cancer deaths. This high case fatality ratio explains the poor survival of the patient. Most of the patients are diagnosed at an advanced stage, which leads to poor outcome. Their clinical presentation are vague and non specific making the diagnosis difficult .The existing screening tests have a low predictive value contributing further to this misery. Early identification and prompt referral to gynecological oncologist is essential for better outcome of the patient

About 30% of ovarian tumors in postmenopausal women are malignant while only 7% of ovarian epithelial tumors in premenopausal are malignant[3].

A thorough pelvic examination, ultrasound assessment and tumor markers are used in preoperative evaluation of ovarian mass. None of these methods individually are effective in diagnosing the disease.

Hence a combined scoring system was developed by Jacob et al in 1990, Risk Malignancy Index using CA 125, USG score and menopausal score. This was called as RMI 1. Later it was modified by Tingulstad et al was named as RMI 2., which was further modified as RMI 3. In 2009, tumor size was also included and new RMI named as RMI 4.

The purpose of this study is to study the demographic profile of ovarian tumors and thereby study the risk factors of ovarian malignancy. Assess the sensitivity and specificity of RMI 2 to discriminate benign and malignant ovarian masses .

AIM OF STUDY

(i) To study the demographic profile of ovarian tumors based on their distribution according to age, parity, body mass index and menstrual history.

(ii) To determine the sensitivity, specificity, positive predictive value and negative predictive value of RMI in diagnosing ovarian tumors

(iii) To assess RMI 2 cut off for differentiating benign and malignant ovarian tumors in South Indian population

REVIEW OF LITERATURE

Ovarian tumors form a complex wide spectrum that includes variety of histological tissue from epithelial, connective tissues, hormone secreting cells to embryonal and germ cells. Amongst the malignant tumors, 80% are epithelial origin. 80% are benign and 20% are malignant.

A woman's risk[4] at birth for having ovarian cancer in her lifetime is nearly 1.4%, and the risk of dying from ovarian cancer is almost 1%.

Patients with ovarian tumor are usually asymptomatic and the signs are non specific. By the time diagnosis is made, they are at advanced stage and the outcome is poor[5]. Although early stage has good prognosis but only 15% of patients have their disease confined to ovary during diagnosis. If 75% of ovarian cancer is diagnosed at stage I death can be reduced to half[6].

Preoperative characterization of ovarian mass determine the management of the patient and appropriate management determine the prognosis. When deciding the type of surgery for patients with ovarian mass, estimating the risk of malignancy is essential. This is because benign mass can be managed conservatively or by fertility sparing surgery. Conversely, malignant tumors require staging laparotomy.

ANATOMY:

Each ovary is a solid, ovoid structure with the shape of an almond. They are intraperitoneal structures lying in the ovarian fossa of Waldeyer on the lateral pelvic wall.

Attachments:

To the posterior layer of the broad ligament – mesoovarium

Lateral pelvic wall – infundibulopelvic ligament.

To the uterus by ovarian ligament.

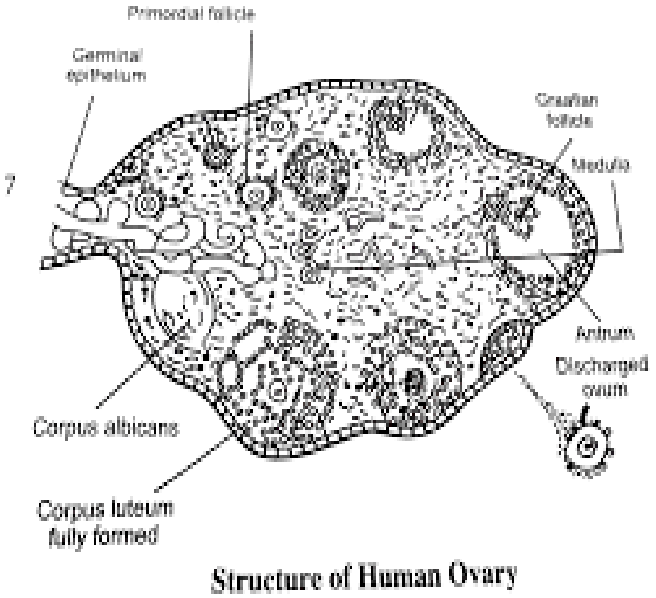


Fig.1 Anatomy of ovary

HISTOLOGY:

The ovary is covered by a single layer of cubical cells called the germinal epithelium which was later named as surface epithelium

Ovary is coated by connective tissue Tunica albuginea.

The cortex contains:

Germ cells

Follicular cells

Cortex is separated from surface epithelium by tunica albuginea. But at a few places follicles are in contact with the epithelium called as cords of pflueger.

Medulla contains blood vessels and hilus cells(secrete androgen)

Blood supply : ovarian artery .

Nerve supply : ovarian plexus- T10, T11.

Lymphatic drainage : Para aortic LN.

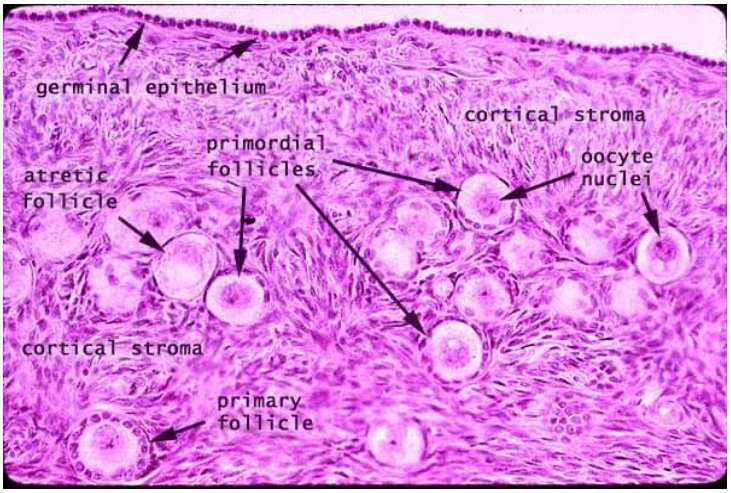


Fig 2:Histology of ovary

PATHOLOGY OF OVARIAN CANCER:

90% of ovarian cancers are derived from cells of the coelomic epithelium or mesothelium.

There are two molecular pathways that lead to the development of ovarian carcinoma:

TYPE 1 :

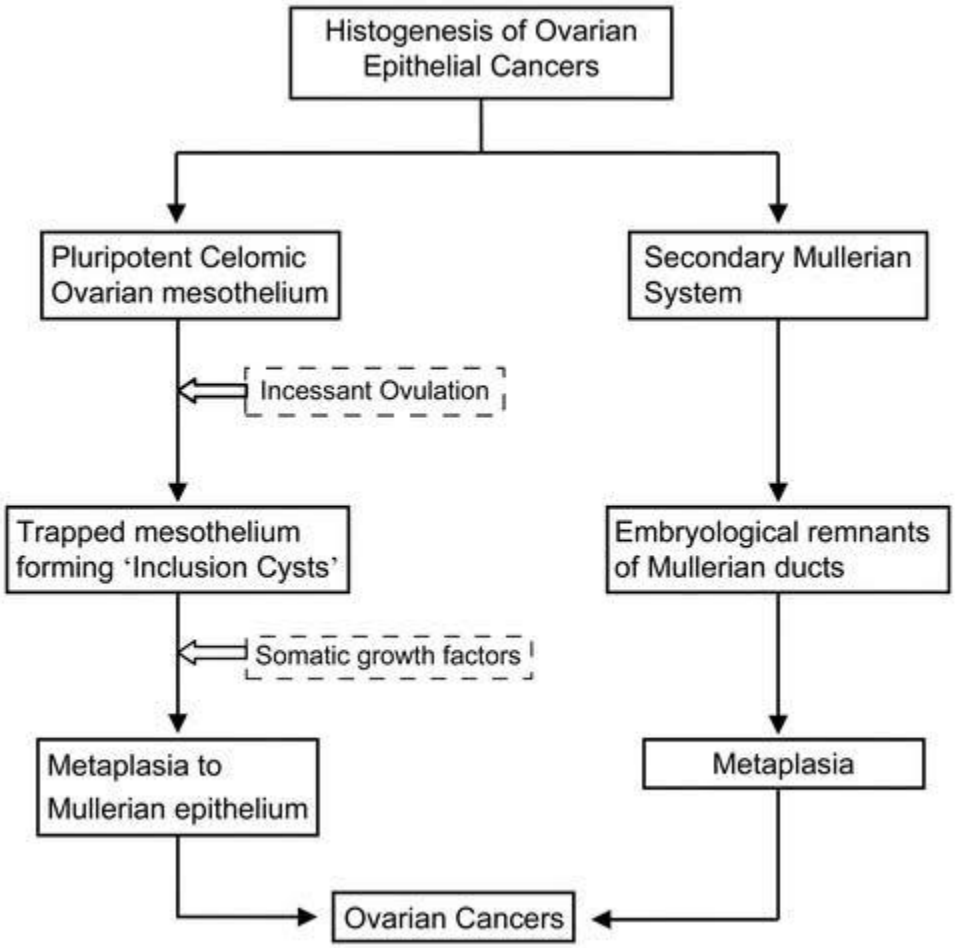
Originate from ovarian surface epithelium and müllerian inclusion

Accounts for early-stage cancers such as endometroid, clear cell, mucinous, and low-grade serous cancers.

Slow growing type

TYPE 2:

- Originate in fimbriae[7 -9] of the distal Fallopian tubal epithelium
- Form high grade serous tumor
- Rapidly growing tumors



TARGET POPULATION:

Two distinct populations are at increased risk for ovarian carcinoma, general population and a high-risk population.

Most of the ovarian tumors are sporadic . Most of them occur in women aged more than 50yrs.

High risk population: Hereditary syndromes accounts for 5–10% of ovarian cancers.

The average risk for ovarian cancer by the age of 70yrs is 40% (35–46%) in BRCA1 mutation carriers and 18% (13–23%) in BRCA2 mutation carrier[10]

EPIDEMIOLOGY

The lifetime risk for a women to develop ovarian cancer is 1:70 to 1:100. Theory of incessant ovulation which means as the frequency of ovulation increases risk of ovarian cancer increases. Also ovarian cancer is an estrogen dependent tumor. Hence all those causes which either increased estrogen or ovulation is risk factor

Risk factors for ovarian cancer include:

- Low parity / nulliparity
- High fat intake
- Obesity
- Diabetes mellitus
- Early menarche
- Late menopause
- Family history of ovarian , Breast and GIT cancer
- Prolonged HRT in postmenopausal women..
- Talc usage
- Genetic predisposition.

Nulliparous women were at 1.5 times the risk of parous women (Donn & Cuttler 1955).Risk decreases with increase in number of full term pregnancies. In a recent US case control study 563 cases, and 523 controls it was found that there was a reduction in risk of 40% with one child, 60% with 2 children, 80% with five or more children (Titus ernset et al).

Menstrual factors are less important than parity in an ovarian cancer risk. Menarche at an earlier age <12yrs are at about 25% greater risk than those with late menarche (>15yr) . Women with irregular cycle length, early menopause are protective.

EXOGENOUS HORMONES :

Combined oral contraceptive pills has a protective effect for ovarian cancer which has been proved beyond doubt . Risk of ovarian cancer reduced by about 50% with 5 year use and protection increases with duration of use (Hannikson et al) After cessation of use the effect last for around 15 years .

Hormone replacement therapy has minimal effect on ovarian cancer while in some have reported moderate increase in risk.

GENETIC SUSCEPTIBILITY:

Ovarian cancer tends to aggravate in families and such cancers tend to occur in younger age. Inheritance has a significant role in about 5% epithelial ovarian cancer, and they are usually serous adenocarcinoma.

BRCA1, BRCA2 Mutations are implicated in 5-10% of malignant ovarian tumors., They also have an increased risk for lynch syndrome (colon, endometrium, ovarian cancer). Women with an inherited BRCA1 gene has 66% risk of breast cancer and 40-50% risk of ovarian cancer .With BRCA2 penetrance of breast cancer is 80% but for ovarian cancer penetrance is only 25% .With one affected family member, relative risk of ovarian cancer was found to be 3,and with 2 relative risk was found to be 7.

OTHER FACTORS:

DIETARY FACTORS: Case control studies in both China & Italy found that high intake of fat and meat are associated with ovarian cancer. In Italian study, it was found that red meat increase the risk by 50% while vegetables decreases it by 50%.

Use of talc powder in genital hygiene associated with 1.5 relative risk of ovarian Cancer.

PROTECTIVE FACTORS:

- Use of OCP pills
- Multiparity.
- Breast feeding
- Pregnancy
- Anovulation
- Tubal ligation
- Hysterectomy

HEREDITARY BREAST AND OVARIAN CANCER SYNDROMES:

Association between breast and ovarian cancer has been found

These usually present at an earlier age.

Associated with BRCA 1 and BRCA 2 mutation..

HEREDITARY NONPOLYPOSIS COLORECTAL CARCINOMA/ LYNCH SYNDROME:

Pattern of inheritance autosomal dominant.

Predisposition to colorectal cancer and other type of malignancy namely endometrial, gastric and ovarian carcinoma.

Due to germ line mismatch repair.

Familial carcinoma accounts for <10% of all ovarian carcinoma

RECOMMENDATION FOR HEREDITARY CANCER

- Genetic counseling is recommended for all women with personal or family history of breast cancer or ovarian cancer.

- Women who wish to preserve their reproductive capacity can undergo screening by transvaginal ultrasonography every 6 months or CA-125 measurement from 30 to 65yrs.

- Oral contraceptives should be recommended to young women before they embark an attempt to have a family

- For those who do not wish to maintain their fertility risk-reducing salpingo-oophorectomy is recommended at age 35 to 40 years for BRCA1 carriers , whereas women with BRCA2 may consider delaying until age 40 to 45 years because of later onset of ovarian cancer

- Women with HNPCC syndrome should undergo periodic colonoscopy, and endometrial biopsy.

WHO CLASSIFICATION OF OVARIAN TUMORS

I Epithelial tumors

1. Serous tumor
2. Mucinous tumor
3. Endometroid tumor
4. Clear cell tumor
5. Brenner tumor
6. Mixed epithelial tumors
7. Undifferentiated Carcinoma
8. Unclassified epithelial tumors.

II Germ cell tumors

1. Dysgerminoma
2. Endodermal sinus tumor
3. Embryonal carcinoma
4. Polyembroyoma
5. Choriocarcinoma
6. Teratoma
7. mixed forms

III Lipid (Lipoid) cell tumors

IV Sex cord (Stromal) tumors

1. Granulosa cell tumor

2. Theca cell tumor

3. Androblastomas: Sertoli leydig cell tumors

4. Gynandroblastomas

5. Unclassified.

V. Gonadoblastomas

1. Pure

2. Mixed with dysgerminoma or other germ cell tumors

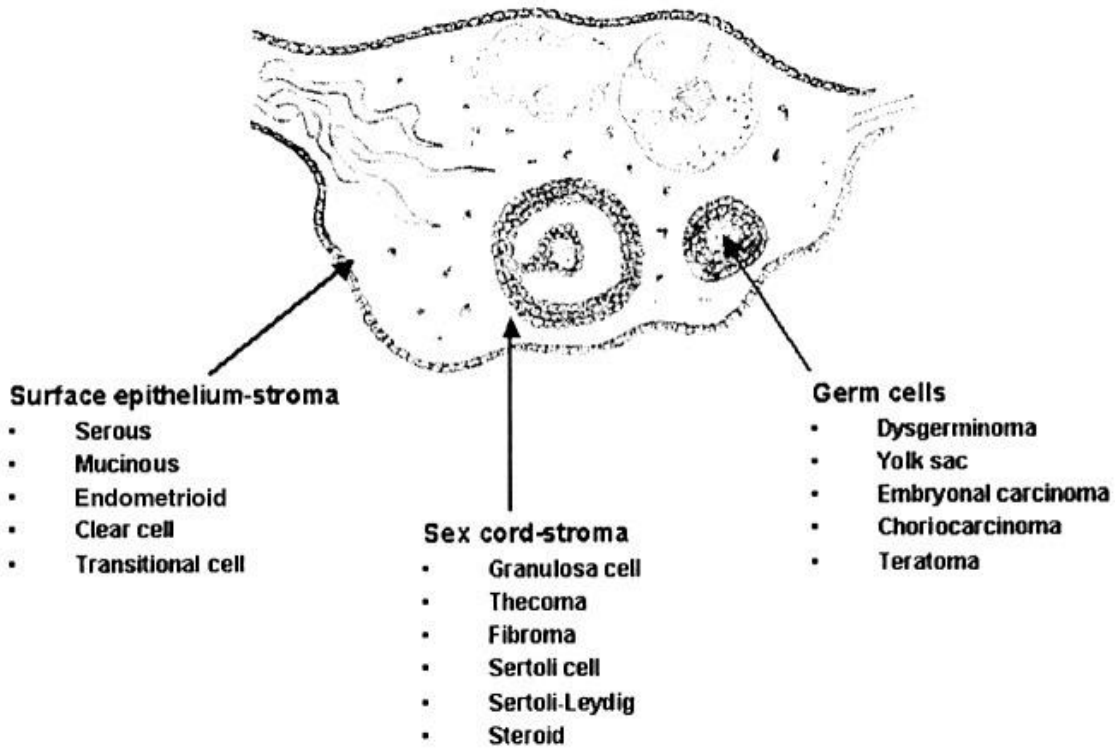
VI Soft tissue tumors not specific to ovary

VII Unclassified tumors

VIII Secondary (metastatic) tumors

IX Tumor like conditions

FIG3. CLASSIFICATION OF OVARIAN CARCINOMA



SEROUS TUMOR

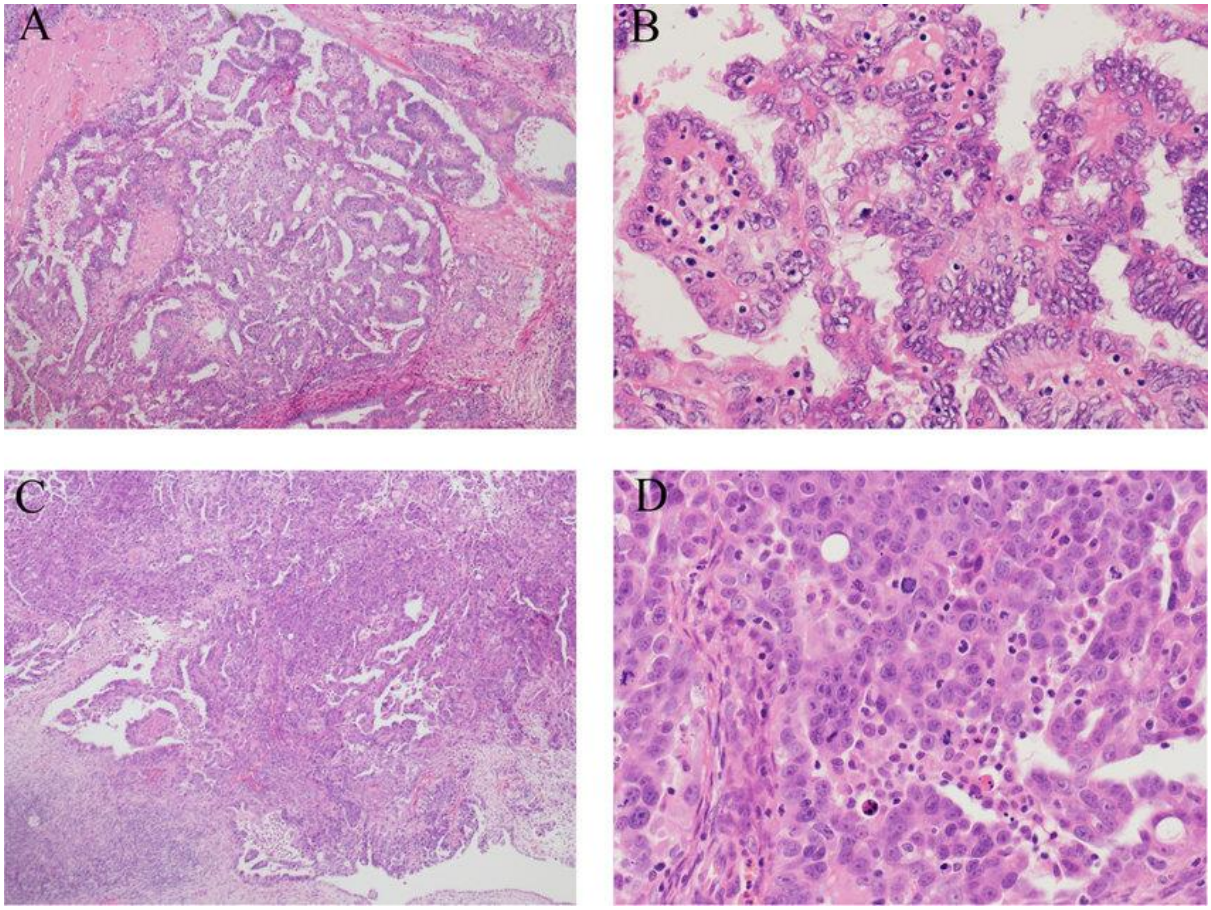
Serous tumors are the most common epithelial ovarian tumor. Benign serous tumors accounts for 60-70% , while malignant tumors form 20-25% and borderline constitute 15%.

Benign serous cystadenoma contain thin walled unilocular or multilocular cyst containing serous fluid. They account for 20% of ovarian tumors.

Serous epithelial cancer usually occurs at 60 to70 yrs .

Type 1 – low grade cancer due to KRAS mutation

Type 2 – rapid growing , aggressive tumors with p53 mutation



(a) and (B) low grade serous cancer

(C) and (D) high grade serous cancer

MUCINOUS TUMORS:

It is second most common after serous tumors. Usually unilateral , bilateral in 10% cases.

Mucinous cancer grow to a large size. Associated with pseudomyxoma peritonei.

The lining epithelium contain intracytoplasmic mucin

ENDOMETROID TUMORS:

They are formed by cells that resemble endometrial lining. Usually associated with endometriosis (15%), endometrial hyperplasia, or endometrial carcinoma (20%).

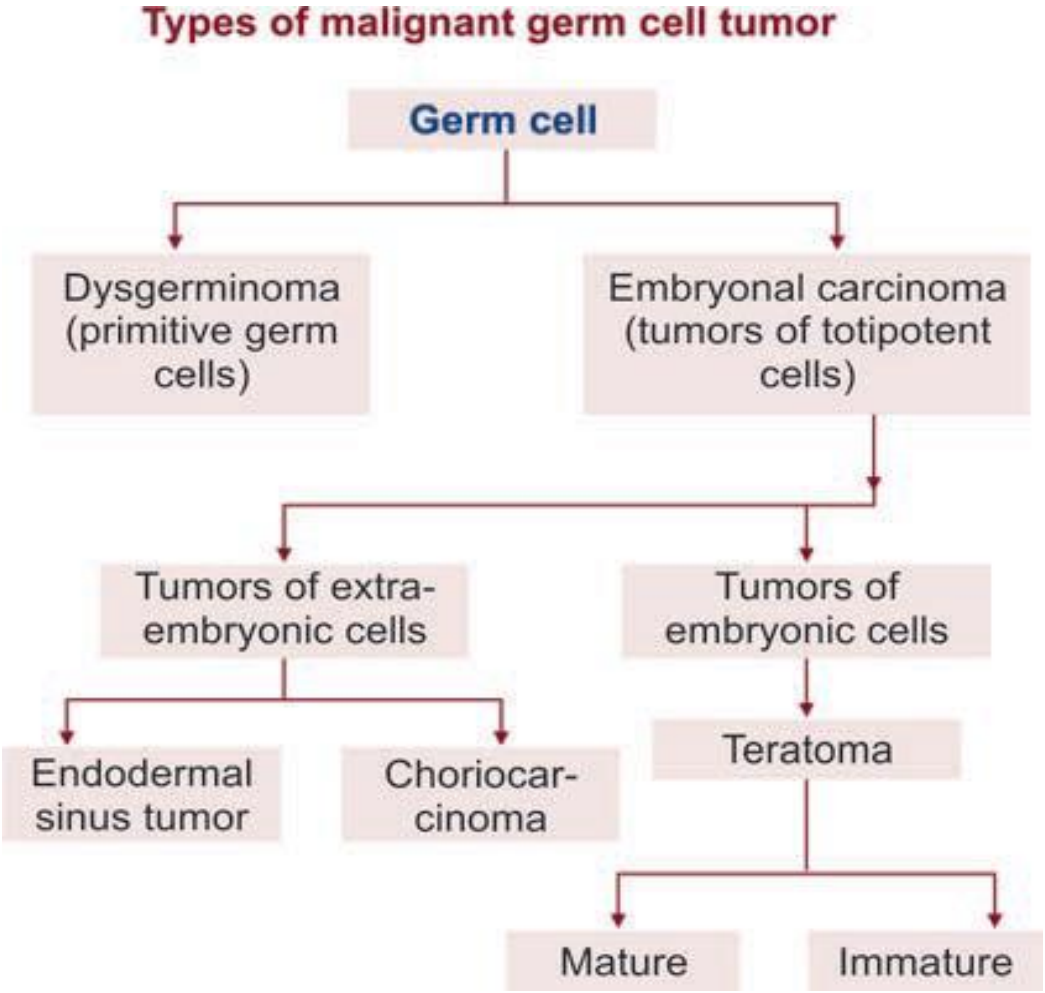
Both Benign and borderline tumors occurs mostly at 60yr .they have low malignant potential

Malignant tumors are predominantly solid and constitute 10-25% of all ovarian cancer.

CLEAR CELL TUMORS:

- It is associated with endometriosis
- Usually high grade tumors
- It is Chemo-resistant
- Histology shows hob nail cell

GERM CELL TUMORS:



- Unilateral tumors
- Age group : 10 to 20years
- Better prognosis

DYSGERMINOMA

- Most common malignant germ cell tumor
- Radio and chemosensitive
- It has good prognosis

- Tumor markers: LDH and placental alkaline phosphatase
- Management: conservative unilateral saplhingo oophorectomy.
- Residual disease treated with chemotherapy- BEP: bleomycin+ etoposide +cisplatin

ENDODERMAL SINUS TUMOR (YOLK SAC TUMOR)

- Rapidly growing. Highly malignant
- It has the worst prognosis
- Tumor markers: AFP, alpha 1 anti trypsin

EMBRYONAL CELL TUMOR:

- Very rare form of GCT
- They secrete estrogen and exhibit signs of precocious puberty and irregular bleeding. Tumor markers - AFP and HCG

CHORIOCARCINOMA:

- Ovarian choriocarcinoma, rare form, formed by placental elements.
- Usually solid and unilateral.
- Tumor marker : HCG
- They are invasive locally , and metastasis early.
- Gestational choriocarcinoma spreads through blood stream while non gestational tumors by lymphatic system.

SEX CORD STROMAL TUMORS:

Least common of all ovarian tumors

Mostly unilateral

ESTROGEN SECRETING TUMOR	**ANDROBLASTOMA**
Granulosa cell tumor	Sertoli cell Tumor
Thecoma	Sertoli and Leydig cell tumor
Fibroma	Leydig cell tumor

GRANULOSA CELL TUMOR:

- Age : occurs at any age
- Always unilateral
- Histology : coffee bean nucleus and call exner bodies
- Metastasis : first involves opposite ovary followed by lumbar region
- Associated with endometrial hyperplasia
- Tumor marker: Inhibin B

THECA CELL TUMOR:

- They resemble theca cells that surrounds the ovarian follicles.
- Usually unilateral, occur in postmenopausal women
- Presents with postmenopausal bleeding, endometrial cancer, endometrial hyperplasia.
- Most of them are benign and surgery is curative.

ARRHENOBLASTOMA:

- Androgen secreting tumors
- Show features of defeminization — atrophy of the breasts and uterus and amenorrhea followed by masculinization (50**%)**
- They may develop cliteromegaly, hirsutism, and finally with breakup of voice.
- Unilateral with high malignant potential.
- HPE shows seminiferous tubules.
- Elevated testosterone levels are seen

GYNANDROBLASTOMA:

- Gynandroblastoma, is a rare, benign tumor with combination of both granulosa cell tumor and arrhenoblastoma.

KRUKENBERG TUMOR:

- These are metastatic ovarian tumors. Primary is usually from stomach and colon.
- Tumor arise by retrograde lymphatic spread.
- Bilateral with smooth surface
- Ovarian capsule is intact and shape is retained.
- Histology : signet ring cells in the background of myxomatous stroma

PATTERNS OF SPREAD:

<table>
<tr><th>TRANSCOELOMIC</th><th>LYMPHATIC</th><th>HEMATOGENOUS</th></tr>
<tr><td>Most Common Route. spread to:</td><td>Para Aortic Lymph Node</td><td rowspan="6">Liver and Lungs</td></tr>
<tr><td>Posterior Culde Sac</td><td rowspan="5">Pelvic Lymph Node</td></tr>
<tr><td>Paracolic gutter</td></tr>
<tr><td>Hemidiaphragm</td></tr>
<tr><td>Mesentries</td></tr>
<tr><td>Omentum</td></tr>
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CLINICAL FEATURES:

Ovarian tumors have no specific presentation.

1. Abdominal distension and discomfort
2. Dyspepsia
3. Abdominal mass
4. Post menopausal bleed

SIGNS OF ADVANCED TUMORS:

1. Loss of weight
2. Loss of appetite
3. Cachexia
4. Fatigue.

SIGNS:

General examination:

- Cachexia and pallor
- Jaundice
- Edema of legs
- Left supraclavicular LN enlargement

Abdominal examination:

- Liver enlarged and nodular
- Mass in the hypogastrium

Per vaginal examination:

- Uterus can be separated from the mass felt per abdomen
- Nodules felt in posterior fornix.

Most of the clinical features are non specific, thus patients presented at an advanced stage. Late diagnosis and early metastasis to other organs are responsible for the poor patient survival. No satisfactory screening method has been developed yet.

80% of the ovarian cancers are epithelial origin and 80% of them are diagnosed only at stage III or IV [10]. The discrimination between benign and malignant ovarian mass is very important for proper management.

CA 125

Also called as Cancer Antigen 125. High molecular weight glycoprotein which is raised in approximately 90% of patients with advanced epithelial ovarian cancer . CA125 is expressed by fetal amniotic, coelomic epithelium, mesothelial cells and Mullerian (tubal, endometrial, and endocervical) epithelium. Therefore they are not specific.

CA125 values less than 35 is considered as normal. This is based on the distribution of values in healthy subjects, where 99% of 888 men and women were found to have levels below 35 kU/L [13,14]. However, CA125 values can show wide variation. The values are influenced by age, race, menstrual cycle, pregnancy, hysterectomy, and other benign conditions. In a postmenopausal patient with CA-125 level >200 U/mL, there is a 96% positive predictive value for malignancy[15,16]. But in premenopausal patients, the specificity is low because raised CA125 is seen in other benign conditions also

Conditions where CA 125 level is elevated:

1. Endometriosis,
2. Fibroid uterus
3. Menstruation
4. Ectopic pregnancy

5. Pelvic inflammatory disease
6. Pregnancy
7. Peritonitis
8. Peritoneal TB
9. Cardiac failure
10. Liver disease
11. Diverticulitis

They have a strong association with serous type of ovarian tumor rather than mucinous. CA-125 is useful for monitoring epithelial ovarian cancer patients during their chemotherapy; Raised levels were found in more than 90% of patients with advanced stage while only 50% of patients with stage I disease[17]

It is used to monitor the disease recurrence. This is based on doubling of CA125 from the upper limit of normal in those patients where the level normalized with treatment.

Various studies confirmed the usefulness of CA125 in detecting epithelial ovarian tumor.

Guppy et al [18] in his study suggested serial changes in CA125 can be used as a reliable indicator of disease response or progression. Based on which patients are classified as responders or progressing disease.

According to Verheijen et al[19], although CA 125 has a limited role in early diagnosis of ovarian cancer, they play an important role in monitoring response to chemotherapy. Unfortunately, a few studies show inadequate sensitivity of CA125 in detecting early ovarian malignancy.

Helzlsouier et al study indicated measurement of serum CA-125 levels, particularly at a reference value of 35 U/mL, is not sufficiently sensitive to be used alone as a screening test for the detection of ovarian cancer.

Steven J skates et al[20] conducted a study to assess the risk of ovarian cancer using serial CA125 compared with a fixed CA125 cut off. His results were, the risk assessment achieved a sensitivity of 86% for preclinical detection of ovarian cancer, whereas CA-125 achieved a sensitivity of 62%.

Various other tumor markers used for screening ovarian cancer are HE4, CA 19-9, CA 15-3, lipid associated sialic acid, osteopontin etc.[22-25]

USG:

A careful physical examination along with imaging techniques helps in the diagnosis. It is used to characterize the features of the mass and the likelihood of benign or malignant. Ultrasound is useful in screening, diagnosis and treatment follow up[26,27]

USG features of malignancy

1. Multiloculation

2. Ovarian volume >10cm3

3. Bilaterality

4. Septal thickness >2mm

5. Cyst wall with >3mm thickness

6. Presence of solid components

7. Papillary excrescences

8. Increased vascularity

9. Doppler resistance index less than 0.40 (RI < 0.40)

10. Presence of ascites

11. Presence of metastasis.

Ultrasound has high sensitivity in diagnosing early ovarian tumor while the specificity remains low.

The risk of malignancy in case of a simple unilocular cyst of size < 5 cm is low, is < 1% in premenopausal women and 1.6% in postmenopausal women

Based on the consensus by the society of radiologist in ultrasound, asymptomatic simple cyst of size <5cm in premenopausal women and size <1cm in postmenopausal women requires no surveillance

Sassone et al[30] devised a scoring system to distinguish benign and malignant masses, with a specificity of 83%, sensitivity of 100%, and positive and negative predictive values of 37 and 100%, respectively. It was based on four variables such as inner wall structure, wall thickness, septum and echogenicity. Each variable has a corresponding value and a total score of > 9 suggest malignancy.

Assessment of Different NEoplasia in the AdneXa (ADNEX) model a scoring program generated by the International Ovarian Tumor Analysis (IOTA) group[28,29]. It contains three clinical and six ultrasound predictors.

Clinical parameters: age, serum CA-125 level, type of center (oncology center vs other hospitals). Ultrasound predictors maximum diameter of lesion, proportion of solid tissue, more than 10 cysts locules, number of papillary projections, acoustic shadows and ascites. Once all the parameters is assessed the application will analyze the chances of benign and malignancy.

According to Poonyakanok et al[31] , the performance of ADNEX model at a 10% cutoff, the sensitivity was 98.4% and specificity was 87.2%.

Mallari et al in 2017 compared the diagnostic accuracy of SASSONE Scoring and ADNEX Model in differentiating benign and malignant ovarian neoplasm. They concluded there was no significant difference in using SASSONE and ADNEX model . However, in cases of suspicious tumors, ADNEX model is more useful in discriminating the type and stage of malignancy.

The limiting factor for early diagnosis of ovarian tumor is lack of standardized terms and procedures in gynecological sonography. A standardized technique for preoperative classification of adnexal masses was defined by IOTA group. Ovarian tumors were classified based on benign and malignant features.

BENIGN (B) FEATURES:

1. Unilocular cyst
2. Presence of solid components with largest diameter<7mm
3. Presence of acoustic shadow.
4. No blood flow
5. Smooth multilocular with largest diameter <10cm.

MALIGNANT (M) FEATURES:

1. Irregular solid tumor
2. Presence of ascites

3. At least four papillary structures
4. Irregular multilocular solid tumor diameter >10cm
5. Very strong blood flow

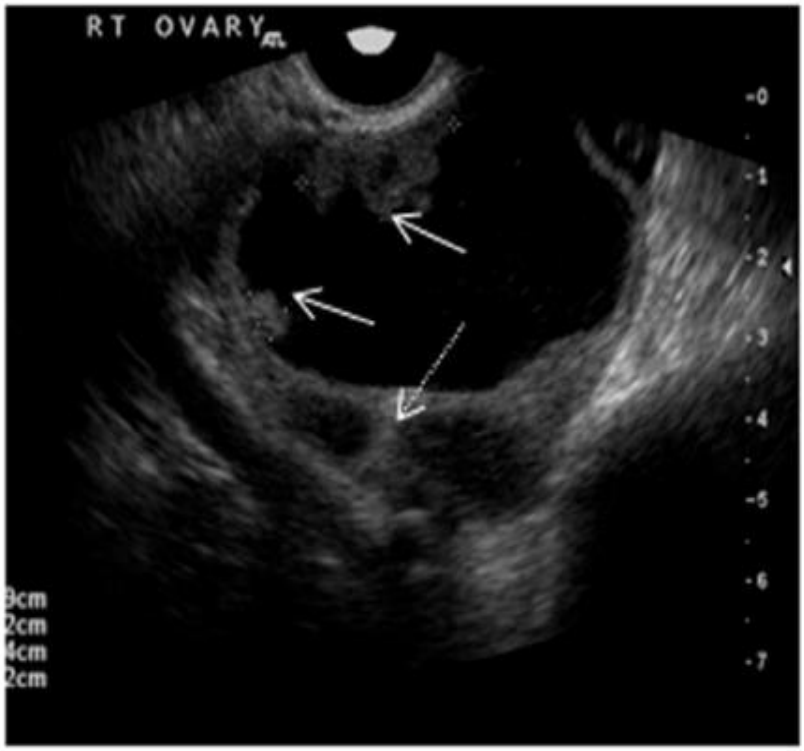
Simple rules were made to discriminate benign and malignancy.

Rule 1:If one or more M features are present in absence of B feature(s), the mass is classified as malignant.

Rule 2: If one or more B features are present in absence of M feature(s), the mass is classified as benign.

Rule 3: If both M features and B features are present, or if no B or M features are present, the result is inconclusive and a second stage test is recommended.

Fig 4. Ultrasound features of malignancy



Presence of papillary nodule and multiloculation

RMI

When used alone, the diagnostic accuracy of demographics, ultrasound (US), and biochemical markers are inadequate. The risk-of-malignancy index (RMI) is a combined parameter based on menopausal status, ultrasound findings, and the serum CA 125 level. It has given significantly better results than the use of a single parameter.The RMI is the product of the imaging scores (*U*), the menopausal score (*M*), and the absolute value of the serum CA 125:

RMI=U×M×CA125

Jacobs et al[32] originated the concept of Risk of Malignancy Index (RMI) in 1990 and it is known as RMI1 .

RMI 1 = $U \times M \times$ CA-125

O abnormality in ultrasound, U =0

1 abnormality in ultrasound, *U*=1

≥2 abnormality in ultrasound, *U*=3;

Premenopausal *M*=1

Postmenopausal *M*=3.

The serum level of CA-125 was applied directly to the calculation .

RMI 1 had a sensitivity of 85.4% and a specificity of 96.9% when using a cut-off level of 200 to indicate malignancy. The main advantage RMI compared with other methods such as color Doppler ultrasonography, or the use of

different tumor markers, is that RMI can be used easily in less-specialized centers.

Tingulstad et al.[33] developed their own model of the RMI in 1996 and it is termed RMI 2. Then this was modified and named as RMI 3 in 1999. The difference between the indices lies in the different scoring of ultrasound score (U) and menopausal status (M).

RMI 2 = $U \times M \times$ CA-125

O or 1 abnormality in US, U =1

≥2 abnormality in US, *U* =4;

Premenopausal *M*=1

Postmenopausal *M*=4.

The serum level of CA-125 was applied directly to the calculation

Tingulstad et al studies showed that the RMI was more accurate than any individual criterion in diagnosing ovarian cancer. Using a RMI cutoff level of 200 to indicate malignancy, the RMI has sensitivity of 80%, specificity of 92% and positive predictive value of 83%. Many other studies also showed similar evidence[34,35]

RMI 3 = $U \times M \times$ CA-125

O or 1 abnormality in ultrasound, U =1

≥2 abnormality in ultrasound, *U* =3;

Premenopausal *M*=1

Postmenopausal *M*=3.

The serum level of CA-125 was applied directly to the calculation

Tingulstad et al while applying RMI 3 criteria found sensitivity and specificity to malignancy were 71% and 92%, respectively.

RMI 4

RMI 4 = *U* × *M* × S × CA-125

O or 1 abnormality in US, U =1

≥2 abnormality in US, *U* =4;

Premenopausal *M*=1

Postmenopausal *M*=4.

Tumor size <7cm = 1

Tumor size >7cm = 2

The serum level of CA-125 was applied directly to the calculation

Yamamoto et al[36] reported RMI 4 sensitivity and specificity of 75% and 91%, respectively, using a cut-off of 450.

	Ultrasound Score (U)	Menopausal Score (M)	Tumor Size (S), cm
RMI I = U × M × CA-125	U = 0 (0 parameter)	M = 1 (premenopausal)	Not applicable
	U = 1 (1 parameter)	M = 3 (postmenopausal)	
	U = 3 (≥2 parameters)		
RMI II = U × M × CA-125	U = 1 (0 or 1 parameter)	M = 1 (pre-menopausal)	Not applicable
	U = 4 (≥2 parameters)	M = 4 (postmenopausal)	
RMIIII = U × M × CA-125	U = 1 (0 or 1 parameter)	M = 1 (premenopausal)	Not applicable
	U = 3 (≥2 parameters)	M = 3 (postmenopausal)	
RMI IV = U × M × S × CA-125	U = 1 (0 or 1 parameter)	M = 1 (premenopausal)	S = 1 (< 7)
	U = 4 (≥2 parameters)	M = 4 (postmenopausal)	S = 2 (≥7)

According to Javdekar Rujuta[37] RMI 2 had a sensitivity of 70.5 %, a specificity of 87.8 %, a positive predictive value of 70.5 %, and negative predictive value of 87.8 %. Menopausal status had sensitivity of 41.1 % ,specificity of 58.5 %, positive predictive value of 29.1 %, and negative predictive value of 70.5 %. Serum Ca-125 level had a sensitivity of 76.4 %, a specificity of 85.3 % . Ultrasound score had a sensitivity of 76.4 % , a specificity of 75.6 %, a positive predictive value of 56.5 %, and a negative predictive value of 88.5 %

Ulusoy et al evaluated 296 patients with ovarian mass. With the cutoff of 200 the sensitivity, specificity was, the positive predictive value and negative predictive value was found to be 71.7%, 80.5%, 67.3%, 83.6% respectively. In 2011 Milan Terzic et al conducted a study involving 81 patients out of which 51 had benign tumors and 30 had malignant ovarian tumors.With RMI 200, the sensitivity, specificity, positive predictive value and negative predictive value was found to be 83.33%,94.12%, 89.29%, and 90.57% respectively.

According to Khawla al Mushali[38] et al both CA-125 and RMI have good validity in the diagnosis of ovarian tumors. CA-125 has higher sensitivity; however, RMI has higher specificity. In combination, CA-125 might be more valid for the diagnosis of malignant ovarian cancer while RMI is more valid for excluding the diagnosis of the tumor

A study by Radhamani[39] showed the incidence of ovarian masses was 93% with the majority (84%) being benign. When both clinical and ultrasound diagnosis were combined, the overall sensitivity, specificity, positive and negative predictive value for diagnosis and discriminating benign and malignant ovarian neoplasms were 87.5%, 96.7%, 70%, and 98.88%, respectively. Their combined accuracy was 96%. Ca-125 as a laboratory test

showed a sensitivity of 62.5% and specificity of 84.25%. RMI <200 showed a sensitivity of 62.5% and specificity of 95.65%.

Obediat et al[40] suggested using a cut-off level of 200 to indicate malignancy, the RMI gave a sensitivity of 90%, specificity of 89%, positive predictive value of 96%, and negative predictive value of 78%

Gany et al suggested each of the RMIs have a different optimal threshold, however using a threshold of 200, RMI 1 had a sensitivity of 66% and a specificity of 91%; RMI 2 had a sensitivity of 74% and a specificity of 79%; and RMI 3 had a sensitivity of 68% and a specificity of 85%

Sarah Waleed Hashim et al studies showed the incidence of ovarian cancer is mainly at age group of ≥50 years. Nulliparity and family history is considered as a risk factor for the development of ovarian cancer . The use of oral contraceptive pills is a protective factor against the development of ovarian cancer. Most of the cases presented in advanced stage at time of diagnosis. Epithelial tumors comprise the most common type.

A study by Rojna Rai[41] et al found Adnexal masses of ovarian origin were most common (*n* = 102, 80.3%), of which 12.7% were malignant. Epithelial ovarian malignancy was the most common malignant ovarian tumor, serous

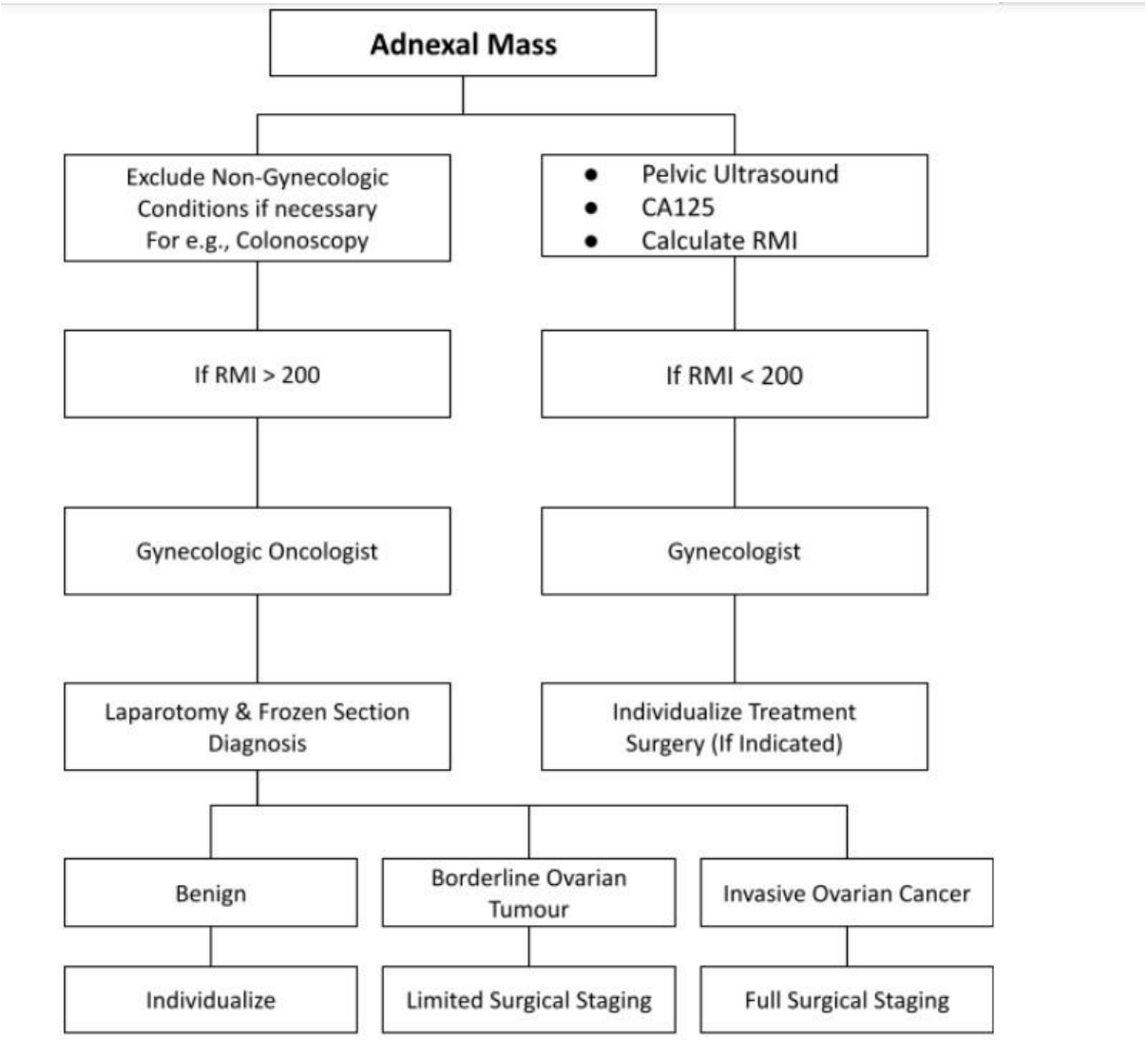
cystadenocarcinoma being the most common. Malignancy was significantly more in older, postmenopausal women with high RMI. Seven out of 11 women with high RMI were diagnosed in Stage 3 or 4. RMI score at cutoff of 200 was 54.6% sensitive and 85.7% specific.

A.B. Pande[42] et al studied with a cut-off point of 236 for RMI was considered which showed a very high sensitivity (72.5%), specificity (98.2%), positive predictive value (98.1%), negative predictive value (74.7%) and diagnostic accuracy (84.13%) for discriminating malignant and benign pelvic masses.

Manjunath[43] et al study confirms that the malignancy risk index is more accurate than the menopausal status, serum CA 125 levels, and ultrasound features separately in diagnosing malignancy. There was no statistically significant difference in the performance of these three different malignancy risk indices in identifying malignancy

Dar sajjid et al studied the demography which showed the mean age of patients was 45±1. years. Most common age group of our patients at presentation was 46-60 years. Majority of patients 70% in our study were from rural area. The major clinical presentation of ovarian in our study was pelvic pain (36%) followed by abdominal distention (34%) and ascites (22%).

According to Velusamy Arul et al ,RMI with a cut-off 150 had sensitivity of 84% and specificity of 97% in detecting ovarian cancer. CA-125>30 had a sensitivity of 84% and a specificity of 83%. An ultrasound score more than 2 had a sensitivity of 96% and specificity of 81%



FIGO staging of the ovary cancer	STAGE	DESCRIPTION
	I	Tumor confined to ovaries or fallopian tube(s)
	IA	Tumor limited to 1 ovary (capsule intact) or fallopian tube; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings
	IB	Tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings
	IC	Tumor limited to 1 or both ovaries or fallopian tubes, with any of the following
	IC1	Surgical spill
	IC2	Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface
	IC3	Malignant cells in the ascites or peritoneal washings
	II	Tumor involves 1 or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or peritoneal cancer
	IIA	Extension and/or implants on uterus and/or fallopian tubes and/or ovaries
	IIB	Extension to other pelvic intraperitoneal tissues
	III	Tumor involves 1 or both ovaries or fallopian tubes, or peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes
	IIIA	Positive retroperitoneal lymph nodes only (cytologically or histologically proven)
	IIIA1(i)	Metastasis up to 10 mm in greatest dimension
	IIIA1(ii)	Metastasis more than 10 mm in greatest dimension
	IIIA2	Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes
	IIIB	Macroscopic peritoneal metastasis beyond the pelvis up to 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes
	IIIC	Macroscopic peritoneal metastasis beyond the pelvis more than 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ)
	IV	Distant metastasis excluding peritoneal metastases
	IVA	Pleural effusion with positive cytology
	IVB	Parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

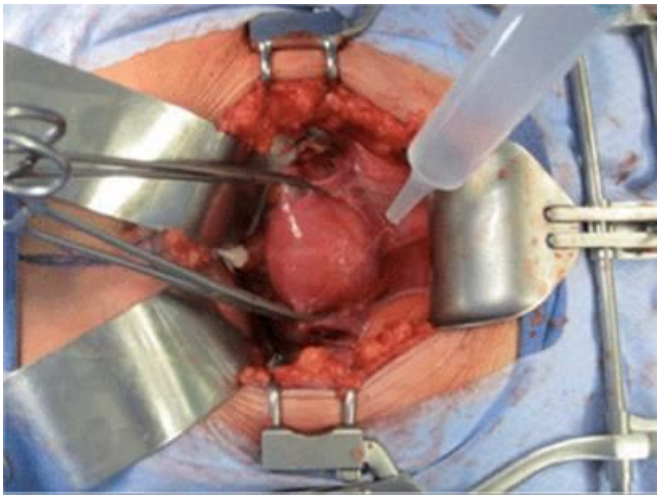
FIGO STAGING OF OVARIAN CANCER

MANAGEMENT

TECHNIQUES FOR SURGICAL STAGING

- A midline incision is advised as it allows adequate access to the abdomen.
- Any free fluid in the pelvic cul-de-sac, should be sent for cytology
- If no free fluid is present, peritoneal wash is done by injecting 50 to 100ml of saline into pelvis, each paracolic gutter, beneath the diaphragm and the same collected

Fig 5.PERITONEAL WASH:



- Systematic exploration of all the intra-abdominal surfaces and viscera done as follows:

Caecum

↓

Paracolic gutter

‘

↓

Ascending colon

↓

Right kidney, liver and gall bladder

↓

Transverse colon

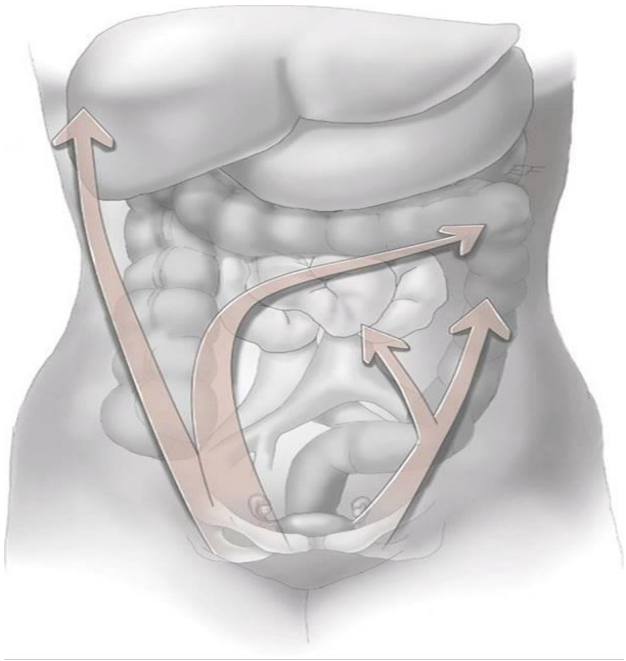
↓

Left hemidipharagm

↓

Descending colon to rectosigmoid colon

Fig 6.ABDOMINAL EXPLORATION IN A STEPWISE MANNNER



- Biopsy to be taken at any suspicious areas or adhesions on the peritoneal surface
- The omentum should be resected from the transverse colon and sent for pathology.
- The retroperitoneal spaces to be examined for pelvic and para aortic lymph nodes

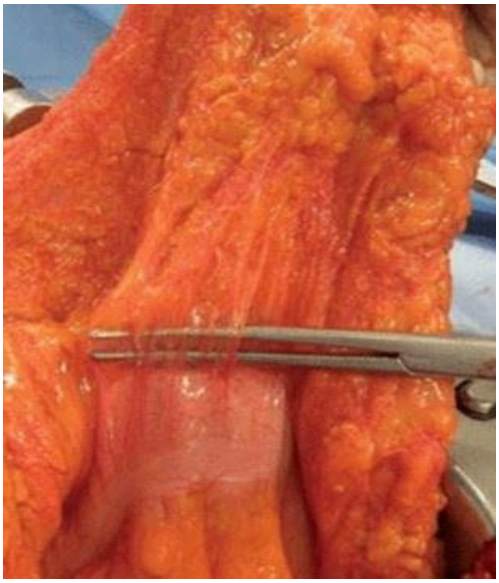


Fig 7.INFRACOLIC OMENECTOMY

PROGNOSTIC VARIABLES IN EARLY STAGE OVARIAN CANCER

LOW RISK	HIGH RISK
Low grade	High grade
No surface excrescence	Surface projections
No ascites	Presence of ascites
Intact capsule	Tumor invades the capsule
No peritoneal cytologic findings	Malignant cells +
Unruptured or intraoperative rupture	preoperative rupture
No dense adherence	Dense adherence

SURGICAL TREATMENT OF OVARIAN CANCER:

Surgery is the keystone in the primary treatment of ovarian malignancy

STAGE 1 LOW RISK

After a thorough surgical staging and confirming no spread beyond ovary, abdominal hysterectomy and bilateral salpingo-oophorectomy are appropriate therapy. In women with stage IA, grade 1 to 2 disease who desire to preserve fertility, uterus and contra lateral ovary can be preserved

STAGE 1 HIGH RISK

Patients with poorly differentiated disease or those with malignant cells either in ascites fluid or in peritoneal washings, must undergo complete surgical staging

ADVANCED STAGE OVARIAN CANCER:

Exploratory Laparotomy

↓

Cytoreductive or debulking surgery

This includes :

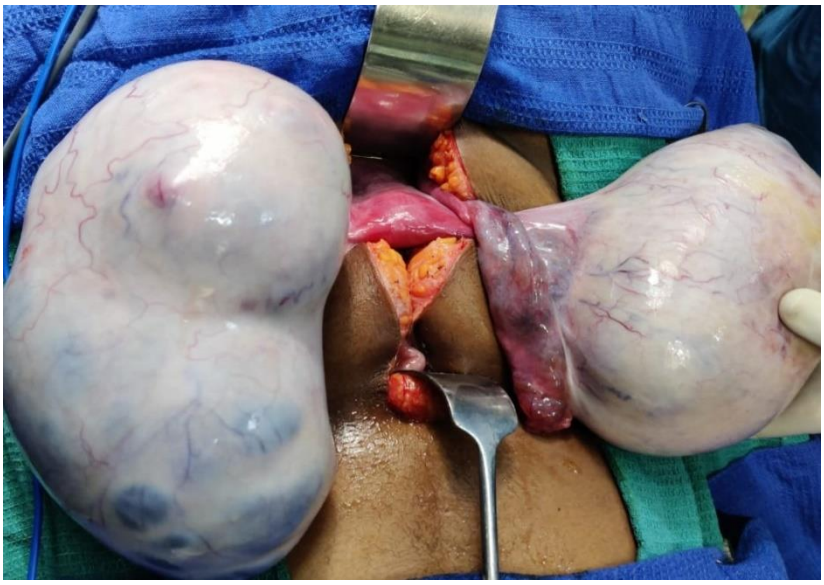
- Total abdominal hysterectomy
- Bilateral salpingo-oophorectomy
- Complete omentectomy
- Retro-peritoneal lymph node sampling
- Resection of any metastatic tumor

Optimum cytoreductive surgery[44-46] aims at reduction of the residual tumor load < 1–2 cm in diameter.

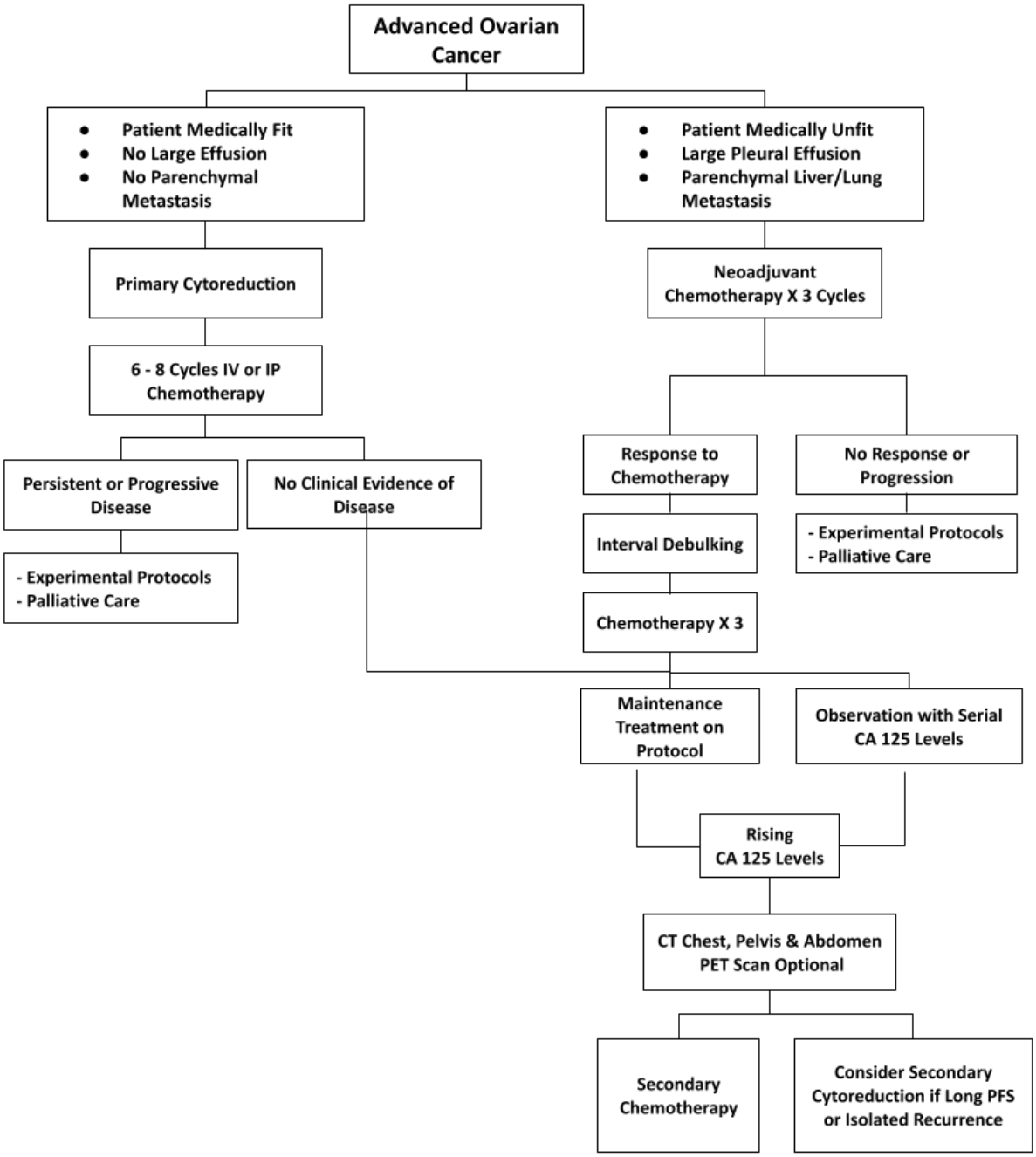
Maximum cytoreductive surgery includes resection of a segment of bowel, bladder or the lymph nodes. Removal of omental cake by debulking improves the outcome of subsequent chemotherapy or radiotherapy.

Large tumor masses have large number of poorly oxygenated cells in the "resting" phase which are resistant to any type of therapy. Lesser the residual tumor mass (< 5 mm) better the survival rate.

Fig 8.INTRA OPERATIVE PICTURE OF OVARIAN TUMOR



MANAGEMENT OF ADVANCED OVARIAN CANCER:



CHEMOTHERAPY

- Stage Ia (grade I) epithelial carcinoma: No adjuvant chemotherapy is required
- All other stage I epithelial cancer : Adjuvant chemotherapy with carboplatin and paclitaxel for six cycles is preferred

Advanced stage disease:

Chemotherapy is given following surgery to improve the patient outcome. Drugs are given for six cycles at 3-4 weekly interval

Combination chemotherapy: Paclitaxel and carboplatin are commonly used.

DRUGS (i.v)	DOSE (mg/m^2)	CYCLE	INTERVAL (weeks)
Cisplatin	75	6	3-4
Paclitaxel	135	6	3-4

COMBINED REGIMEN

DRUGS	CAP(mg/m^2)	CP (mg/m^2)
CYCLOPHOSPHAMIDE ©	500	700-1000
ADRIAMYCIN (A)	50	
CISPLATIN (P)	50	50- 100

Neoadjuvant chemotherapy and interval cytoreductive surgery:

Cytoreductive surgery done after few cycles of chemotherapy

Indications:

- Advanced stage ovarian cancer
- High risk for surgery
- Associated with co morbidities
- Predicted to be suboptimal resection.

ADVANTAGES

- Early clinical improvement.
- Reduced morbidity
- Optimum cytoreduction is possible.

PROGNOSTIC FACTORS :

It includes – pathological and clinical factors.

PATHOLOGICAL FACTORS:

- In general, histologic type is not of prognostic signifcance, with the exception of clear cell and mucinous carcinomas,which has the worst prognosis

- Due to heterogeneity of tumors and observation bias , the value of histology as an independent prognostic factor has not been established.

CLINICAL FACTORS

In patients with early stage ovarian cancer factors that determine the prognosis are substage, grade,age , histology subtype positive cytology, dense adherence and capsular rupture.

Prognostic factors depends on:

Surgical stage of the disease — worse beyond stage II.

Histological type — endometrioid tumor has got a higher survival rate than serous type because the former tumor is highly well-differentiated. „

Histological grade of the tumor — higher the grade, poorer the prognosis. „

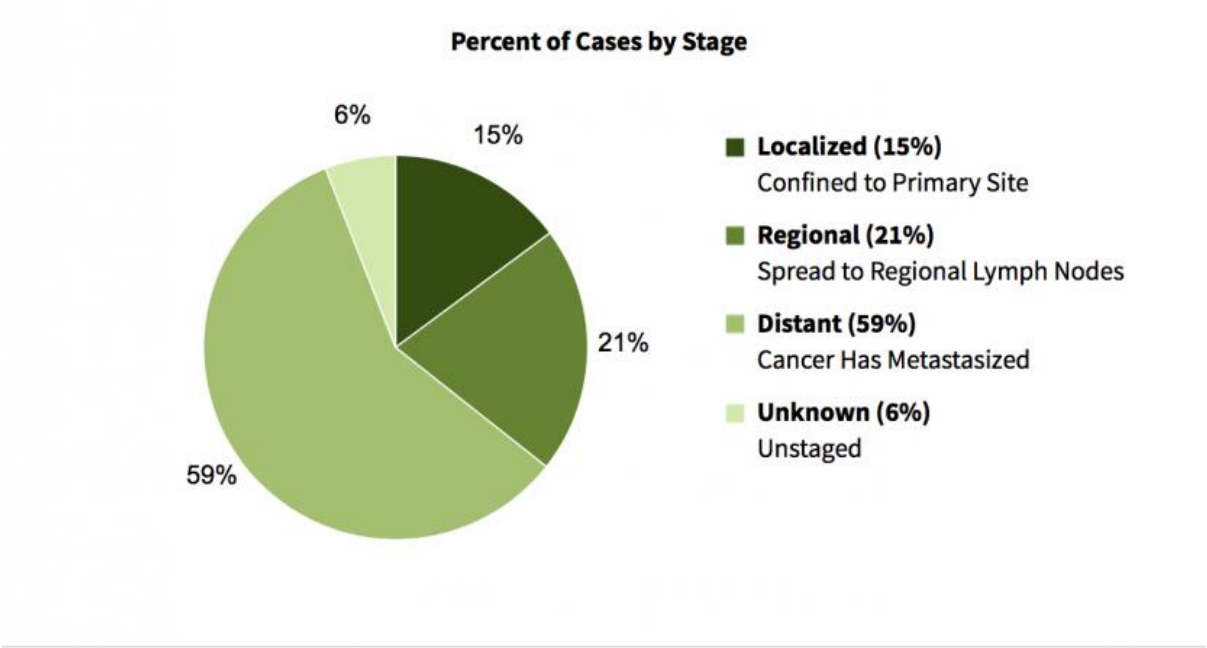
Peritoneal cytology — positive malignant cells, higher the risk.

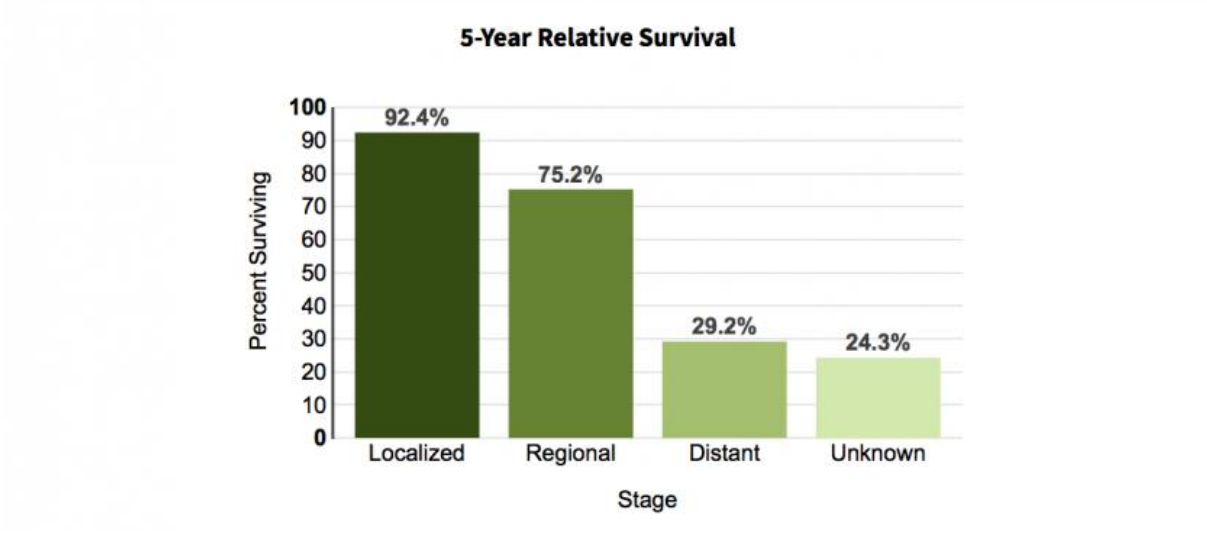
Presence of ascites — higher the risk.

Presence of metastatic disease before cytoreductive surgery — poor the prognosis and shorter the survival.

Volume of residual tumor after primary surgery — when < 5 mm better the prognosis. „

Ploidy status – diploid tumors are prognostically better compared to aneuploid tumors.





FIVE YEAR SURVIVAL RATE BY STAGE AT DIAGNOSIS

MATERIALS AND METHODS

This study was conducted in the Institute of Obstetrics and Gynecology and ISO KGH, Madras medical college, Chennai during the period of october 2020 to october 2021

Study design: Prospective study

Study population: The study consists of 120 patients who were admitted in our hospital with ovarian mass.

Inclusion criteria:

Patients with ovarian mass planned for surgical intervention

Exclusion criteria:

- Age <15yrs
- Pregnancy with adnexal mass
- Patients not willing for surgery
- Non operable ovarian mass.

The study was performed after Institutional ethical committee approval. The objective of the study was explained in detail and written consent was obtained from the patients included in the study.

At admission, detailed history including patient age, socioeconomic status, parity, body mass index , details of menstrual history, age at menarche and menopause, marital history, contraceptive history, family history, personal history was obtained. General, physical,systemic, pelvic examination was performed.

Ultrasound examination was performed using a 3.5-MHz abdominal convex transducer in patients with full bladder or 7.5-MHz vaginal probe in patients after empting the bladder. Ultrasound score was given for the following features:

1. Bilaterality
2. Multiloculations
3. Solid areas
4. Ascites
5. Metastasis

ULTRASOUND FEATURES	SCORING SYSTEM(U)
0 or 1 abnormality.	1
2 or more abnormality	4

5ml of venous blood will be collected for serum CA 125 estimation. Abnormal CA125 is defined as serum levels >35U/ml in postmenopausal women. CA 125 was determined by radioimmunoassay.

Menopausal score is M = 1 if premenopausal and M = 4 if postmenopausal.CA 125 levels will be substituted as such in the formula Menopausal status will be noted. Menopause is defined as one or more year of amenorrhea.

Once all parameters assessed RMI calculated using the formula

RMI : U * M * CA125

RMI is calculated. Histopathological diagnosis is considered as gold standard for defining the outcome.

RMI will be evaluated for sensitivity, specificity, positive predictive value and negative predictive ,with reference to actual presence of benign or malignant tumor.

STATISTICAL ANALYSIS:

Data were analyzed using chi-square tests. Descriptive statistics were used for demographic data and summarized as mean with standard deviation or frequency with percentage. Univariate analyses to determine the association of each parameter were performed using Student's t-test.

The independent association was then determined by logistic regression.The diagnostic performances of each test were reported as sensitivity, specificity, positive predictive value, and negative predictive value with 95% confidence interval.

RESULTS

The participants were recruited based on the inclusion and the exclusion criteria .The study participants were analysed based on the following headings

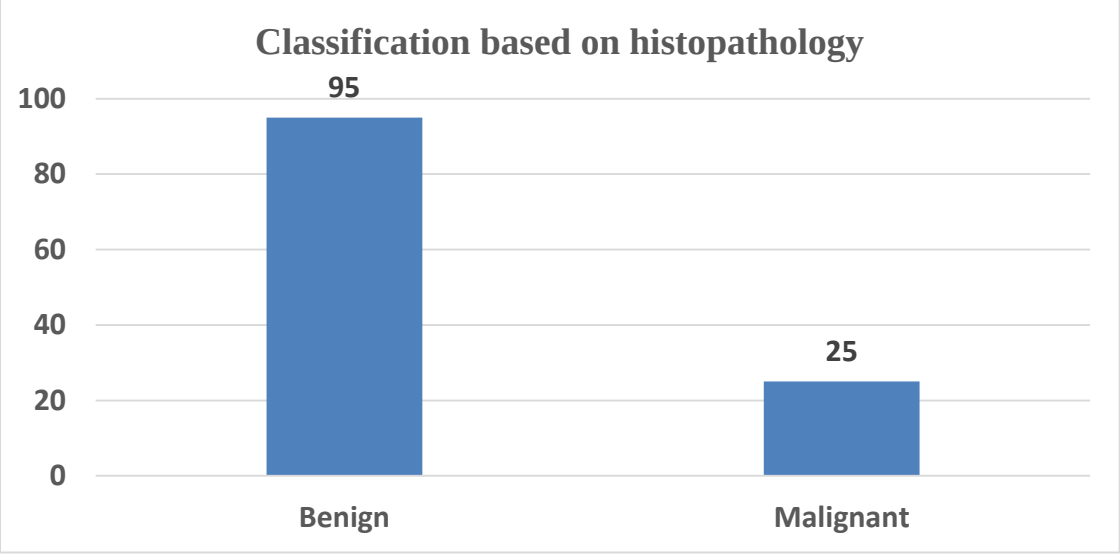
1.Baseline characteristics of the study participants

2.Based on the ovarian marker classification

3.Based of RMI

First the study participants were classified into two study groups based on their histopathological classification:

Figure 1:Classification of the ovarian mass based on the histopathology:



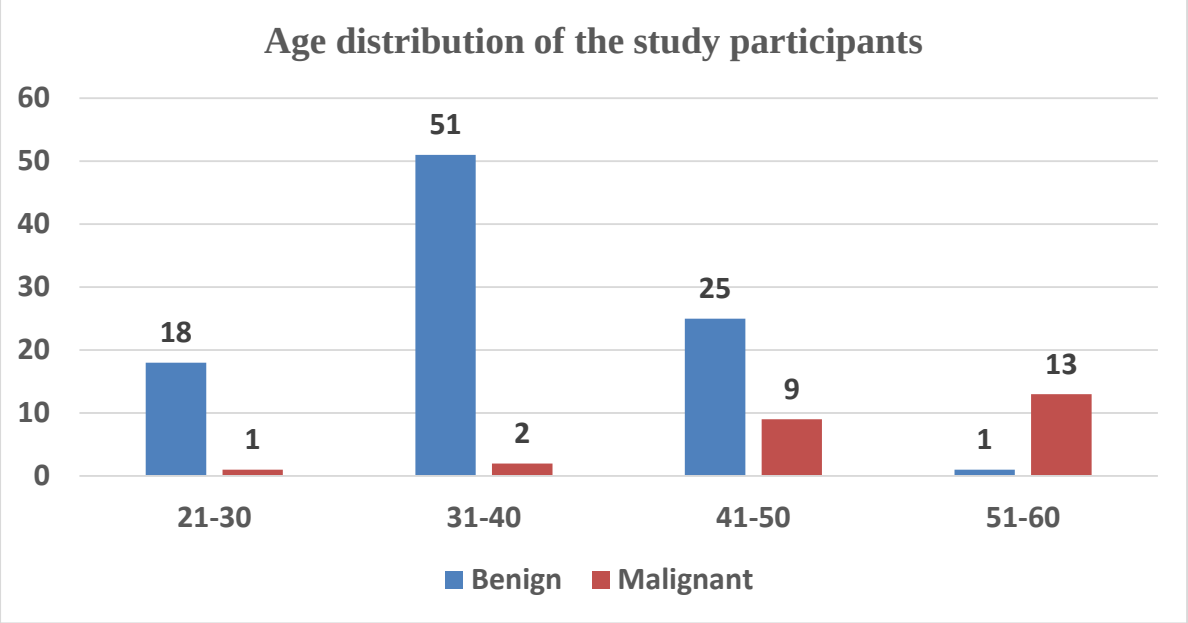
Majority of our study participants have benign type of ovarian tumor 95(79.2%) followed by the malignant 25(20.8%).

Table 1: Distribution according to the nature of tumor in HPE

Types of ovarian tumour	Number	Percentage
Benign	95	79.2%
Malignant	25	20.8%

About 21% had malignant lesions while majority 79% had benign pathology.

Figure2:Age distribution of the study participants:



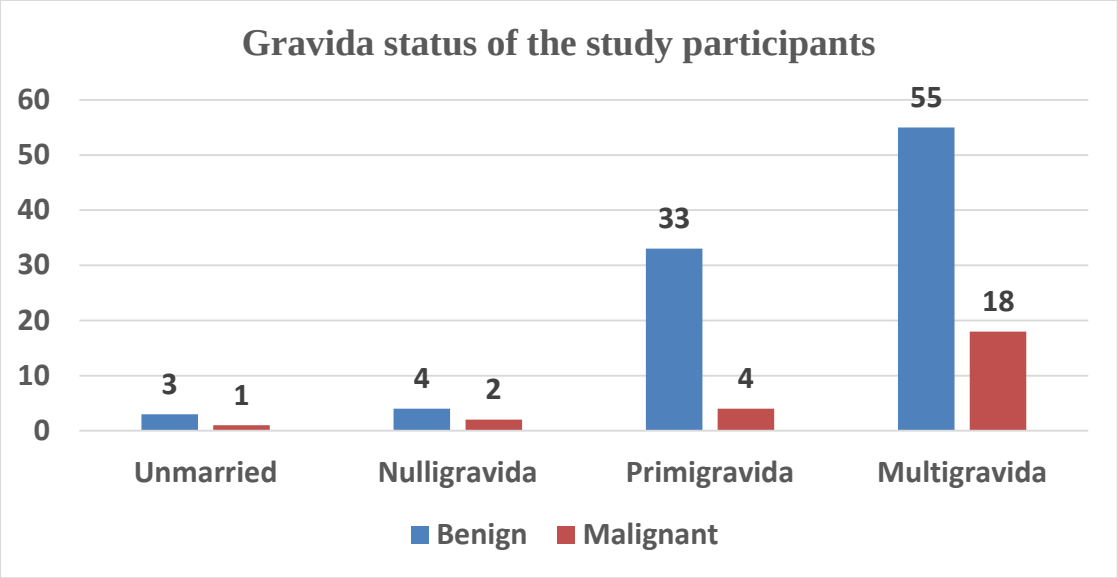
The mean age of the study participants in the benign type is 36.70±6.41 with minimum age of 23 and maximum age of 52.The mean age of the study participants in the malignant type is 48.28±7.32 with minimum age of 30 and maximum age of 58

Table 2:Distribution of age among the study participants

Age category	Benign	Malignant	P value
21-30	18(18.9%)	1(4%)	<0.00001
31-40	51(53.7%)	2(8%)	
41-50	25(26.3%)	9(36%)	
51-60	1(1.1%)	13(52%)	
Total	95(100%)	25(100%)	

In Benign type of tumors the most common age of distribution 31-40 years 51(53.7%) followed by the 41-50 years of age 25(26.3%).In malignant type of tumors the most common age group is 51-60 years 13(52%) followed by 41-50 years of age 9(36%).There is a difference between the age distribution in both the groups and the difference is found to be statistically significant.

Figure 3:Gravida status of the study participants



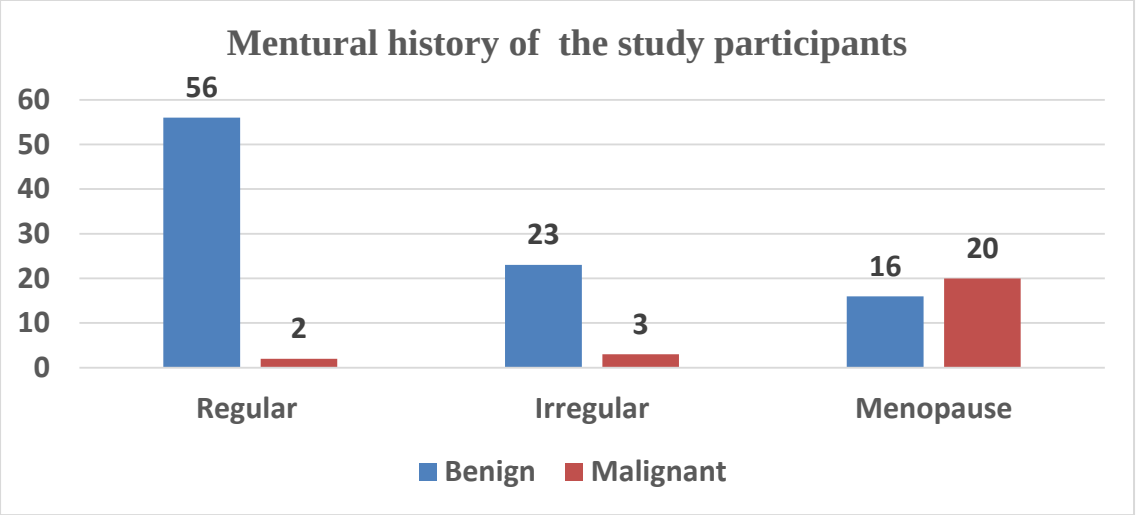
In our study participants the multigravida were more (Benign 55,Malignant -18) compared to primigravida (Benign-33 ,Malignant -4).

Table 3:Gravida status of the study participants

Gravida status	**Benign**	**Malignant**	**P value**
Unmarried	3(3.2%)	1(4%)	0.2
Nulligravida	4(4.2%)	2(8%)	
Primigravida	33(34.7%)	4(16%)	
Multigravida	55(57.9%)	18(72%)	
Total	95(100%)	25(100%)	

Among the study participants in benign type 3(3.2%) were unmarried and 4(4.2%) were nulligravida and in malignant type 1(4%) were nulligravida and 2(8%) were unmarried.

Figure 4:Menstrual history of the study participants:



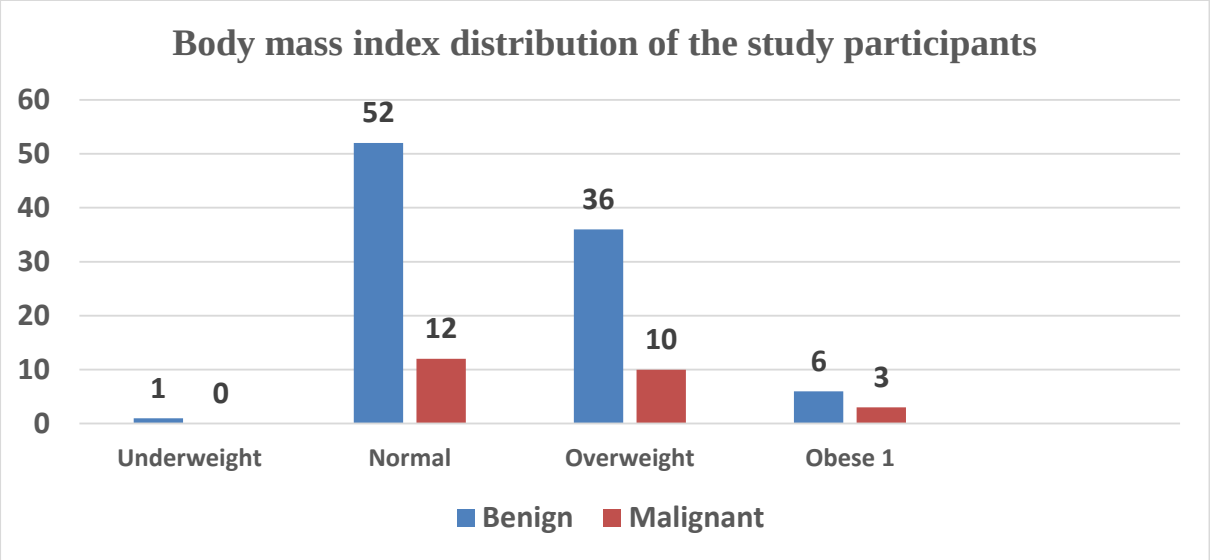
Among the study participants majority have a regular menstrual cycle (Benign - 56,Malignant -2)followed by irregular menstrual cycle(Benign -23,Malignant-3)

Table 4:History of menstrual cycle

menstrual pattern	**Benign**	**Malignant**	**P value**
Regular	56(59%)	2(8%)	**<0.0001**
Irregular	24(25%)	3(12%)	
Menopause	15(16%)	20(80%)	
Total	95(100%)	25(100%)	

In malignant group majority of the study participants had attained menopause 20(80%) where in benign type only 15(16%) attained menopause.There is a difference between these two groups and the difference is found to be not statistically significant**.**

Figure 5:Body mass index distribution of the study participants:



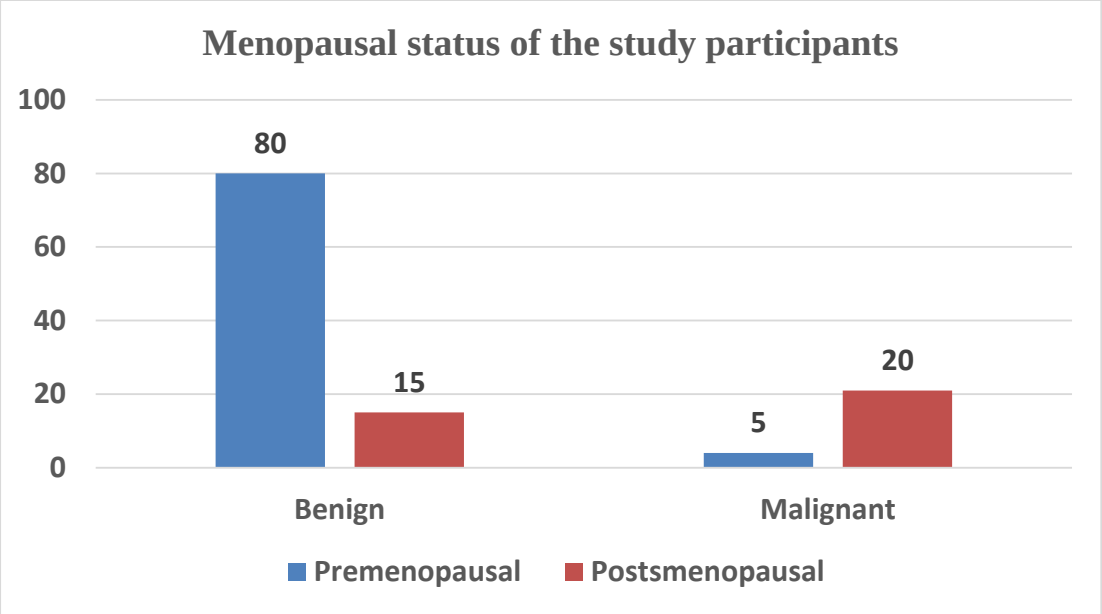
Majority of the study participants were have normal body mass index in both the groups(Benign -52,Malignant-12) followed by Overweight (Benign -36,Malignant-10)

Table 5:Body mass index distribution of the study participants:

Body mass index	**Benign**	**Malignant**	**P value**
Underweight	1(1.1%)	0	**0.27**
Normal	52(54.7%)	12(48%)	
Overweight	36(37.9%)	10(40%)	
Obese class	6(6.3%)	3(12%)	
Total	95(100%)	25(100%)	

In benign type both underweight 1(1.2%) and obese class 6(6.3%) were there in the study participants whereas in malignant only overweight 10(40%) and obese class 3(12%) were present.There is a difference between the body mass distribution but it is not statistically significant.

Figure 6:Menopausal status of the study participants:



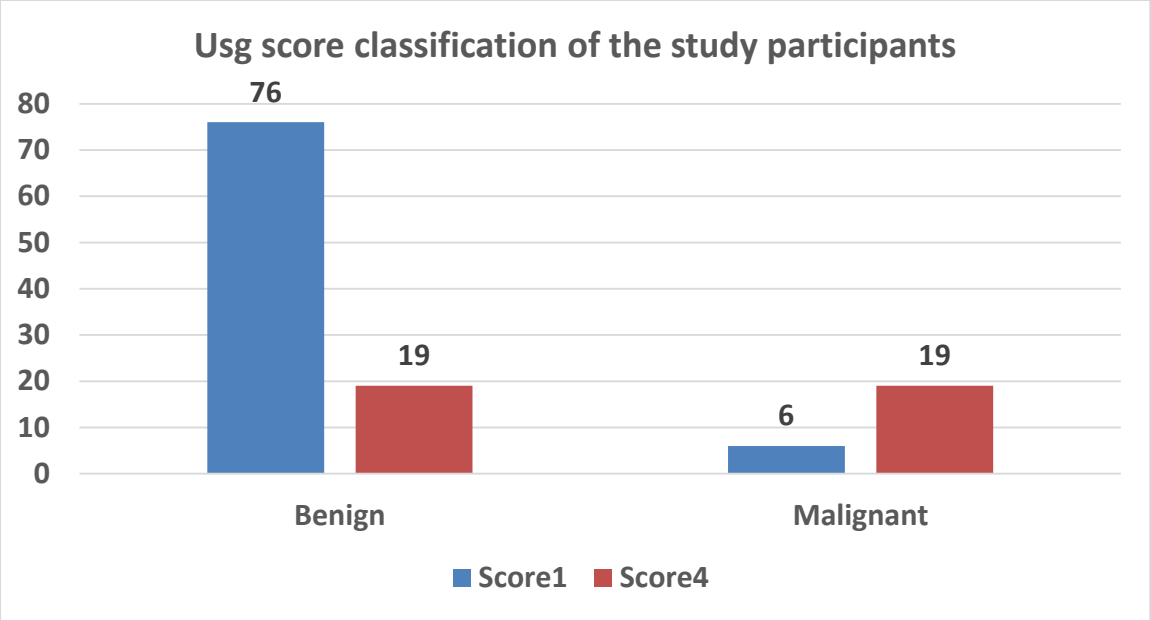
In our study in benign type majority of the participants were premenopausal 80(84.2%) and in malignant type postmenopausal was 20 comprising 80%.

Table 6:Menopausal status of the study participants

Menopausal status	**Benign**	**Malignant**	**P value**
Premenopausal	80(84.2%)	5(20%)	<0.0001
Postmenopausal	15(15.8%)	25(80%)	
Total	95(100%)	25(100%)	

There is a difference between the menopausal types in both the groups and the difference if found to be statistically significant.

Figure 7:USG score of the study participants



Among the benign type majority of the study participants 76 have 0 or 1 abnormality whereas in malignant type 19 have score 4.

Table 7:USG score of the study participants

USG score	Benign	Malignant	P value
USG score 1	76(80%)	6(24%)	<0.0001
USG score 4	19(20%)	19(76%)	
Total	95(100%)	25(100%)	

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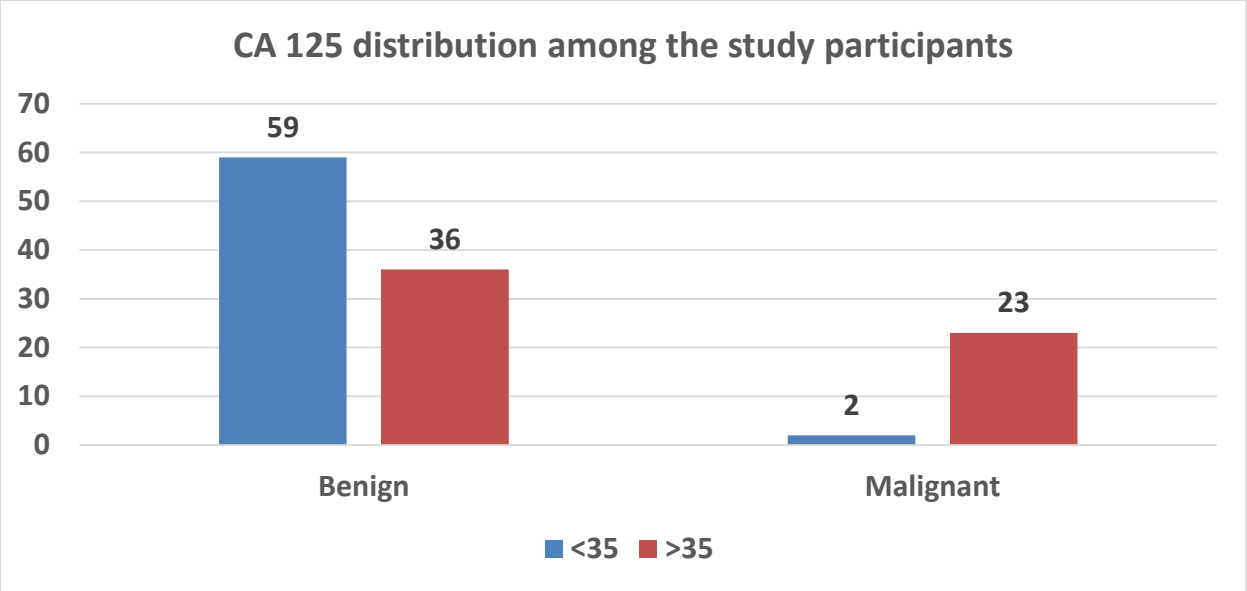
There is a difference between the USG score of the two groups benign and the malignant and the difference is found to be statistically significant.

Figure 8:CA 125 distribution among the study participants



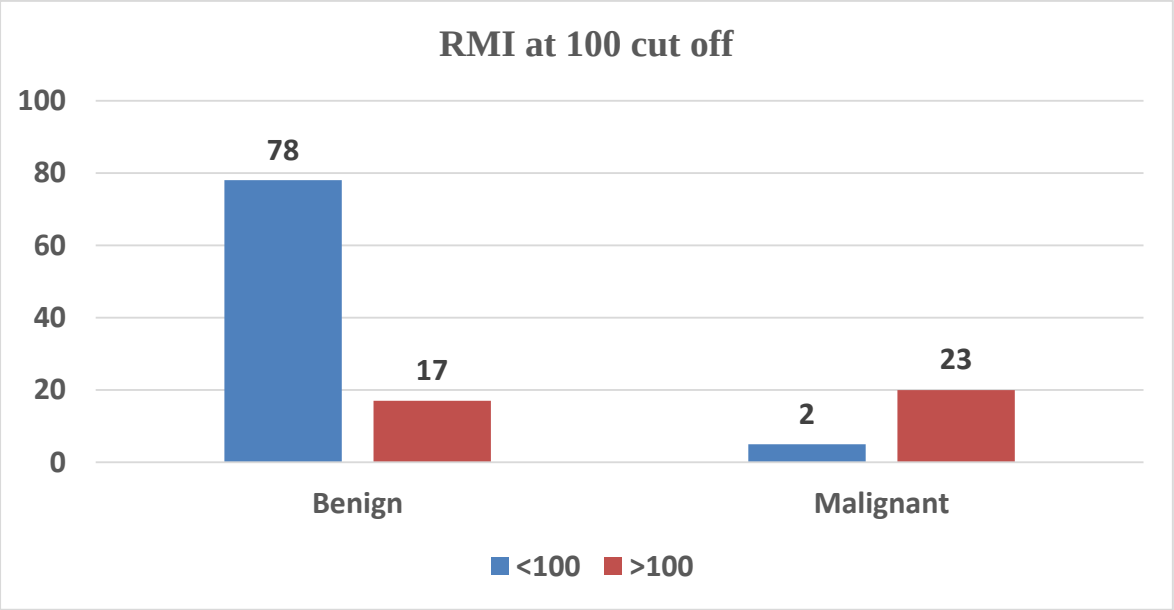
In Benign type majority of the study participants 59(62.1%) have <35 cut off whereas in malignant type 23(92%) has >35 cut off

Table 8: CA 125 Cut off of the study participants

CA125	Benign	Malignant	P value
<35	59(62.1%)	2(8%)	<0.0001
>35	36(37.9%)	23(92%)	
Total	95(100%)	25(100%)	

There is a difference in the distribution of the CA125 marker between benign and the malignant group and the difference is found to be statistically significant.

Figure 9:RMI cut off 100



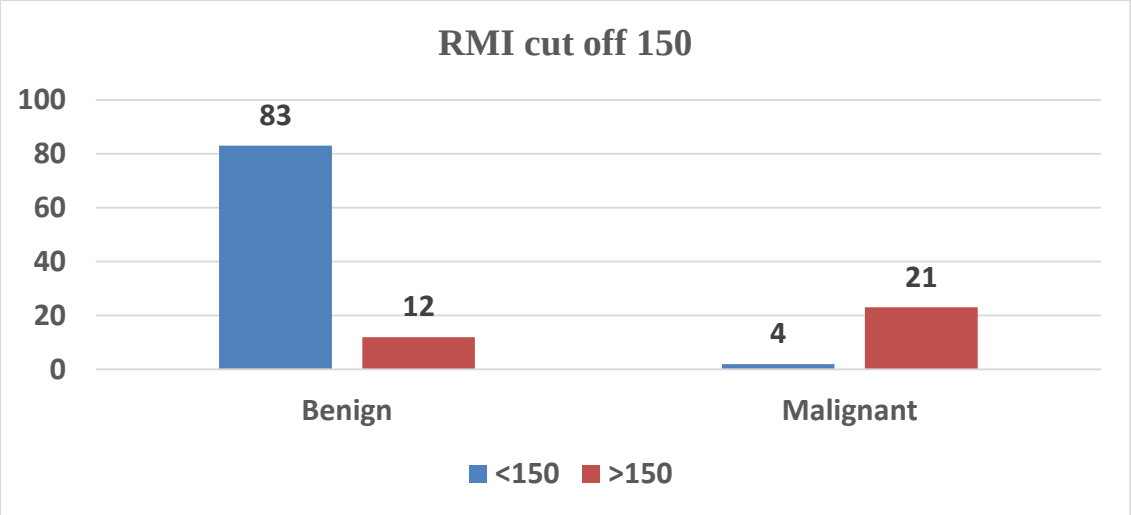
With the RMI cut off <100 17(17.9%) of benign tumor and with cut off of >100 23(92%) of malignant tumor was found.

Table 9:RMI cut off 100

RMI cut off 100	**Benign**	**Malignant**
<100	78(82.1%)	2(8%)
>100	17(17.9%))	23(92%)
Total	95(100%)	25(100%)

The sensitivity of the test is 92% and specificity of the test is 82.1%.The positive predictive value is 57.5% and the negative predictive value is 98.7%.

Figure 10:RMI cut off at 150



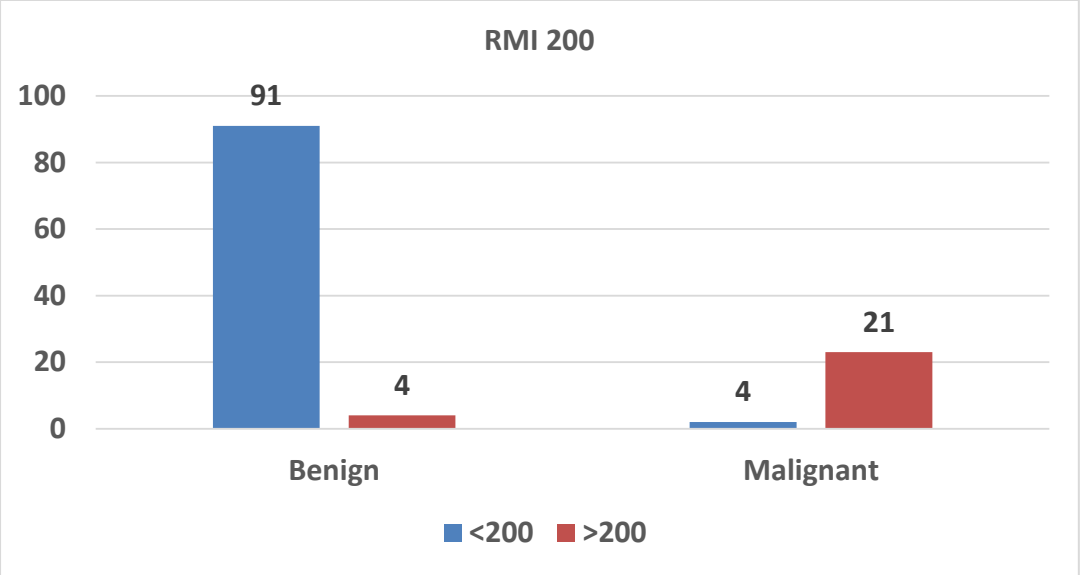
Around 83(87.4%) of the study participants with benign tumour and 12(12.6%) of malignant tumor was found with this RMI cut off <150.In >150 cut off 4(16%) of benign tumour and the 21(84%) of malignant tumor was found.

Table 10:RMI cut off 150

RMI cut off 150	**Benign**	**Malignant**
<150	83(87.4%)	4(16%)
>150	12(12.6%)	21(84%)
Total	95(100%)	25(100%)

The sensitivity of the test is 84 % and the specificity is 87.4%.The positive predictive value is 63.6% and the negative predictive value is 95.4%

Figure 11:RMI cut off 200



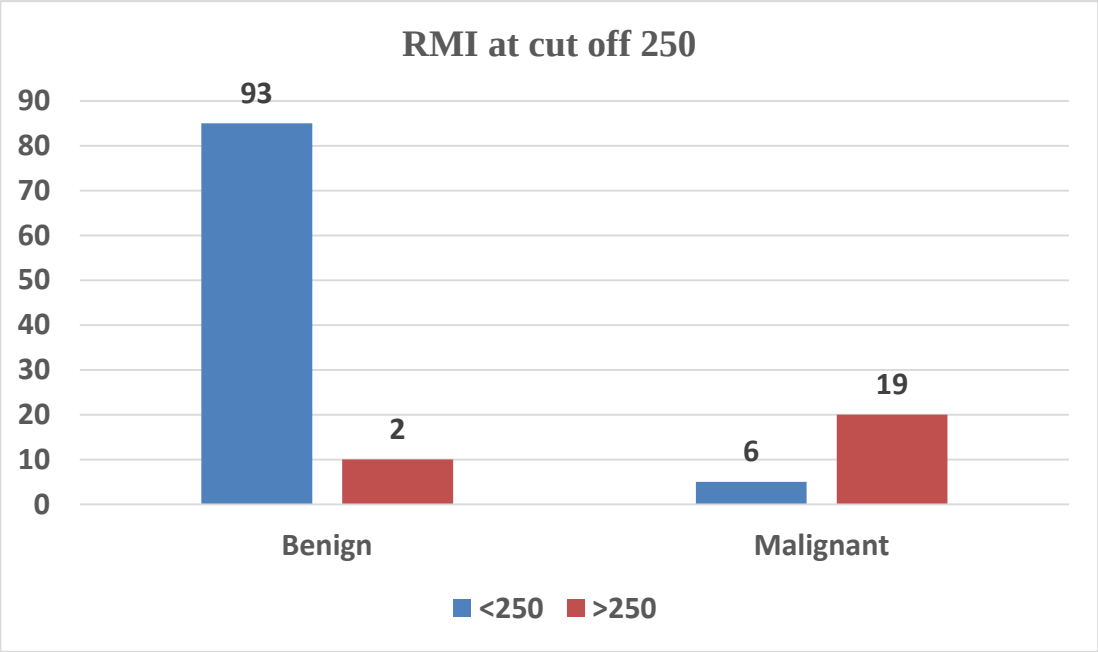
In our study for RMI <200 91(95.8%) of benign tumour and 4(4.2%) of malignant tumour was found and for RMI >200 2(8%) of benign and 23(92%) of malignant tumour was found.

Table 11:RMI cut off 200

RMI cut off 200	**Benign**	**Malignant**
<200	91 (95.8%)	4(16%)
>200	4(4.2%)	21(84%)
Total	95(100%)	25(100%)

The sensitivity of the test is 84% and the specificity of the test is 95.8% .The positive predictive value is 84% and the negative predictive value is 95.7%

Figure 12:RMI at cut off 250



Among the study participants for <250 cut off 93(97%) of benign tumour and for cut off >250 : 19(76%) of malignant tumour is found.

Table 12:RMI cut off 250

RMI cut off 250	**Benign**	**Malignant**
<250	93(97.9%)	6(24%)
>250	2(2.1%)	19(76%)
Total	95(100%)	25(100%)

The sensitivity of the test was 76% ,specificity is 98%.The positive predictive value was 90.5% and the negative predictive value was 94%

Table 13:Comparison of Risk malignancy index for various cut offs

RMI	SENSITIVITY	SPECIFICITY	PPV	NPV
100	92%	82%	57.5%	98.7%
150	84%	87%	63.6%	95.4%
200	84%	95%	84%	95.7%
250	76%	97%	90.4%	94%

The discrimination of benign and malignant tumour was high with cut off 200.The specificity was highest with cut off 200.As the cut off of RMI increases the sensitivity also increases.The positive predictive value was found to be highest in cut off 200 and negative predictive value increases gradually as RMI cut off increases.

Table 13:Comparison of Different parameters in RMI

	SENSITIVITY	SPECIFICITY	PPV	NPV
Menopause	84.21%	84%	95.2%	84%
USG score	80%	76%	92.6%	50%
CA125	62.1%	92%	96.7%	38.9%
RMI	84%	95%	84%	95.7%

The RMI has high sensitivity and negative predictive and positive predictive value.The sensitivity and specificity was decreased in USG score and the menopause score.

Table 14: Prevalence of benign tumors in our study

Benign Types	**Number**	**Percentage**
Serous cystadenoma	34	36%
Mucinous cystadenoma	28	29%
Dermoid	12	13%
Corpus luteal cyst	5	5.3%
Follicular cyst	4	4.%
Papillary serous cystadenoma	1	1.1%
Simple serous cyst	11	11.6
Total	95	100%

The most common benign tumour to occur is Serous cystadenoma 34(36%) followed by mucinous type 28(29%).Papillary serous cystadenoma is rare in our study participants 1(1.1%)

Benign types	**Number**	**Percentage**
Serous cystadenocarcinoma	11	44%
Endometroid adenocarcinoma	4	16%
Mucous Cystadenocarcinoma	4	16%
Papillary serous cystadenocarcinoma	2	8%
Granulosa cell carcinoma	1	4%
Atypical proliferative serous carcinoma	1	4%
Dysgerminoma	1	4%
Krukenberg	1	4%
Total	25	100%

The most common type serouscystadenocarcinoma is 11(44%) followed by endometroid adenocarcinoma 4(16%) and Mucous cystadenocarcinoma 4(16%)

DISCUSSION

The aim of this study is to evaluate the role of RMI 2 in distinguishing malignant from benign ovarian mass. This was a prospective study conducted on 120 patients admitted with ovarian mass over a period of one year. In the present study 95 patients had benign and 25 patients had malignant pathology. This conveys 79% benign and 21 % malignant lesion, which is comparable to Morgan et al studies where 75% had benign and 25 % of ovarian mass had malignancy.

In our study, the peak incidence of malignancy was at 51 to 60yrs during which 52% had malignancy. Among the benign tumor, the peak age group was at 31 to 40yrs with 53.7%. Suggesting that the risk of malignancy increases with increased age.

Relationship between age and outcome of ovarian cancer is unclear.Many studies have reported that young age is associated with improved outcome while few stated age is not an independent prognostic factor. Usually oldage is associated with advanced stage and low survival

84% of the post-menopausal women had malignancy while 16% of the premenopausal had malignancy. Among the menstruating women, 8 % of regular cycle and 12 % of irregular cycle had malignancy.

Anderson et al in a cohort study reported that waist- hip ratio is associated with increased risk of ovarian cancer.Beehler et al stated that relationship between obesity and risk of ovarian cancer is related to menopausal status. Obesity before menopause had increased risk of malignancy .

Leizman et al reported that obesity has increased risk of ovarian cancer and increased mortality for those affected.

In our study, 12 % of the obese and 40% of overweight had malignancy.

Infertility increases the risk of ovarian cancer. 8% of nulligravida had ovarian malignancy.

Though ultrasound has high potential in discriminating benign and malignant tumors. But they are non specific if there is no volume , morphological features and is subjected to examiner's expertise. 76% of malignant ovarian mass had ultrasound score 4 in the present study

In our study, the sensitivity of Ultrasonographic score was 76% and specificity was 80%, the positive predictive value was 50% and negative predictive value was 92%.

The difference in proportion of benign and malignant having USG score 4 (20% vs 90%) was statistically significant.

CA 125 with cut off 35 had a

Sensitivity : 92%

Specificity : 62%

PPV : 50%

NPV : 92.6%

This was comparable to Rachmasari studies according to which sensitivity, specificity, positive predictive and negative predictive value was 81%, 60%, 48% and 88% respectively.

RMI was more accurate compared to individual criteria in discriminating benign and malignant tumors.

The high false positive rate of ultrasound in premenopausal women is indicated as the limiting factor. CA 125 is unreliable in differentiating malignant from benign mass due to its high false positive rate and low specificity.

RMI translated the morphological features of ovarian mass into numerical data thereby reducing examiner bias. RMI was calculated using the formula for each patient included in the study (n=120). Out of 120 patients, the RMI with cut off value of 200,95 patients had benign tumor and 25 patients had malignant tumor.

True positive - 21 cases

True negative - 91 cases

False positive - 4 cases

False negative - 4 cases

Total - 120 cases

One of the aims of our study was to determine RMI cut off for discriminating malignancy for our population . The performance of sensitivity, specificity, positive predictive value and negative predictive value of RMI at various cutoff levels of 100,150, 200, 250, were analyzed. At a cut off level of100, the RMI had highest sensitivity (92%) and negative predictivevalue (98.7%).The specificity (82%) and positive predictive value(57.5%) were low. As the cut off levels are increased, the sensitivitydecreases and specificity increases. RMI at cut off value of 250, had the highest specificity (97%) and positive predictive value (90.4%).

The sensitivity was low 76%. Many studies have shown that the best cut off value of RMI is 200. In our study, the performance of RMIat 200 is statistically significant with sensitivity 84%,specificity 95%, positive predictive value 84% and negative predictive value 95.7%.

COMPARISON OF PREVIOUS STUDIES WITH PRESENT STUDY

STUDY	SENSITIVITY	SPECIFICITY	PPV	NPV
Jacob et al	85%	97%	-	-
Tingulstad 1996	71%	96%	89%	88%
Tingulstad 1999	71%	92%	69%	92%
Morgante e al	58%	95%	78%	87%
Obeidat et al	90%	89%	96%	78%
Manjunath et al	73%	91%	93%	67%
Our study	84%	95%	84%	95%

In this study, RMI 2 showed the best performance in predicting malignancy, compared with the other t indices. At the cutoff point 200 (above which the probability of malignancy of masses was high) RMI 2 had the most area under the curve , showing the greatest concordance with pathological results.

SUMMARY

In my study 120 patients admitted at IOG and ISO KGH with ovarian mass were included after fulfilling inclusion and exclusion criteria.

The mean age of the study participants in benign type was 36yrs while 48yrs for malignant type. proper history elicitation, general examination and pelvic examination was done.

Ultrasonogram of pelvis was done for all the cases. An ultrasound score was given based on the presence of multiloculations, solid components, bilaterality, presence of ascites and evidence of intra-abdominal metastases. A score of 1 was given if no or presence of one feature and score 4 was given if two or more features were present.

Serum CA 125 was measured for all patients in our study .

Menopausal score was given as M=4 if women is postmenopausal ., M=1 if the women in pre-menopausal group.

RMI was calculated ,

RMI = U × M × CA 125

According to the RMI, the method of surgery was planned for all patients. After surgery, specimen was sent for histopathological analysis which was considered as a gold standard in defining the final diagnosis.

Out of 120 patients in our study 79% were benign tumors and 21% were malignant tumors. The sensitivity, specificity, positive predictive value and negative predictive value of the ultrasound score in this study was 76%, 80%, 50% and 92.6% respectively.

The sensitivity , specificity , positive predictive value and negative predictive value of serum CA125 with cut off value of 35U/ml was 92%, 62%,38.9% and 96.7% respectively.

In this study by using the RMI with cut off value 200,the sensitivity, specificity, positive predictive value and negative predictive value was 84%, 95%, 84% and 95.7% respectively.

After comparing the RMI with various cut off values, the best results were attained by using the cut off value of 200. This study concludes that RMI 2 cut off 200 is accurate in distinguishing malignant and benign ovarian mass for south Indian population.

CONCLUSION

Differentiation of benign and malignant ovarian tumor is an important step in the preoperative evaluation of ovarian mass. In the absence of definitive biomarker Risk Malignancy Index is a combined parameter incorporating menopausal status, ultrasound score and CA 125 is a better estimate in diagnosing ovarian mass and early referral to gynecological oncologist.

The optimal cut off point that best distinguishes benign from malignant ovarian mass for RMI is 200 in the present study

RMI is simple to calculate , easy applicable and effective method.