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Correlation between MRI, Frozen Section and Histopathological Findings in Carcinoma Endometrium

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INTRODUCTION

Endometrial carcinoma is the most common pelvic gynecological malignancy in industrialized countries and the incidence is increasing. Approximately 75% cases occur in postmenopausal women.

Adenocarcinomas account for 90% of endometrial neoplasms, whereas uterine sarcomas are relatively rare and account for only 2%–6%; the remaining histologic types include adenocarcinoma with squamous cell differentiation and adenosquamous carcinoma. Endometrial cancer is staged surgically with the International Federation of Gynecology and Obstetrics (FIGO) system, which underwent a major revision in 2009.

Treatment and prognosis depends on a number of factors, including stage, depth of myometrial invasion, cervical extension, lymphovascular invasion, histologic grade and nodal status.

Depth of myometrial invasion is the most important morphologic prognostic factor correlating with tumor grade, presence of lymph node metastases and overall patient survival.

Deep (more than 50%) myometrial infiltration is an indication for pelvic and para aortic nodal dissection as an adjunct to hysterectomy and salpingo-oophorectomy.

Lymphadenectomy for early stage (stage 1) endometrial cancer remains controversial. The histological subtype and grade are also established prognostic markers influencing therapy. The overall 5 year survival of endometrial carcinoma is 80% ranging from 20-91% for different tumour stages. Approximately 75% of endometrial carcinomas are diagnosed with the tumours confined to the uterus corpus.

Although, clinical evaluation with diagnostic imaging has not yet proved to be accurate enough in the evaluation of tumour extent to replace surgical staging it may enable an optimization of the surgical procedure and a better tailored therapeutic strategy.

MRI (Magnetic resonance imaging), thanks to the possibility of accurately assessing the anatomy of the uterine wall and pelvic structures, is currently preferred over CT and USG in the local staging of gynecological malignancies.

Frozen section is used in differentiating tumor grade, myometrial invasion, and cervical extension of the tumor in gynecologic operations. If there is any doubt in the preoperative diagnosis of the patient, frozen section can be helpful to make the diagnosis.

AIMS AND OBJECTIVES

To correlate between preoperative MRI, intraoperative Frozen section and postoperative Histopathological findings:

- Depth of myometrial invasion
- Cervical involvement
- Lymph nodes

REVIEW OF LITERATURE

Endometrial cancer is the fourth most common cancer after breast, lung and colorectal cancers. About 2-3% women develop endometrial cancer in their lifetime. (1) It is a disease of postmenopausal women with a peak incidence in the 6th & 7th decade of life. Only 2-5% occur before 40 years. Prognosis is better than other gynecological cancers due to early diagnosis. 75% patients are diagnosed in Stage I. Estrogen has been implicated as a causative factor

EPIDEMIOLOGY (2)

- Type 1: 75-85%
 - Young, perimenopausal
 - Prolonged exposure to estrogens
- Type 2: Without estrogen stimulation
 - Atrophic endometrium
 - Less differential and poor prognosis

ETIOLOGY: (3-8)

- Age: 65-75 years , only 2-5% < 40 years
- Excessive endogenous/exogenous oestrogens. Unopposed oestrogen therapy in postmenopausal women increases risk of Endometrial cancer by 6-8 times.
- Nulliparity
- Chronic anovulation as in PCO
- Late menopause
- Obesity- aromatization of adrenal androgens in fat tissue
 - risk is 3times for patient 21-50 pounds overweight
 - 10 times for patient > 50 pounds overweight
- Granulosa-theca cell tumors of the ovary (a rare estrogen secreting ovarian tumor)
- Cirrhosis of the liver - decreases degradation of estrogen
- Endometrial hyperplasia
- Tamoxifen - an anti-estrogen used in the treatment of breast Ca has weak estrogenic activity on the genital tract.

Increased risk of Endometrial Ca when used \geq 5 Years.
- Increased risk in women with breast, ovarian (endometrial type) & colorectal Ca (Lynch 2 syndrome)

- Diabetes mellitus
- Hypertension
- Previous pelvic radiation therapy
- Family H/O of endometrial Ca

ENDOMETRIAL HYPERPLASIA: (9)

- Excessive proliferation of the endometrial glands & to a lesser extent endometrial stroma
- Continuous and uninterrupted oestrogen stimulation of endometrium in absence of progesterone
- Only 25% of patients have H/O of hyperplasia

CLASSIFICATION:

The International Society of Gynecological Pathologists have come up recently with classification of endometrial hyperplasia. (10)

Table-1: Classification of Hyperplasia

TYPE	PROGRESSION TO CANCER
Simple (Cystic without atypia)	1%
Complex(Adenomatous without atypia)	5%
Simple (Cystic with atypia)	8%
Complex (Adenomatous with atypia)	40%

Hyperplasia without atypia (not premalignant):

A) Simple

- Microscopically- crowding of the glands in the stroma
- Glands are cystically dilated with increased *glandular-stromal ratio* & give a “*Swiss cheese*” appearance
- Commonly asymptomatic
- 80% regress

B) Complex hyperplasia without atypia

- A complex crowded appearance of the glands with very little stroma
- Epithelial stratification & mitotic activity
- 80% regress

- 85% reversal with progestin

Hyperplasia with atypia (pre-malignant):

Histologically - endometrial glands are lined by enlarged cells with increased nuclear: cytoplasmic ratios

The nuclei are irregular with coarse chromatin clumping, lost polarity & prominent nucleoli

- 50-94% regress with progestin therapy
- A higher rate of relapse after stopping treatment compared to that of lesions without atypia

A) Simple

B) Complex

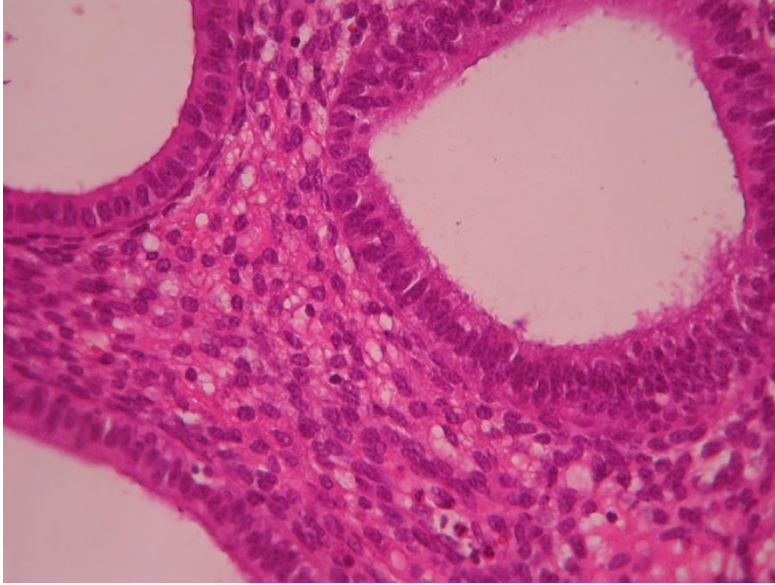


Figure- 1: Simple hyperplasia:

Glands are lined by pseudostratified uniform and oval nuclei

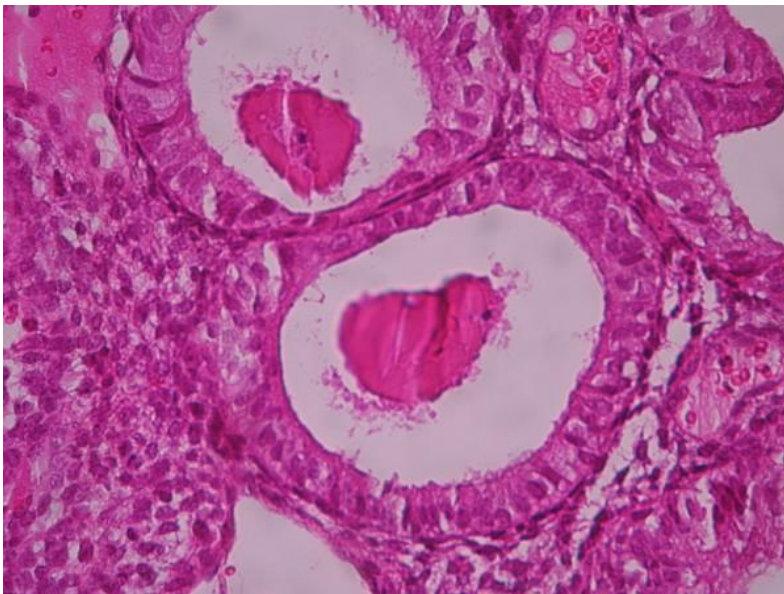


Figure- 2:Complex hyperplasia:

The glands are lined by separate, scanty endometrial stroma from each other. The nuclei are uniform and oval.

Risk of endometrial hyperplasia progressing to carcinoma is related to the presence of severity of cytologic atypia.

The premalignant potential of hyperplasia is influenced by age, underlying ovarian disease, endocrinopathy, obesity and exogenous hormone exposure.

25-43% of patients with atypical hyperplasia detected in endometrial biopsy or curettage specimen will have an associated usually well differentiated endometrial carcinoma detected during hysterectomy. (11)

CARCINOMA IN SITU

Histologically differentiated from carcinoma by:

- Presence of intervening stroma between abnormal glands
- There is no evidence of invasion

CLINICAL FEATURES: (12)

- Abnormal vaginal bleeding- most common 90%
- Perimenopausal patient
 - c/o heavy flow at the time of menses

- persistent intermenstrual bleeding
- pre or post menstrual spotting
- polymenorrhea that fails to respond to hormonal treatment
- Postmenopausal bleeding is the most common mode of presentation (c/o intermittent spotting)
- Postmenopausal vaginal discharge -10%
- Hematometra or pyometra
- Symptoms due to local or distant metastases (pelvic pressure or discomfort)
- Asymptomatic women

SPREAD:

1. Direct spread

- Through the endometrial cavity - to Cervix
- Through the fallopian tubes - to ovaries & peritoneal cavity
- Through the invading myometrium - to serosal surface, parametrium & pelvic wall
- Rarely - direct invasion of the pubic bone

2. Lymphatic spread

- Never occurs without myometrial invasion

- The incidence of involvement is related to the degree of differentiation & depth of myometrial involvement
 - Pelvic lymphnodes - common 35%
 - Para-aortic lymphnodes - 10-20% rarely involved without pelvic nodes.
 - Inguinal lymphnodes - rare
3. Hematogenous spread to the lungs
- Uncommon with the primary tumor limited to the uterus
 - Occurs with recurrent or disseminated disease

DIAGNOSIS:

1. History:

A careful and complete history is very important.

Detailed information includes:

- Age
- Marital status
- Parity
- Presenting complaints
- Menstrual history

Intermenstrual intervals (number of days, regularity)

Volume (heavy, light, variable)

Duration (normal, prolonged, consistent, variable)

- Obstetric history
- Past history
- Family history
- Systemic illness (renal, hepatic, coagulopathy, thyroid, diabetes, hypertension)
- History of medications (hormones, anticoagulants, anticancer drugs like tamoxifen)

2. Examination

a. General examination:

- Height
- Weight
- Breast examination
- Pallor

b. Per abdomen examination:

For any palpable masses

c. Per speculum examination:

On per speculum examination vagina and cervix is examined for any growth, discharge, any cervical or vaginal lesions

d. Per vaginal examination:

- uterine size (normal or enlarged)
- contours (smooth, symmetrical or irregular)
- consistency (firm or soft)
- mobility
- tenderness
- any mass felt through fornices especially ovarian masses
- parametrial involvement in malignancy

e. Per rectal examination:

If malignancy is suspected, then per rectal examination helps in diagnosing any rectal involvement and adherence to the rectum.

In majority of women with true anovulatory bleeding, menstrual history alone can establish the diagnosis without any additional laboratory evaluation or imaging.

INVESTIGATIONS:

1] Laboratory Investigations:

1) Complete blood count:

- Haemoglobin estimation in severe bleeding
- Exclude thrombocytopenia
- Coagulation profile

2] Liver and renal function tests

3] Blood sugar

4] Pap smear:

Pap smear is not reliable for endometrial carcinomas. It can detect only 30% cases.

2] Imaging modalities

Imaging modalities like Ultrasonography, CT and MRI can be used to:-

- Identify the organic causes of bleeding like PCO, ovarian tumours, cysts
- Assess endometrial thickness by TVS
- Delineate endometrial polyps by saline sonography
- Identify endometrial lesions or myometrial invasion by endometrial carcinoma with MRI

Ultrasonography (USG):

USG is most widely used imaging modality for diagnosis of any organic lesions in patients with abnormal uterine bleeding.

Transvaginal USG is preferable to Transabdominal USG because of the better quality of its images. A standard TVS can provide valuable information.

The first and foremost information is endometrial thickness.

If endometrial thickness is less than 5mm it indicates denuded endometrium.

Endometrial thickness 5-12mm is considered within normal range.

An endometrial thickness of greater than 12mm is suspicious and warrants further evaluation like endometrial sampling and histopathology. (12)

In endometrial carcinoma the USG findings are: (13)

- Thickened endometrium
- Polypoidal endometrial mass
- Hyperechoic endometrium with irregular outline
- Intrauterine fluid

Figure- 3: Transabdominal and Transvaginal Probes



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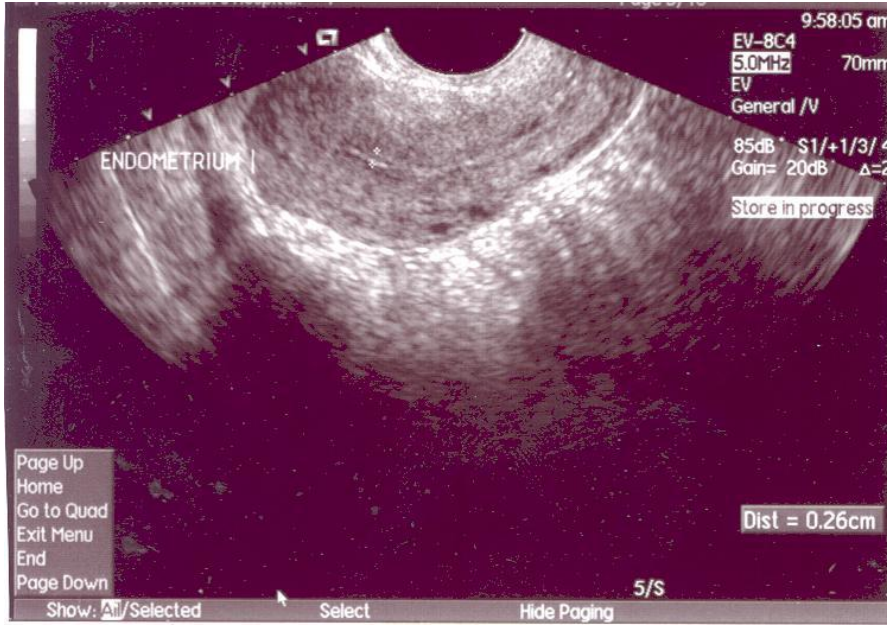


Figure- 4: Normal thin (atrophic) postmenopausal endometrium (3mm thickness)



Figure- 4: Normal thickened postmenopausal endometrium (18mm thickness)

MRI:

MRI is found to be superior to CT in delineation of pelvic organs in multiple planes. (14)

It can differentiate the different zones of endometrium, inner and outer myometrium clearly and can measure the depth of myometrial invasion in endometrial carcinoma.

It can determine the invasion of bladder, rectum, parametrium and uterine body.

However, MRI is more expensive than CT and hence not used routinely used imaging modality.

Prognosis depends on a number of factors, including stage, depth of myometrial invasion, lymphovascular invasion, histologic grade, and nodal status.

Depth of myometrial invasion is the most important morphologic prognostic factor, correlating with tumor grade, presence of lymph node metastases, and overall patient survival. Consequently, preoperative information about depth of myometrial invasion and histologic grade is essential in tailoring the surgical approach for these patients. Magnetic resonance (MR) imaging can accurately help assess the depth of myometrial invasion, whereas histologic grade can be determined with endometrial sampling. This information allows the selection of

patients for pelvic or paraaortic lymph node sampling while obviating radical surgery in patients with a low risk of recurrent disease or significant comorbidities.

Lymphadenectomy for early-stage (stage I) endometrial cancer remains controversial.

In 2008 *Beneditti Panacici et al* and in 2009 *Kitchener et al* investigated whether pelvic lymphadenectomy could improve the survival of women with early-stage endometrial cancer. Both studies reported no benefit in overall or recurrence-free survival in the patients randomized to lymphadenectomy. (16, 17)

The recent SEPAL study (survival effect of paraaortic lymphadenectomy in endometrial cancer) conducted by *Todo Y et al* showed that pelvic and paraaortic lymphadenectomy improves outcome in patients with an intermediate or high risk of recurrent disease. (18)

Peter Beddy et al acknowledged that MR imaging findings are an important predictor of lymph node metastases and when combined with tumor grade and histologic findings, could be useful in selecting patients at low risk for recurrence. (19)

MR imaging can also allow accurate assessment of more advanced disease such as cervical stromal invasion or adnexal involvement. Additional information from an MR imaging staging examination (eg, uterine size, tumor volume, presence of

ascites or adnexal disease) may help determine whether the surgical approach should be transabdominal, transvaginal, or laparoscopic.

Diffusion-weighted and dynamic multiphase contrast medium-enhanced MR imaging sequences have been shown to improve the accuracy of MR imaging in assessing the depth of myometrial invasion and can be used to assess tumor response to therapy and to differentiate tumor recurrence from post treatment changes. (20, 21, 22)

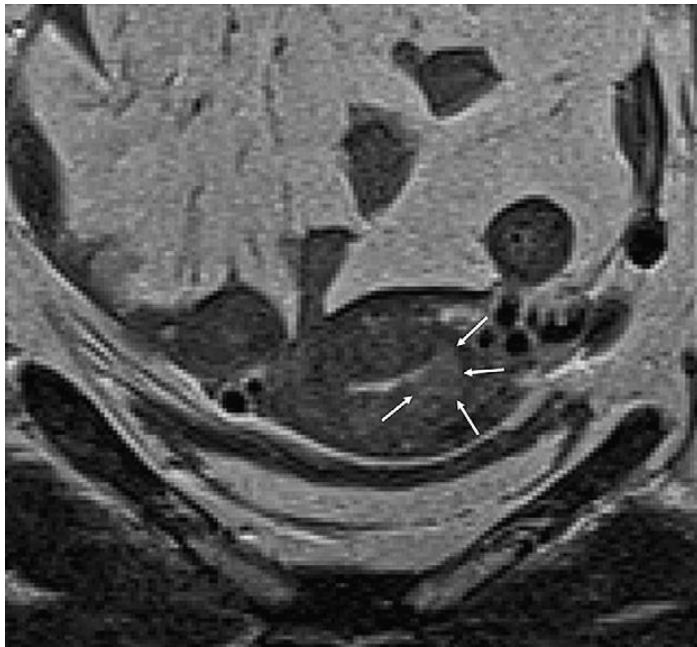
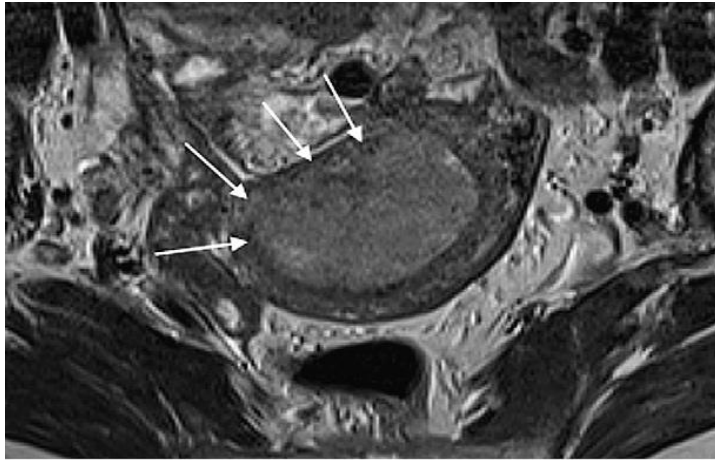
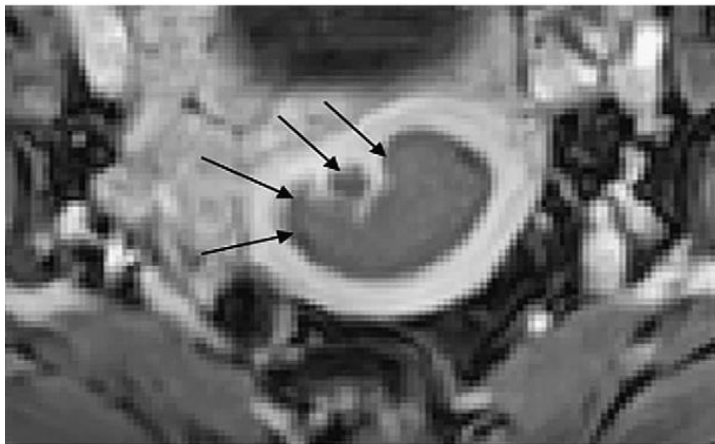


Figure- 6: Stage IA endometrial carcinoma (endometrioid, grade 1) in a 69-year-old woman. Axial, T2-weighted image shows a hyperintense endometrial lesion

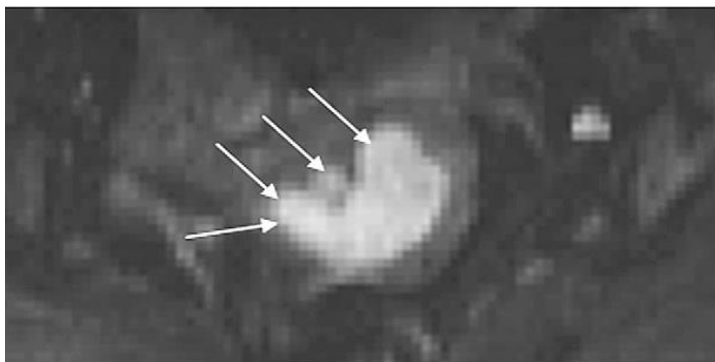
with an irregular junctional zone in the upper left part of the uterine cavity (arrows) invading less than 50% of the myometrium.



(a)



(b)



(c)

Figure- 7:Stage IB endometrial carcinoma (endometrioid, grade 1) in a 53-year-old woman. Axial, T2-weighted image (a) depicts a hyperintense large endometrial lesion disrupting the junctional zone (arrows) indicating myometrial invasion. On the axial, contrast enhanced (120 s delay), T1-weighted image (b), the tumour, which invades more than 50% of the myometrium, is sharply demarcated (arrows) and appears distinctly hypointense relative to the myometrium.

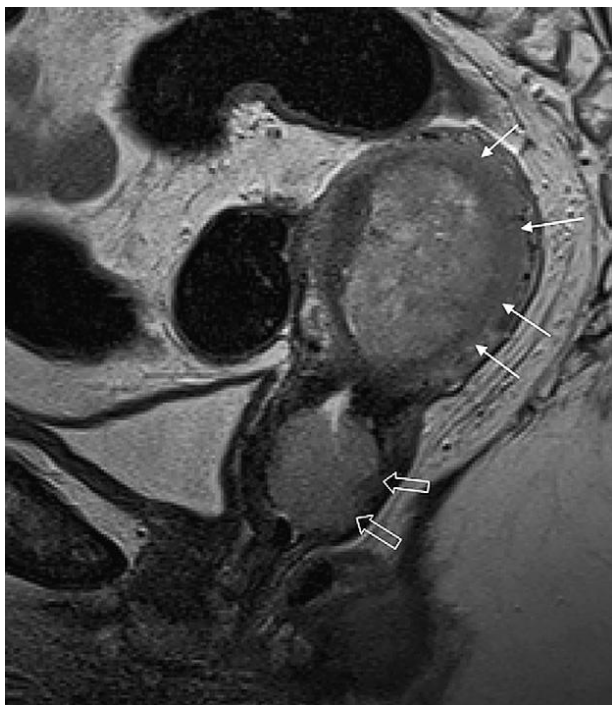


Figure -8: Stage II endometrial carcinoma (clear cell) in a 70-year-old woman. Sagittal, T2-weighted image depicts hyperintense tumours in the uterine cavity and cervix without visible continuity. The uterine tumour invades more than 50% of

the posterior myometrial wall (closed arrows) and the cervical tumour invades the posterior cervical stroma (open arrows).

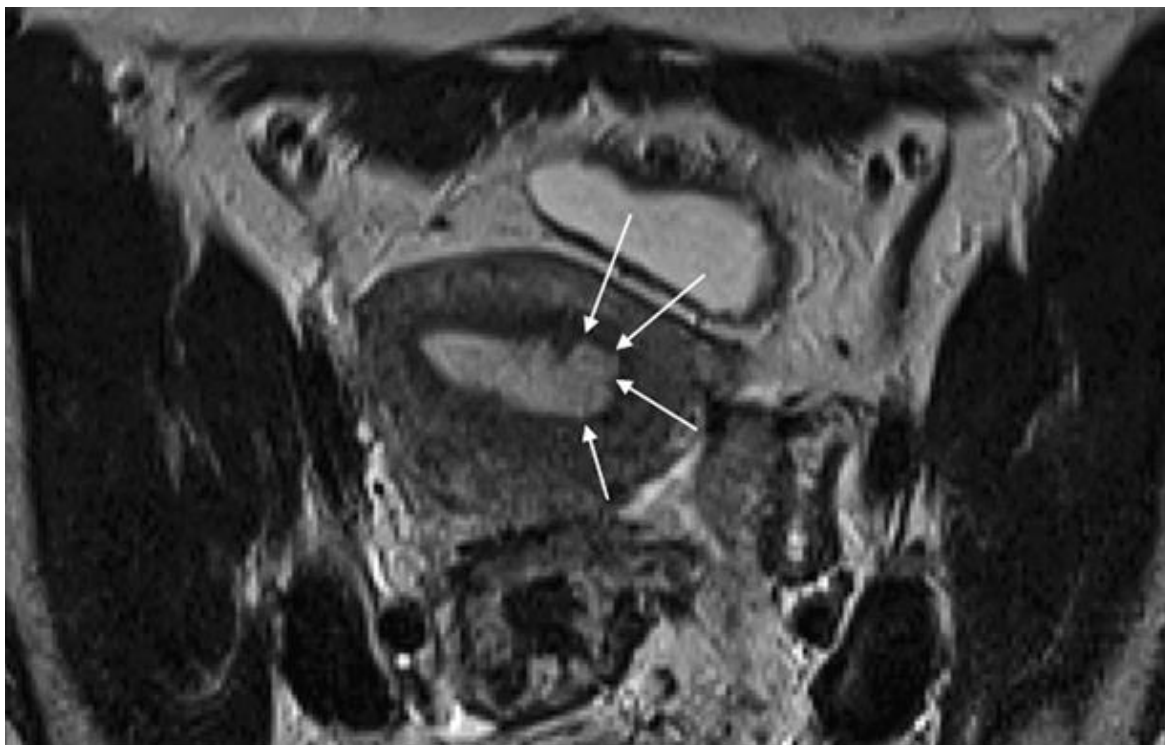
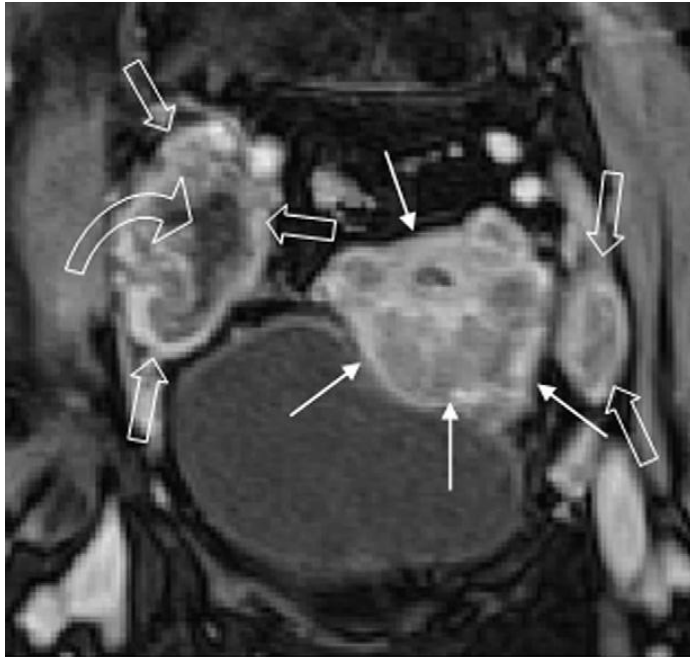
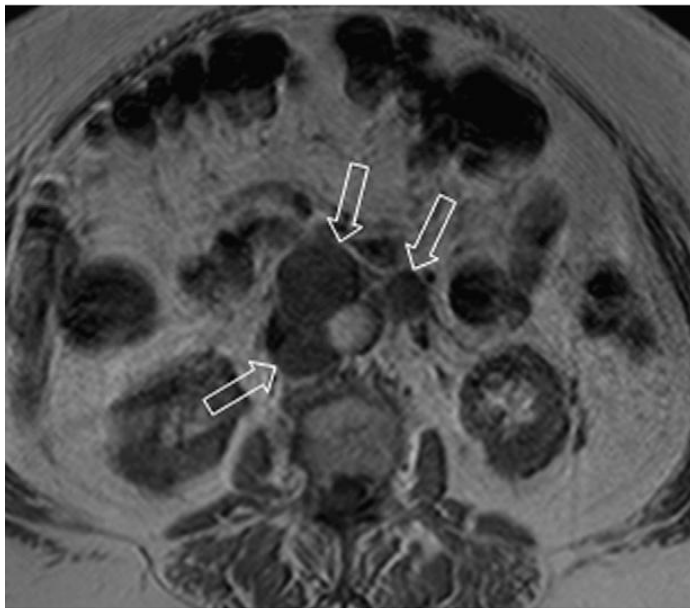


Figure-9: Stage IIIA endometrial carcinoma (endometrioid, grade 1: metastasis to one pelvic lymph node) in a 42-year-old woman.

Characteristic time intensity curves (a) of normal subendometrial myometrium (ROI 1, upper curve), deep myometrium (ROI 2, middle curve), and endometrial carcinoma (ROI 3, lower curve). The subendometrial myometrium displays an early peak enhancement (at w30 s), prior to the peak enhancement of the deep myometrium (at w120 s). The endometrial carcinoma is hypovascular with lower intensities than the myometrium.



(a)



(b)

Figure -10: Stage IIIC2 endometrial carcinosarcoma in a 73-year-old woman.

Axial, contrast-enhanced T1-weighted image (a) (120 s delay) depicts a large, multilobulate, and hypointense tumour invading the serosa of the corpus uteri (closed arrows) with regional tumour spread to the parametrium and to pelvic

lymph nodes (open arrows). The uterine tumour has similar intensity to that of the pelvic metastatic lesions. An area of central necrosis is seen in the right metastatic lesion (curved open arrow). T1-weighted MRI at the level of the renal hilus (b) depicts paraaortal enlarged metastatic lymph nodes (open arrows).

Table -2: Revised surgical staging FIGO (2009) of endometrial cancer with

MRI findings:

FIGO stage	Pathological findings	MRI findings
Stage I IA	Tumour confined to the corpus uteri No or less than half myometrial invasion	The endometrial mass is confined to the endometrium or invades <50% of the myometrial wall with disruption of the JZ.
IB	Invasion equal to or more than half of the myometrium	Mass invades 50% or more of the myometrium with a preserved stripe
Stage II	Tumour invades cervical stroma, but does not	Disruption of the low-signal intensity inner cervical stroma (T2).

	extend beyond the uterus	Disruption of the cervical epithelium enhancement (CE T1).
Stage III	Local or regional spread of the tumour	-
IIIA	Tumour invades the serosa of the corpus uteri and/or adnexae	Disruption of continuity of the outer myometrium or presence of nodules on the peritoneal surface or adnexa
IIIB	Vaginal and/or parametrial involvement	Tumour extension into upper vagina and/or parametrium.
IIIC	Metastases to pelvic and/or para-aortic lymph nodes	Enlarged pelvic and/or para-aortic lymph nodes (cut-off value: >10 mm for short-axis diameter)
IIIC1	Positive pelvic nodes	Enlarged pelvic lymph nodes
IIIC2	Positive para-aortic lymph nodes with or without positive pelvic lymph nodes	Enlarged para-aortic lymph nodes.
Stage IV	Tumour invades bladder and/or bowel mucosa,	Tumour extension into bladder/rectum with disruption of the hypointense signal of the

	and/or distant metastases	bladder or rectal wall.
IVA	Tumour invasion of bladder and/or bowel mucosa	Tumour extension into bladder/rectum with disruption of the hypointense signal of bladder or rectal wall.
IV B	Distant metastases, including intra-abdominal metastases and/or inguinal lymph nodes	Intraperitoneal metastases in peritoneum or omentum. Distant (haematogenous) metastases to lung bones or liver. Distant lymph nodes metastases.

CE T1, contrast enhanced T1-weighted imaging; FIGO, International Federation of Gynaecology and Obstetrics; JZ, junctional zone; T2, T2-weighted imaging. a Exclusively endocervical glandular involvement should be considered stage I. b Positive cytology should be reported separately without changing the stage. 2 I.S. Haldorsen, H.B. Salvesen / Clinical Radiology xxx (2011) 1e11.

In postmenopausal women, there is thinning of the myometrium secondary to uterine involution, which can make accurate assessment of the depth of myometrial invasion challenging at conventional MR imaging (23,24). Other commonly reported pitfalls in assessing the depth of myometrial invasion include tumor extension into the cornua, myometrial compression from a polypoid tumor, poor tumor-to-myometrium contrast and the presence of leiomyomas or adenomyosis. (22, 25, 26, 27).

Endometrial Biopsy:

Endometrial biopsy is the most commonly used test for dysfunction uterine bleeding.

It is indicated in all women with DUB who are 35 years of age or older since their risk of developing malignancy is high.

Most endometrial biopsies can be performed in outpatients and have the advantage of being simple, quick, safe, inexpensive, convenient and avoiding the need of anaesthesia.

The two most commonly used devices are the Pipelle and the Vabra aspiration biopsy.

There are several limitations to all of these methods. The most important is that they are blind procedures and thus not all of the endometrial surface will be sampled. Both the Pipelle and Vabra curettes may miss the endometrial polyps.



Figure -10: Outpatient endometrial biopsy devices A) Panoramic view



Figure -10: Outpatient endometrial biopsy devices B) Magnified view



Figure- 11: Outpatient endometrial biopsy A) Insertion of endometrial biopsy device into the uterus



Figure- 11: Outpatient endometrial biopsy B) Endmetrial tissue specimen

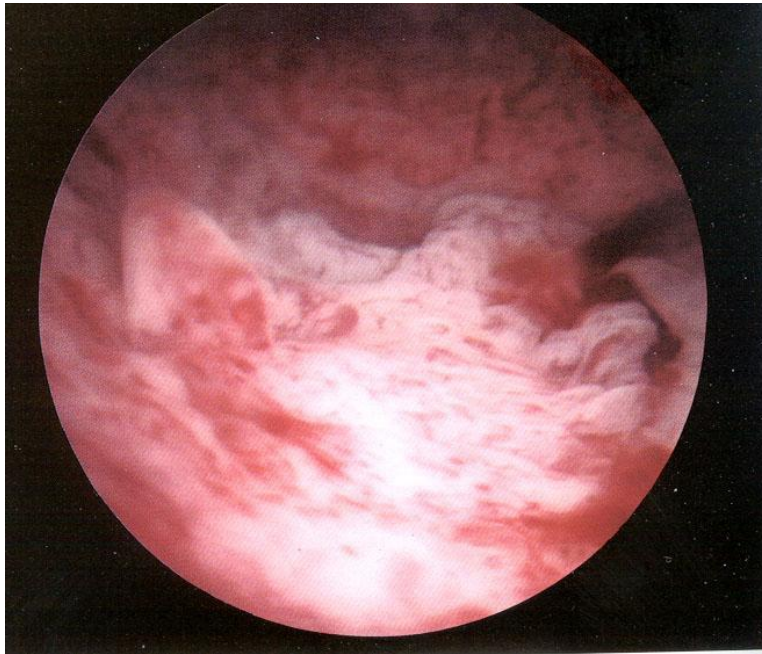


Figure-12: Hysteroscopic views of the endometrium.

- A) Normal view showing thin, atrophic postmenopausal endometrium
- B) Abnormal view showing thickened, irregular and vascular endometrium

HISTOPATHOLOGY:

- Microscopically - hyperplasia & anaplasia of glands
- Invasion of stroma, myometrium, or vascular spaces

1. Adenocarcinomas - 80-85%

Types:

- Variants
- Villoglandular
- Secretory
- With squamous differentiation

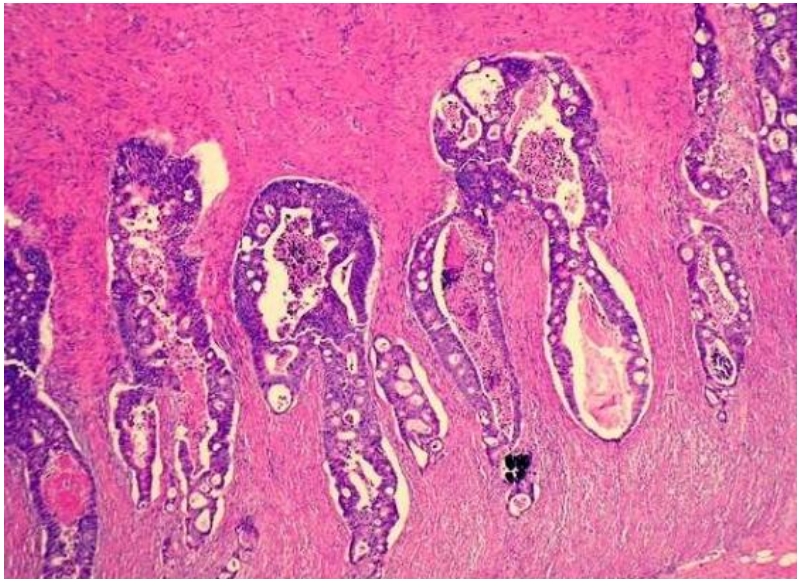


Figure-13: Endometroid adenocarcinoma showing myometrial invasion

2. Adenocarcinoma with squamous differentiation -5%

- Malignant glands with benign squamous metaplasia

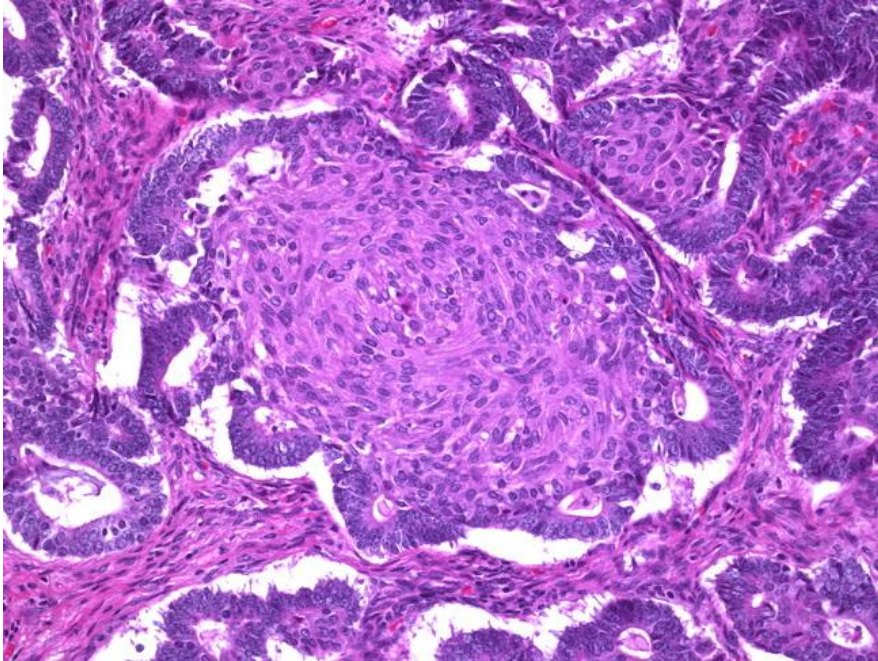


Figure-14: Adenocarcinoma with squamous differentiation

3. Papillary Serous Ca - 10%

- Older women
- Less likely to have hyperestrogenic state
- Similar to Papillary Serous Ca of the ovaries and fallopian tubes
(3-4%) (31-34)
- Psammoma bodies
- Spread early through peritoneal surfaces of the pelvis & abdomen
- Invasion of the myometrium & lymphatic system
- Prognosis unfavorable

- Recurrence

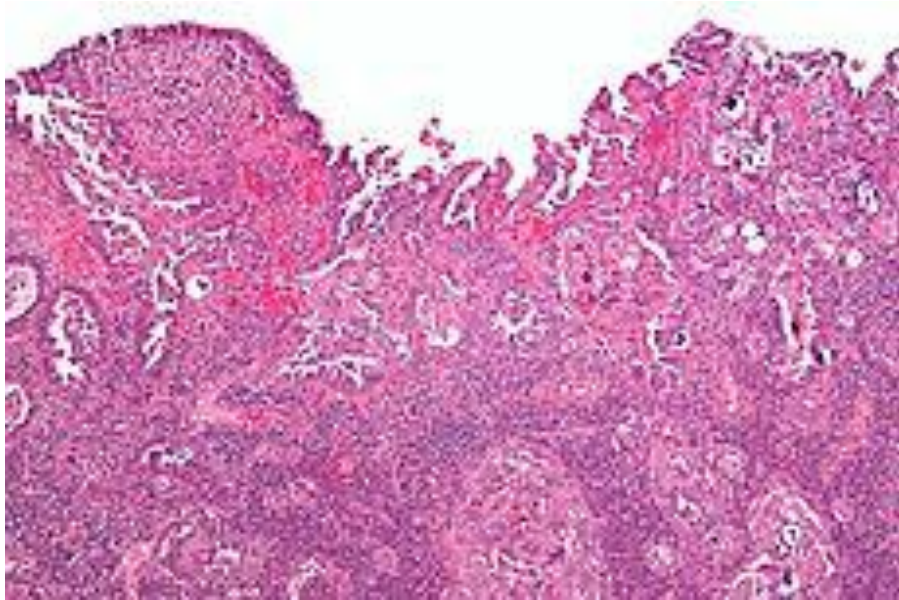


Figure -15: Papillary serous carcinoma

4. Clear cell Ca - <5% (35,36,37)

- Microscopic appearance - mixed histology papillary, tubular, glandular & cystic pattern are possible. Often cells have hobnail configuration arranged in papillae with hyalinised stalks.
- Commonly high grade & aggressive
- Seen in advanced stages
- Older women
- Not associated with hyperestrogenic states
- Behaves like ovarian Ca

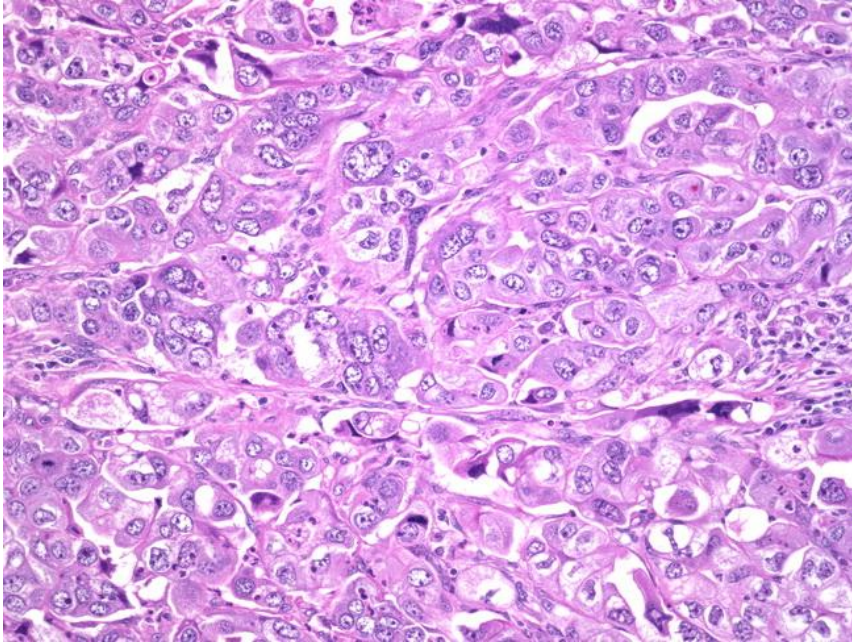


Figure-16: Clear cell carcinoma

5. Mucinous Ca - 5%

- More than half of the tumour is composed of cells with intracytoplasmic mucin (38, 39)
- well differentiated
- good prognosis
- Positive immunohistochemical staining with vimentin (40)

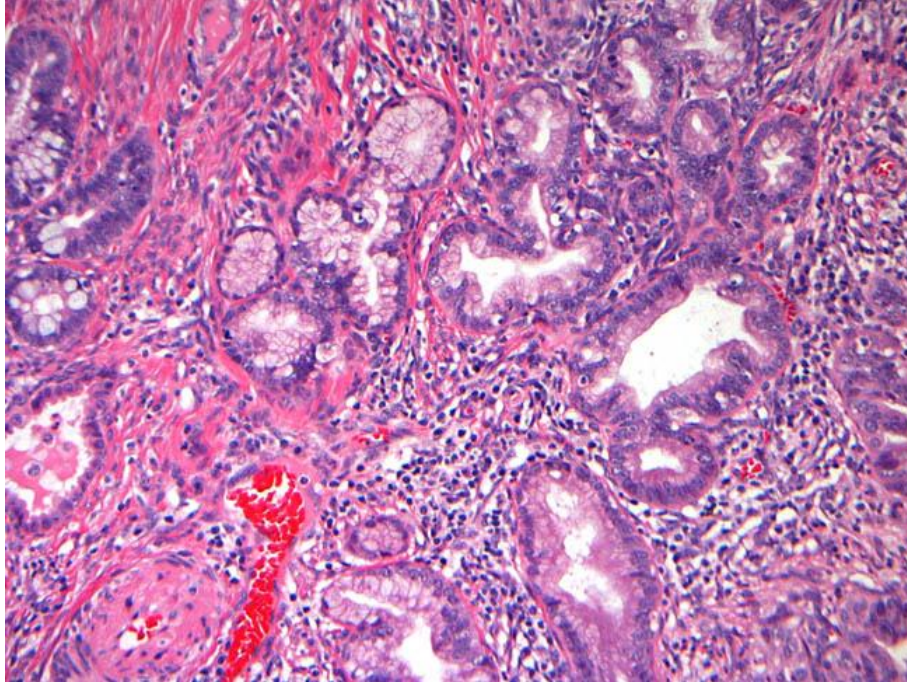


Figure- 17: Mucinous carcinoma

6. Secretory Ca - 1-2%

- Exhibit sub-nuclear or supra-nuclear vacuoles - resembling early secretory endometrium
- Behaves like typical endometrial cancer

7. Squamous cell Ca - extremely rare

- Associated with - Cervical stenosis, pyometra & inflammation
- Poor prognosis with an estimated 36% survival rate in clinical stage 1. (41)

The endometroid endometrial carcinomas are graded according to the degree of architectural and nuclear characteristics. (42)

G1: Well differentiated tumours

G2: Moderately differentiated tumours

G3: Poorly differentiated/ undifferentiated tumours

STAGING:

Cancer staging is one of the most fundamental activities in oncology and is of pivotal importance to the modern management of cancer patients. It is structured to represent a major prognostic factor in predicting patients' outcome and lending order to the complex dynamic behavior of a cancer. (43)

The main objectives of any good staging system essential to an evidence-based approach to cancer are: to aid the clinician in planning treatment; to provide indication of prognosis; to assist the physician in evaluating the results of treatment; to facilitate the exchange of information between treatment centers, thus disseminating knowledge; and to contribute to continuing investigations into human malignancies.

A good staging system must have 3 basic characteristics: it must be valid, reliable, and practical. The first staging system for gynecological cancers appeared around

the time of the 20th century and applied to the carcinoma of the cervix uteri-the most common cancer affecting women in high income countries at that time.

The classification and staging of the other gynecological malignancies was not put forward until the 1950s. Over the years, these staging classifications; with the exception of cervical cancer and gestational trophoblastic neoplasia, have shifted from a clinical to a surgical-pathological basis. (44)

Clinical Staging:

Clinical staging, according to 1971 FIGO system, should be performed only in those patients who are not surgical candidates due to their poor medical condition or the degree of disease spread.

The current FIGO staging is surgical which has supplanted the old clinical system. With improvements in preoperative and postoperative care, anaesthesia administration and surgical techniques, almost all patients are medically fit for operative therapy.

Surgical evaluation and staging have been the cornerstone of management since 1988, when the International Federation of Gynecology and Obstetrics (FIGO) system was changed from clinical to surgical staging.

Staging includes peritoneal washings for cytology, careful exploration of the abdomen and pelvis with biopsy of any suspicious lesions, total hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymphadenectomy.

The method and extent of lymph node dissection have not been uniformly defined and remain controversial. In seeking the optimal care for women with endometrial cancer, the aim is to avoid both overtreatment (i.e, sparing a patient unnecessary surgery or radiotherapy) and undertreatment (i.e, not treating a patient with occult involvement of her lymph nodes).

Impact of Surgical Staging on Clinical Care

It has been argued that the information obtained from comprehensive surgical staging significantly impacts postoperative management. (45)

In 2005, in a study of 181 patients with grade 1 disease, *Ben-Shachar et al* (46) reported that adjuvant treatment was avoided in 17% of patients as a result of negative staging results. The results of surgical staging also led to adjuvant treatment in 12% of patients who were found to have extrauterine disease or other high-risk characteristics.

In 2009, in a study by *Peter Frederick et al*, surgical staging significantly impacted postoperative treatment in a significant number of patients. Therefore, several

authors recommend comprehensive surgical staging to be performed on all patients with endometrial cancer, including those with grade 1 disease. (47)

Surgical staging of endometrial cancer was first proposed in 1988, and the staging system was updated in 2009. (48)

The previous staging of the FIGO system subdivided stage I tumors into IA, IB, and IC tumors.

Table 3 -:FIGO staging of endometrial carcinoma 2009

Stage	Description
IA	Tumor confined to uterus, <50% myometrial invasion
IB	Tumor confined to uterus, ≥50% myometrial invasion
II	Cervical stromal invasion
IIIA	Tumor invasion into serosa or adnexa
IIIB	Vaginal or parametrial involvement
IIIC1	Pelvic node involvement
IIIC2	Paraortic node involvement

IVA	Tumor invasion into bladder or bowel mucosa
IVB	Distant metastases (including abdominal metastases) or inguinal lymph node involvement

Stage IA tumors were confined to the endometrial complex, stage IB tumors invaded only the inner half of the myometrium (<50% of the depth of the myometrium), and stage IC tumors invaded the outer half of the myometrium ($\geq 50\%$ of the depth of the myometrium).

In the 2009 revised FIGO staging system, tumors confined to the endometrium as well as those invading the inner half of the myometrium are designated as stage IA tumors (48, 44), and tumors invading the outer half of the myometrium are designated as stage IB tumors . These changes may improve the diagnostic accuracy of MR imaging. With the old staging system, differentiating between stage IA and IB tumors could be challenging in patients with loss of junctional zone definition or in lesions with poor tumor-to-myometrium contrast, both of which are common pitfalls in endometrial cancer staging. (22, 25, 49)

The amalgamation of stage IA and IB tumors into a new stage IA should alleviate this problem.

Stage II tumors were previously subdivided into stage IIA and IIB tumors, with IIA tumors characterized by endocervical glandular invasion and IIB tumors by cervical stromal invasion. The new system, no longer has subsets IIA and IIB. Instead, tumors with endocervical glandular invasion are now considered stage I tumors, and tumors with cervical stromal invasion are defined as stage II tumors.

Stage III is still composed of three subdivisions: IIIA, IIIB, and IIIC. Stage IIIA tumors invade the serosa or adnexa, and stage IIIB tumors invade the vagina or parametrium. Previously, stage IIIC referred to any lymphadenopathy (pelvic or retroperitoneal); in the new FIGO system, however, stage IIIC is divided into stage IIIC1, which is characterized by pelvic lymph node involvement, and stage IIIC2, which is characterized by paraaortic lymph node involvement. These changes reflect prognostic data that suggest a worse outcome in patients with involvement of paraaortic nodes than in those with involvement of pelvic nodes only. (50)

Stage IV remains unchanged: Stage IVA tumors extend into adjacent bladder or bowel, and stage IVB tumors have distant metastases (eg, to the liver or lungs).

FROZEN SECTION:

The incidence of lymph node metastasis is related to the depth of invasion and tumor grade.

Intraoperative frozen section might identify patients who are at risk for extrauterine spread and required complete surgical staging.

Frozen section may help to further stratify for the risk of final pathology but is not entirely accurate. (51)

Case et al. evaluated in a prospective-blinded study the accuracy of frozen section in surgical management of endometrial cancer. There was a poor correlation between frozen and final section: only 67% for invasion depth and 58% for tumour grade. This study demonstrated a clinically relevant upstaging in 18% of patient who underwent lymphadenectomy. (52)

Another study by *Frumovitz et al.* verified that the combination of intraoperative frozen section analysis for histological grade and depth of myometrial invasion correlates poorly with final pathologic grade and stage in patients with apparent grade I and II tumor. (53)

The finding of negative pelvic nodes at intraoperative frozen section has been proposed to guide further surgical management during surgical staging of endometrial cancer.

A recent study by *Papadia et al.* confirmed that frozen section underestimated the risk of lymph node involvement in 16% of cases when compared with final section pathology. (54)

The consequence of errors that lead to suboptimal surgical management can be significant. Patients in whom the features of high risk uterine disease are not identified at the time of primary surgery will not be surgically staged and will therefore all require extended field radiotherapy or further surgery.

In contrast, those patients with features of high risk uterine disease who were staged and found to have negative lymph node pathology may safely have radiotherapy omitted. The combination of surgery and radiotherapy is associated with significant morbidity in 12% patients.

Conversely, patients incorrectly identified with high risk uterine disease at the time of primary hysterectomy will have surgical staging performed when it is not indicated. This will increase operating time and blood loss, although major complications are uncommon. (55-58)

Factors responsible for inaccuracy in frozen section reports have been documented. (59, 60)

The most common are interpretation or difficulties associated with technical artifacts.

Other causes for inaccuracy include inadequate sampling, time constraints.

TREATMENT:

Endometrial Hyperplasia:

The purpose of treating simple or complex endometrial hyperplasia without atypia is to control abnormal uterine bleeding, which is the most common presentation of the disorder and to prevent progression to cancer, although this risk is very low (less than 1-3 %). Atypical endometrial hyperplasia also requires therapy but due to the significant risk of endometrial cancer (17-53%), treatment recommendations typically include surgery.

1) Endometrial hyperplasia without atypia diagnosed on histopathological examination of endometrium can be corrected by progestin therapy or by D & C alone.

Progestin therapy can be cyclic i.e medroxyprogesterone acetate (MPA) 10mg for 14 days per month or norethindrone acetate 5 mg daily for 14 days per month.

Even oral contraceptives and levonorgestrel containing intrauterine device can be used for this purpose. (61)

Therapy should be continued for atleast 2-3 months and a repeat endometrial biopsy can be taken 3-4 weeks after completion of therapy to assess the response.

Data suggests that most women with endometrial hyperplasia without atypia will respond to progestin therapy and are not at increased risk of endometrial carcinoma. (62)

2) Endometrial hyperplasia with atypia:

Atypical endometrial hyperplasia is considered a part of continuum with endometrial cancer and hence it is best treated surgically i.e hysterectomy.

However, in women who are interested in preserving their child bearing and reproductive functions or those who are medically poor candidates for surgery can be advised cyclic progestin therapy but more potent and longer duration of therapy is required.

Continuous progesterone therapy with megestrol acetate 80 mg twice a day which can be increased to 160 mg twice a day is the most reliable treatment for reversing complex or atypical hyperplasia. (63)

A repeat endometrial biopsy is done after 3 months. If atypical hyperplasia persists, then higher dose of progestins are given as continuous therapy.

If a repeat endometrial biopsy again shows endometrial hyperplasia then, hysterectomy is the only method of choice.

Persistent disease at 7-9 months was predictive of treatment failure. Hysterectomy is recommended for treatment failures.

However, these patients should be under strict surveillance and should undergo periodic transvaginal sonogram or endometrial biopsy. Repeating an endometrial biopsy every 6-12 months should be considered initially.

Women who do not wish to retain their child bearing function or are unable to comply with regular treatment and follow up should however be advised hysterectomy without trial of progestin therapy.

SURGICAL TREATMENT:

Once the diagnosis of endometrial carcinoma is established by endometrial sampling and histopathology, hysterectomy remains the main stay of treatment.

Extrafascial hysterectomy is the preferred treatment in early endometrial carcinoma. Surgery involves removal of uterus, bilateral tubes and ovaries and vaginal cuff.

In advanced Carcinoma endometrium Stage 2, Radical hysterectomy is the method of choice. This involves Total Abdominal Hysterectomy+ Bilateral Salpingo-ophorectomy, upper half of vagina, draining lymph nodes- Parametrial, internal and external iliac groups and sometimes common iliac nodes. Para-aortic lymph node sampling is done.



Figure: Surgical management of patients with stage I-II endometrial carcinoma

Radiation Therapy:

Primary surgery followed by individualized radiation therapy is the most widely accepted treatment for early- stage endometrial cancers.

Landgren et al and Abayomi et al showed that radiotherapy is effective treatment for patients with inoperable endometrial cancer.(64,65)

Although radiation alone can produce excellent survival and local control, it should be considered definitive treatment only if the operative risk is estimated to exceed 10-15% risk of recurrence than radiation treatment alone.

Patterns of metasatatic dissemination:

There are four potential routes of metastasis.

1. Contiguous extension: Histologic grade 3 and lymphovascular space invasion are proven predictors of vaginal relapse in Stage 1 endometrial cancer. (66)
2. Hematogenous: Deep myometrial invasion is the strongest predictor of hematogenous recurrence. (67)
3. Lymphatic: Lymphatic failure more likely to occur when cervical stromal involvement or positive lymph nodes are present. (68)

4. Peritoneal :

- Stage 4 disease or
- Stage 2 or 3 with two or more of the following risk factors: cervical invasion, peritoneal cytology results positive, positive lymph nodes or nonendometroid histologic findings. (69)

Modalities of postoperative treatment:

1. Observation:

Patients with grades 1 and 2 lesions without myometrial invasion or any of the risk factors have an excellent prognosis and require no postoperative therapy.

2. Vaginal vault radiation:

Vaginal brachytherapy is an attractive alternative to external radiation therapy.

Pearcey and Petereit established HDR dosing of 21 Gy to 5 mm depth in 3 fractions as the standard brachytherapy dose providing local control rates of 98%- 100%. (70)

Mariani A et al showed that patients with Grade 3 histology and lymphovascular space invasion are proven predictors of vaginal relapse in Stage 1 endometrial cancer and are most likely to benefit from vaginal vault brachytherapy. (66)

3. External pelvic radiation:

Radiation therapy traditionally was suggested to patients who were deemed to have intermediate or high risk of recurrence, according to grade and depth of myometrial invasion. Patients with extrauterine pelvic disease, including adnexal spread, parametrial involvement and pelvic node metastasis in the absence of extrapelvic disease are likely to benefit from postoperative pelvic radiation.

The **PORTEC** trial tested the role of postoperative pelvic radiation therapy for presumed Stage 1 endometrial cancer. Locoregional recurrence was more in the surgery group as compared to postoperative pelvic radiation group. (71)

Keys HM in the GOG99 trial showed that overall survival rates were not significantly improved in patients receiving postoperative pelvic radiation compared with those treated only with surgery. (72)

In the **Astec** trial, it was proved that external beam radiation therapy in patients at intermediate to high risk of recurrence has no significant effect on overall survival. (73)

4. Extended Field Radiation:

Patients with histologically proven para-aortic node metastasis and no other evidence of disease spread outside the pelvis should be treated with extended – field radiation.

Potish RA et al in 1985 and **Rose PG** in 1992 showed that extended field radiotherapy appears to improve survival in patients with endometrial cancer with positive para-aortic lymph nodes. (74, 75)

5. Whole Abdomen Radiation:

It is usually reserved for patients with Stages 3 and 4 of endometrial cancer.

It may be considered for patients with serous or carcinosarcomas which have propensity for upper abdominal recurrence.

Corn BW et al proved that in patients treated with surgical Stage 3 endometrial cancer with whole abdomen radiation, patients with spread to adnexa, positive peritoneal cytology or both had a 5-year relapse-free

survival of 90% whereas all patients with macroscopic disease beyond the adnexa had recurrence. (76)

In 2006, *Randall ME et al* proved the superiority of chemotherapy over whole-abdominal radiotherapy in advanced endometrial cancer. (77)

6. Progestins:

Since most endometrial cancers have both oestrogen and progesterone receptors and progestins were successfully used to treat metastatic endometrial cancer. Postoperative adjuvant progestin therapy attempted to reduce risk of recurrence.

7. Chemotherapy:

In case of advanced disease, chemotherapy is now the standard.

Stage 3 and 4:

In locally advanced disease: Adjuvant chemotherapy followed by pelvic radiation is done. Combination chemotherapy is commonly used.

Drugs comprise: cisplatin, adriamycin and cyclophosphamide.

External pelvic and intracavitary radiation followed by extended hysterectomy 6 weeks later is done in cases of:

- Highly anaplastic tumour
- Papillary serous carcinoma
- Clear cell carcinoma

Chemotherapy:

Chemotherapy is used in advanced or recurrent cases or in metastatic lesions.

Progestogens: give good response in well differentiated carcinomas with adequate oestrogen and progesterone receptors.

Any one of the drugs, 17 hydroxyprogesterone caproate (1 gm/wk IM), medroxyprogesterone acetate (1 gm/wk IM or 150 mg/ day oral) or megestrol acetate (160 mg/day) is used for atleast 3 months.

Tamoxifen: is a nonsteroid with antioestrogenic and weakly oestrogenic property. It is used 10 mg twice daily with progesterone therapy.

Cytotoxic drugs: are used singly or in combination. Commonly used are cisplatin, cyclophosphamide, adriamycin, carboplatin and paclitaxel.

Recurrent disease:

- Radiation therapy is the choice for isolated recurrence following surgical treatment.
- Exenterative surgery for recurrent endometrial cancer is of limited value.
- Hormonal and chemotherapy have also been used depending on individual case.

Overall survival depends on the stage at diagnosis.

5 year relative survival rates by FIGO stage (78)

Stage	5 year survival
1A	88%
1B	75%
2	69%
3A	58%
3B	50%
3C	47%
4A	17%
4B	15%

RISK FACTORS:

- Depth of myometrial invasion - increasing depth of invasion is associated with increasing likelihood of extrauterine spread and recurrence
- Age
- Histological grade-strongly associated with prognosis (79-85)
 - grade I - 90% limited to endometrium or inner ½ of the myometrium
 - grade II - 50% invading the outer half of the myometrium
- Histological type
 - Nonendometroid histologic subtypes account for 10% and carry an increased risk for recurrence and distant spread.(86,87)
 - Adenocarcinoma - best prognosis
 - clear cell & papillary serous types - poorer prognosis
- Lymphovascular space involvement – independent risk factor in terms of survival & recurrence (88-91)
- Isthmus-cervix extension- associated with increased risk for extrauterine disease, lymphnode metastasis and recurrence especially cervical stromal invasion. (68)
- Adnexal involvement

- Lymphnode metastasis- most important prognostic factor in clinical early stage endometrial cancer.
- Intraperitoneal tumour
- Tumour size (92,93)
- Peritoneal cytology – associated with increased recurrence and decreased survival. Hence treatment is recommended for positive cytology.(94-96)
- Hormone receptor status.- Estrogen and progesterone are prognostic indicators independent of grade. (97-103)
- DNA ploidy/proliferative index
- Genetic /Molecular tumour markers

MATERIALS AND METHODS

This prospective study was carried out in the department of Obstetrics and Gynaecology at Kokilaben Dhirubhai Ambani Hospital, Mumbai from March 2013 to March 2014 after approval of the Ethics Committee.

Study included 50 patients who were diagnosed with Endometrial Cancer and have undergone surgery here. Only operable patients were included.

Sample Size: 50

Sample size was not based on previous studies. Since, we get limited number of cases, we decided to take all the cases based on inclusion criteria. On an average, 3-4 patients of Carcinoma of the Endometrium come to our hospital every month. Hence, over 13 months about 50 patients are seen.

Study period: March 2013 to March 2014

MR Imaging protocol:

Renal function test was done for all patients. If serum creatinine was in normal value, the non-ionic contrast was given. The patient should void approximately 1 hour before the examination to ensure that the bladder is partially filled, since a full bladder may degrade T2 weighted MR images. A 1.5 Tesla MR unit was used with a dedicated phased-array pelvic coil.

Surgical specimens were sectioned across the longitudinal plane of the uterus. The depth of myometrial invasion was estimated macroscopically and microscopically without awareness of MR findings and was staged according to FIGO classification.

Ultimately, MRI findings were compared with the Frozen section and pathological reports.

All patients underwent staging surgery including total hysterectomy and bilateral salpingo-oophorectomy. For suspicious cases, lymphadenectomy was performed.

Statistical Methodology:

Qualitative data was represented in form of frequency and percentage.

Association between qualitative variables was assessed by Chi-Square test with Continuity Correction for all 2 X 2 tables and with or without Continuity Correction in rest and Fisher's Exact test for all 2 X 2 tables where p-value of Chi-Square test is not valid due to small counts.

Quantitative data was represented using mean \pm sd and Median & IQR (Interquartile range).

Diagnostic efficacy of MRI vs. Frozen section, MRI vs. Histopathology and Frozen sections. Histopathology for various tumour characteristics was calculated through Sensitivity, Specificity, PPV, NPV, Positive Likelihood measurements.

Measurement of agreement between MRI and Frozen section, MRI and Histopathology and Frozen section and Histopathology for various tumour characteristics was assessed using Cohen's kappa coefficient.

Interpretation of Kappa was done as follows:

- Poor agreement = Less than 0.20
- Fair agreement = 0.20 to 0.40
- Moderate agreement = 0.40 to 0.60

- Good agreement = 0.60 to 0.80
- Very good agreement = 0.80 to 1.00

Results were graphically represented where deemed necessary.

Statistical Software:

SPSS V. 13 and Microsoft Excel were used for most analysis and graphical representation respectively.

Proper history, clinical examination (general, systemic, local) including per speculum and bimanual pelvic examination were done. Patients underwent various evaluation procedures like Ultrasonography, Dilatation and Curettage, Hysteroscopy biopsy, MRI, Intraoperative Frozen section.

Treatment modalities offered were Surgical management which included Total Abdominal Hysterectomy +Bilateral Salpingo-opherectomy+ Pelvic Lymphadenectomy and Total Abdominal Hysterectomy +Bilateral Salpingo-opherectomy+ Pelvic Lymphadenectomy+ Para-aortic node sampling.

OBSERVATIONS AND RESULTS

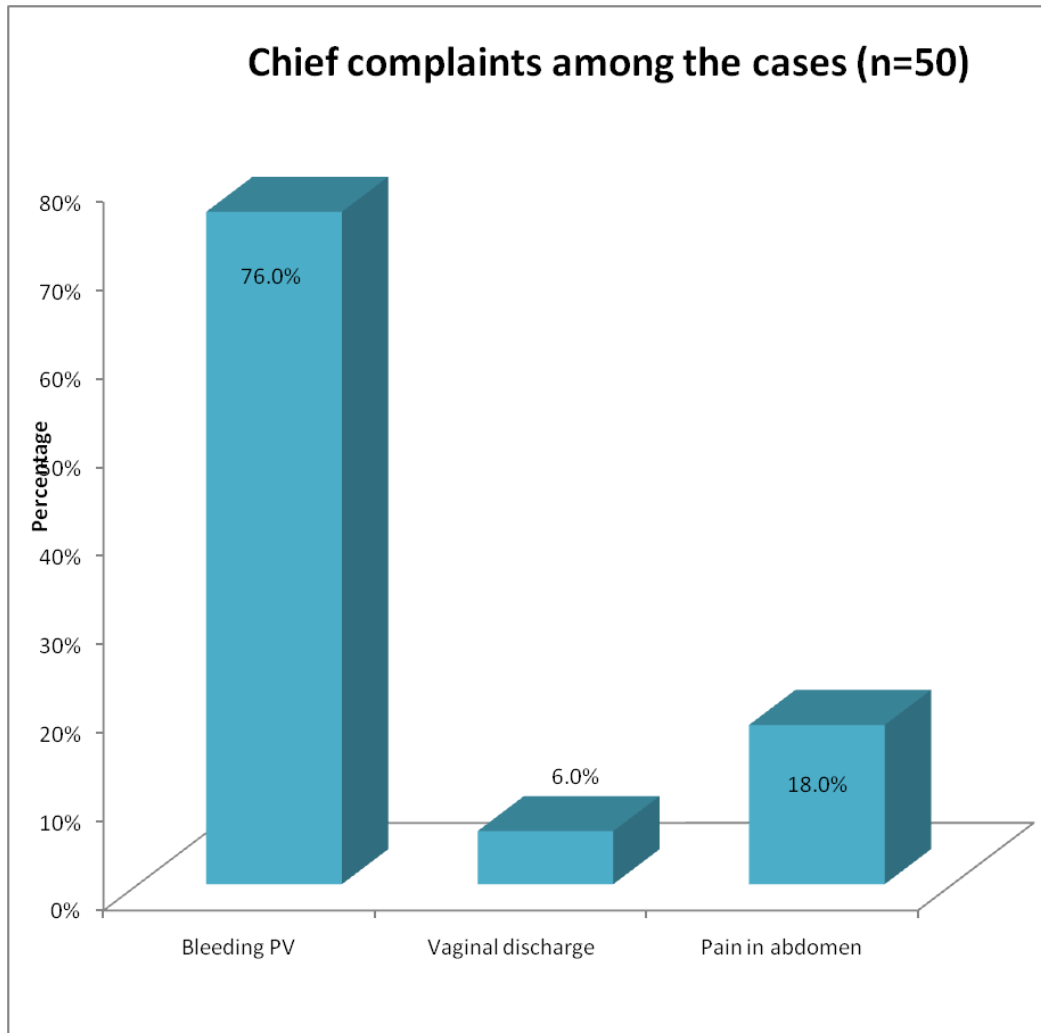
Table No: 5 - Chief complaints

Chief complaints	No.	Percentage (n=50)
Bleeding PV	38	76.0%
Vaginal discharge	3	6.0%
Pain in abdomen	9	18.0%

Patients presented with complaints such as postmenopausal bleeding, vaginal discharge and pain in abdomen.

Interpretation of Table No 5:

Out of 50 patients, 38(76%) had postmenopausal bleeding, 3(6%) had vaginal discharge and 9(18%) had pain in abdomen. Hence it can be concluded that postmenopausal bleeding is the most common complaint in CA endometrium.



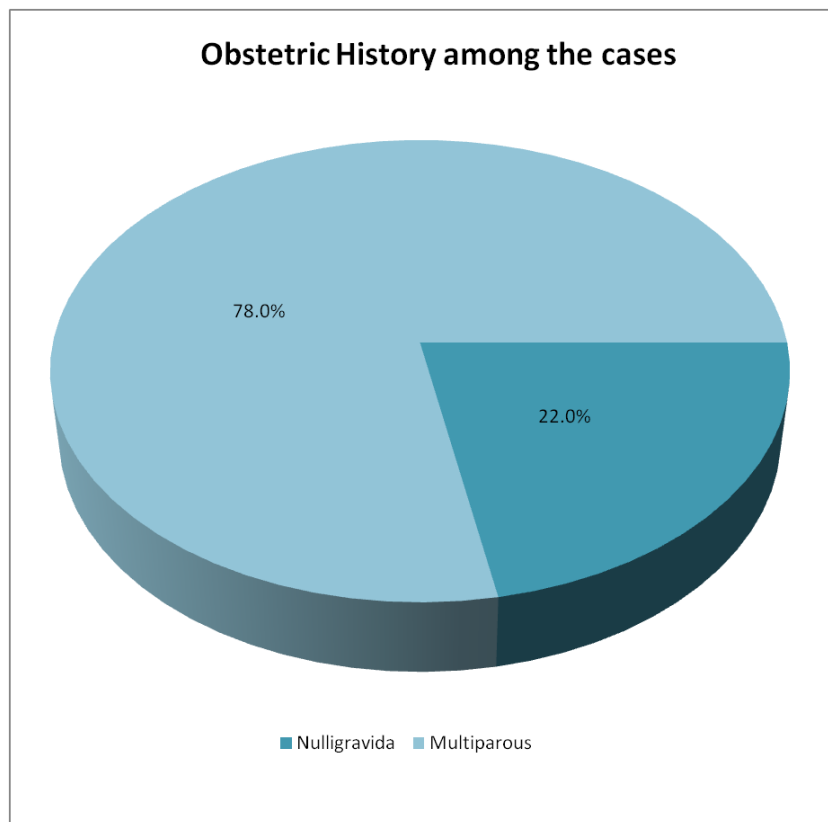
Graph 1: Chief complaints among the cases (n=50)

Table No. 6 : Obstetric History

Obstetric History	No.	Percentage
Nulligravida	11	22.0%
Multiparous	39	78.0%
Total	50	100.0%

Interpretation of table no 6:

In our study, 39 out of 50 patients i.e 78% were multiparous and 11 patients, i.e 22% were nulliparous.



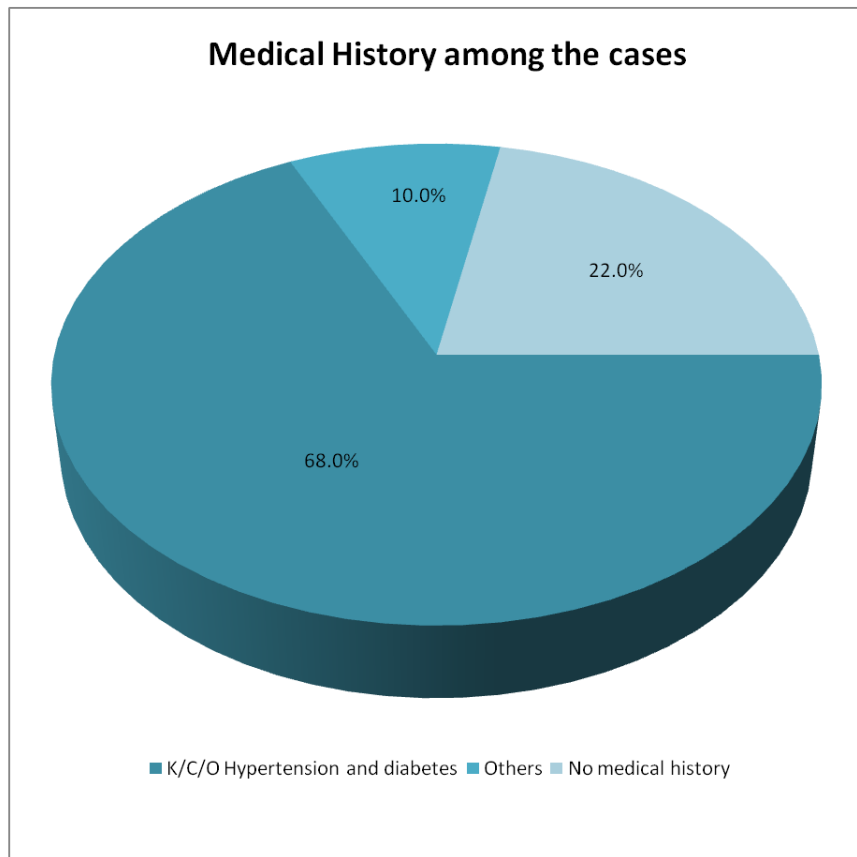
Graph 2: Obstetric History among the cases

Table No. 7 : Medical History

Medical History	No.	Percentage
K/C/O Hypertension and diabetes	34	68.0%
Others	5	10.0%
No medical history	11	22.0%
Total	50	100.0%

Interpretation of Table No 7 :

In our study, out of 50 patients 34(68%) had hypertension and /or diabetes, 5(10%) had other medical illness and 11(22%) had no medical history. Hence, it can be concluded that hypertension and diabetes are the most common risk factors.



Graph 3: Medical History among the cases

Table no 8 :-Endometrial thickness on USG

Endometrial thickness on USG	No.	Percentage
Less than 4mm	0	0.0%
More than 4mm	50	100.0%

Interpretation of Table no 8:

In all patients endometrial thickness was more than 4mm.

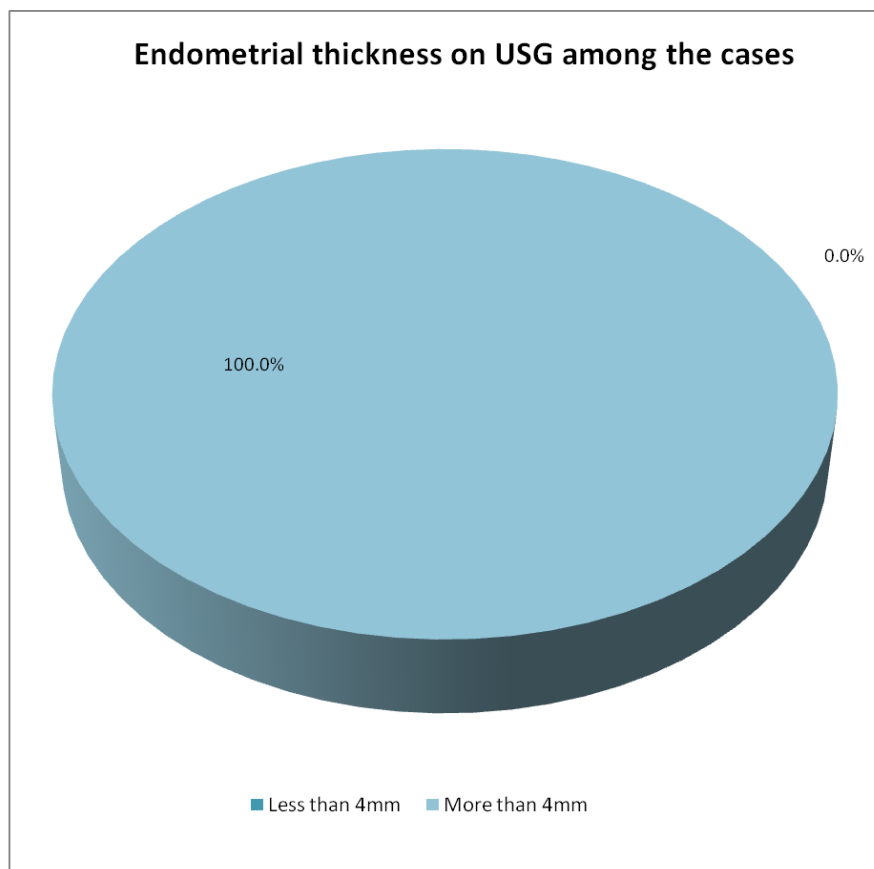
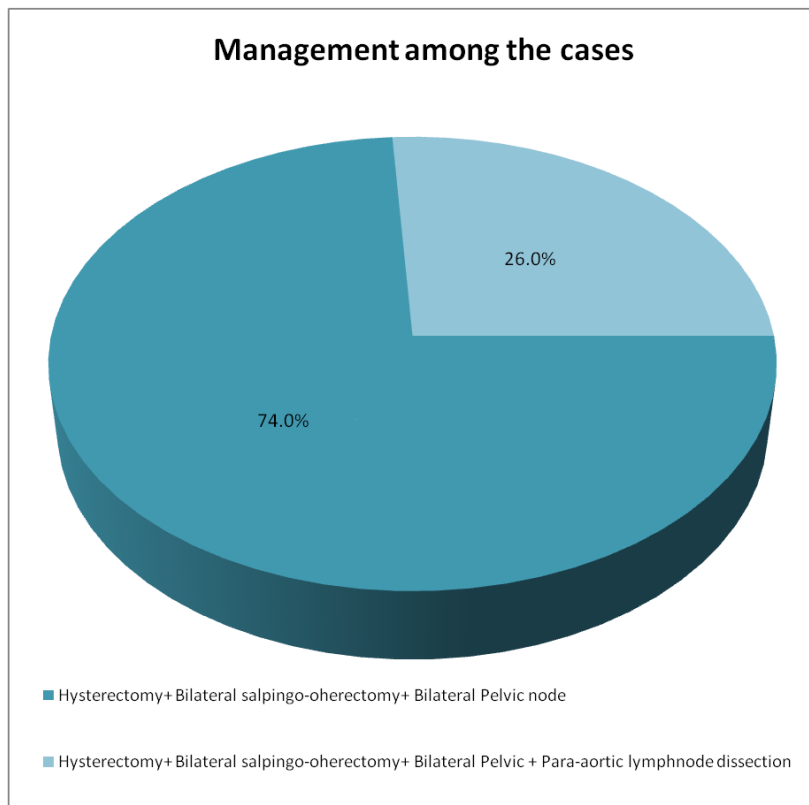
**Graph 4: Endometrial thickness on USG among the cases**

Table no 9:-Management (M)

Management (M)	No.	Percentage
Hysterectomy+ Bilateral salpingo- oherectomy+ Bilateral Pelvic node dissection	37	74.0%
Hysterectomy+ Bilateral salpingo- oherectomy+ Bilateral Pelvic + Para-aortic lymphnode dissection	13	26.0%
Total	50	100.0%

Interpretation of Table no 9:

37 out of 50 patients i.e 74% underwent Total Abdominal Hysterectomy + Bilateral Salpingo-oophorectomy+ Pelvic Lymphadenectomy and 13 patients i.e 26% underwent Total Abdominal Hysterectomy + Bilateral Salpingo-oophorectomy+ Pelvic and Paraortic node dissection either by open route or laparoscopic route.



Graph 5: Management among the cases

Table No. 10 : Correlation between Depth of Invasion on MRI and Frozen section

MRI-Depth of invasion		Frozen section-Depth of invasion		Total
		More than 50%	Less than 50%	
More than 50%	No.	6	7	13
	%	46.2%	53.8%	100.0%
Less than 50%	No.	0	37	37
	%	0.0%	100.0%	100.0%
Total	No.	6	44	50
	%	12.0%	88.0%	100.0%

Diagnostic & Agreement tests	Estimate	Lower 95% CI	Upper 95% CI
Sensitivity	100.00%	54.07%	100.0%
Specificity	84.09%	69.93%	93.36%
Predictive value of positive test	46.15%	19.22%	74.87%
Predictive value of negative test	100.00%	90.51%	100.0%

Likelihood ratio of positive test	6.286	3.187	12.399
Likelihood ratio of negative test	0.000		

Measure of Agreement-Kappa	Value	p-value	Agreement is-
	0.559	1.06E-05	Significant

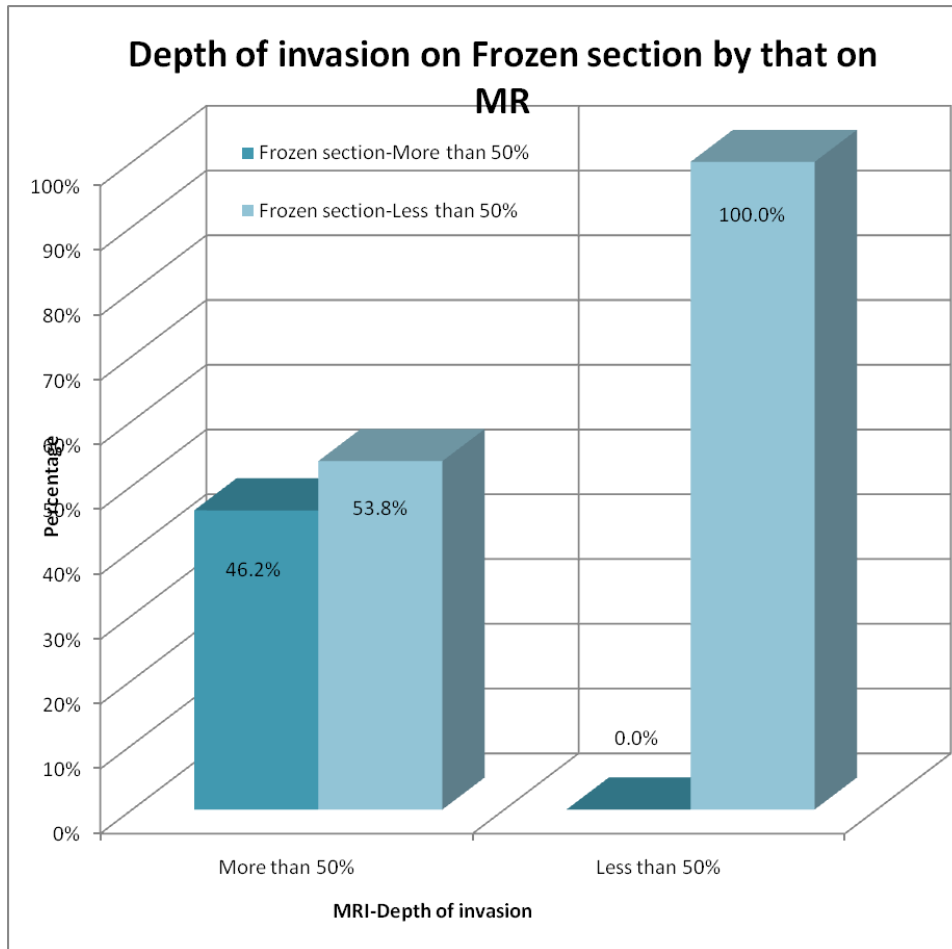
Interpretation of Table no 10:

Out of 13 patients who showed more than 50% myometrial invasion on MRI, only 6 (46.2%) patients showed more than 50% myometrial invasion on Frozen section.

Out of 37 patients who showed less than 50% myometrial invasion on MRI, all patients i.e 100% showed less than 50 % myometrial invasion on Frozen section.

The correlation was 100% sensitive and 84.09% specific, PPV 46.15% and NPV 100%.

The result shows a statistically significant correlation between depth of invasion on MRI and Frozen section using Kappa (value 0.559).



Graph 6: Depth of invasion on Frozen section by that on MR

Table No. 11 : Correlation between Depth of Invasion on MRI and Histopathology

MRI-Depth of invasion		Histopathology-Depth of invasion		Total
		More than 50%	Less than 50%	
More than 50%	No.	9	4	13

	%	69.2%	30.8%	100.0%
Less than 50%	No.	0	37	37
	%	0.0%	100.0%	100.0%
Total	No.	9	41	50
	%	18.0%	82.0%	100.0%

Diagnostic & Agreement tests	Estimate	Lower 95% CI	Upper 95% CI
Sensitivity	100.00%	66.37%	100.0%
Specificity	90.24%	76.87%	97.28%
Predictive value of positive test	69.23%	38.57%	90.91%
Predictive value of negative test	100.00%	90.51%	100.0%
Likelihood ratio of positive test	10.250	4.040	26.003
Likelihood ratio of negative test	0.000		

Measure of Agreement-Kappa	Value	p-value	Agreement is-
	0.769	2.28E-08	Significant

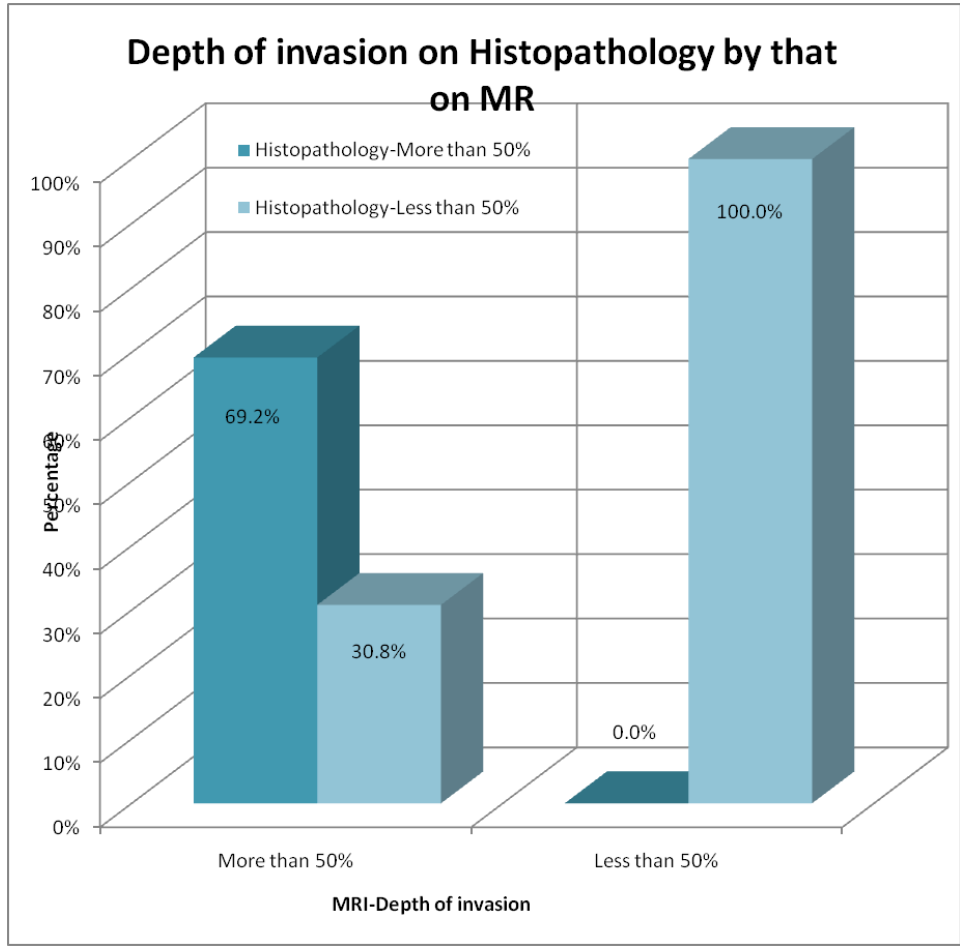
Interpretation of Table no 11:

Out of 13 patients who showed more than 50% myometrial invasion on MRI, only 9 patients i.e 69.2% showed more than 50% myometrial invasion on Histopathology.

All 37(100%) patients who showed less than 50% myometrial invasion on MRI also showed less than 50% myometrial invasion on Histopathology.

The sensitivity was 100%, specificity 90.24%, positive predictive value 69.23%, negative predictive value 100%.

The result shows a statistically significant correlation between depth of invasion on MRI and Histopathology using Kappa (value 0.769)



Graph 7: Depth of invasion on Histopathology by that on MR

Table No. 12 : Correlation between Depth of Invasion on Frozen section and Histopathology

Frozen section-Depth of invasion		Histopathology-Depth of invasion		Total
		More than 50%	Less than 50%	
More than 50%	No.	6	0	6
	%	100.0%	0.0%	100.0%
Less than 50%	No.	3	41	44
	%	6.8%	93.2%	100.0%
Total	No.	9	41	50
	%	18.0%	82.0%	100.0%

Diagnostic & Agreement tests	Estimate	Lower 95% CI	Upper 95% CI
Sensitivity	66.67%	29.93%	92.51%
Specificity	100.00%	91.40%	100.0%
Predictive value of positive test	100.00%	54.07%	100.0%
Predictive value of negative test	93.18%	81.34%	98.57%
Likelihood ratio of positive test			

Likelihood ratio of negative test	0.333	0.132	0.840
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Measure of Agreement-Kappa	Value	p-value	Agreement is-
	0.766	2.50E-08	Significant

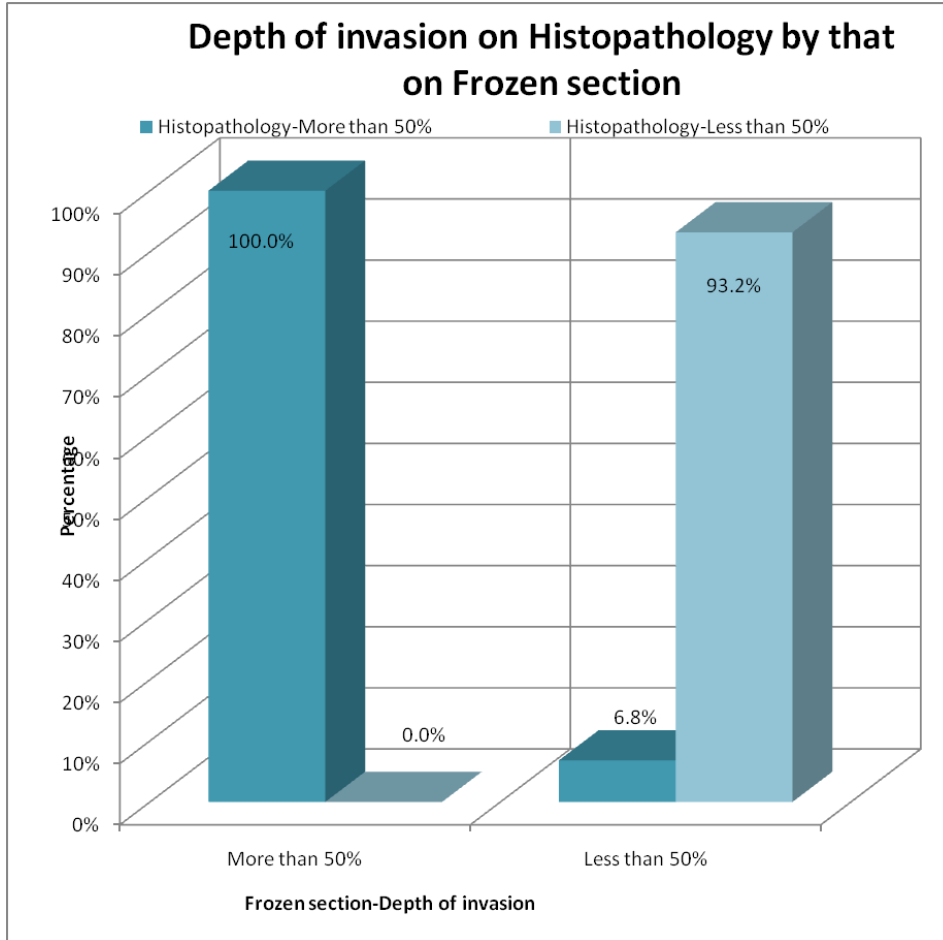
Interpretation of Table no 12:

All 6 patients who showed more than 50% myometrial invasion on Frozen section had more than 50% myometrial invasion on Histopathology also.

Out of 44 patients who showed less than 50% myometrial invasion on Frozen section, 41 (93.2%) showed less than 50 % myometrial invasion on Histopathology also.

The correlation was 66.67% sensitive and 100% specific. PPV was 100% and NPV was 93.18%.

The result shows a statistically significant correlation between depth of invasion on Frozen section and Histopatholog using Kappa (value 0.766)



Graph 8: Depth of invasion on Histopathology by that on Frozen section

Correlation between cervical infiltration on MRI and Frozen section:

Out of 50 patients who showed no cervical infiltration on MRI, 47 (94%) patients showed no cervical infiltration on Frozen section.

Only 3(6%) patients who showed glandular infiltration on Frozen section did not show cervical infiltration on MRI.

Hence, the correlation between the two is significant.

Table No.13 : Correlation between cervical infiltration on Frozen section and Histopathology:

Frozen section-Cervical infiltration		Histopathology- Cervical infiltration	
		Glandular	Not involved
Glandular	No.	3	0
	%	100.0%	0.0%
Not involved	No.	0	47
	%	0.0%	100.0%
Total	No.	3	47
	%	6.0%	94.0%

Diagnostic & Agreement tests	<i>Estimate</i>	<i>Lower 95% CI</i>	<i>Upper 95% CI</i>
Sensitivity	100.00%	29.24%	100.0%
Specificity	100.00%	92.45%	100.0%
Predictive value of positive test	100.00%	29.24%	100.0%
Predictive value of negative test	100.00%	92.45%	100.0%
Likelihood ratio of positive test			
Likelihood ratio of negative test	0.000		

Measure of Agreement-Kappa	Value	p-value	Agreement is-
	1.000	1.54E-12	Significant

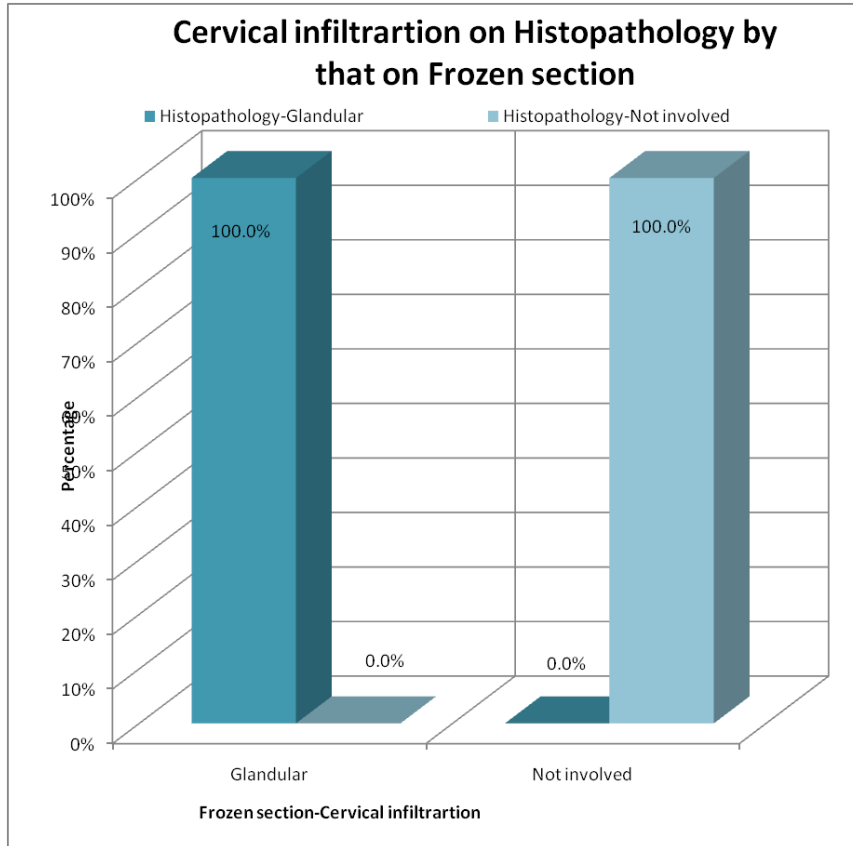
Interpretation of Table no 13:

3 patients who showed cervical glandular infiltration on Frozen section also showed cervical infiltration on Histopathology (100%).

47 out of 50 patients who showed no cervical infiltration on Frozen section also showed no cervical infiltration on Histopathology (100%).

The correlation was 100% sensitive and 100% specific. PPV 100%, NPV 100%.

The result shows a statistically significant correlation between Cervical Infiltration on Frozen section and Histopathology using Kappa (value 1).



Graph 9: Cervical infiltration on Histopathology by that on Frozen section

Correlation between cervical infiltration on MRI and Histopathology:

Out of 50 patients who showed no cervical infiltration on MRI, 47 (94%) patients showed no cervical infiltration on Histopathology.

Only 3(6%) patients who showed glandular infiltration on Histopathology did not show cervical infiltration on MRI.

Hence, the correlation between the two is significant.

Table No. 14 : Correlation between Lymph nodes on MRI and Frozen Section:

MRI-Lymph nodes		Frozen section- Lymph node		Total
		Yes	No	
Yes	No.	5	7	12
	%	41.7%	58.3%	100.0%
No	No.	1	37	38
	%	2.6%	97.4%	100.0%
Total	No.	6	44	50
	%	12.0%	88.0%	100.0%

Diagnostic & Agreement tests	Estimate	Lower 95% CI	Upper 95% CI
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Sensitivity	83.33%	35.88%	99.58%
Specificity	84.09%	69.93%	93.36%
Predictive value of positive test	41.67%	15.17%	72.33%
Predictive value of negative test	97.37%	86.19%	99.93%
Likelihood ratio of positive test	5.238	2.431	11.288
Likelihood ratio of negative test	0.198	0.033	1.192

Measure of Agreement-Kappa	Value	p-value	Agreement is-
		0.471	0.000286

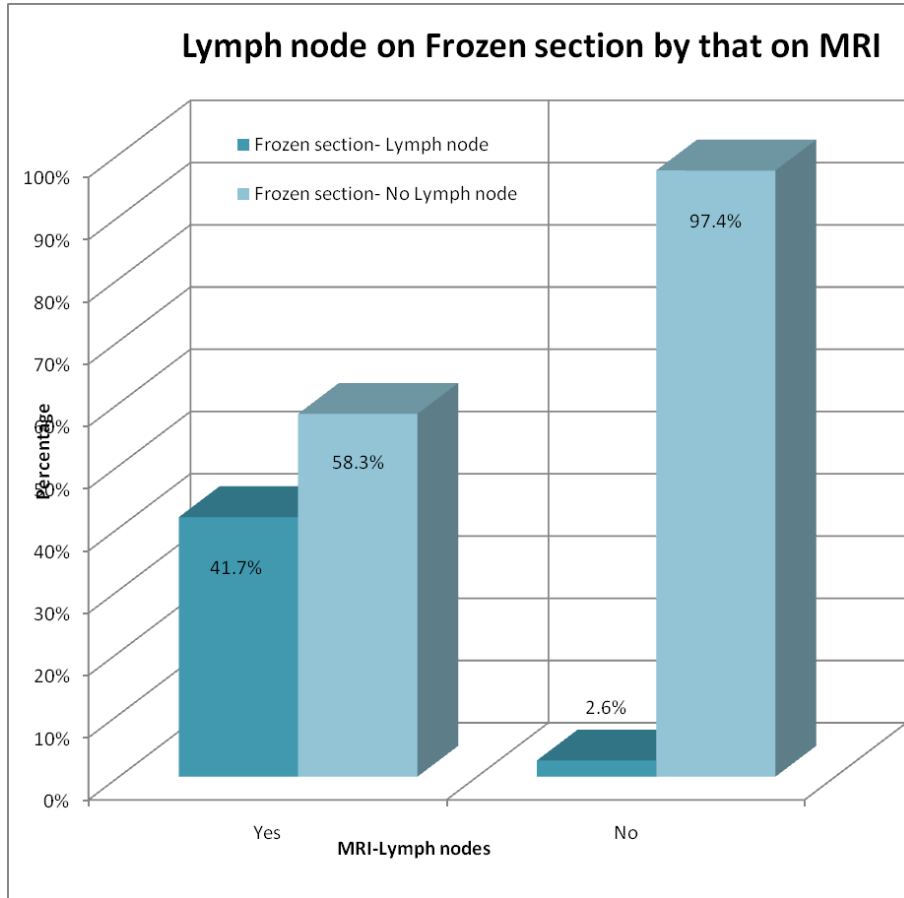
Interpretation of Table no 14:

Out of 12 patients who had lymph nodal involvement on MRI, 5 patients i.e 41.7% had lymph nodes on Frozen Section also.

Out of 38 patients who had no lymph node involvement on MRI, 37 patients (97.4%) had no lymph node involvement on Frozen section also.

The correlation was 83.33% sensitive and 84.09% specific. PPV 41.67% was and NPV 97.37%.

The result shows a statistically significant correlation between Lymph node on Frozen section and MRI using Kappa (value 0.471).



Graph 10: Lymph node on Frozen section by that on MRI

Table No.15 : Correlation between lymph node involvement on MRI and

Histopathology:

MRI-Lymph nodes	Histopathology-Lymph Nodes		Total
	Yes	No	

Yes	No.	3	9	12
	%	25.0%	75.0%	100.0%
No	No.	1	37	38
	%	2.6%	97.4%	100.0%
	No.	4	46	50
	%	8.0%	92.0%	100.0%

Diagnostic & Agreement tests	Estimate	Lower 95% CI	Upper 95% CI
Sensitivity	75.00%	19.41%	99.37%
Specificity	80.43%	66.09%	90.64%
Predictive value of positive test	25.00%	5.49%	57.19%
Predictive value of negative test	97.37%	86.19%	99.93%
Likelihood ratio of positive test	3.833	1.698	8.656
Likelihood ratio of negative test	0.311	0.057	1.707

Measure of Agreement-Kappa	Value	p-value	Agreement is-
	0.290	0.013	Significant

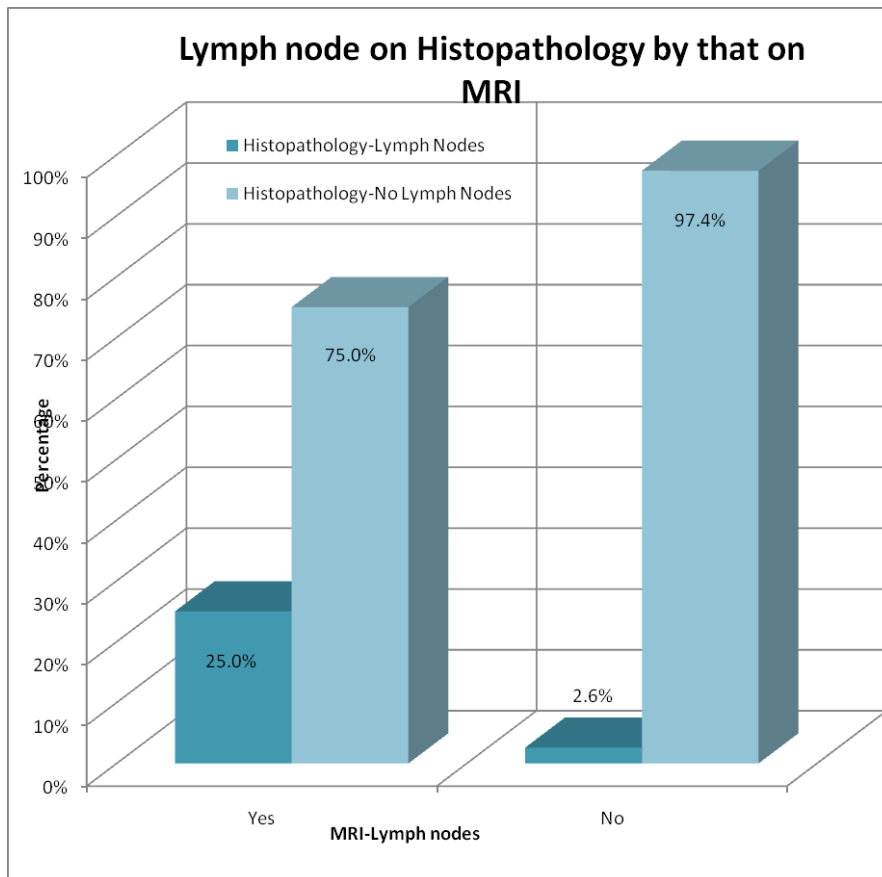
Interpretation of Table no 15:

Out of 12 patients who had lymph node involvement on MRI, 3 patients i.e 25% had lymph node involvement on Histopathology also.

Out of 38 patients who had no lymph node involvement on MRI, 37 patients i.e 97.4% had no lymph node involvement on Histopathology also.

The correlation was 75% sensitive and 80.43% specific. PPV 25% and NPV was 97.37%.

The result shows a statistically significant correlation between Lymph node involvement on MRI and Histopathology using Kappa (value 0.290).



Graph 11: Lymph node on Histopathology by that on MRI

Table No 16 : Correlation between lymph nodes on Frozen section and**Histopathology:-**

Frozen section- Lymph node		Histopathology-Lymph Nodes		Total
		Yes	No	
Yes	No.	3	3	6
	%	50.0%	50.0%	100.0%
No	No.	1	43	44
	%	2.3%	97.7%	100.0%
Total	No.	4	46	50
	%	8.0%	92.0%	100.0%

Diagnostic & Agreement tests	Estimate	Lower 95% CI	Upper 95% CI
Sensitivity	75.00%	19.41%	99.37%
Specificity	93.48%	82.10%	98.63%
Predictive value of positive test	50.00%	11.81%	88.19%
Predictive value of negative test	97.73%	87.98%	99.94%
Likelihood ratio of positive test	11.500	3.356	39.411
Likelihood ratio of negative test	0.267	0.049	1.463

Measure of Agreement-Kappa	Value	p-value	Agreement is-
	0.558	5.29E-05	Significant

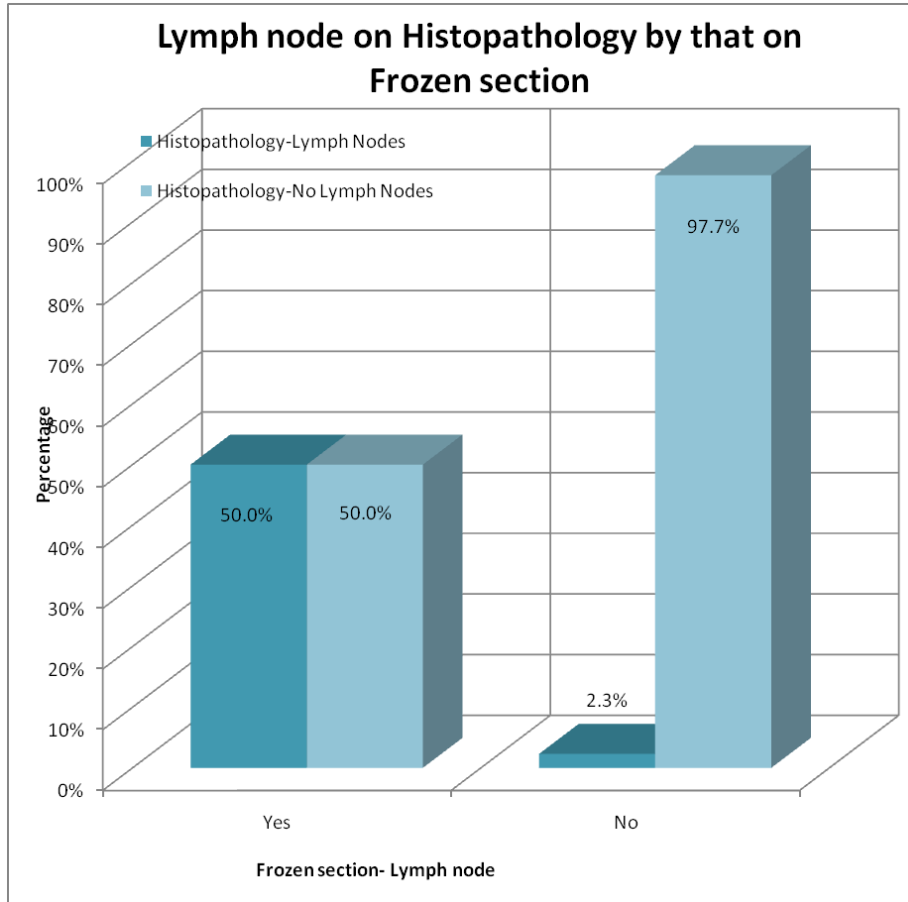
Interpretation of Table no 16:

Out of 6 patients who had positive lymph nodes on Frozen section, 3 patients i.e 50% had positive lymph nodes on Histopathology.

Out of 44 patients who had no lymph nodes on Frozen section, 43 patients i.e 97.7% had no lymph nodes on Histopathology.

The correlation was 75% sensitive and 93.48% specific. PPV was 50% and NPV was 97.73%.

The result shows a statistically significant correlation between Lymph nodal involvement on Frozen section and Histopathology using Kappa (value 0.558).



Graph 12: Lymph node on Histopathology by that on Frozen section

Table No. 17 : Correlation between Grade on Frozen section and Histopathology:

Frozen section-Grade	Histopathology-Grade		Total
	1	2	

1	No.	28	6	34
	%	82.4%	17.6%	100.0%
2	No.	3	13	16
	%	18.8%	81.3%	100.0%
Total	No.	31	19	50
	%	62.0%	38.0%	100.0%

Chi-Square Tests	Value	df	p-value	Association is-
Pearson Chi-Square	18.681	1	1.55E-05	Significant
Continuity Correction	16.079	1	6.08E-05	Significant
Fisher's Exact Test			0.00002589	Significant

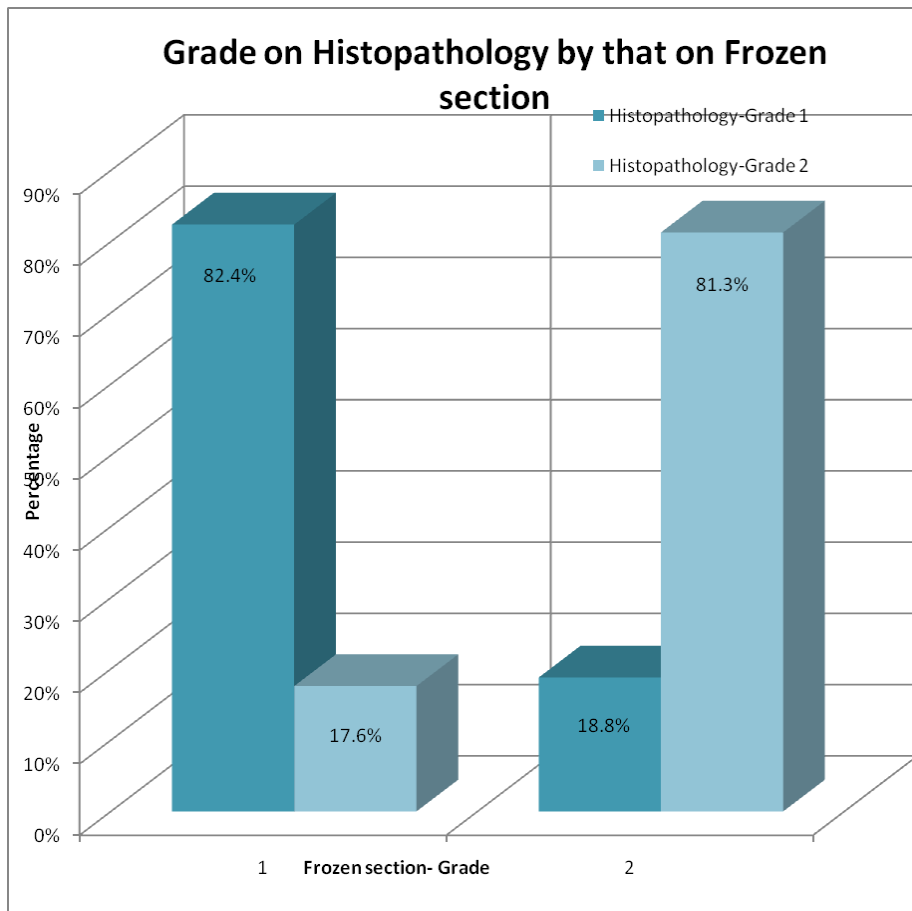
Measure of Agreement-Kappa	Value	p-value	Agreement is-
	0.606	1.54E-05	Significant

Interpretation of Table no 17:

Out of 34 patients who showed Grade 1 on Frozen section, 28 patients i.e 82.4% showed Grade 1 on Histopathology also.

Out of 16 patients who showed Grade 2 on Frozen section, 13 patients i.e 81.3% showed Grade 2 on Histopathology also.

The result shows a statistically significant correlation between Grading on Frozen section and Histopathology using Kappa (value 0.606).



Graph 13: Grade on Histopathology by that on Frozen section

DISCUSSION

The prognosis of endometrial cancer is more favorable in respect to other gynecological malignancies with a 5 year survival rate of 84%.

75% patients with endometrial cancer are diagnosed at stage 1 and are curable by simple hysterectomy. (104, 81)

The histological grade and the stage of disease (depth of myometrial invasion, cervical involvement) are predictive of the occurrence of extrauterine spread and pelvic or lumboaortic nodal metastases and affect prognosis and treatment. (105, 106, 107)

Based on the stage of the disease, the treatment options include surgery, radiation therapy, hormone therapy and chemotherapy. Therefore, pre-treatment staging allows to define the type and extent of therapy. (106)

In patients at high risk of extrauterine disease or nodal metastases (grade 3, deep myometrial and/or cervical infiltration), lymphadenectomy and preoperative or postoperative radiation therapy are indicated. (106, 108)

Postmenopausal Vaginal bleeding is the most common symptom of endometrial carcinoma.

According to *Gambrell et al* in approximately 10% of woman with postmenopausal bleeding will be diagnosed with endometrial carcinoma. (109)

Smith et al also found that about 90% women with endometrial carcinoma have vaginal bleeding as their only presenting symptom. (12)

In this study of 50 patients, 38(76%) had postmenopausal bleeding.

Thus our study proves that postmenopausal bleeding is the most common complaint in CA endometrium as seen in other studies also.

Type 2 diabetes is related to hyperinsulinemia which may increase free oestrogen levels by decreasing the concentration of sex hormone binding globulin. (110,111)

Hyperinsulinemia may also affect the Insulin Growth Factor system. Increasing levels of IGF-1 and IGF binding protein have been associated with endometrial cancer particularly in obese women. (112)

In a study by *Parazzini et al*, an increased risk of endometrial cancer in diabetic women has been reported. (113)

Salazar-Martinez et al also proved that diabetic women are more prone to endometrial cancer. (114)

Tooke JE showed that hypertension has a moderate association with endometrial cancer risk. (115)

The biological mechanism linking hypertension to endometrial cancer is unclear but has been related to insulin resistance.

In our study, out of 50 patients 34(68%) had hypertension and /or diabetes .Hence, it can be concluded that hypertension and diabetes are the most common risk factors which correlates with other studies also.

Depth of invasion on MRI and Frozen section:

Kisu et al conducted a study to compare myometrial invasion retrospectively on MRI and Frozen section.

They concluded that the accuracy and sensitivity of frozen sections were significantly higher ($p < 0.001$) than MRI whereas the specificity of the methods did not differ. (116)

In our experience, out of 13 patients who showed more than 50% myometrial invasion on MRI, only 6 (46.2%) patients showed more than 50% myometrial invasion on Frozen section.

Out of 37 patients who showed less than 50% myometrial invasion on MRI, all patients i.e 100% showed less than 50 % myometrial invasion on Frozen section.

The correlation was 100% sensitive and 84.09% specific, PPV 46.15% and NPV 100%.

Hence, we can conclude that myometrial invasion on MRI and Frozen section can be correlated.

Depth of invasion on MRI and Histopathology:

Agreement between MRI and histopathology has been observed in 90% of cases, with good sensitivity and diagnostic accuracy for the identification of deep myometrial infiltration by *Manfredi et al.* (23)

Fatemeh Zamani et al showed the correlation of myometrial involvement in MRI and Histopathology. (117)

The Kappa for agreement was 0.656. (Table 18)

Table- 18 : Correlation of MR Imaging with Histopathologic Results in 54**Patients**

	Myometrial Invasion in Pathology			Total
	None	< 50%	≥ 50%	
No myometrial invasion in MRI	9	7	0	16
< 50% myometrial invasion in MRI	0	19	3	22
≥ 50% myometrial invasion in MRI	0	2	14	16
Total	9	28	17	54

Our study showed that out of 13 patients who showed more than 50% myometrial invasion on MRI, only 9 patients i.e 69.2% showed more than 50% myometrial invasion on Histopathology.

All 37 patients who showed less than 50% myometrial invasion on MRI also showed less than 50% myometrial invasion on Histopathology.

The sensitivity was 100%, specificity 90.24%, positive predictive value 69.23%, negative predictive value 100%.

The Kappa for agreement between depth of invasion on MRI and Histopathology was 0.769.

All the studies show good agreement between myometrial invasion on MRI and Histopathology.

Depth of invasion Frozen Section and Histopathology:

In a study by *Julie A et al*, the observed agreement between Frozen Section and Histopathology with respect to depth of myometrial invasion was extremely high with Kappa 0.89. (118)

Richardson et al Depth of myometrial invasion compared the depth of invasion on Frozen section and Histopathology. (119)

Table- 19: The depth of tumour invasion on frozen section reporting compared to the final histopathology of the uterus.

Final histopathology of myometrial invasion	Frozen section diagnosis	
	<50% myometrial invasion	>= 50% myometrial invasion
<50%	128 (94.8)	4 (5.4)
>=50% myometrial invasion	7 (5.2)	70 (94.6)
Total	135 (100)	74 (100)

The sensitivity of frozen section for identifying deeply invasive lesions was found to be 78.57% with a specificity of 100%, a PPV of 100% and a NPV of 94%.

Case et al. evaluated in a prospective-blinded study the accuracy of frozen section in surgical management of endometrial cancer. There was a poor correlation between frozen and final section: only 67% for invasion depth. (52)

Another study by *Frumovitz et al.* verified that the combination of intraoperative frozen section analysis for histological depth of myometrial invasion correlates

poorly with final pathologic stage in patients with apparent grade I and II tumor.
(53)

In our experience, all 6 patients who showed more than 50% myometrial invasion on Frozen section had more than 50% myometrial invasion on Histopathology also.

Out of 44 patients who showed less than 50% myometrial invasion on Frozen section, 41 (93.2%) showed less than 50 % myometrial invasion on Histopathology also.

The correlation was 66.67% sensitive and 100% specific. PPV was 100% and NPV was 93.18%.

The result shows a statistically significant correlation between depth of invasion on Frozen section and Histopathology using Kappa (value 0.766)

Cervical involvement on Frozen Section and Histopathology:

Richardson KJ compared cervical involvement on Frozen section and Histopathology. (119)

Table-20: Comparison of cervical involvement identified on frozen section with definitive histology results

		Definitive histology: cervical involvement		
		Involved	Not Involved	Total
Frozen section: Cervical involvement	Involved	4	0	4
	Not involved	3	23	26
	Total	7	23	30

The sensitivity was 57.1%, specificity 100%, PPV 100% and NPV 88.5%.

In our study, 3 patients who showed cervical glandular infiltration on Frozen section also showed cervical infiltration on Histopathology (100%).

47 out of 50 patients who showed no cervical infiltration on Frozen section also showed cervical infiltration on Histopathology (100%).

The correlation was 100% sensitive and 100% specific. PPV 100%, NPV 100%.

The result shows a statistically significant correlation between Cervical Infiltration on Frozen section and Histopathology using Kappa (value 1).

Cervical involvement on MRI and Histopathology:

According to a study by *Fatemeh Zamani et al* (117), the correlation of cervical invasion in MRI and the final pathology report, 29 out of 46 patients (63%) without cervical involvement in MRI did not have any cervical invasion in the surgicopathological report, 13 patients (28.3%) had only mucosal and four patients (8.7%) had stromal involvement.

One out of two patients (50%) with mucosal involvement in MRI had mucosal and another one had stromal involvement. In the case of mucosal involvement, the PPV was only 50% and the accuracy decreased to 74.07%.

In case of cervical stromal involvement in the MRI report, all of them had stromal invasion in the pathology report (100% correlation between MRI and pathology). For cervical stromal involvement, the sensitivity, specificity, diagnostic accuracy, PPV and NPV and positive and negative likelihood ratios of MRI were 54.54%, 100%, 90.74%, 100%, 89.58%, 2.85 and 0.95, respectively (calculated with 95% confidence intervals).

For agreement between MRI report and pathology of cervix, the Kappa was 0.347.

In our study, none of the 50 patients showed cervical invasion on MRI.

3 out of 50 patients showed cervical invasion on Histopathology suggesting no correlation between MRI and Histopathology.

Correlation of Lymph node involvement on Frozen section and Histopathology:

The finding of negative pelvic nodes at intraoperative frozen section has been proposed to guide further surgical management during surgical staging of endometrial cancer.

A recent study by *Papadia et al.* confirmed that frozen section underestimated the risk of lymph node involvement in 16% of cases when compared with final section pathology (54)

Another trial by *Pristauz et al.* verified that intraoperative frozen section of pelvic nodes is not accurate to tailor the extent of lymphadenectomy. In this study, examination of pelvic nodes had a sensitivity of 41% and a false negative rate of 59%. (120)

In our experience, the correlation was 75% sensitive and 93.48% specific. PPV 50% and NPV was 97.73%.

The result shows a statistically significant correlation between Lymph nodal involvement on Frozen section and Histopathology using Kappa (value 0.558).

Correlation of Lymph node involvement on MRI and Histopathology:

S. Cabrita et al showed that considering lymph node invasion, MRI demonstrated a sensitivity of just 17%, a specificity of 99%, a diagnostic accuracy of 89%, a PPV of 66% and NPV of 90%. (121)

In a study, *Hricak H et al* proved that MRI had limited specificity in detecting pelvic and para-aortic lymph nodes. (26)

When determining whether or not to perform routine lymphadenectomy, a key issue that must be considered is if lymphadenectomy improves outcomes in a patient population that has excellent disease-free survival.

Hidaka et al compared 68 patients with early stage disease who underwent complete lymphadenectomy with 60 patients who did not undergo lymphadenectomy. (122)

Disease-free survival, overall survival, perioperative complications, and blood transfusions were compared. Overall, there was no significant difference in

disease-free and overall survival between the two groups. However, mean operative time (237 vs 132 minutes), estimated blood loss (771 vs 259 mL), transfusion requirement (23 vs 2 patients), and postoperative leg lymphedema (11 vs 0 patients) were all significantly greater in the lymphadenectomy group.

Although this study was not powered to detect differences in survival, it confirmed earlier reports that low risk patients without complete lymphadenectomy had an excellent prognosis.

In contrast, *Kilgore et al* found that lymphadenectomy did impact survival. Three groups of endometrial cancer patients were compared retrospectively. (56)

One group underwent multiple pelvic node sampling (average of 11 nodes) . A second group of 205 patients had limited pelvic node sampling (average of 4 nodes) from fewer than 4 sites, and the third group of 208 patients were not sampled.

The patients who had multiple-site pelvic node sampling had significantly better overall survival than the patients who did not have lymph node sampling ($P = .0002$).

Multiple-site pelvic node sampling offered survival benefit in both low-risk and high-risk patients. Additionally, lower recurrence rates were observed in patients with multiple-site pelvic node sampling compared to those patients without node sampling ($P = .019$). This study suggests that the extent of lymph node dissection may be an important consideration when assessing the potential benefits of lymphadenectomy.

Morbidity from Lymph node dissections and radiotherapy:

It has been argued that the complications from surgical staging may be worse than the side effects of radiotherapy.

Morbidity from lymphadenectomy includes lymphedema, symptomatic lymphocyst, deep vein thrombosis, and blood transfusion. (123)

In a study comparing 191 surgically staged endometrial cancer patients with 101 non-staged patients; *Moore et al* (124) did not find significant differences in estimated blood loss, blood transfusions, or vascular injuries between the staged and unstaged groups.

There was also no difference in infection rates and length of hospital admission postoperatively.

In a prospective trial of 77 patients, *Larson et al* (59) noted that lymph node sampling resulted in surgeries lasting an average of 40 minutes longer with greater estimated blood loss (approximately 120mL).

There was also a longer average postoperative hospital stay for the surgically staged group. However, lymph node sampling did not result in an increased risk of febrile morbidity, blood transfusion, postoperative complications, or mortality in this study. In general, morbidity from lymphadenectomy is limited if performed by a skilled surgeon.

Morbidity from whole pelvic radiation includes deleterious effects on small and large bowel, urinary bladder, and vaginal function.

Adverse gastrointestinal effects are the most common, ranging from mild diarrhea and abdominal cramping to bleeding and obstruction.

Urinary bladder complications include dysuria, hematuria, incontinence, fistula, and necrosis.

In a retrospective study of 317 patients with endometrial cancer treated with postoperative radiotherapy, late complications were documented in 51%, with 11% of patients suffering from grade 3 or 4 complications. (126)

Surgical staging may avoid these potential morbidities by decreasing the utilization of radiotherapy.

Correlation between lymph node involvement on MRI and Histopathology:

Our study showed that Out of 12 patients who had lymph node involvement on MRI, 3 patients i.e 25% had lymph node involvement on Histopathology also.

Out of 38 patients who had no lymph node involvement on MRI, 37 patients i.e 97.4% had no lymph node involvement on Histopathology also.

The correlation was 75% sensitive and 80.43% specific. PPV 25% and NPV was 97.37%.

The result shows a statistically significant correlation between Lymph node involvement on MRI and Histopathology using Kappa (value 0.290).

Correlation between Tumour grading on Frozen section and Histopathology:

Julie et al observed that agreement between Frozen section and Histopathology with respect to tumour grade was high. Kappa = 0.72(118)

Table 21: Tumour grade on frozen section reporting compared to histopathology of the uterus. Values are given as n (%).

Final histopathology	Frozen section diagnosis		
	Grade 1	Grade 2	Grade 3
Grade 1	151 (91.5)	4 (12.1%)	1 (9.1)
Grade 2	12 (7.3)	29 (81.8)	3 (27.3)
Grade 3	2 (1.2)	2 (6.1)	7 (63.6)
Total	165 (100)	33 (100)	11 (100)

Richardson et al, when assessing high-grade (grade 3) lesions, frozen section identified five, whereas definitive histology found eight patients to be have high-grade lesions. Thus, the sensitivity of frozen section for identifying high-grade lesions was 62.5% and the specificity 98.1%, with a PPV of 83.3% and a NPV 94.6%. Frozen section was found to be accurate in 95.1% of cases. (119)

Table 22: Tumour grade on frozen section reporting compared to histopathology of the uterus

		Definitive histology: grade		
		Grade 3	Grade <3	Total
Frozen section: grade	Grade 3	5	1	6
	Grade <3	3	52	55
	Total	8	53	61

Case et al in a prospective –blinded study found that the correlation between tumour grade on Frozen section and Histopathology was 58%. (52)

Frumovitz et al verified that there was poor correlation between Frozen section and Histopathology for tumour grading. (53)

In our experience, Out of 34 patients who showed Grade 1 on Frozen section, 28 patients i.e 82.4% showed Grade 1 on Histopathology also.

Out of 16 patients who showed Grade 2 on Frozen section, 13 patients i.e 81.3% showed Grade 2 on Histopathology also.

The result shows a statistically significant correlation between Grading on Frozen section and Histopathology using Kappa (value 0.606).

Retroperitoneal lymph node metastasis is a significant prognostic factor for patients with endometrial cancer. The risk of paraaortic nodal metastasis can be related to the presence

of adnexal metastasis and/or pelvic lymph nodes metastasis: paraaortic lymph nodes are positive in 38%–52% of cases with positive pelvic lymph nodes, in 20%–57% with adnexal metastasis, and in only 2% with negative pelvic nodes . (126)

In other trials, a range from 28.6% to 66.7% of patients with pelvic metastasis had concomitant positive paraaortic nodes. (81,126-128)

Mariani et al. demonstrated that 47% of patients with pelvic lymph nodes metastasis also have positive paraaortic lymph nodes or will submit a relapse in paraaortic region. (129)

Mariani et al. reported the potential therapeutic role of paraaortic lymphadenectomy in node positive patient with endometrial cancer. (130,131)

The 5-year progression free and overall survival rates were significantly better in paraaortic lymphadenectomy group.

Sanjeev Kumar et al showed the agreement between the Frozen Section and Histopathology for the following parameters in the table below.

Table-23: (%) Agreement between frozen section and paraffin section with the corresponding agreement statistic (Kappa) for different variables in endometrial cancer.

Variable	% Agreement	Kappa	(95% Confidence Interval for Kappa)	P
Myometrial invasion	72	0.61	0.53–0.69	<0.0001
Cervical invasion	86.9	0.78	0.65–0.91	0.002
Lymphovascular space invasion	68.3	0.60	0.52–0.69	0.01
Grade	65.3	0.58	0.51–0.68	0.003

From the available studies we could conclude that paraaortic lymphadenectomy might have a therapeutic role at least for high-risk patients.

CONCLUSION

Endometrial carcinoma is the most common pelvic gynaecological malignancy in industrialized countries, and the incidence is increasing.

Treatment and prognosis is influenced by surgical stage with evaluation of the depth of myometrial invasion, cervical extension and the presence of lymph node and distant metastases. The histological subtype and grade are also established prognostic markers influencing therapy. The overall 5-year survival of endometrial carcinoma is 80%. Approximately 75% of endometrial carcinomas are diagnosed with the tumours confined to the uterine corpus

Magnetic resonance imaging (MRI) has long been established as a valuable diagnostic tool in the preoperative diagnostic staging of endometrial carcinomas.

Intraoperative Frozen section might identify patients who are at risk for extrauterine spread and require complete surgical staging.

The surgical procedure and therapeutic strategy in endometrial carcinoma are highly dependent on the FIGO stage. For low-risk stage I endometrial cancer,

hysterectomy with bilateral salpingo-oophorectomy is the standard surgical procedure including cytological evaluation of the peritoneal fluid or intraperitoneal cell washings. Systematic pelvic and para-aortic lymphadenectomy is part of the surgical FIGO staging scheme.

The risk of lymph node metastases is highly correlated with the extent of myometrial tumour infiltration and histopathological subtype and grade. Lymph node metastases occur in only 3-5% of the patients with superficially infiltrating, well-differentiated, endometrioid tumours as opposed to 20% of patients with poorly differentiated tumours with deep myometrial invasion.

Therefore, in order to reduce the number of unnecessary nodal sampling procedures, some apply a tailored approach to pelvic- and para-aortic lymphadenectomy according to the preoperative identification of high- and intermediate-risk patients based on depth of myometrial invasion, histological subtype, and grade.

This prospective study was done to study the correlation between MRI, Frozen section and Histopathological findings in Carcinoma of the Endometrium.

Preoperative MRI, intraoperative Frozen section and postoperative Histopathology was done in all patients.

We emphasized on the following:

1. Complete surgical staging: Role of lymphadenectomy in endometrial cancer;
2. Preoperative evaluation: Predictors of lymph node metastasis;
3. Intraoperative detection of lymph node metastasis;
4. Extent of lymphadenectomy;
5. Surgical approach for staging of endometrial cancer.

Highest incidence was seen in postmenopausal women. It was observed that women with history of diabetes or hypertension or both were significantly associated with increased risk of Carcinoma of the endometrium. 68% patients with Carcinoma of the Endometrium had hypertension or diabetes or both.

Most common presentation was vaginal bleeding. (76%)

The present study shows that there is significant correlation between MRI, Frozen Section and Histopathological findings i.e myometrial invasion, cervical invasion and lymph node in a patient of Carcinoma of the Endometrium.

MRI can accurately assess myometrial invasion and cervical infiltration. MRI is also an important predictor of lymph node metastasis and when combined with Frozen section findings could be used to select patients at low risk of recurrence.

This information allows the selection of patients for pelvic or paraaortic lymph node sampling while obviating radical surgery in patients with low risk of recurrent disease or significant comorbidities.

It also helps in planning postoperative adjuvant therapy.

State-of-the-art staging is usually done surgically, but correct non-invasive staging by imaging modalities predicting myometrial and cervical invasion could allow us to decide on the surgical approach in advance and to select patients who need chemotherapy or radiation therapy.

Imaging identification of nodal involvement may provide an indication for lymphadenectomy and the extent of nodal involvement on imaging studies in nonsurgical patients may help to plan the extension of radiation therapy.

When different imaging modalities were compared for their efficacy in detecting deep myometrial invasion, MRI was found to have better diagnostic performance than transvaginal ultrasonography and computed tomography.

Because of the high contrast and spatial resolution and the absence of radiation exposure, MRI is an optimal diagnostic tool for the study of the female pelvis. MR images provide a detailed picture of the uterine wall, with identification of the different layers. This means that the depth of infiltration can be established.

MRI is the only imaging modality allowing 1-step assessment of lymph nodes, myometrium, and cervix, reaching a diagnostic accuracy of 80-90%

The results of the present study indicate that Frozen section compares favorably in accuracy with Magnetic Resonance Imaging. Hence, it should play an important role in directing primary operative management.

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INFORMED CONSENT FORM FOR STUDY PARTICIPANTS

Information Sheet

Purpose of the study. As part of the requirements for DNB primary training, I have to carry out a research study. The study is concerned with the correlation between MRI, Frozen section and Histopathological findings in Carcinoma of the Endometrium.

What will the study involve? The study will involve collection of basic details and complaints of participants and data from the advised investigations would be collected to generate results.

Why have you been asked to take part? You have been asked because you have presented with the complaints suggestive of Carcinoma of the Endometrium.

Do you have to take part? *Participation is voluntary not mandatory. You have the option of withdrawing before the study commences (even if you have agreed to participate) or discontinuing after data collection has started.*

Will your participation in the study be kept anonymous? *Yes – I will ensure that no clues to your identity appear in the thesis. Any extracts from what you say that are quoted in the thesis will be entirely anonymous.*

What will happen to the results? The results will be presented in the thesis. They will be seen by my supervisor, a second marker and the external examiner. The thesis may be read by future students on the course. The study may be published in a research journal.

Who has reviewed this study? Study is reviewed by Institutional Scientific and Ethics Board (ISEB).

Consent Form

Iagree to participate in study entitled “Correlation between MRI, Frozen section and Histopathological findings in a patient of Carcinoma of the Endometrium.” in a tertiary care centre conducted by Dr. Namrita Sheregar.

The purpose and nature of the study has been explained to me in details.

I am participating voluntarily.

I understand that I can withdraw from the study, without repercussions, at any time, whether before it starts or while I am participating.

I understand that anonymity will be ensured in the write-up by disguising my identity.

I understand that disguised extracts from my details may be quoted in the thesis and in any subsequent publications if I give permission below.

Signed.....

Date.....

Name.....

Study Proforma

Sr. No.

NAME

AGE

MARRIED / UNMARRIED

UHID NO.

DOA

DOS

DOD

Presenting complaints:

1. Bleeding pv
2. Vaginal discharge
3. Pain in abdomen
4. Bowel/Bladder complaints
5. Others

Menstrual history: Menarche / Menopause _____ age in years

Present Menstrual: LMP _____, _____ / _____ days flow, scanty/ moderate/ heavy,
pain, clots, reg/ irreg.

USG: Size

MRI:

Myometrial invasion

1. No invasion
2. Less than 50% or 50%
3. More than 50%

Size of tumour

1. less than 2 cm
2. More than 2 cm

Location

1. Fundal
2. Anterior wall
3. Posterior wall
4. Lateral wall
5. Isthmus

Cervical involvement

1. Glandular involvement
2. Infiltrating cervix

Lymph nodes:

Frozen Section:

Grade

Type

Depth of invasion

Cervical involvement

Size

Lymph node

Final HPR:

Grade

Type

Depth of invasion

Cervical involvement

Lymph node

Diagnosis _____

Management:

