"ROLE OF MAGNETIC RESONANCE IMAGING IN EVALUATION OF CARCINOMA CERVIX"

By

Dr. DARSHAN A. V., M.B.B.S.

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Under the Guidance of

Dr. ANIL KUMAR SAKALECHA, MD (RD),
Professor, Department of Radiodiagnosis

And Co-Guidance of

Dr. GOMATHI M, MS (OBG),
Professor, Department of Obstetrics and Gynaecology

DEPARTMENT OF RADIODIAGNOSIS,

SRI DEVARAJ URS MEDICAL COLLEGE
TAMAKA, KOLAR-563101

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SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

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Dr. DARSHAN A. V.
Postgraduate in Radiodiagnosis
Sri Devaraj Urs Medical College
Tamaka, Kolar

Date:

Place: Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

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Dr. ANIL KUMAR SAKALECHA, MD
Professor
Department of Radiodiagnosis
Sri Devaraj Urs Medical College
Tamaka, Kolar

Date:
Place: Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH TAMAKA, KOLAR, KARNATAKA

CERTIFICATE BY THE CO- GUIDE

This is to certify that the dissertation entitled "**ROLE OF MAGNETIC RESONANCE IMAGING IN EVALUATIONOF CARCINOMA CERVIX**" is a bonafide research work done by **Dr. DARSHAN A. V.**, under my co-guidance and supervision of **Dr. GOMATHI M.**, MS (OBG) Department of Obstetrics and Gynecology at **Sri Devaraj Urs Medical College and Research Center, Kolar,** in partial fulfillment of the requirement for the degree of **"M.D. IN RADIODIAGNOSIS"**.

Date:

Place: Kolar

GOMATHI M., MS

PROFESSOR,

Department of Obstetrics and Gynecology,

Sri Devaraj Urs Medical College and

Research Centre, Tamaka

Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

CERTIFICATE BY THE HEAD OF DEPARTMENT

This is to certify that the dissertation entitled "**ROLE OF MAGNETIC RESONANCE IMAGING IN EVALUATION OF CARCINOMA CERVIX"** is a bonafide research work done by **Dr. DARSHAN A. V.,** under direct guidance and supervision of **Dr. ANIL KUMAR SAKALECHA**, Professor, Department of Radiodiagnosis& under the co-guidance of Professor, **Dr. GOMATHI M**., MS (OBG) Department of Obstetrics and Gynecology, at Sri Devaraj Urs Medical College, Kolar**,** in partial fulfilment of the requirement for the degree of "**M.D. IN RADIODIAGNOSIS"**.

Dr. N. RACHEGOWDA, MD
Professor & HOD
Department of Radiodiagnosis
Sri Devaraj Urs Medical College
Tamaka, Kolar

Date:

Place: Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

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This is to certify that the dissertation entitled **"ROLE OF MAGNETIC RESONANCE IMAGING IN EVALUATION OF CARCINOMA CERVIX"** is a bonafide research work done by **Dr. DARSHAN A. V.** under the direct guidance and supervision of **Dr. ANIL KUMAR SAKALECHA,** Professor, Department of Radiodiagnosis & under the co-guidance of Professor, **Dr. GOMATHI M**., MS (OBG) Department of Obstetrics and Gynecology, Sri Devaraj Urs Medical College, Kolar, in partial fulfilment of University regulation for the award "**M.D. DEGREE IN RADIODIAGNOSIS**".

Dr. N. RACHEGOWDA,
Professor & HOD
Department of Radiodiagnosis,
Sri Devaraj Urs Medical College,
Tamaka, Kolar

Date:
Place: Kolar

Dr. M. L. HARENDRA KUMAR
Principal,
Sri Devaraj Urs Medical College
Tamaka, Kolar

Date:
Place: Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

ETHICAL COMMITTEE CERTIFICATE

This is to certify that the Ethical committee of Sri Devaraj Urs Medical College, Tamaka, and Kolar has unanimously approved

Dr. DARSHAN A. V.

Post-Graduate student in the subject of

RADIODIAGNOSIS at Sri Devaraj Urs Medical College, Kolar

to take up the Dissertation work entitled

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SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTER, TAMAKA, KOLAR, KARNATAKA.

Member Secretary

Sri Devaraj Urs Medical College,

Kolar–563 101.

Date:

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Darshan	Professor, Dept. of Radio-Diagnosis, R.L.J. Hospital & Research Centre, Tamaka, Kolar-563 101
Signature of Student	Signature of Supervisor
	03/12/18
Head of the Department	
Dept. of Radio - Diagnosis, R.L.J. Hospital & Research Centre, Tamaka, Kolar - 563 101.	
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Dr. DARSHAN A. V

LIST OF ABBREVIATIONS

CT	Computed tomography
DNA	Deoxyribonucleic acid
DWI	Diffusion weighted images
FDA	Food and Drug Administration
FIGO	Federation of gynecology and obstetrics
FSE	Fast spin echo
GE	General electric
HPV	Human papilloma virus
IVU	Intravenous urogram
LSIL	Low-grade squamous intraepithelial
MR	Magnetic resonance
MRI	Magnetic resonance imaging
MRS	Magnetic resonance spectroscopy
NMR	Nuclear magnetic resonance
N	Total number of patients
OCP	Oral contraceptive pill
PET	Positron emission tomography

PET-CT	Positron emission tomography-Computed tomography
Rb	Retinoblastoma
SCJ	Squamocolumnar junction
SE	Spin echo
STIR	Short tau inversion recovery
T1 WI	T1 relaxation time
T2 WI	T2 relaxation time
TVS	Transvaginal
TZ	Transition zone
USPIO	Ultra small particles of iron oxide

ABSTRACT

Background: Carcinoma cervix is the second most common cancer in women in the developing countries with incidence of about 12%. The treatment of choice for carcinoma cervix is completely dependent on its staging and hence an accurate pretreatment staging is important. MRI has an ability of excellent soft tissue characterization, thereby permitting better identification of stromal and parametrial invasion and thus plays an important role in staging of carcinoma cervix.

Aims and objectives: 1. To document morphological changes in histopathologically diagnosed carcinoma cervix with regional lymph node involvement by MRI. 2. To stage carcinoma cervix by MRI under FIGO guidelines. 3. To compare MRI FIGO staging with clinical FIGO staging in carcinoma cervix.

Materials and methods: This descriptive observational study was carried out over a period of 18 months from January 2017 to June 2018 in 103 patients with histopathologically proved carcinoma cervix who underwent MRI of pelvis. Patients who met the inclusion/exclusion criteria were included in the study.

Results: Majority of patients in our study was mostly concentrated in the middle age group (80%). Most of the patients (n=70; 67%) had parity of 1-3 in our study. 72 (73%) out of 103 patients were postmenopausal. Most common clinical presentation in our study was discharge per vagina (n=93; 90%) followed by post-menopausal bleeding (n=67; 65%). 98 (95.2%) patients in our study were diagnosed with squamous cell carcinoma. On clinical staging, most of the patient were equally staged as IIB (n=47,

45.6%) and IIIB (n=45; 43.6%) followed by IVA (n=5; 4.8 %). On MRI, majority of the patients were staged under stage IIB (47 patients) and stage IVA (35 patients).

MRI staging after clinical staging have redistributed the cases among IIB and IIIB. On comparing clinical and MRI staging, it was noted that less than half (n=49) of the cases were staged correctly.

Conclusion: MRI is encouraged for cervical cancer staging. There seems to be good correlation between MRI and histopathology. Evaluation of carcinoma cervix by MRI accurately predicts the nodal status and the degree of myometrial and parametrial invasion. MRI is the preferred imaging technique for tumor detection and invasion evaluation in advanced stage disease. A combined imaging and histopathological approach is warranted in the management of carcinoma cervix. MRI has been proposed as better alternative for initial screening of cervical cancer instead of cystoscopy and proctoscopy.

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INTRODUCTION

Carcinoma cervix is the second most common cancer in women in India with an incidence of 22.9% and contributing to 20.7% of all cancer-related deaths in women. It is also notorious for being the second most common cancer to affect the overall population with an incidence of 12.1% and accounting for up to 10% of all cancer-related deaths (men and women combined)[1].

The choice of treatment for carcinoma cervix is completely dependent on its staging and hence an accurate pretreatment staging is important[2].

The International Federation of Gynecology and Obstetrics (FIGO) staging is widely used for treatment planning and is based on findings at clinical examination. However there are significant inaccuracies in the clinical FIGO staging system, with an error of 24%–39% in gynecologic examinations. Metastasis to local, regional, pelvic or paraaortic lymph nodes cannot be assessed by clinical examination and also the tumor volume and its extension to the bladder and or rectum is difficult to define, which are critically important for treatment planning[3].

Magnetic resonance imaging (MRI) has an excellent soft tissue characterization, thereby permitting identification of stromal and parametrial invasion and hence it has an important role in staging of carcinoma cervix[4].

In Indian rural setup, there is an increasing trend in incidence of carcinoma cervix[5]. The study purpose is to evaluate the role of MRI for accurate pretreatment staging in carcinoma cervix in this rural setup.

Objectives

AIMS AND OBJECTIVES

The aims and objectives of the study are:

1. To document morphological changes in histopathologically diagnosed carcinoma cervix with regional lymph node involvement by MRI.

2. To stage carcinoma cervix by MRI under FIGO guidelines.

3. To compare MRI FIGO staging with clinical FIGO staging in carcinoma cervix.

Review of Literature

REVIEW OF LITERATURE

Historic background

MRI is a newer technology, yet its history spans more than a century and is renowned for several Nobel Prizes and key innovations in science and technology. The study of MRI was launched in 1882 with a major breakthrough in Physics: namely, the discovery of the rotating magnetic field by Nikola Tesla. In his honor, "Tesla" became the international unit of magnetic flux density, which calibrates the strength of the magnetic field used in all MRI systems.

In 1952, Herman Carr produced a one-dimensional MRI image. In 1971 Raymond Damadian, an Armenian-American physician, scientist and professor at the Downstate Medical Centre State University of New York reported that normal tissue and tumors can be distinguished in vivo by nuclear magnetic resonance ("NMR")[6] . In 1972 Damadian created a first MRI machine.

Lauterbur published the first nuclear magnetic resonance image and the first cross-sectional image of a living mouse in 1973. Damadian, along with Larry Minkoff and Michael Goldsmith, performed the first MRI body scan of a human being in 1977. Mansfield was successful and in 1978 presented the first cross-section images of a finger and the abdomen[7]. In 1980, Paul Bottomley joined the GE Research Center in Schenectady, New York, and his team ordered the highest field-strength magnet then available a 1.5T system and built the first high-field and overcame problems of coil

design, RF penetration and signal-to-noise ratio to build the first whole-body MRI/MRS scanner.

Paul Lauterbur of the University of Illinois at Urbana-Champaign and Sir Peter Mansfield of the University of Nottingham were awarded Nobel Prize in Physiology or Medicine in 2003 for their "discoveries concerning magnetic resonance imaging.

The final step towards advancing the clinical use of MRI was to build a magnet scanner, which was accomplished in 1977 and approved for clinical use by the FDA (Food and Drug Administration) in 1984. In addition, gadolinium, an MRI contrast agent, was patented and approved by the FDA four years later. Clinical MRI is a rather young field that has yielded extraordinary achievements, most of which occurred in the United States[7].

Anatomy of cervix

Cervix is a fibromuscular organ which connects uterine body to vagina. The post-pubertal, nulliparous women will have cervix which is narrower and more cylindrical measuring about 4 cm in length and 3 cm in diameter. The proximal part continues with the uterine body above the internal os and the distal part opens into the vagina after the external os. The external os is circular, whereas after delivery it becomes transverse slit.

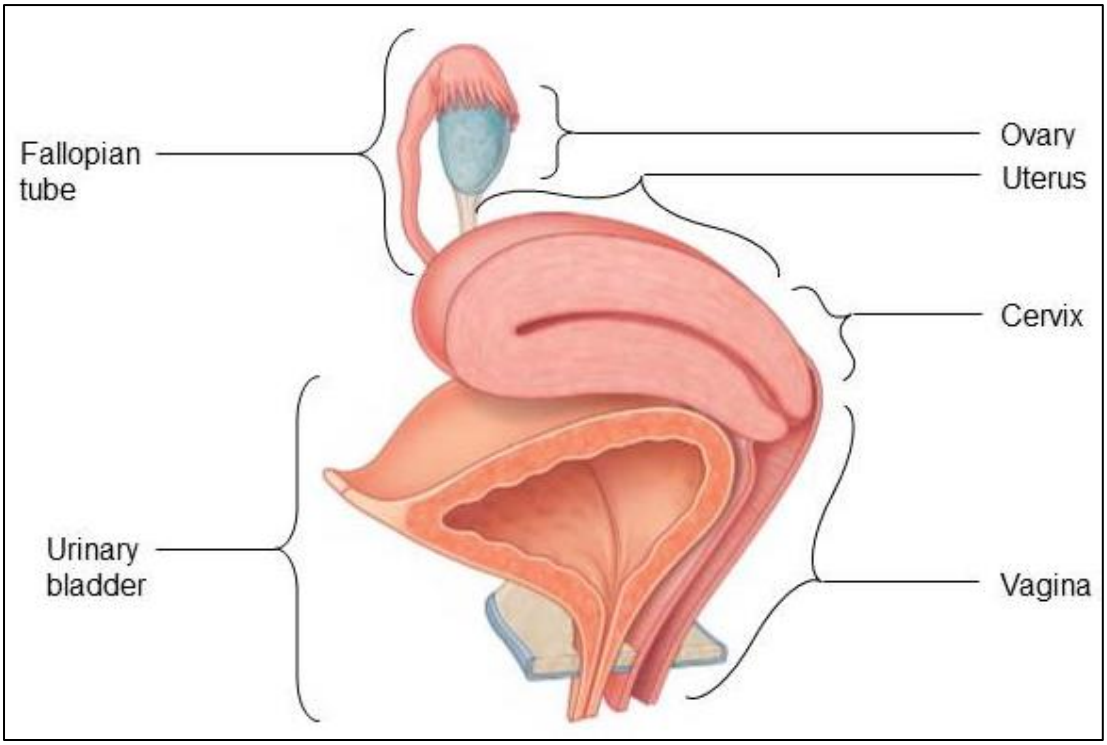

Figure 1: Uterus and cervix.

The upper one third of cervix is formed by narrow segment, isthmus. During first month of pregnancy this portion remains unaffected however, from second month onwards it gradually form the lower uterine segment. The caudal portion of the cervix enters the cranial end of the vagina and hence it is divided into supravaginal and vaginal parts[8].

The supravaginal part is posterior to urinary bladder which is separated by the parametrium. The parametrium continues on either side of the cervix and extends laterally in between two layers of the broad ligaments[8].

The cervix has several different epithelial cell linings. The glandular epithelium is columnar cells that lines endocervical canal whereas the ectocervix is

lined by squamous epithelium. The squamous epithelium meets the glandular epithelium at the squamocolumnar junction (SCJ). The SCJ originates in the endocervical canal, but as it is dynamic and moves during early adolescence and first pregnancy, the SCJ comes to lie on the ectocervix and becomes the new SCJ. The epithelium at SCJs is the transition zone (TZ), and its position is also variable. It may be of variable size and usually becomes more ectocervical during a woman's reproductive age and returning to an endocervical position after menopause[9].

The stroma of the cervix is composed of dense, fibromuscular tissue through which vascular, lymphatic, and nerve supplies to the cervix and forms a complex plexus[9].

The internal iliac arteries supply the cervix through the cervical and vaginal branches of the uterine arteries. The cervical branches of the uterine arteries courses in lateral to cervix at the 3 o'clock and 9 o'clock positions and the veins of the cervix run parallel to the arteries and drain into the hypogastric venous plexus. The lymphatics from the cervix drain into the common iliac, external iliac, internal iliac, obturator, and parametrial lymph nodes[9].

The nerve supply to the cervix is from the hypogastric plexus. The endocervix has extensive sensory nerve endings, whereas there are very few in the ectocervix.

Hence, procedures such as biopsy, thermal coagulation, and cryotherapy are relatively well tolerated in most women. Also, the cervix of a parous woman tends to

have slightly lower sensory perception due to damaged nerve endings during childbirth. Because sympathetic and parasympathetic fibres are also abundant in the endocervix, dilatation and curettage may lead to vasovagal reaction[9].

MRI anatomy of cervix uteri

Internal os separates cervix from uterine body. On MRI, normal cervix show three different zones identified on high resolution T2 weighted sequences. Central hyperintense zone consists of the endocervical canal which contains mucosa, secretions and longitudinal folds. Next to this is the middle zone which is the inner fibromuscular zone appearing hypointense on T2 weighted sequences. This zone is made of fibrous stroma and dense smooth muscles. The outer most peripheral zone demonstrates isointense signal on T2 weighted sequences corresponding to the outer fibromuscular zone (Figure **3**).

On post contrast T1 weighted sequences there is no obvious distinction between the layers of the cervix. However on contrast administration the mucosa enhances more rapidly than the fibro muscular zone.[10]

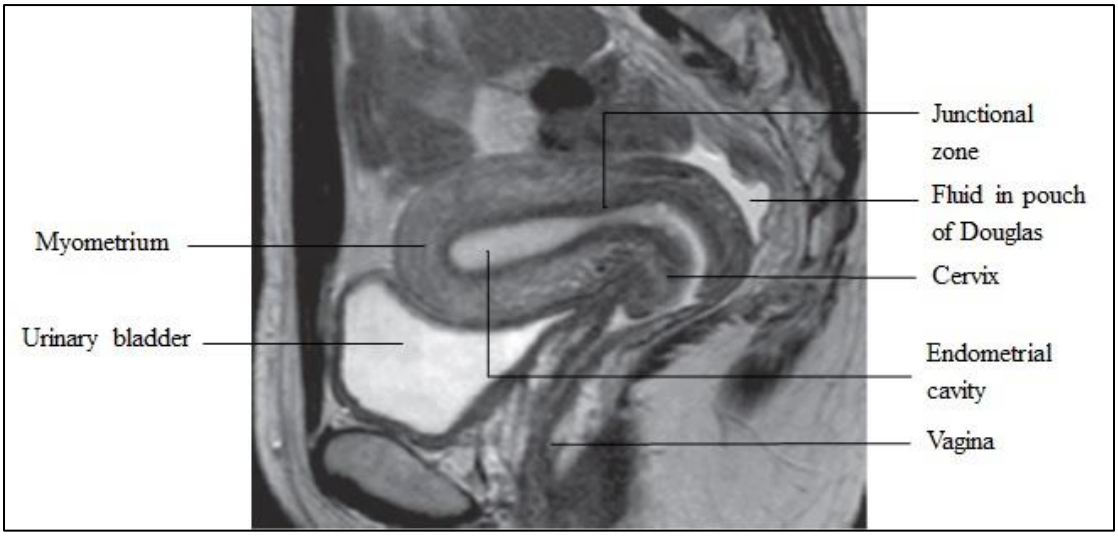

Figure 2: T2W Sagittal section of Uterus and Cervix.

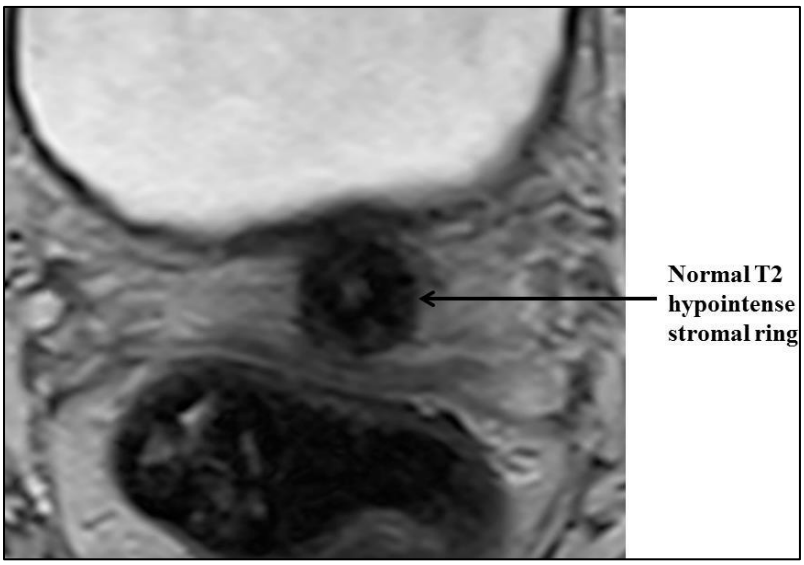

Figure 3: Normal T2 hypointense stromal ring

Carcinoma cervix

The difficulties in evaluation of patients with carcinoma cervix clinically are the estimation of tumor size, especially in primary endocervical tumor; the assessment of parametrium, pelvic sidewall invasion; lymph node evaluation and distant metastasis. Modern cross-sectional imaging, which can assist in the evaluation of these prognostic factors, has become an important adjunct to clinical assessment of cervical cancer.

Current cross-sectional imaging has not been incorporated into the FIGO guidelines for routine pretreatment diagnostic evaluation of carcinoma cervix. This is due to the belief that staging methods should be universally available and that staging should serve as a standardized means of communication between institutions around the world.

Histologically, squamous cell carcinoma is the commonest type. Other types are adenocarcinoma, adenoid-cystic, adenoid-basal, and small cell carcinoma[11].

The most important etiological factor is exposure to human papilloma virus (HPV), types 16 and 18. The introduction of the vaccine against HPV 16 and 18 is likely to have a major impact on disease prevention. Other risk factors include smoking; lower socio-economic class and oral contraceptive pill (OCP). Most patients with invasive cervical cancer are asymptomatic at its early phase, and patients with advanced disease typically present with abnormal vaginal bleeding[11].

Pathophysiology of carcinoma cervix

Tumorigenesis

Most women readily clear HPV, but those with persistent infection may develop preinvasive dysplastic cervical lesions and from such lesions, squamous cell carcinoma arises at the squamo-columnar junction. In general, progression from dysplasia to invasive cancer requires several years, although times can vary widely. The molecular alterations involved with cervical carcinogenesis are complex and not fully understood. Carcinogenesis currently is suspected to result from the interactive effects among environmental insults, host immunity and somatic-cell genomic variations[12].

Increasing evidence suggests that HPV oncoproteins may be a critical component of continued cancer cell proliferation. Unlike low-risk serotypes, oncogenic HPV serotypes can integrate into human DNA. As a result, with infection, oncogenic HPV's early replication proteins E1 and E2 enable the virus to replicate within cervical cells. These protein levels are high in early HPV infection. They can lead to cytological changes detected as low-grade squamous intraepithelial (LSIL) on Pap smears[12].

Amplification of viral replication and subsequent transformation of normal cells into tumor cells may follow. Specifically, the viral gene products E6 and E7 oncoproteins are implicated in this transformation. E7 protein binds to the retinoblastoma (Rb) tumor suppressor protein, whereas E6 binds to the p53 tumor

suppressor protein. In both instances, binding leads to degradation of these suppressor proteins. The E6 effect of p53 degradation is well studied and linked with the proliferation and immortalization of cervical cells[12].

Tumor Spread

Following tumorigenesis, the pattern of local growth may be exophytic if a cancer arises from the ectocervix, or may be endophytic if it arises from the endocervical canal. Lesions lower in the canal and on the ectocervix are more likely to be clinically visible during physical examination. Alternatively, growth may be infiltrative, and shows ulcerations if necrosis accompanies growth. As primary lesions enlarge and lymphatic involvement progresses, local invasion increases and will eventually become extensive[12].

Tumor detection and size:

Tumor should be at least 1 cm in diameter for good correlation between MRI and histopathology[13] as microscopic extension outside the uterine cervix on MRI is not reliable[14]. The limitations of MRI in tumor detection are:

1. No detection

2. Difficulty in margin delineation

3. Confusion between peri-tumoral soft tissue reaction and scars

These are relevant if the tumor is confined only to cervix. A study on 60 patients had false positive diagnosis on MRI for IA1 tumors was 33.0% and false negatives was 50.0%[15]. Cone biopsy in these cases helps to differentiate scar tissue form tumor.

FIGO staging system of cancer cervix and its limitations:

FIGO is a worldwide organization established for staging of gynecological malignancies. In 1958, FIGO gained global acceptance for annual reporting. FIGO staging for carcinoma cervix is mainly based on clinical evaluation. Hence in every case of carcinoma cervix thorough clinical evaluation should be performed.

FIGO staging for carcinoma cervix permits the following examinations: inspection, palpation, colposcopy, endocervical curettage, hysteroscopy, cystoscopy, proctoscopy, intravenous urography and radiographic examination of the lungs and skeleton. Patients with suspicion for urinary bladder or rectal infiltrations should be confirmed with biopsy.

Conization or amputation of the cervix is regarded as a clinical examination. Disease extension to uterine body cannot be evaluated clinically in all cases. Hence extension to the corpus is disregarded in FIGO staging. Treatment in patients with carcinoma cervix is completely dependent on the stage they belong. Therefore accurate pretreatment staging of carcinoma cervix is important. Clinical FIGO staging is inaccurate and is often subject to multiple errors. Clinical staging shows error of 20%-35% depending on the stage of the disease[16,17]. Patients with metastasis to

regional, pelvic or para-aortic lymph nodes can be detected on clinical examination in 25 % of patients.

Involvement of urinary bladder and rectum is difficult to determine on clinical examination. However, clinical examination is subjective[16]. Pretreatment laparotomy is not recommended as it may hamper subsequent radiation therapy. There are fewer studies to determine the benefits of staging surgically in patients with cervix cancer[18,19,20].

Contrast studies which include intravenous urogram (IVU) and barium enema should be done in selected patients. IVU is performed before radical hysterectomy to demonstrate the course of the ureter. Barium enema is done to determine rectal mucosa involvement. Skeletal radiograph should be done when patients report with specific symptoms related to bone metastasis. Chest radiograph should be performed to rule out distant metastasis to lungs. Its incidence is <10% in general population[21,22]. Ultrasound is the investigation usually done after clinical examination. It gives additional information regarding uterine extensions and urinary tract involvement. Transvaginal (TVS) as well as transrectal sonography is being tried these days in staging carcinoma cervix[23].

Huskin WJ et al[24], in their study have said that bone scan labeled with technetium phosphate is useful technique in detecting bone metastasis. Patients presenting with symptoms like bone pains or increased levels of alkaline phosphatase are said to have high detection of metastasis on bone scan. Since bone scan is expensive, it is usually used when indicated only and not as a part of routine

screening. At times bone metastasis can be clinically silent and the patients might be completely asymptomatic[24].

With the advent of newer modalities like cross sectional imaging, extended clinical staging has been developed without changing the official FIGO guidelines. Use of MRI is gaining acceptance in treatment planning and use of conventional radiographic technique is decreasing[25].

In the year 2009, FIGO revised the staging of carcinoma cervix based on the clinical examination alone. The cross sectional imaging and surgical staging was not considered for staging and the same staging guidelines are being followed globally (Table 1)[26].

Recently FIGO gynecologic oncology committee have revised the staging guidelines which now includes clinical examination with certain procedures and imaging as well as pathological findings, if available so as to assign appropriate staging[27].

Table 1: FIGO staging of carcinoma cervix (2009 Guide lines) [26]

Stage Description
Stage I: Carcinoma strictly confined to the cervix; extension to the uterine corpus should be disregarded. The diagnosis of both Stages IA1 and IA2 should be based on microscopic examination of removed tissue, preferably a cone biopsy, which must include the entire lesion.
Stage IA: Invasive cancer identified only on microscopically with depth of invasion ≤ 5 mm and width ≤ 7 mm in diameter.
Stage IA1: Measured invasion of the stroma is ≤ 3 mm in depth.
Stage IA2: Measured invasion of stroma > 3 mm but ≤ 5 mm in depth.
Stage IB: Clinically visible lesions confined only to the uterine cervix or pre-clinical disease more than Stage IA[a].
Stage IB1: Clinically visible lesion ≤ 4 cm in greatest dimension.
Stage IB2: Clinically visible lesion > 4 cm in greatest dimension.
Stage II: Carcinoma extending beyond uterine cervix, but not extend upto pelvic side walls. Lesion involves the vagina, but not beyond lower third.
Stage IIA: No obvious parametrial involvement.
Stage IIA1: Clinically visualized lesion ≤ 4cm in greatest dimension.
Stage IIA2: Clinically visualized lesion > 4cm in greatest dimension
Stage IIB: Obvious parametrial involvement.
Stage III: Carcinoma extending upto pelvic sidewalls and/or lower third of vagina and causing hydroureteronephrosis or non-functioning kidney[b].
Stage IIIA: Involvement of lower third of vagina with no extension upto the pelvic sidewall.
Stage IIIB: Involvement of pelvic sidewalls and/or hydroureteronephrosis or nonfunctioning kidneys.
Stage IV: Carcinoma extended beyond the true pelvis or has clinically involved the bladder and or rectum.
Stage IVA: Spread of the tumour to adjacent pelvic organs.
Stage IVB: Spread to distant organs.
When in doubt, the lower staging should be assigned. a. All macroscopically visualized lesions with superficial invasion are staged as IB. Measured depth of stromal invasion is > 5.00 mm and a horizontal extension of > 7.00 mm. Depth of invasion should be > 5.00 mm from the base of the epithelium and it should always be reported in mm, even in the cases with minimal stromal invasion (~1 mm). The involvement of vascular or lymphatic channels should not alter the stage allotment b. On rectal examination, between tumor and lateral pelvic wall there should be no cancer free space. All cases with non-functioning kidneys and hydroureteronephrosis are included unless the cause is specified.

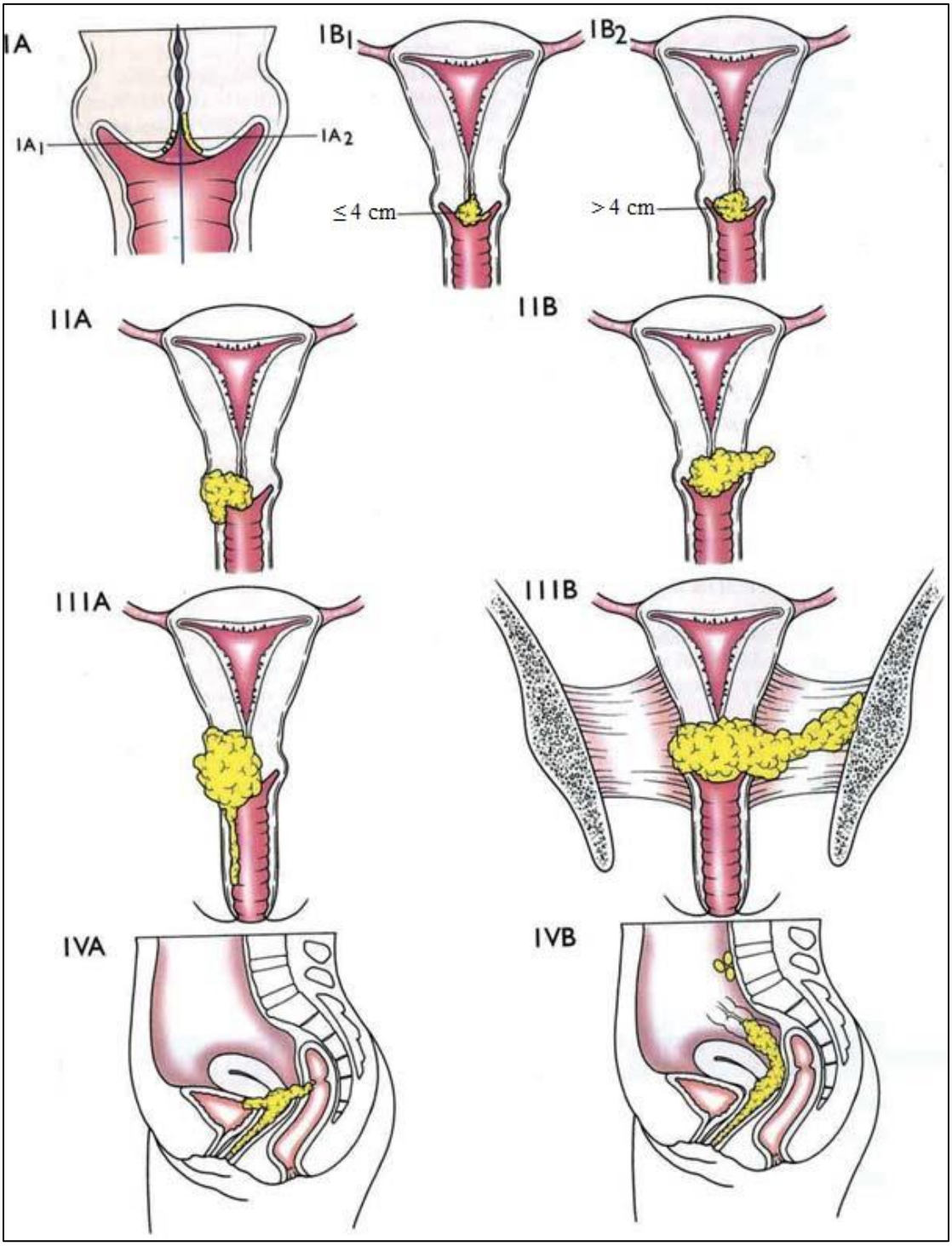

Figure 4. Staging of carcinoma cervix according to FIGO guidelines[2].

Limitations of clinical staging:

1) Clinical examination skills are subjective.
2) Examination under anesthesia may be required if necessary.
3) Cannot show the exact extent of tumor.
4) Corpus uteri infiltration cannot be evaluated.
5) Urinary bladder and rectal involvement is also difficult to define.
6) Pelvic lymph nodal metastasis cannot be assessed.
7) Incomplete unless combined with other investigations.

Other difficulties of FIGO staging determining the prognosis are:

1) It does not take tumor size into consideration.
2) Urinary bladder and rectal invasion are missed if tumor has not extended upto mucosa.
3) Corpus uteri involvement is not taken into account.

MRI in staging of carcinoma cervix

The FIGO staging system can be readily applied to MRI appearances.

Stage IA:

Stage IA (micro-invasive) tumors usually show no visible disease on T2-weighted images. MRI is usually normal in stage IA. The shape of the cervix may be distorted due to diagnostic cone biopsy. A visible tumor is clinically staged as IB or higher.

Tumor detection on MRI in patients having primary tumor >1 cm^3 has sensitivity and specificity of 82.89% and 84.21% respectively. For tumor size <1 cm^3, the sensitivity and specificity is 44.0% and 94.29%, respectively[23].

Stage IB:

Clinically visible lesions confined only to the uterine cervix or preclinical disease greater than Stage IA and all macroscopically visualized lesions with superficial invasion are staged as IB. Vertical stromal invasion from the base of the epithelium should be > 5.00 mm and a horizontal extension of > 7.00 mm. The involvement of vascular or lymphatic channels will not alter the stage allotment[26]**.**

A study conducted by Lien HH et al on 45 patients with stromal invasion on MR sagittal T2 weighted sequence documented the logarithmic transforms of values

in both MRI and histopathological examination. The authors concluded that reliable information can be obtained regarding the depth of tumor invasion.[28].

` MRI provides valuable information in defining involvement of internal cervical os. Detection of endometrial and myometrial invasion is also better appreciated on MRI[28]. MRI has a sensitivity and specificity of 90.0% and a 98.0%[26].

Stage IIA:

Disease is considered IIA when the tumor extends beyond the cervix. Stage IIA is characterized by invasion of proximal two thirds of the vagina only. Vaginal invasion is detected by loss of normal low intensity of the vagina or with hyperintense thickening of the vagina[29].

MR is highly sensitive in detecting vaginal invasion (86-93%). Large tumors may cause confusion by stretching the vaginal fornices and resulting in false positive cases. However clinical assessment in determining vaginal invasion is said to be pretty sensitive.

Stage IIB:

Differentiating Stage IIA and IIB is most important factor in determining treatment options. Presence of parametrial invasion will upstage the disease to IIB. The treatment of choice for stage I to IIA is surgery and IIB or greater is radiotherapy.

Normal parametrium shows a T2 hypointense stromal ring surrounding the cervix on MRI. Disruption of this ring with irregular tumor margin extension to the parametrium are signs of invasion[17,30].

Preservation of a hypointense fibrous stromal ring at T2 weighted MRI has more negative predictive value in evaluation of parametrial invasion[31,32]. With disruption of the stromal ring but no definite parametrial mass, there may be microscopic invasion (false-negative findings). Complete disruption of this ring with nodular or irregular tumor signal intensity extending into the parametrium is reliable signs of invasion. Linear fat stranding around the cervical mass is suggestive of parametrial invasion but may be due to peritumoral inflammatory tissue as well (false positive findings)[31,32]. Unilateral or bilateral parametrial invasion is a definite contraindication to surgery. Contrast material–enhanced T1-weighted imaging has not proved to be more accurate than T2-weighted imaging in this setting.

Stage III:

Stage III cancer is defined as extension of tumor beyond the cervix to the lower third of vagina (stage IIIA), extension to one or both of the pelvic side walls (stage IIIB), or causes encasement and obstruction of ureter causing hydroureter (stage IIIB). Patients at this stage are treated with radiotherapy and chemotherapy[33].

On MRI, an irregular T2 heterogenous hyperintense lesion extending caudally upto the lower third of vagina without any obstructive urological features is staged as IIIA. If the mass has extended beyond the uterus to reach one or both the pelvic side

walls and causing obstructive uropathy features with hydroureter on MRI are staged as IIIB.

Stage IVA

Cystoscopy can document the infiltration of tumor upto the mucosa of urinary bladder, but the lesions invading the muscular layers or the serosa alone may not be picked up on cystoscopy. Serosa invasion is also said to be a contraindication for curative hysterectomy, as the urinary bladder may not be separable from the cervical lesion during surgery. Urinary bladder invasion may be associated with fistula formation as well[34].

Stage IVB:

Bone metastasis in carcinoma cervix is said to be very infrequent. Metastasis occurs by direct extension of the disease, rarely by adjacent metastatic lymph nodes and haematogenous spread. MR imaging has a great role in demonstrating spread to bone.

Lymph nodal spread:

The presence of lymph nodal metastasis does not change the clinical FIGO stage of the disease, but it has a role in the treatment selection and prognosis. Lymph nodal involvement on MRI demonstrates diffusion restriction and heterogenous post contrast enhancement.

It is already known that lymph node metastasis is a very strong prognostic factor in these patients and approximately 8% to 26% of early-stage patients who undergo radical surgery will have distant lymph node metastasis[35].

Adjuvant chemoradiation improves survival in patients with lymph nodal metastasis[3]. They usually undergo postoperative chemoradiation to deal with the remnant disease and or lymph nodes if left unexcised. However, unfortunately the combination of surgery and postoperative radiation is associated with severe morbidity and complications[36].

A lymph node specific MR contrast agent has been developed that allows the identification of malignant nodal infiltration independent of the lymph node size. This novel MR contrast agent is classified as a nanoparticle (mean diameter, 30 nm), and is composed of an iron oxide core, coated with low molecular weight dextran. The class of these MR contrast agents is collectively known as ultra-small particles of iron oxide (USPIO). The particles are injected intravenously, and are engulfed by macrophages in the reticuloendothelial system, predominantly within the lymph nodes[37].

Uptake of USPIO results in marked loss of signal intensity (darkening) of the nodes on T2 and T2 weighted sequences because of a susceptibility artifacts caused by the iron. Metastatic tissue within the node displaces the normal macrophages thereby preventing contrast uptake. Thus lymph node continues to remain high in signal intensity on T2 weighted MRI[37].

Routine MRI evaluation of carcinoma cervix does not need addition of contrast agent, as it has shown no advantage in tumor detection. However, cases with ambiguity in tumor extension and in early stage disease contrast enhanced MRI helps in accurate staging[38].

Diffusion weighted imaging (DWI) is an advanced sequence based on the diffusion of the water molecules. DWI is not performed routinely for carcinoma cervix however recent studies have shown that addition of this sequence along with apparent diffusion co-efficient (ADC) mapping can provide valuable information about the histological type of carcinoma cervix[39].

Clinical studies

The FIGO recommends a clinical staging system for carcinoma cervix that includes inspection, palpation (if needed under anesthesia), barium enema, colposcopy, hysteroscopy, endocervical curettage, cystoscopy, proctoscopy and intravenous urography[40], which are invasive, time consuming and associated with radiation. Alternatively, MRI is an appropriate option for cervical cancer staging without time consuming and with no risk of radiation[41]

Studies have shown that MRI staging of carcinoma cervix is preferred to clinical FIGO staging for deciding on the treatment modality when there is an ambiguity in assessing the parametrium[42].

MRI is most reliable noninvasive imaging method without side effects of ionizing radiation and has high resolution helping in accurate detection of cervical tumor and its invasion to adjacent organs and lymph nodes[41].

A review article on MRI in malignant neoplasms of the uterine corpus and cervix quotes that MRI is not officially incorporated in the FIGO staging system, but it is widely accepted as the most reliable imaging modality for appropriate diagnosis, staging, treatment planning and follow-up of cervical cancer[43].

A study conducted in 70 women showed that MRI has an accuracy of 98.5% in differentiating stage ≤IIA, correctly delineating operable from inoperable stages of carcinoma cervix, thereby helping in appropriate treatment planning[42].

Stage IA:

According to Sahdev et al[44], MRI evaluation of microscopic stage IA tumor revealed sensitivity and specificity for tumor detection of 65.0% and 77.0%, respectively. Total false-positives were 30.6% (19/62) possibly due to post-biopsy edema or chronic inflammation.

A study conducted on 20 patients with administration of bacteriostatic vaginal gel before pelvic MRI. This improves visualization of the upper vagina and fornices and also it is inexpensive, well tolerated, and can improve the diagnostic usefulness of MRI staging of cervical carcinoma[45].

De Souza et al[46] conducted a study on 119 patients with microinvasive tumor using endovaginal coil on MRI had sensitivity and specificity of 96.9% and 59.1% respectively. They concluded that use of endovaginal coil was invaluable in planning fertility conserving surgeries or radical surgeries in early stage carcinoma cervix due to its low specificity and false positive results.

Stage IB:

Seki H et al[47], showed that lesions with stromal invasion of three mm or less were not picked up on MRI. Dynamic MRI is said to be a more reliable technique in detecting lesions of stromal invasion more than three mm. Dynamic MRI were obtained every 20 seconds for three minutes without breath holding technique. The first two minutes after contrast administration is known as the early dynamic phase and the latter two minutes as the late dynamic phase.

A study conducted by Bipat et al[48] on 21 patients reposted that internal os is well visualized on MRI. Authors observed zero false negatives for uterine corpus involvement and 3 false positives for invasion of uterine body.

A review article by Follen M et al[49] have quoted that endocervical lesions are well picked up on MRI.

Stage IIA:

A study conducted by Choi et al[15] on 23 patients for evaluating carcinoma cervix on MRI. The authors reported sensitivity and specificity of 87.0% and 79.0% respectively.

A study by Sheu et al[29], on patients with carcinoma cervix who underwent MRI documented vaginal invasion in 9 patients. On comparing with histopathology, two patients were false negatives, six were false positives and one was correlating. The authors documented sensitivity and specificity of 75.0% and 88.0% respectively for detection of vaginal invasion.

Stage IIB:

A review article on invasive carcinoma cervix states that parametrial invasion requires tumor margin protruding through the segmental disruption of hypointense stromal ring. Authors documented accuracy, sensitivity and specificity ranging between 82%-94%, 20% - l00% and 80% - 98% respectively in detecting parametrial invasion on MRI[50].

Hricak H et al[51] documented that parametrial invasion is present when there is disruption of full thickness of the stroma combined with one or more of the following findings:

1) Irregular interphase between the stroma and the parametrium

2) Asymmetric tumor bulge or

3) Vascular encasement

They hence concluded MRI should become the initial examination of choice to rule out early parametrial invasion.

Recent studies have suggested better specificity in detection of parametrial involvement on MRI. Fujiwara et al[52] demonstrated a sensitivity of 67.8% and a specificity of 95.7% for parametrial involvement detection on MRI. Fischerova et al[23] in their study documented sensitivity and specificity of 50.0% and 97.8% respectively in detection of parametrial invasion on MRI[53].

Another study by Hricak H et al[54], documented that tumor-fat interphase may be clearly appreciated on T2-weighted FSE (Fast Spin Echo) images than on conventional T2 weighted images. However, addition of fat suppression gadolinium enhanced MR images with T2 weighted FSE images did not improve the accuracy for detection of parametrial invasion.

Togashi K et al[17] prospectively evaluated 67 patients and they used the criteria of disruption of full thickness of cervical stroma with areas of altered signal intensity within the parametrium on T2 weighted sequence for staging as IIB on MRI.

Evaluation of parametrial invasion may be difficult in the case of a markedly anteverted uterus or a large exophytic tumor on the cervical lip. Endocervical lesions have higher incidence of parametrial invasion[50].

Few studies documented the accuracy for determining parametrial invasion on MRI to range between 82% - 94% (Hricak et al[55] 88%, Togashi et al[17]89%, Kim et al[56]92%) with sensitivity ranging between 80% - 98%[16,30,57]. Positive and negative predictive values were 89% and 100% respectively[58].

Lam WW et al[59] investigated the role of short tau inversion recovery (STIR) sequence in patients with carcinoma cervix for evaluation of parametrial invasion. Axial images of the cervical region using T1 weighted spin echo (SE), T2 fast spin echo (FSE), STIR and T1 weighted dynamic gadolinium enhanced SE sequence were obtained in 38 patients with cervical carcinoma. All the images were assessed for the presence or absence of parametrial invasion. They concluded that dynamic T1 weighted imaging is less accurate than STIR and T2 weighted FSE sequences. STIR has similar accuracy as T2 in evaluation of parametrial invasion; hence any one of the sequences can be used.

Scheilder J et al[60] used fat suppression to study parametrial invasion. 35 patients of carcinoma cervix were studied with T2 SE, STIR, and contrast enhanced sequence with or without fat suppression. Authors concluded that in MR diagnosis of parametrial invasion, the addition of fat suppression or gadolinium enhanced MR images did not improve the accuracy with T2 weighted spin echo sequences alone.

A study by Hricak et al[61] focused on MRI capability to detect advanced cancer stage (IIB) and the authors documented sensitivity and specificity of 53.0% and 75.0% respectively. A study conducted by Choi et al[15] analysed 226 patients with invasive carcinoma cervix on MRI. The reported a sensitivity of 38.0% and an

accuracy of 94.0% in evaluation of parametrial invasion. They concluded that the increase in tumor volume decreases the specificity in evaluating parametrial invasion.

Stage III:

Hricak H et al[55] conducted a study on MR imaging in patients with cervical carcinoma and authors documented criteria for MRI findings of lateral pelvic wall invasion:

1) Tumor less than 3 mm from the pelvic side wall,

2) Vascular encasement or

3) Increased signal intensity of the adjacent muscles on T2 weighted images.

The former two criteria are better evaluated on T1 weighted or proton weighted images than on T2. They conducted their study on 57 patients and determined that the overall accuracy was 95% while sensitivity was 86% and specificity was 96%.

Hricak H et al[51] have shown that there is often discrepancy between clinical staging and MRI findings. Hence a tumor found to be invading into lateral pelvic wall on clinical examination may not show the same finding on MRI

Stage IVA:

A study by Kim SH et al[62], have proposed that utero-vesical space can be best evaluated on sagittal T2 weighted images. MR had sensitivity, specificity, positive

predictive value and an accuracy of 83%, 100%, 99% and 99% respectively in detecting urinary bladder invasion.

MR features of definite urinary bladder invasion are

1. Disruption in low signal intensity of the posterior urinary bladder wall adjacent to cervical mass on T2 weighted sagittal images,
2. Nodularity and irregularity of the anterior aspect of the posterior bladder wall and
3. Soft tissue strands in the utero-vesical space.

A study conducted on 97 patients of carcinoma cervix stage IIIB – IVA who underwent MRI documented that, urinary bladder mucosal invasion provides an accurate prognosis when compared to patients with or without invasion of muscle or serosa of bladder wall. They also concluded that mucosal invasion provides more accurate prognosis than pathological evidence of bladder mucosal invasion and hence cystoscopic biopsy can be avoided[63].

Lien HH[50] has reported that the cervical lesion infrequently extends into rectum due to the presence of pouch of Douglas which separates it from the posterior fornix of the vagina. Sagittal T2 weighted images are said to offer the best information. The two most commonly applied criteria are

1) Segmental thickening and
2) Loss of normal low signal intensity of the anterior rectal wall on T2 weighted sequences.

Scheilder J et al[64] documented that rectal invasion usually occurs by the spread of disease along uterosacral ligaments. The commonly criteria used are altered signal intensity of anterior rectal wall with segmental thickening. Hertel et al[65], in their study reported MRI sensitivity and specificity of 50.0% and 86.0% respectively for rectal invasion.

Stage IVB:

Lien HH et al[50] mentioned that combination of T1 weighted and STIR sequences are highly sensitive in detecting bone metastasis. Bone marrow is replaced by fat as age progress and hence normal bone marrow appears hyperintense on T1 weighted sequence and hypointense on STIR sequence. In the presence of lesion, the signal characters of bone marrow alter and appear hypointense on T1 and hyperintense on STIR sequence.

Lymph nodal involvement:

Sachdev et al[44] suggests that the prediction of nodal status was most accurate when a 9 mm cut-off was applied to the short-axis diameter of the lymph node on MRI. De Souza et al[46], using a cut-off volume of 5.2 cm^3, observed that lymph node metastasis could be predicted with 78.6% sensitivity and 72.5% specificity on MRI.

A cut-off tumor volume of 2.8 cm^3 improves sensitivity to 89.0% but this gives a poor specificity of only 67.0%. Park et al[66], reports that using 10 mm diameter

as cut-off for maximum tumor diameter provided a sensitivity and specificity of 57.0% and 73.0%, respectively in detection of lymph nodal metastasis, while Narayan et al[67] with the same cut-off observed a MRI sensitivity of 50.0%.

Hricak H et al[68] have reported that altered signal intensity alone on MRI is difficult to appreciate the difference between inflammatory and metastatic nodes. Lymph nodes >10 mm size are considered abnormal. Malignant nodes are usually round in shape as compared to inflammatory nodes which are oval in shape.

Schielder. J et al[64] conducted a comparative study between lymphangiography, CT and MRI to analyze lymph nodes. They concluded that MR being noninvasive is better than lymphangiography in detecting lymph nodal metastasis. However no statistically significant difference was noted between CT and MRI.

Current data show that metabolic imaging with PET is a reliable alternative to conventional imaging for lymph node evaluation in patients with cervical cancer. Rose et al[69], have reported that for detection of para-aortic nodes, PET had sensitivity and specificity of 75% and 92% respectively. Lin et al[70] have also reported 86% sensitivity, 94% specificity and 92% accuracy for PET in detecting para-aortic lymph node metastasis. Reinhardt et al[71] compared the accuracy in diagnosis for detecting metastatic lymphadenopathy in patients with carcinoma cervix by MRI and PET. The author documented sensitivity of 91% with PET and 73% with MRI, and specificity of 100% with PET and 83% with MRI.

Kim SH et al[72] studied 167 patients. They classified the lymph nodes based on the location. The regional lymph nodes included are the lymph nodes of the parametrium, obturator, external, internal and common iliac chain and paraaortic lymph nodes. Microscopic tumor deposition is not detected on MRI. Similar degree of enhancement was noted between true positive and false positive nodes. Authors also mentioned that T2 weighted sequence was not enough sensitive in detecting metastatic lymph nodes. Finally conclusion stated that MRI was fairly sensitive in detecting lymph nodal metastasis with minimal axial diameter criteria.

Materials and methods

MATERIALS AND METHODS

Source of data:

This hospital based observational study was conducted over eighteen months on 127 patients diagnosed with carcinoma cervix and referred for MR imaging of pelvis to Department of Radio-Diagnosis at R.L. Jalappa Hospital attached to Sri Devaraj Urs Medical College, Tamaka, Kolar. 103 patients were included in the study after they met the inclusion/exclusion criteria (Table 4). An informed consent in their own language was taken from individuals for their willingness to participate in the study.

Inclusion Criteria:

All patients with histopathologically diagnosed carcinoma cervix and have undergone MRI evaluation of pelvis.

Exclusion Criteria:

- Claustrophobic
- Metallic implants in pelvis,
- Pacemaker
- Recurrent cases of carcinoma cervix.
- Post chemo/radiotherapy.
- No follow-up, either due to loss of contact or death.

Method of collection of data:

Baseline data was collected from the patients along with pertinent clinical history, relevant lab investigations and histopathological report. MRI of pelvis was performed on patients with histopathologically confirmed carcinoma cervix in 1.5 Tesla, 18 channel, MR Scanner (Siemens Magnetom Avanto®) (

Figure **6**).

Parameters used for MRI

The patients are in supine position and following sequences were performed in pelvis:

1. Sagittal and axial T1 and T2-weighted fast spin echo,
2. Coronal Short Tau Inversion Recovery (STIR);
3. Single-shot echo-planner diffusion weighted and
4. Contrast enhanced study (I.V gadolinium injection) was performed wherever required. Patient's renal function was assessed in the form of blood urea and serum creatinine levels and only patients with normal renal function underwent contrast study.

The MRI staging of tumor was done as per FIGO guidelines (2009)[26]. The clinical and MRI FIGO staging are compared. The final diagnosis was documented and compared whenever available.

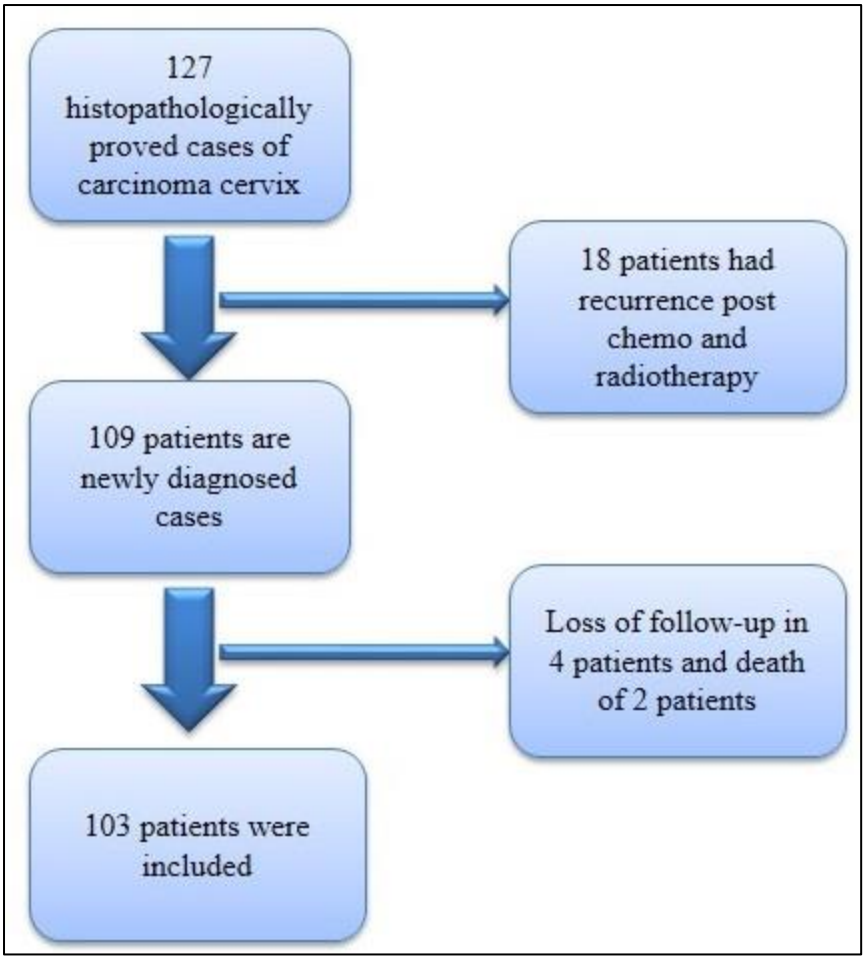

Figure 5: Schematic representation of patients included in study.

Data Analysis:

Collected data was recorded into Microsoft® Excel® and was analyzed using OpenEpi® software. Chi square test was applied to assess the statistical significance. A *P* value of <.001 was considered as statistically significant. The agreement between MRI and clinical staging was evaluated using kappa (κ) statistics: $\kappa \leq 0.2$ indicated poor agreement; κ of 0.21 to 0.40 indicated fair agreement, κ of 0.41 to 0.60 indicated moderate agreement, κ 0.61 to 0.80 indicated good agreement and κ of 0.81 to 1.00 indicated excellent agreement.

All newly diagnosed cases of carcinoma cervix received one week of antibiotic therapy following which thorough clinical examination was performed. Chest X-ray, cystoscopy and proctoscopy were performed and clinical stage was assigned based on the 2009 FIGO system[26].

The following parameters were assessed on MRI:

1) Corpus uteri involvement

2) Infiltration of vagina

3) Parametrial Invasion

4) Invasion of pelvic side walls

5) Infiltration of bladder and rectum

6) Involvement of ureter

7) Pelvic lymph nodes

8) Pyometra.

MRI findings and stage were compared with clinical staging. Surgical biopsy and histopathological correlation is done wherever available.

Figure 6: Siemens Magnetom Avanto® 1.5 T MRI scanner used in the study. (Inset pelvic coil).

Results

RESULTS

Distribution of patients based on age.

Table 2: Age Wise Distribution

Age group (in years)	Number of patients	Percentage (%)
20-29	0	0
30-39	12	12.0
40-49	29	28.0
50-59	28	27.0
60-69	26	25.0
70-79	8	8.0
>80	0	0

The majority of patients in our study was mostly concentrated in the middle age group (80%) i.e. 40-49 years (n=29; 28%), 50-59 years (n=28, 27%) and 60-69 years (n=26; 25%) (Table 2 &Figure 7).

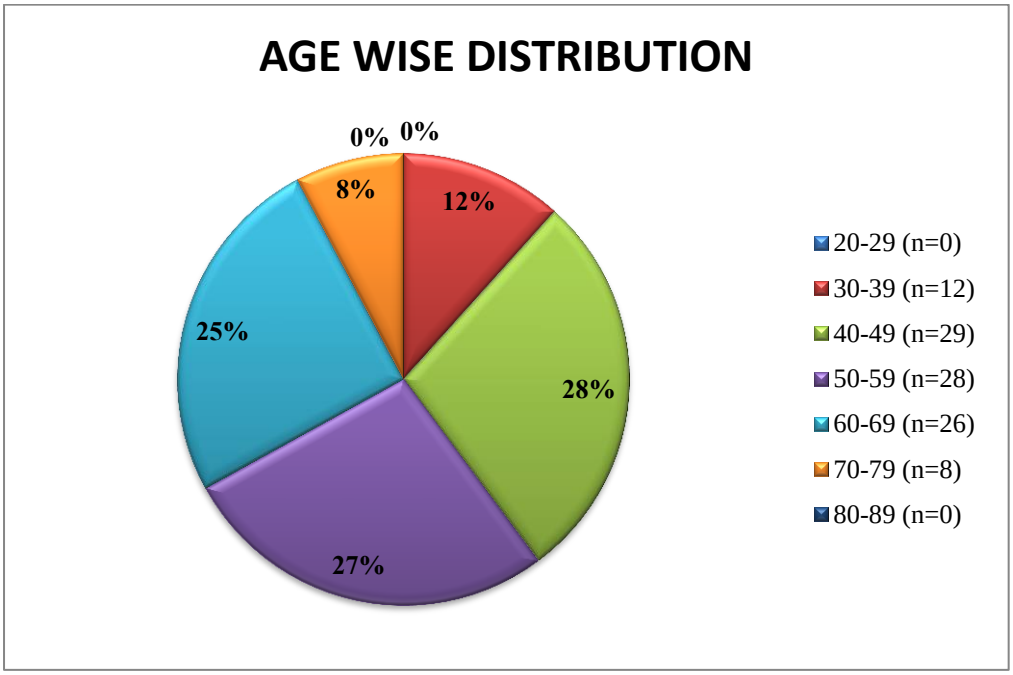

Figure 7: Age wise distribution

Distribution of patients based on parity

Table 3: Parity wise distribution

Parity	Number of patients
1-3	70
4-6	25
7-9	8

Most of the patients (n=70; 67%) had parity of 1-3 in our study. None of the patients were nulliparous (Table 3 &Figure 8).

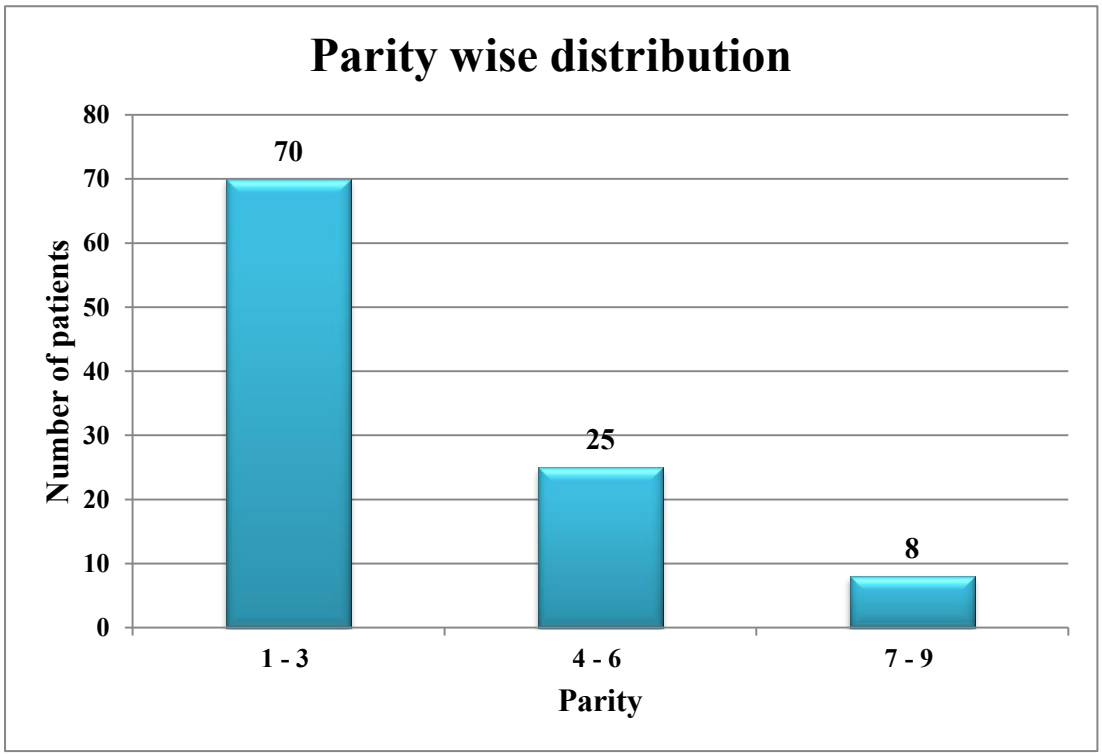

Figure 8: Parity wise distribution.

Distribution of patients based on menstrual status

Table 4: Distribution based on menstrual status

Post-menopausal	72
Pre-menopausal	31

72 (73%) of 103 patients were postmenopausal, remaining 31 (27%) were premenopausal (Table 4 & Figure 9).

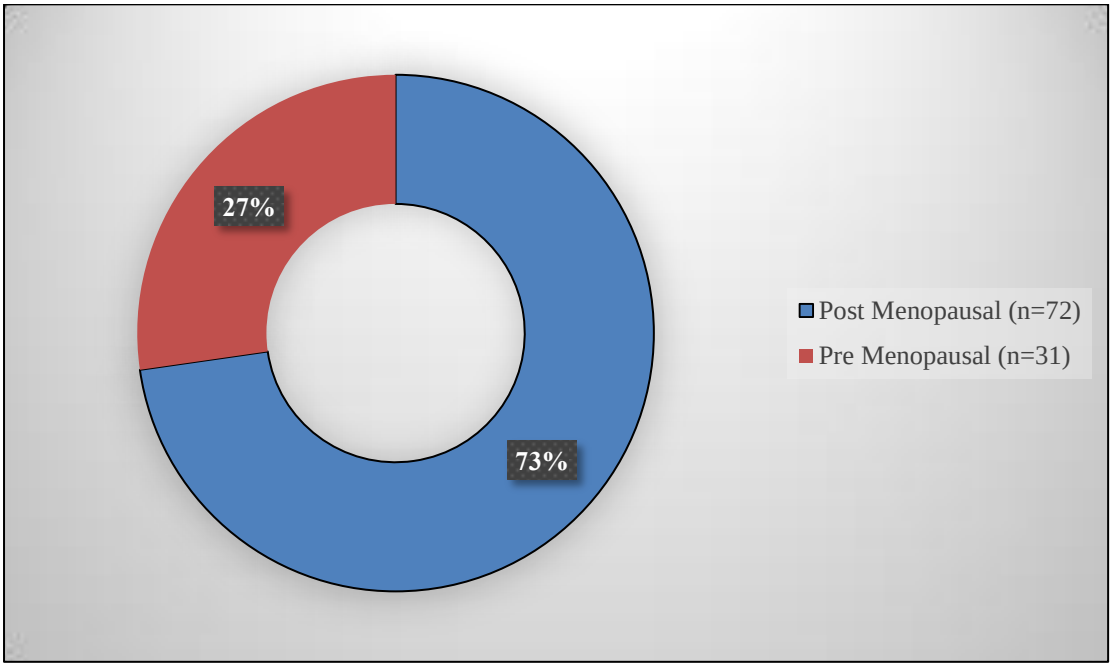

Figure 9: Distribution based on menstrual status

Distribution based on clinical presentation

Table 5: Distribution based on clinical presentation

Presentation	Number of patients	Percentage
Discharge per vagina	93	90%
Post-menopausal bleed	67	65%
Intermenstrual bleed	27	26%
Post coital bleed	8	7%
Asymptomatic	2	1.9%

Many patients in our study had multiple symptom but most common clinical presentation was discharge per vagina (n=93; 90%) followed by post-menopausal bleeding (n=67; 65%). Only two patients (1.9%) were asymptomatic and picked up on routine screening (Figure 10 & Table 5).

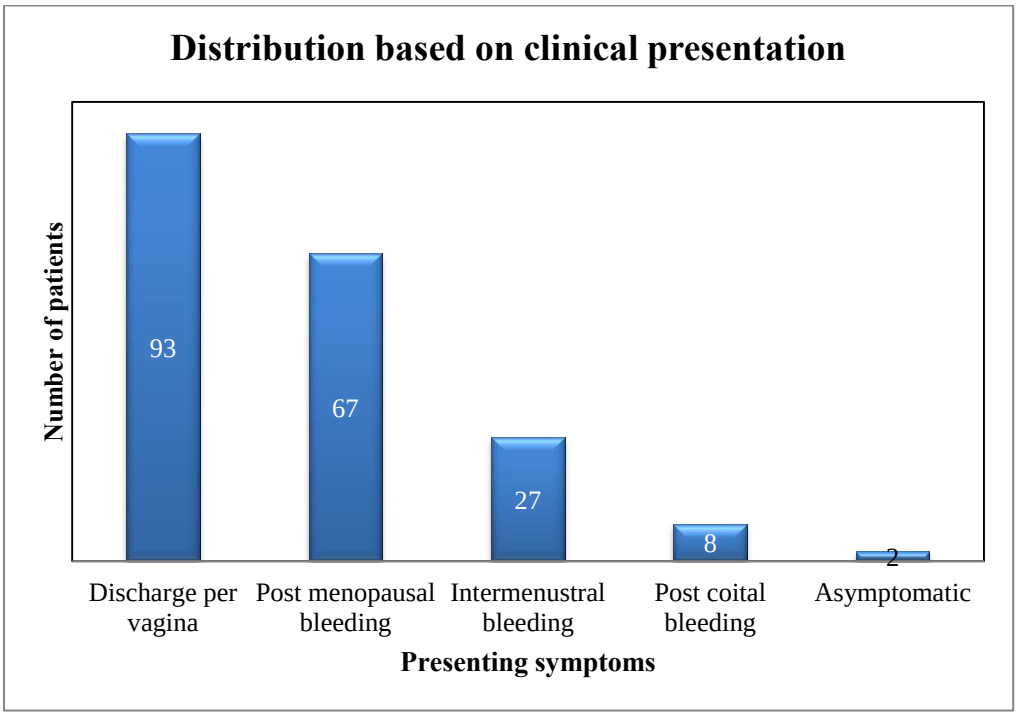

Figure 10: Distribution based on clinical presentation

Histopathological distribution:

Table 6: Histopathological distribution

Histopathology	Number of cases	Percentage
Squamous cell carcinoma	98	95.2%
Adenocarcinoma	5	4.8%

98 (95.2%) patients in our study were diagnosed with squamous cell carcinoma and remaining five (4.8%) were adenocarcinoma (Table 6 & Figure 11).

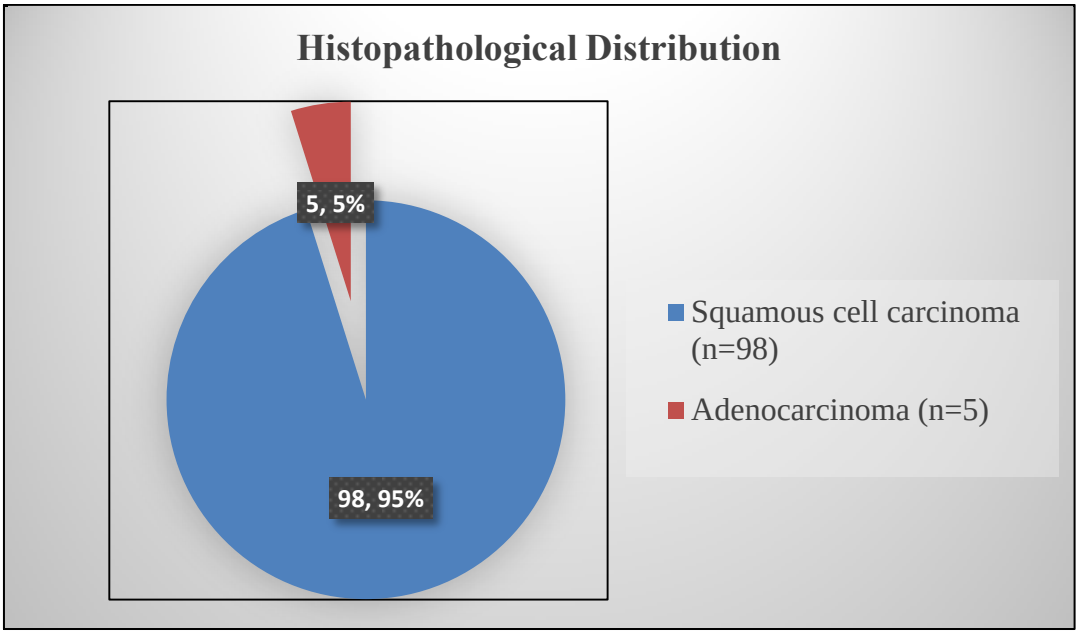

Figure 11: Histopathological distribution

Among the five patients with adenocarcinoma, three are between the age group of 30 – 39 years and remaining two patients are between the age group 40 – 49 years.

Distribution based on clinical staging

Table 7: Distribution based on clinical staging

FIGO* Stage	IA	IB	IIA	IIB	IIIA	IIIB	IVA	IVB
Number of patients	0	1	2	47	3	45	5	0
Percentage (%)	0	0.97	1.94	45.63	2.91	43.68	4.85	0

*FIGO –International federation of gynecology and obstetrics

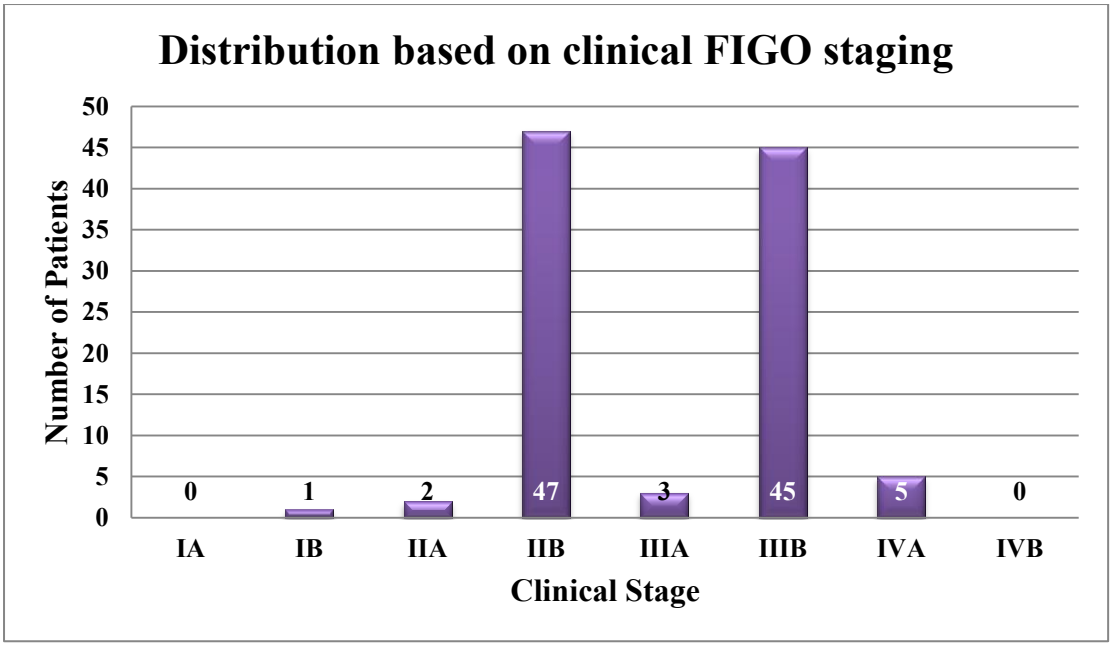

Figure 12: Distribution based on clinical FIGO staging

On clinical staging, most of the patient were equally staged as IIB (n=47, 45.6%) and IIIB (n=45; 43.6%) followed by IVA (n=5; 4.8 %). Only one patient (stage IB) had invasive carcinoma with invasion ≥5 mm (greater than stage IA) and lesion is limited to the cervix. For two patients (stage IIA), involvement was limited to upper two-thirds of the vagina without involving parametrial. For three patients (stage IIIA) the carcinoma involves the lower third of the vagina, with no extension to the pelvic wall. The carcinoma has extended beyond the true pelvis or had involved (biopsy proven) the mucosae of the urinary bladder or rectum in five patients were staged as IVA (Figure 12 & Table 7).

Distribution based on MRI staging:

Table 8: Distribution based on MRI staging

Stage	FIGO IA	FIGO IB	FIGO IIA	FIGO IIB	FIGO IIIA	FIGO IIIB	FIGO IVA	FIGO IVB
Number of patients	0	1	8	47	5	5	35	2
Percentage (%)	0	0.97	7.76	45.63	4.85	4.85	33.98	1.94

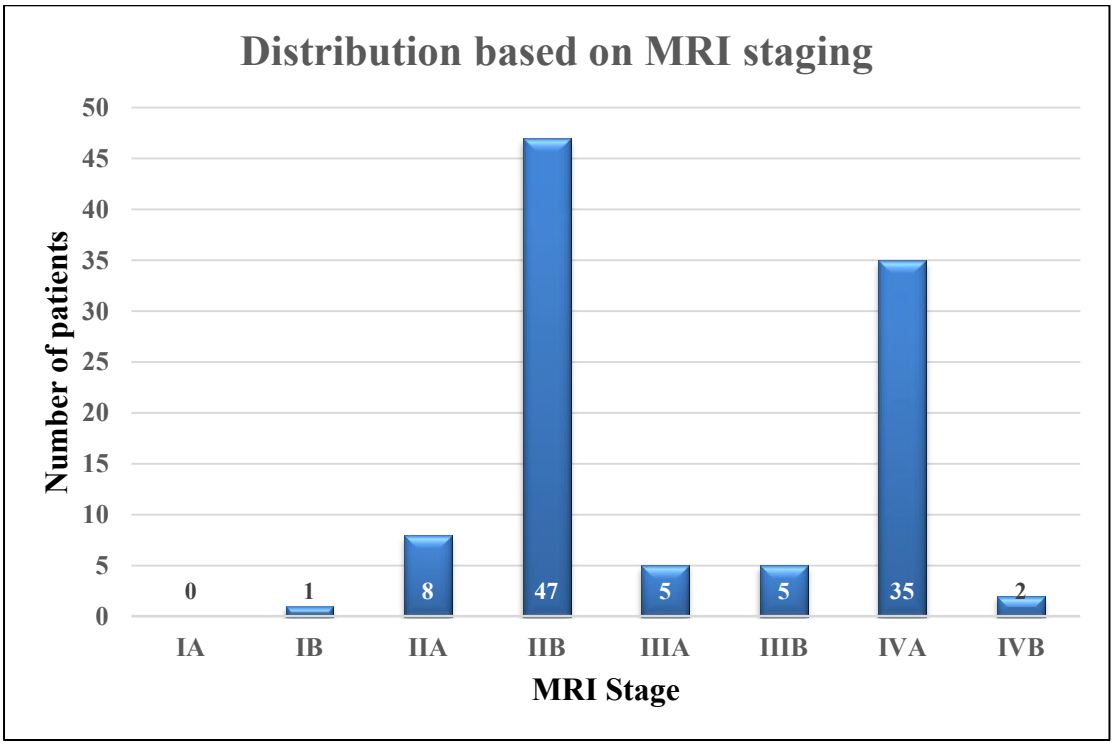

Figure 13: Distribution based on MRI staging

On MRI, majority of the patients were staged under stage IIB (47 patients) and stage IVA (35 patients). Only one patient (FIGO - IB) had invasive carcinoma with invasion ≥5 mm (greater than Stage IA) and lesion is limited to the cervix. Eight patients (FIGO - IIA) had invasion to upper 2/3rd of vagina with no obvious invasion into parametrium. Five (4.85%) patients each were staged as IIIA and IIIB respectively. Two out of 103 patients showed distant metastasis (Table 8 &Figure 13).

Distribution based on clinical & MR FIGO staging:

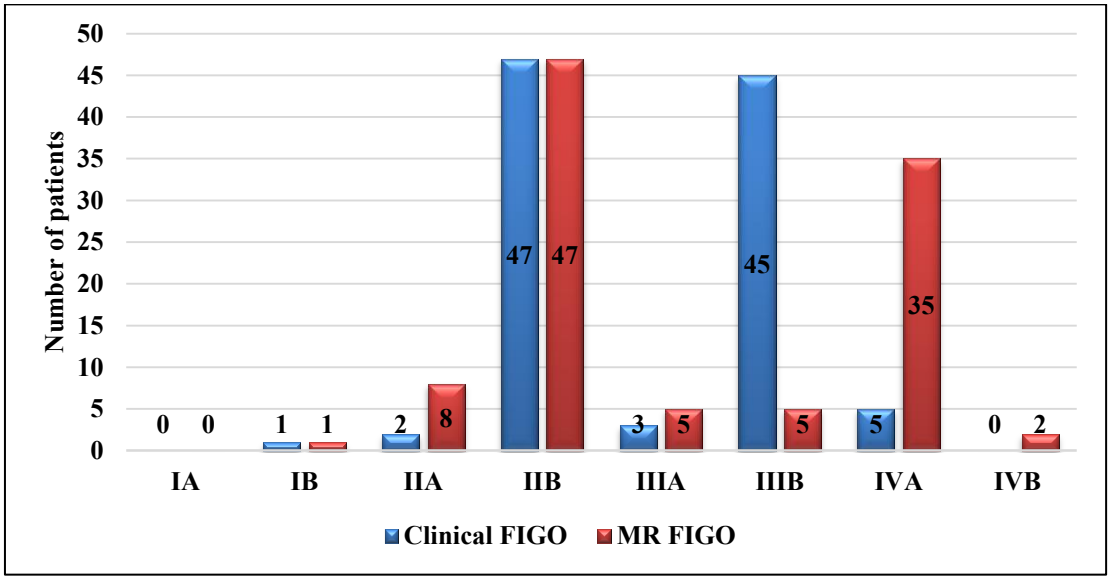

Figure 14: Comparison between clinical and MR FIGO staging

MRI staging after clinical staging have redistributed the cases among IIB and IIIB. Though the number of stage IIB cases remains same but were redistributed to IIIB and IVA. Most of the clinically stage IIIB cases were assigned stage IVA on MRI as it can clearly delineate the spread of the disease (Figure 14).

Table 9: Comparison between clinical and MR staging

Stage	FIGO IA	FIGO IB	FIGO IIA	FIGO IIB	FIGO IIIA	FIGO IIIB	FIGO IVA	FIGO IVB	N=103
MR IA	-	-	-	-	-	-	-	-	0
MR IB	-	-	-	1	-	-	-	-	1
MR IIA	-	1	2	4	-	1	-	-	8
MR IIB	-	-	-	36	1	10	-	-	47
MR IIIA	-	-	-	1	1	3	-	-	5
MR IIIB	-	-	-	-	-	5	-	-	5
MR IVA	-	-	-	4	1	25	5	-	35
MR IVB	-	-	-	1	-	1	-	-	2
Total	0	1	2	47	3	45	5	0	103

FIGO – International federation of gynecology and obstetrics
MR – Magnetic resonance
N – Total number of patients

On comparing clinical and MRI staging, it was noted that less than half (n=49) of the cases were staged correctly. It was found that, on clinical staging large number of cases was seen in IIB and IIIB. On MR staging, these cases were found to be redistributed among IIB and IVA (Table 9).

Cases correctly staged, under staged & over staged clinically:

Table 10: Cases correctly staged, under staged & over staged clinically.

MR Stage	N=103	Correctly staged	Under staged clinically	Over staged clinically
MR IA	0	-	-	-
MR IB	1	0	0	1
MR IIA	8	2	1	5
MR IIB	47	36	0	11
MR IIIA	5	1	1	3
MR IIIB	5	5	0	0
MR IV A	35	5	30	0
MR IV B	2	0	2	0
Total	**103**	**49 (47.5%)**	**34 (33.0%)**	**20 (19.4%)**

On comparing clinical staging with MRI staging, it revealed that 49 (47.5%) patients were correctly staged clinically. 20 (19.4%) patients were over staged and 34 (33.0%) patients were under staged clinically (Table 10). Almost 88.2% of the patients who were understaged clinically belonged to stage IVA on MRI and 55% of the patients who were overstaged clinically belonged to stage IIB on MRI.

Histopathological staging compared with clinical & MR staging

Histopathological correlation was only available in 56 patients up to MR stage IIB. Though surgery was indicated as treatment up to stage ≤IIA we had availability of surgical specimen up to stage IIB. All surgical specimens were examined and histopathological staging was given. On histopathological correlation, it was found

that MRI staging was 100% sensitive up to stage IIB. There were disparity between clinical staging and histopathological correlation (Table 11).

Table 11: Comparison of histopathological, MRI & clinical FIGO staging.

Stage	Histopathology	MRI	Clinical
IA	0	0	0
IB	1	1	1
IIA	8	8	2
IIB	47	47	41
IIIA	0	0	1
IIIB	0	0	11
IVA	0	0	0
IVB	0	0	0
Total	**56**	**56**	**56**

A. Stage IA (n=0):

In our study, clinically no patients were diagnosed with cervical intraepithelial neoplasia and the same was correlated with MRI.

B. Stage IB (n=1):

Table 12: Histopathologically proven stage IB cases.

Stage IB (n=1)	Correctly staged	Overstaged	Understaged
MRI	1	0	0
Clinical	0	1	0

One patient was diagnosed as stage IB on MRI and on histopathological examination, the lesion showed no evidence of extension of the disease beyond the cervix. This patient was clinically overstaged as IIB (Table 12).

C. Stage IIA (n=8):

Table 13: Histopathologically proven stage IIA cases.

Stage IIA (n=8)	Correctly staged	Overstaged	Understaged
MRI	**8**	**0**	**0**
Clinical	**2**	**5**	**1**

Eight patients were staged as IIA on MRI. Out of these eight patients only two was correctly staged clinically. Vaginal invasion was missed in one patient and hence was understaged as stage IB. Clinically five patients were overstaged of which, four were staged IIB as they were presumed to invade parametrium and one was staged as IIIB due to deranged renal function test; however it was later proved to be a case of chronic kidney disease and not because of pelvic wall extension or hydroureteronephrosis. Eight cases staged as IIA on MR correlated well with the histopathological findings, giving a sensitivity and specificity of 100% (Table 13).

D. Stage IIB (n=47):

Table 14: Histopathologically proven stage IIB cases.

Stage IIB	Correctly staged	Over staged	Under staged
MRI	47	0	0
Clinical	36	11	0

On MRI 47 patients were correctly staged as IIB when compared to histopathology. But on clinical staging, only 36 patients were staged correctly and 11 of them were over staged (Table 14). Among these 11 patients, one was staged IIIA and rest 10 were staged IIIB.

E. Stage IIIA (n=5):

Table 15: Comparison of Stage IIIA cases**.**

Stage IIIA	Correctly staged	Over staged	Under staged
MRI	5	0	0
Clinical	1	3	1

On MRI five patients were correctly staged as IIIA. But on clinical staging, only one patient was staged correctly. Three of them were overstaged as IIIB and the other one was understaged as IIB clinically. (Table 15).

F. Stage IIIB (n=5):

Table 16: Comparison of stage IIIB cases.

Stage IIIA	Correctly staged	Over staged	Under staged
MRI	5	0	0
Clinical	5	0	0

Both on MRI and clinical staging, five patients were correctly staged as IIIB. None of these cases were overstaged or understaged clinically (Table 16).

G. Stage IVA & IVB:

A total of 35 cases were staged as IVA and two cases were staged IVB. Among the 35 cases of IVA, 12 cases had isolated bladder involvement, five cases had isolated rectal involvement and rest of the 18 cases had involvement of both urinary bladder and rectum.

Urinary bladder involvement:

Table 17: Comparison between MR and FIGO staging of urinary bladder involvement.

Bladder involvement	MRI	Clinical FIGO
Mucosa	30	5
Muscle	1	0

On cystoscopy five patients showed bladder mucosal involvement and on MRI mucosal involvement was seen in 30 patients and one patient showed infiltration only

upto bladder smooth muscle. On cystoscopy, bladder invasion was obvious only when there was mucosal invasion and muscle infiltrations were not picked up (Table 17).

Rectal involvement:

Table 18: Comparison between MR and FIGO staging of rectal involvement.

Rectal involvement	MRI	Clinical FIGO
Mucosa	23	4
Muscle	6	0

Clinically rectal invasion was seen only in four patients who showed evidence of rectal mucosal invasion on proctoscopy. 23 patients on MR imaging showed rectal mucosal infiltration. Six patients had only rectal muscle infiltration and no obvious mucosal involvement. Similar to bladder invasion, rectal invasion is only picked up clinically when there is obvious mucosal invasion (Table 18).

Distant metastasis (n=2):

Two patients on MRI showed metastasis to pelvic bones and one of them showed hepatic metastasis as well. Both the cases were under staged clinically as IIB and IIIB. The patient who was staged MRI IIIB had both hepatic and bony metastasis.

H. Uterine body infiltration:

Table 19: Uterine body infiltration

Stage	MR IA	MR IB	MR IIA	MR IIB	MR IIIA	MR IIIB	MR IVA	MR IVB
Number of patients	0	0	8	46	5	5	35	2
Percentage (%)	0	0	7.1	45	5	5	34	1.9

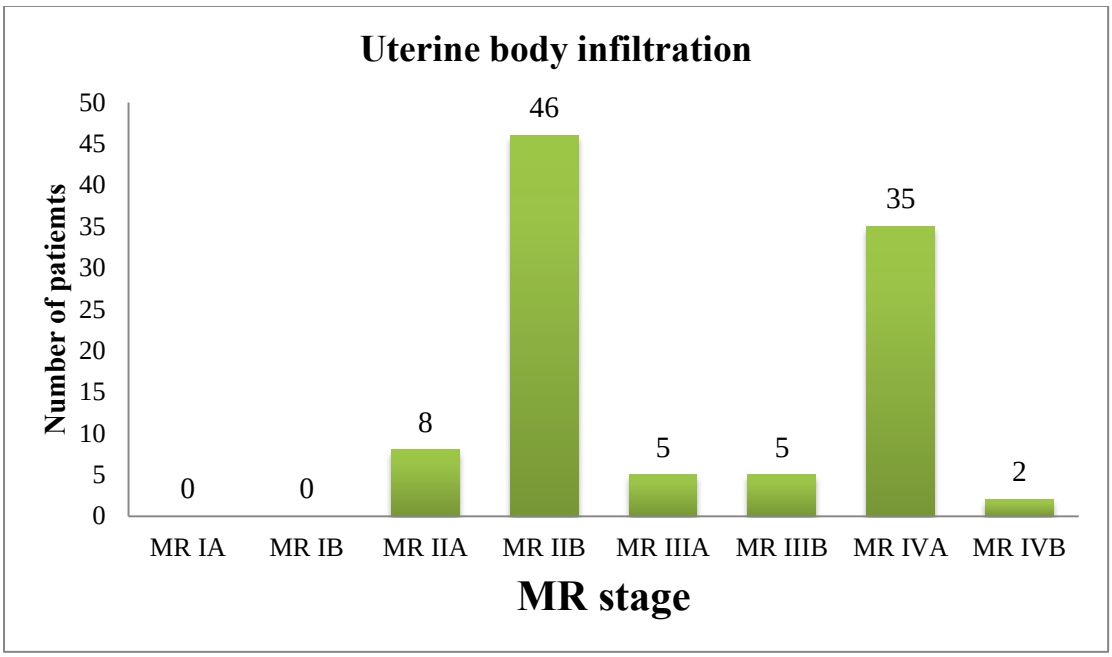

Figure 15: Uterine body infiltration

Total of 101 (98%) patients out of 103 showed uterine body infiltration. 46 (45%) out of them belong to IIB, 35 (34%) stage IVA. Among the remaining 20 cases, eight (7%) cases to IIA, five (5%) cases to IIIA, five (5%) cases to IIIB and two cases to IVB (Table 19 & Figure 15).

I. Lymph nodal involvement

Stage wise distribution of lymph nodal involvement

Table 20: Local parameters associated with lymph nodal involvement.

Stage	MR IA	MR IB	MR IIA	MR IIB	MR IIIA	MR IIIB	MR IVA	MR IVB
Number of patients	**0**	**0**	**3**	**27**	**5**	**5**	**28**	**2**
Percentage (%)	0	0	4.28	38.57	7.14	7.14	40	2.85

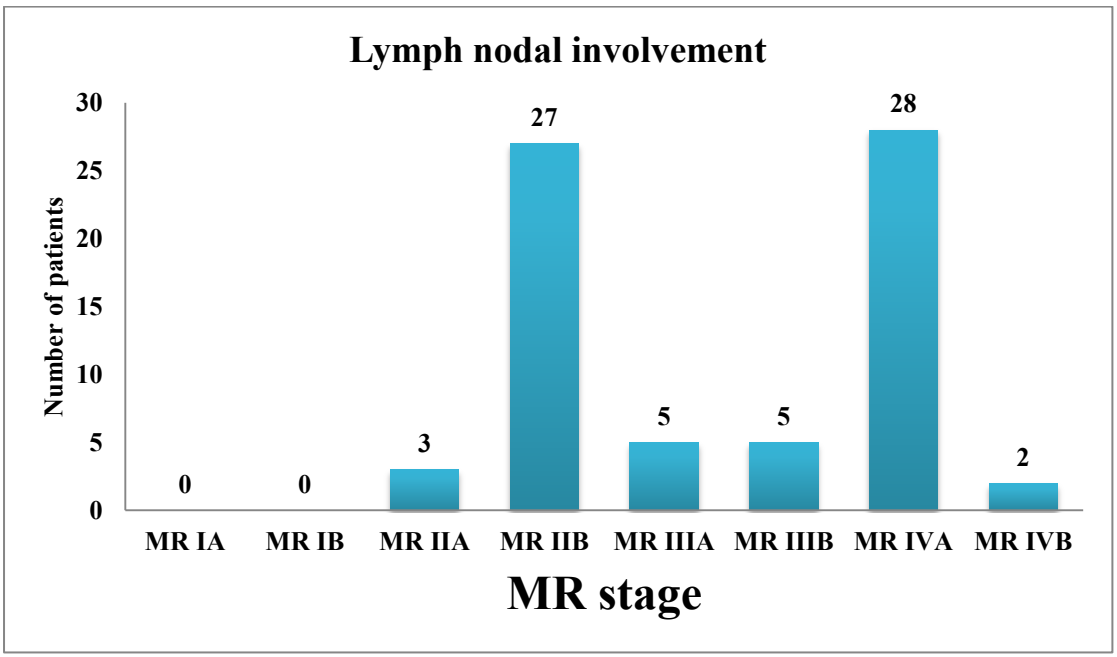

Figure 16: Stage wise distribution of lymph nodal involvement

On MR Imaging, out of the 103 patients, 70 (67%) showed evidence of lymph nodal metastasis. 28 (40%) patients out of these 70 belong to MR stage IVA, 27 (38%) to stage IIB, five (7.1%) each to IIA and IIIB, three (4.2%) to IIA and two

(2.8%) to IVB. Patients with disease confined to cervix had no lymph nodal spread on MRI (Figure 16 & Table 20).

Local parameters associated with lymph nodal involvement:

Table 21: Local parameters associated with lymph nodal involvement.

Parameter	Number of cases	Percentage (%)
Uterine body	69	98
Vaginal	69	98
Parametrial	67	95
Lateral pelvic wall	5	7
Urinary Bladder	24	34
Rectal	21	30

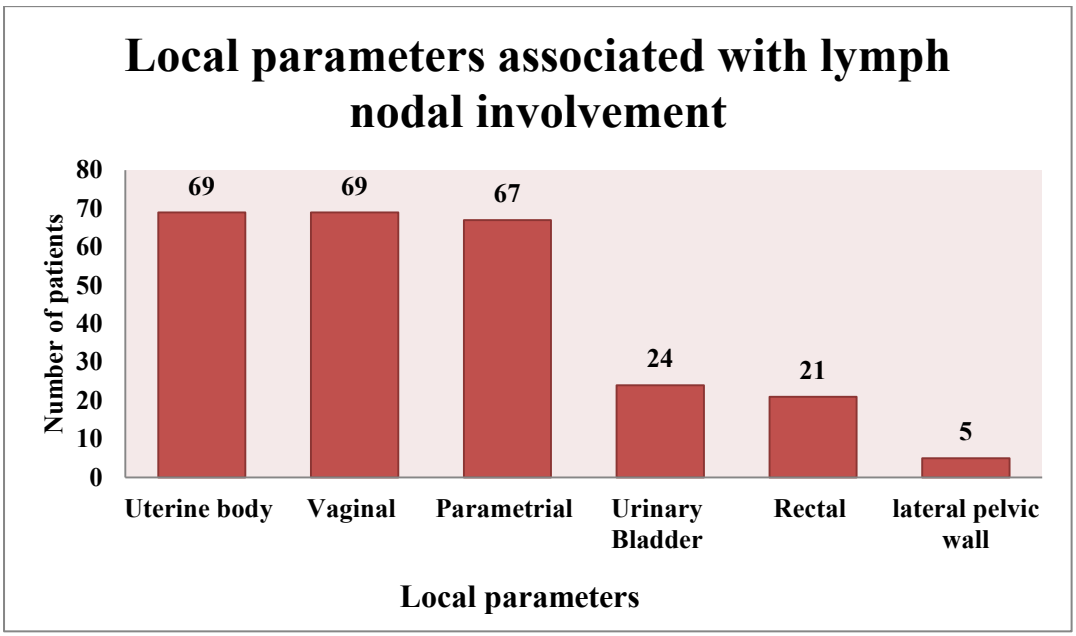

Figure 17: Local parameters associated with lymph nodal involvement.

Six local parameters associated with lymph nodal metastasis were assessed in our study. Uterine body, vaginal and parametrial invasion were the local parameter which were highly associated with lymph nodal metastasis. 69 (98%) out of the 70 patients with lymph nodal involvement had uterine body and vaginal involvement. Parametrial invasion was noted in 67 (95%) out of 70 patients with lymph nodal metastasis which was the next local parameter associated. Urinary bladder involvement and rectal involvement were noted in 24 (34%) and 21 (30%) out of the 70 patients with lymph nodal metastasis respectively. Only five patients (7%) with lateral pelvic wall involvement were associated with lymph nodal metastasis (Table 21 & Figure 17).

Associated findings:

In our study the most common associated finding was pyometra (n=11, 10.67%) secondary to cervical stenosis caused by the mass. The next common association was involvement of unilateral or bilateral fallopian tube causing hydrosalphinx (n=7; 6.79%) and less common association was hematometra (n=3; 2.91%) (Figure 18).

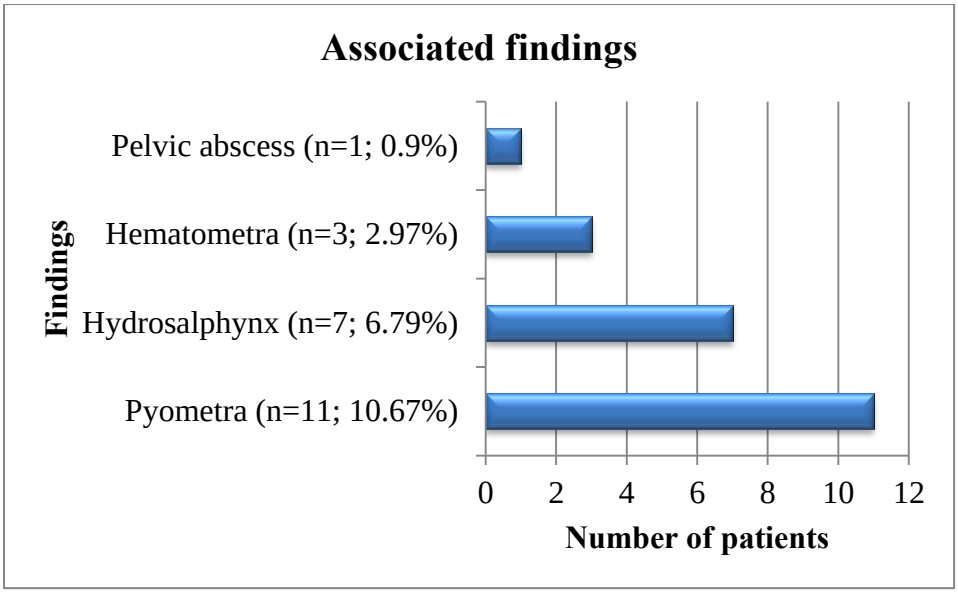

Figure 18: Associated findings on MRI

There is significant difference between clinical and MRI staging of carcinoma cervix (P<0.001; chi square test). The kappa value of the study was found to be 0.33 which interprets that the two methods of staging are in fair agreement with each other.

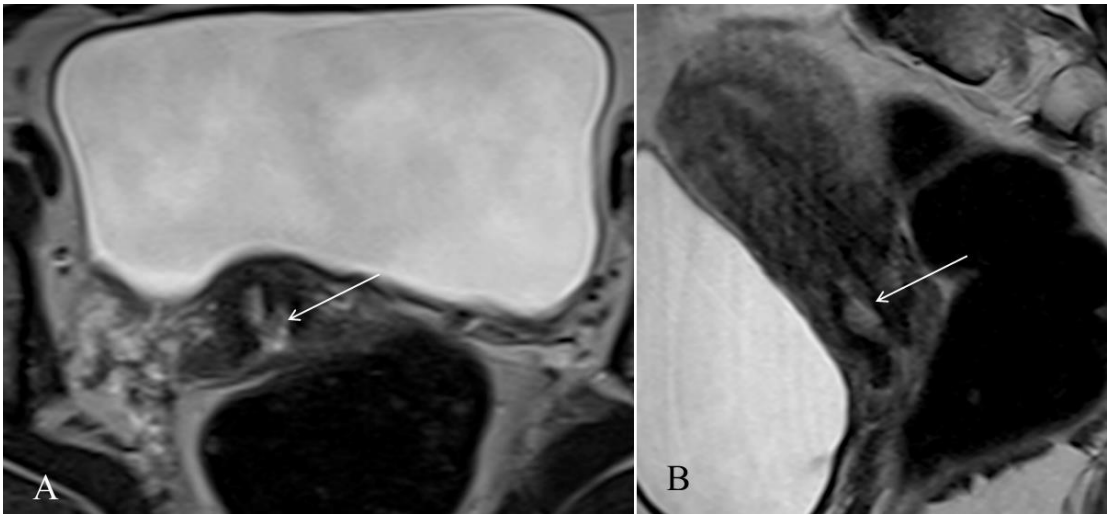

Figure 19: (A) Axial and (B) Sagittal T2 weighted MRI showing hyperintense lesion confined to cervix (white arrow), staged as IB.

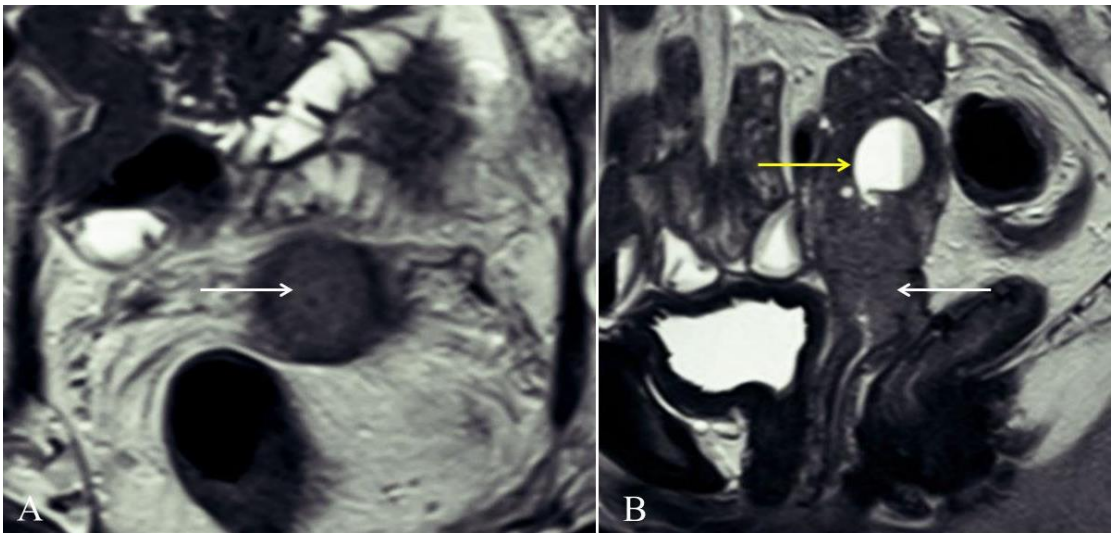

Figure 20: (A) Axial and (B) Sagittal T2 weighted MRI showing mass (white arrow) extending to lower uterine segment but no obvious breach in cervical stromal ring. Mass is causing cervical stenosis leading to endometrial collection (yellow arrow), staged as IIA.

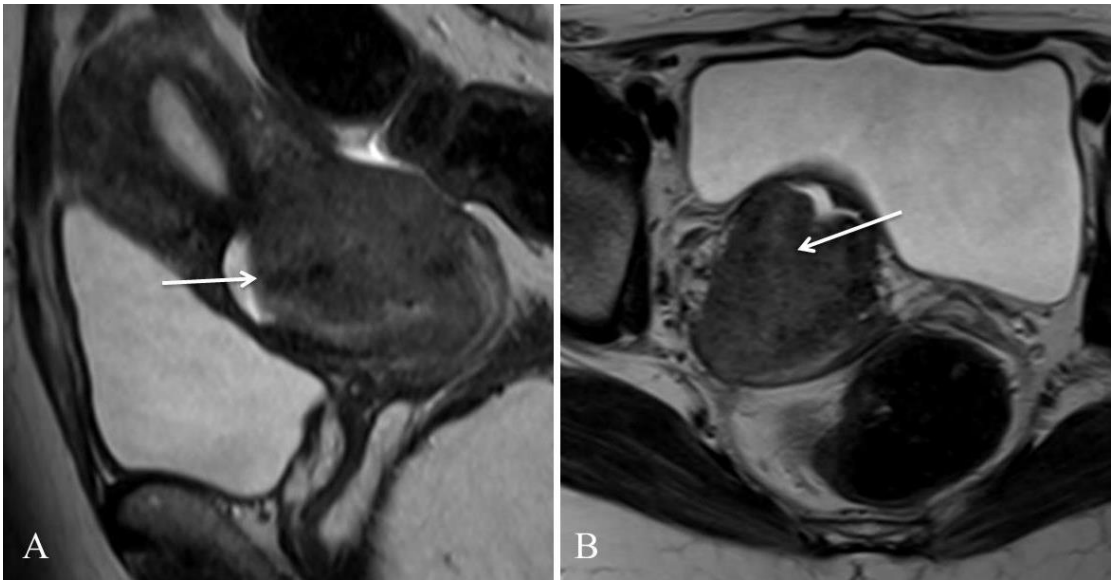

Figure 21: Sagittal (A) and Axial (B) T2 weighted MRI showing cervical mass (white arrow) extending to bilateral parametrium with mild endometrial collection staged as IIB.

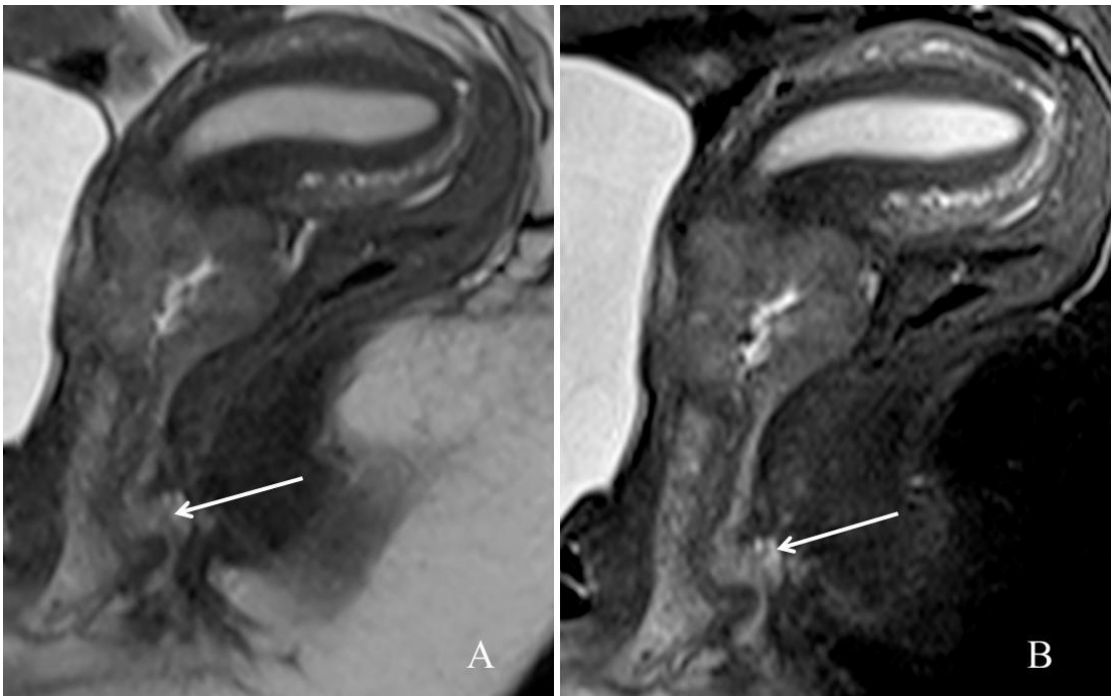

Figure 22: Sagittal T2 (A) and STIR (B) MRI showing extension of cervical mass to lower third of vagina (white arrow) staged as IIIA.

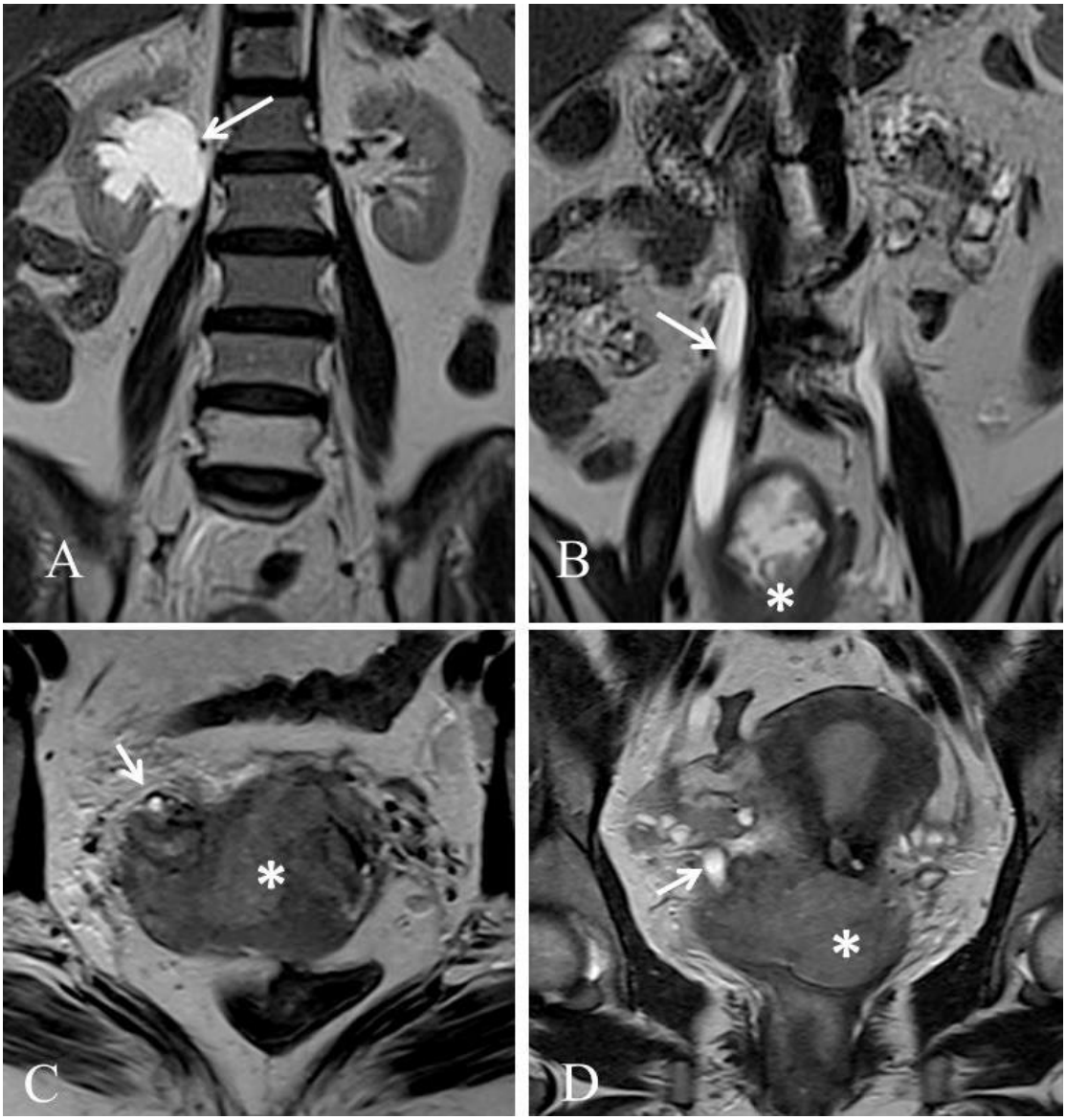

Figure 23: Coronal (A) ,(B), (D) and Axial (C) T2 weighted MRI showing cervical mass (white asterisk*) extending to bilateral parametrium and involving right distal ureter causing hydroureteronephrosis (white arrow), staged as IIIB.

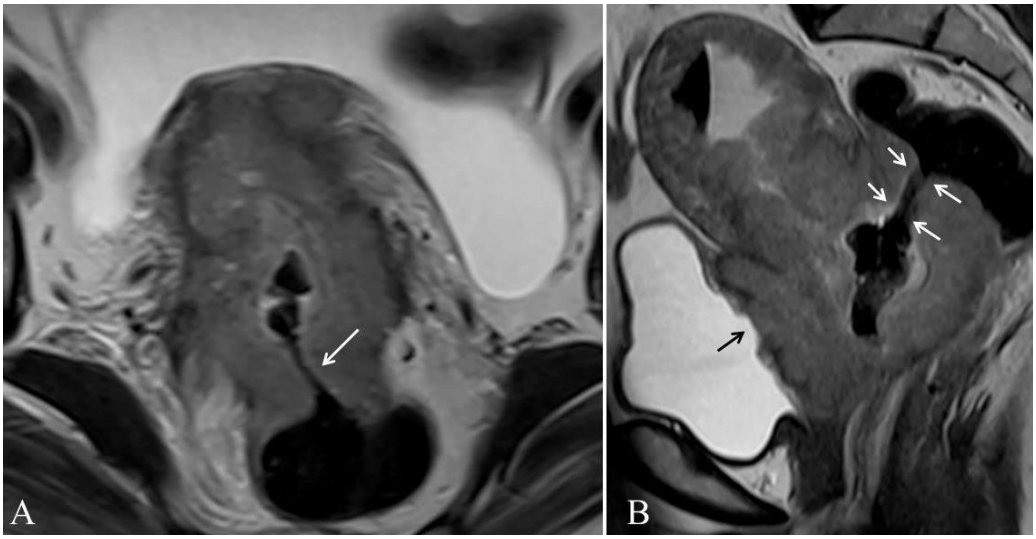

Figure 24: (A) Axial and (B) Sagittal T2 weighted MRI showing tumor extension to rectum causing rectocervical fistula (white arrow) and also to posterior wall of urinary bladder (black arrow), staged IVA.

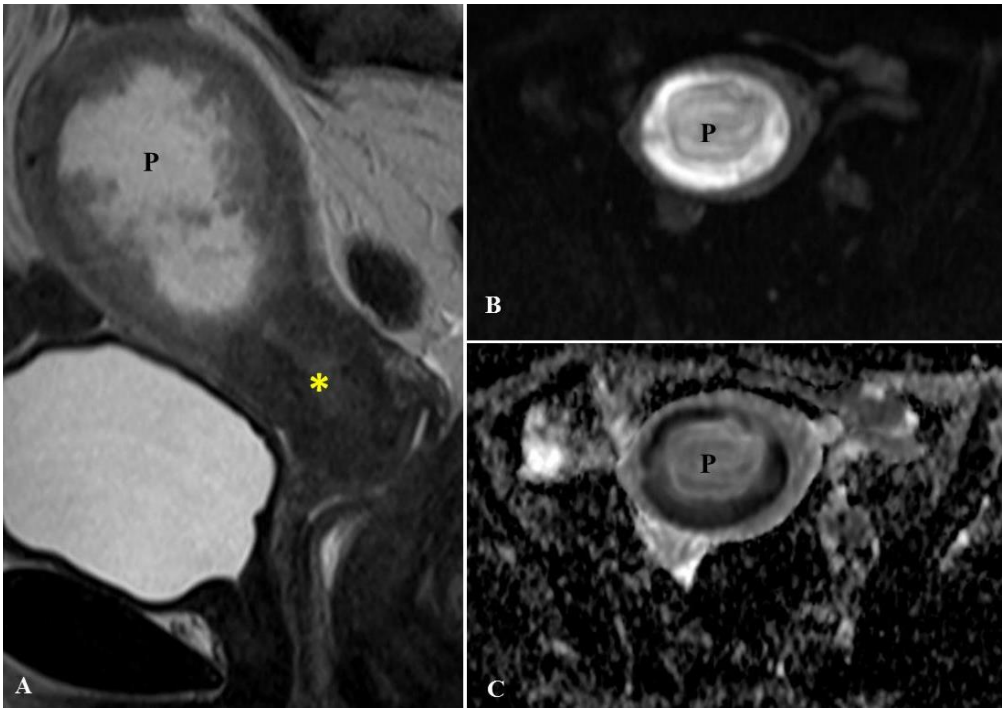

Figure 25: (A) Sagittal T2 weighted MRI showing mass in the cervix (yellow asterisk*) extending to lower uterine segment causing cervical stenosis and pyometra (P). Diffusion weighted MRI (B) showing hyperintense signal of pyometra which on corresponding ADC map (C) showing restricted diffusion.

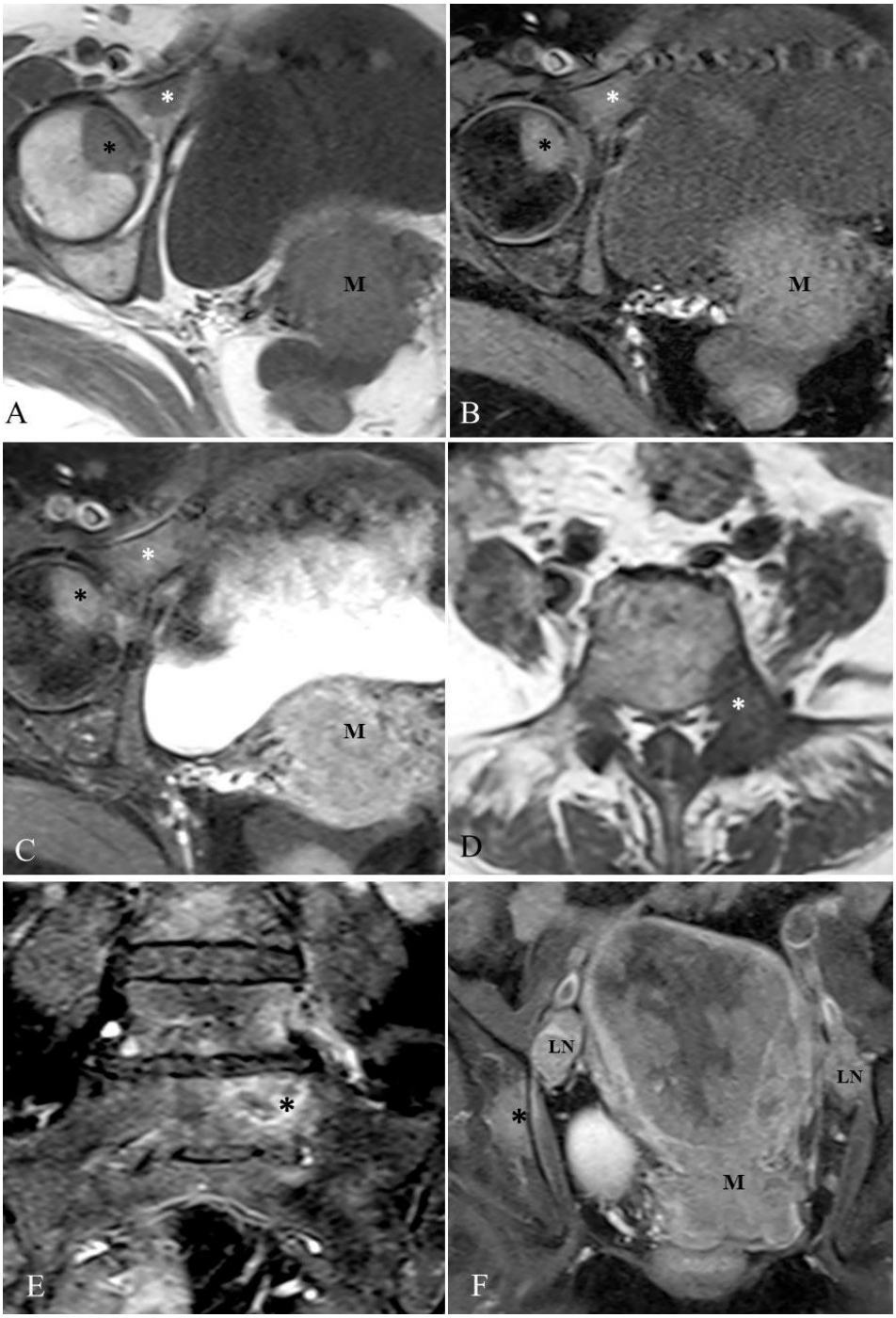

Figure 26: Axial T1 (A), STIR (B), T1 post-contrast (C) MRI showing cervical mass (M) withT1 hypo, STIR hyperintense and heterogeneously enhancing metastatic lesion in the head of femur (black asterisk *) and superior pubic ramus on right side (white asterisk *). Axial T1 (D) and coronal STIR (E) MRI showing metastatic lesion in pedicle, lamina of L5 (black asterisk *) and body of S1 vertebra on left side. Coronal post-contrast T1 fat saturated (F) MRI showing heterogenous enhancement of the cervical mass (M) with heterogeneously enhancing metastasis to right iliac bone (black asterisk *) and bilateral internal iliac chain lymph nodes (LN).

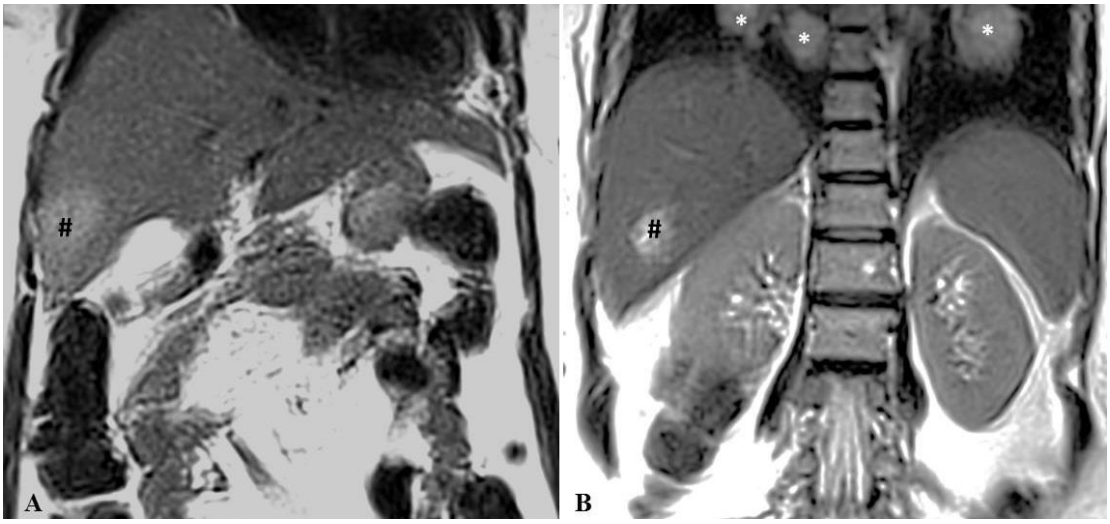

Figure 27: Coronal T2 weighted MRI (A) and (B) showing hyperintense metastatic lesion (#) involving segment six of right lobe and multiple hyperintense nodular lesions (*) in bilateral lower lung fields.

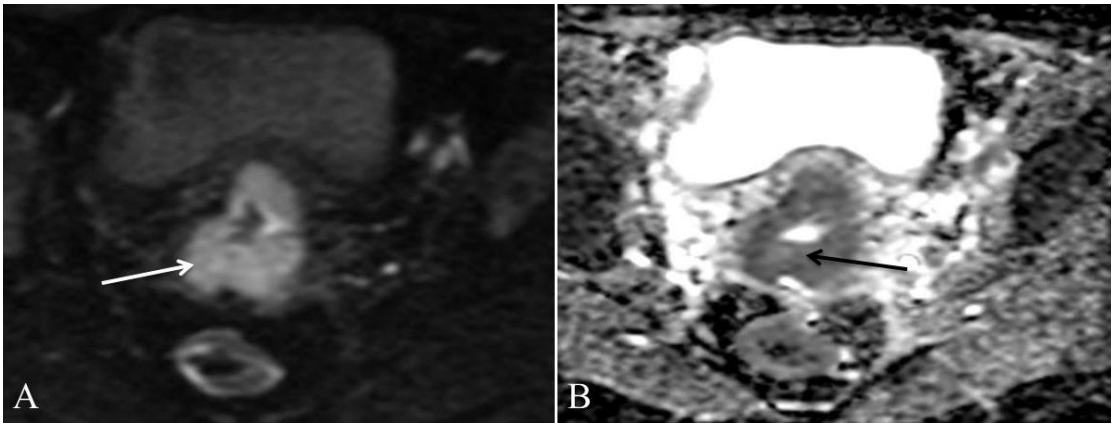

Figure 28: Diffusion weighted MRI (A) of cervix showing hyperintense signal (white arrow) which on corresponding ADC mapping (B) showing restricted diffusion (black arrow).

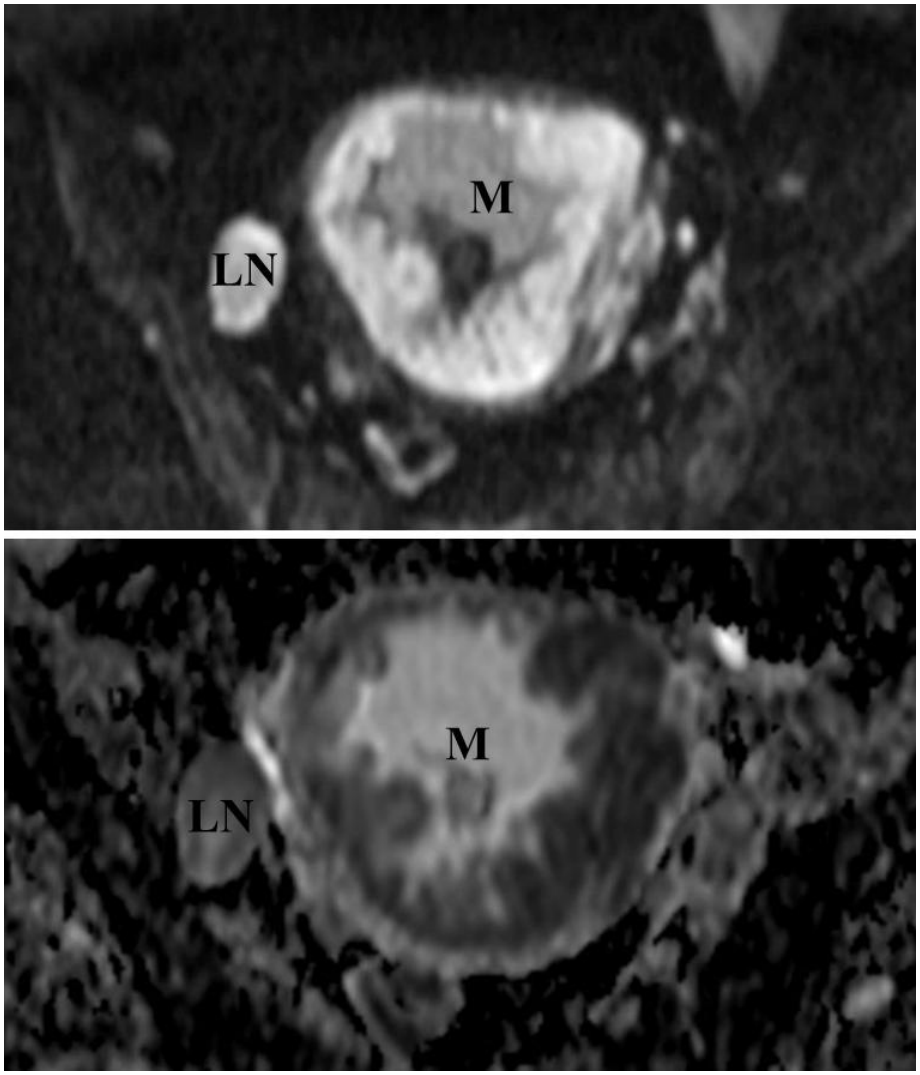

Figure 29: Diffusion weighted MRI (A) showing high signal intensity involving a large metastatic right internal iliac chain lymphnode (LN) and cervical mass (M) which on corresponding ADC mapping (B) image showing restricted diffusion.

Discussion

DISCUSSION:

The FIGO staging system was updated in 2009 and is commonly used for treatment planning but is inadequate in the evaluation of prognostic factors like tumor volume and nodal status. MRI is the preferred imaging modality for cervical cancer.

Staging plays an important role in prognosis as well as treatment planning. Prognosis of the disease at the time of diagnosis depends on the volume and extent of disease.

Unavailability of MRI for staging the disease in rural population and its high cost was a hindrance for optimal evaluation of the disease in the population below poverty line. Introduction of newer schemes by the government at a subsidiary cost and making MRI available in almost all the government hospitals in our region have led to increase in number of MRI studies.

The sample size in our study was 103 biopsy proven cases of carcinoma cervix. Majority of the women in our study were postmenopausal (73%) and in middle age group (80%) i.e.40-49 years (n=29), 50-59 years (n=28) and 60-69 years (n=26). Most of the women had a parity of 1-3 (67%). Discharge per vaginum was the most common presentation with which patients presented in our study.

A study was conducted on 50 patients for the assessment of diagnostic efficacy of diffusion weighted (DWI) sequence in the imaging of carcinoma cervix. They concluded that acquiring DWI additional to conventional sequences provided 100% sensitivity and 84.8% specificity for detecting the tumor[73].

A study on 45 patients with carcinoma cervix was evaluated by Kumar JU et al to assess the need of contrast MRI. The authors concluded that contrast was needed only in selected patients with ambiguity in plain study. They also documented that, postcontrast T1 weighted sequence has no additional value when compared with unenhanced T1 and T2 weighted imaging[38].

Stage IA:

Stage IA being micro invasive can only be diagnosed on microscopy and is normal on MR imaging. On routine MRI, stage IA shows no abnormal signal. There were no cases of clinical stage IA cervical cancer in our study. According to Kim SH et al[56], the resolution of MRI is not enough to detect microscopic lesions and therefore lesions from stage IB onwards only can be picked up.

Stage IB:

Stage IB is a clinically invasive lesion confined only to the cervix. Stage IB lesion appears hyperintense on T2 and STIR sequences with evidence of enhancement on post contrast T1 weighted images.

On MRI, one patient was corresponding to stage IB which correlated with histopathology, but this patient was clinically staged as IIB. Hence we had sensitivity and specificity of 100% in detecting stage IB lesions on MRI. One patient was diagnosed as stage IB clinically but on MR imaging it was staged as IIA.

Stage IIA:

Stage IIA is extension of the cervical lesion into the proximal two-thirds of the vagina. Disruption of the hypointense vaginal wall with hyperintense lesion on T2 and enhancement on contrast administration were used as signs of vaginal invasion. Similar criteria were used by Togashi K et al[17] and Hricak H et al[55].

There were eight cases diagnosed with stage IIA on MRI of which all were staged correctly on histopathology. However, only two of these patients were staged as IIA clinically. Thus MRI showed a sensitivity and specificity of 100% in diagnosing stage IIA lesions (Table 22).

Table 22: Comparison of stage IIA cases between clinical, MRI and histopathology.

Stage IIA (n=8)	Clinical	MRI	Histopathology
Number of patients	2	8	8

As mentioned before, two patients who were staged as IIA on clinical examination showed relevant signal changes involving the vagina on MRI. Hence

both the cases were correctly staged as IIA. Among the rest six cases of MRI staged IIA, one case was staged as IB, four cases were staged as IIB and one case was staged as IIIB (Table 23).

Table 23: Distribution of MRI IIA cases under clinical FIGO staging.

Clinical FIGO Stage	IB	IIA	IIB	IIIB
MR IIA (n=8)	1	2	4	1

Togashi K et al[17], in their study of 67 patients had three cases of histopathologically confirmed vaginal invasion. On MRI two cases were overstaged as IIB and the other one was understaged as IB.

Stage IIB:

Stage IIB is when the lesion is infiltrating into the parametrium with no extension to lateral pelvic walls. On MRI, T2 hypointense stromal ring is seen surrounding the cervix which when disrupted by extending tumoral margins to the parametrium are said to be signs of definitive invasion[30].

Table 24: Clinical FIGO staging compared with MR IIB cases.

Stage (n=47)	Clinical FIGO IIB	MR IIB	Histopathology
Number of patients	36	47	47

Table 25: MR IIB cases distribution compared with clinical staging.

Stage (n=47)	FIGO IIB	FIGO IIIA	FIGO IIIB
MR IIB	36	1	10

Forty seven patients on MR imaging showed involvement of the parametrium and hence they were staged as IIB. On clinical staging, 36 of these 47 patients were correctly staged as IIB and 11 cases were over staged. Among the 11 patients, one was staged as IIIA where parametrial invasion was overstaged with infiltration to lateral pelvic walls without hydroureteronephrosis and rest ten patients with hydroureteronephrosis were staged as IIIB. No patients were understaged clinically. Our study showed 100% sensitivity and specificity for staging IIB on MRI (Table 24 & Table 25).

Hricak H et al[55], in their study have documented that peritumoral edema and increased vascularity adjacent to the tumor can result in hyperintense signal on T2 weighted images and then mistaken for parametrial involvement by the tumor (Table 26).

Table 26: Correlation with other clinical studies for stage IIB

Stage IIB	MRI	Histopathology	Percentage (%)
Present Study	47	47	100
Hricak et al[55]	13	17	76
Togashi et al[17]	17	19	89

Hricak H et al[55] and Togashi K et al[17] had false negative cases in their study. The most probable reason is failure to diagnose parametrial invasion as they were microscopic.

A retrospective study by Park et al[66] on 36 patients documented 84.4% accuracy on MRI in detecting parametrial invasion. They concluded that MRI provides an accurate evaluation of tumor extension, but accuracy in lymph nodal metastasis detection is lower than PET.A study by Choi et al[15] on 226 patients reported 94.0% accuracy on MRI for evaluation of parametrial invasion.

A study conducted by Testa et al[58] on 33 patients with invasive carcinoma cervix for evaluation of parametrial extension by MRI and ultrasound documented low sensitivity of 40.0% and 60% respectively.

Postema et al[74] reviewed 103 patients with parametrial invasion on MRI by two observers. The authors documented a sensitivity and specificity of 20.0% and 97.0% for observer 1 and 60% and 73% for observer 2 respectively. Finally authors concluded that detection of parametrial invasion on MRI was relatively insensitive as MRI interpretation might show interobserver variability.

Stage IIIA:

Stage IIIA is defined as infiltration to lower third of the vagina with no involvement of the lateral pelvic walls. Clinically there were three patients staged as IIIA but on MRI, one patient showed extension of disease to the adjacent pelvic organ

and another showed only parametrial invasion but no extension to lower third of the vagina. MRI was able to detect and accurately stage the disease in all these patients (Table 27).

Table 27: FIGO IIIA cases compared with MRI staging.

Stage	MR IIB	MR IIIA	MR IVB
Clinical FIGO IIIA (n=3)	**1**	**1**	**1**

On MRI, five cases were staged IIIA, out of which only one was appropriately staged clinically. One was understaged as IIB because vaginal infiltration to lower third was not obvious on clinical examination. Three were overstaged as IIIB because of altered renal function test secondary to medical renal disease but no ureteral involvement was noted (Table 28).

Table 28: MRI stage IIIA cases compared with FIGO staging.

Stage	FIGO IIB	FIGO IIIA	FIGO IIIB
MR IIIA (n=5)	1	1	3

Stage IIIB:

Stage IIIB is defined as extension of the lesion beyond the parametrium with invasion to the lateral pelvic wall.

Criteria used in our study were:

1. Tumor less than 3 mm from the pelvic side walls,

2. Vascular encasement,
3. Presence of hydroureter or
4. Increased signal in the adjacent muscles (obturator internus, pyriformis and levator ani).

Togashi K et al[17] and Hricak H et al[55] had used similar criteria in their study for lateral pelvic wall invasion.

In our study, five patients were stage as IIIB on MR imaging whereas clinically 45 patients were labeled as stage IIIB. Five out of 45 patients were corresponding to MRI staging, 14 patients were understaged and 26 cases were overstaged on MRI. All the 14 patients had no disease extension to lateral pelvic wall but were overstaged clinically due to abnormal results of renal function test secondary to medical causes rather than tumoral involvement of ureter Among the 26 cases, 25 patient showed adjacent pelvic organ infiltrations and one case had bony metastasis which was not assessed clinically, hence they were understaged clinically (

Table **29**).

Table 29: FIGO IIIB cases compared with MR staging

Stage	MR IIA	MR IIB	MR IIIA	MR IIIB	MR IVA	MR IVB
FIGO IIIB (n=45)	1	10	3	5	25	1

A study by Hricak et al[55] on 57 patients documented 5 stage IIIB carcinoma cervix on MRI of which four had extension to lateral pelvic walls on histopathology.

Togashi et al[17] in their study on 67 patients, one patient with stage IIIB disease was understaged as IIB on MR imaging.

We had small number of patients with extension of carcinoma to lateral pelvic wall and no surgical correlation was available either. However according to literature MRI is better in detecting pelvic side walls infiltration and helps in planning for radiotherapy.

Stage IVA:

Disruption of normal hypointense wall of urinary bladder or rectum with or without mass protruding into the lumen was considered as invasion and staged as IVA. The presence of bullous edema alone is insufficient to stage tumor as IVA Togashi et al[17] and Hricak H et al[55] have done their study based on similar MRI findings as well.

A total of 35 cases were staged as IVA on MRI and 5 cases (14.28%) were staged appropriately on clinical staging. Majority of the cases (n=25; 71.4 %) were staged as IIIB followed by IIB (n=4; 11.4%) and IIIA (n=1; 2.85%).

Urinary bladder involvement:

Among the 35 cases of IVA on MRI, 12 cases had isolated bladder involvement, five cases had isolated rectal involvement and rest of the 18 cases had involvement of both urinary bladder and rectum.

Table 30: Cases with isolated urinary bladder involvement.

Bladder involvement	MRI	FIGO
Total number of patients	30	5
Isolated bladder involvement	12	1
Combined bladder and rectal involvement	18	4

Cystoscopy was performed on five patients who showed evidence of bladder mucosal invasion in the form of exuberant growth and mucosal edema. The biopsy from edematous mucosa revealed malignant infiltration. These patients also had symptoms of cystitis and hematuria. On MRI, all these patients showed mucosal involvement (Table 30).

Among the five patients who underwent cystoscopy, four patients showed involvement of rectum which was proven by proctoscopy and one patient had isolated bladder involvement clinically. Very large prolific mass were seen in all cases involving both bladder and rectum. In patients with no clinical symptoms and normal mucosa on cystoscopy, MRI helps in proper detection of bladder involvement.

Rectal involvement:

Table 31: Cases with rectal involvement.

Rectal Involvement	MRI	FIGO
Total number of patients	23	4
Isolated rectal involvement	5	0
Combined bladder and rectal involvement	18	4

Proctoscopy was done in four patients who had symptoms of bleeding per rectum. They also showed invasion of urinary bladder mucosa on cystoscopy.

Rectal mucosal invasion was seen in 23 patients on MRI, among which 18 patients had both urinary bladder and rectal mucosal invasion. Five patients had isolated rectal invasion (Table 31).

There is less data regarding rectal invasion on MRI in patients with carcinoma cervix. Rockall et al[75], found 10 false positives out of 112 patients with 100.0% sensitivity and 91.0% specificity. According to Rajaram et al[76]., MRI correctly assessed disease invasion into both spaces with accuracy of 88.9% in vesicocervical space and 66.7% for rectovaginal space . Rockall et al highlighted 13 false positives out of 112 patients with 100.0% sensitivity and 88.0% specificity for detection of bladder involvement on MRI[75].

Hertel et al, documented sensitivity and specificity of 64.0% and 88.0% respectively for detection of detectable bladder involvement on MRI[65]. A study by Postema et al reported sensitivity of 77.0% and specificity of 97.0% for detection of bladder involvement on MRI[74].

Stage IVB:

Bone spread:

Stage IVB is when there is distant spread of disease beyond pelvis or shows skeletal metastasis. We had two patients who had involvement of pelvic bone on MR imaging and hence were staged as stage IVB. The bone lesions were hyperintense on T2 and STIR sequences and showed evidence of enhancement on post contrast T1 weighted images.

The above two MRI staged IVB patients are clinically staged as IIB and IIIB. Both cases however did not have involvement of urinary bladder and rectum on MRI. The clinical stage IIIB case also had hepatic metastasis which was detected incidentally on MRI but histopathological confirmation was not available.

Lymphadenopathy:

On MRI, lymph nodal metastasis was found in 70 out of the 103 patients. These lymph nodes were iso to hypointense on T1 weighted images and hyperintense on T2 and STIR weighted sequences with enhancement on post contrast images. Lymph nodes >10 mm in short axis were taken as significant in our study. This

criterion was used by Hricak H et al[55] and Togashi K et al[17] in their study. Patients with disease confined only to the cervix showed no lymph nodal involvement on MR imaging.

Table 32: Stage wise lymph nodal distribution.

Stage	MR IIA	MR IIB	MR IIIA	MR IIIB	MR IVA	MR IVB
Number of patients	3	27	5	5	28	2
Percentage (%)	4	38	7	7	40	3

Most of the patients with lymph nodal involvement in our study belong to stage IVA (n=28; 40%) and IIB (n=27; 38%) (Table 32).

In our study we used six different local morphological parameters as the criteria to assess lymph nodal metastasis. These included involvement of –

1. Uterine body,
2. Vagina,
3. Parametrium,
4. Lateral pelvic wall,
5. Rectal mucosa
6. Urinary bladder mucosa

Table 33: Local parameters with lymph nodal metastasis.

Parameter	Percentage (%)
Uterine body	**98**
Vagina	**98**
Parametrium	**95**
Urinary Bladder mucosa	**34**
Rectal mucosa	**30**
Lateral pelvic wall	**7**

According to our study, uterine body and vaginal invasion was associated with lymph nodal metastasis. 69 (98%) out of the 70 patients with lymph nodal involvement had involvement of uterine body and vagina as well. Parametrial involvement was the next local parameter which was associated with lymph node involvement. 67 (95%) out of the 70 patients with lymph nodal metastasis had parametrial involvement (Table 33).

Table 34: Patients with bladder invasion having lymph nodal spread.

Patients with bladder invasion	Patients with bladder invasion having lymph nodal spread	Percentage (%)
30	24	80

Table 35: Patients with rectal invasion having lymph nodal spread.

Patients with rectal invasion	Patients with rectal invasion having lymph nodal spread	Percentage (%)
23	21	91

In our study it was found that most of the cases with involvement of rectum, urinary bladder or bone also had evidence of lymph nodal spread. Hence we concluded that, once the disease has reached stage IV, lymph nodal spread is likely high (Table 34 & Table 35).

A recent article documented an accuracy of 78% on PET-CT compared to 67% by MRI in detecting pelvic lymph nodal metastasis greater than 10 mm. The authors concluded that though MRI provides accurate information about local extension of tumor but PET-CT is more accurate in evaluating pelvic lymph nodal metastasis[66].

LIMITATIONS

1. Sample size in our study was only 103 so a much larger sample size is required to conduct a more extensive study.
2. Surgical staging with histopathological confirmation wasn't available in all the cases as surgery is only performed upto stage IIA. This would be an inherent limitation of the study

Conclusion

CONCLUSION

- MRI is encouraged for staging of carcinoma cervix. There seems to be good correlation between MRI and histopathology. If T2 weighted MRI shows intact cervical stromal ring then there is least probability of extension of the disease to parametrium.
- MRI evaluation also provides valuable information about extension to proximal structures.
- Evaluation of carcinoma cervix by MRI accurately assesses the lymph nodal, myometrial and parametrial involvement.
- MRI has good tissue contrast; MRI is the preferred imaging technique for tumor detection and invasion evaluation in advanced stage disease. MRI is far superior to CT and ultrasound in preoperative staging of the disease.
- A combined imaging and histopathological approach is warranted in the management of carcinoma cervix.
- MRI has been proposed as better alternative for initial screening of cervical cancer instead of cystoscopy and proctoscopy.
- There is no gold standard for assessment of staging in carcinoma cervix, as all the stages of disease are not operated and hence surgical specimen are not available.

Summary

SUMMARY

This was a hospital based prospective study conducted from January 2017 to July 2018 to evaluate the usefulness of MRI in patients with invasive cervical cancer.
A total of 103 biopsy proven cases of carcinoma cervix were assessed in this study.

All patients in our study were parous with 80% of the patients in the age group of 40-69 years. Surgical correlation was available up to stage IIA, but all cases of any stage had histopathological confirmation by biopsy. All the patients with stage > IIB were treated with radiotherapy. In our study MRI had 100% sensitivity in detecting lesions upto stage IIA. In our study it was seen that MR played a significant role in deciding the presence of parametrial invasion. Presence of low signal intensity rim around the cervix on T2 suggests that the lesion in confined only to the cervix. Disruption of this low signal intensity rim is suggestive of parametrial invasion. According to our study T2 weighted was the sequence of choice to detect parametrial invasion.

MRI proved to be more accurate in detecting lateral pelvic wall invasion compared to clinical examination. MRI helped in avoiding over-diagnosing lateral pelvic wall invasion and hence helped in planning the exact field for radiotherapy. Bladder and rectal invasion was obvious clinically only when there was mucosal infiltration. Here again MRI played an important role in detecting bladder and rectal muscular wall invasion and accurately stage the disease. Another important finding seen in our study was corpus uteri infiltration which was not picked up on clinical examination but was well assessed on MR imaging.

Presence of metastatic pelvic or abdominal lymph node is one of the important prognostic factors in patients with carcinoma cervix. MRI was far superior in picking up lymph nodes when compared to clinical examination. Our study documented that lymph nodal metastasis is highly associated with involvement of uterine body, vagina and parametrium. MRI could also detect skeletal metastasis to pelvic bones and hepatic metastasis which provided valuable information in precisely staging the disease.

Evaluation of the disease extension at the time of diagnosis is highly important for optimal selection of treatment option and accurately analyzing the prognosis for patients with carcinoma cervix.

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Annexures

ANNEXURE – I

PROFORMA

Demographic details:

Name:

Age:

Socio-economic status:

Clinical History:

Local Examination:

Histopathological Diagnosis:

MRI Findings:

MRI diagnosis:

Final diagnosis:

ANNEXURE – II

INFORMED CONSENT FORM

Study title: ROLE OF MAGNETIC RESONANCE IMAGING IN EVALUATION OF CARCINOMA CERVIX

Chief researcher/ PG guide's name: Dr. ANIL KUMAR SAKALECHA

Principal investigator: Dr. DARSHAN A V

Name of the subject:

Age :

Gender :

a. I have been informed in my own language that this study involves MRI and use of contrast material as part of procedure. I have been explained thoroughly and understand its complication and possible side effects.
b. I understand that the medical information produced by this study will become part of institutional record and will be kept confidential by the said institute.
c. I understand that my participation is voluntary and may refuse to participate or may withdraw my consent and discontinue participation at any time without prejudice to my present or future care at this institution.
d. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
e. I confirm that Dr. ANIL KUMAR SAKALECHA / Dr. DARSHAN A V (chief researcher/ name of PG guide) has explained to me the purpose of research and the study procedure that I will undergo and the possible risks and discomforts that i may experience, in my own language. I hereby agree to give valid consent to participate as a subject in this research project.

ANNEXURE – II

Participant's signature/thumb impression

Signature of the witness: Date:

1)

2)

I have explained to _____ (subject) the purpose of the research, the possible risk and benefits to the best of my ability.

Chief Researcher/ Guide signature Date:

ANNEXURE – II

ROLE OF MAGNETIC RESONANCE IMAGING IN EVALUATION OF CARCINOMA CERVIX

Patient Information Sheet

Principal Investigator: Dr. Darshan A V/ Dr. Anil Kumar Sakalecha

I, Dr. Darshan A V, post-graduate student in Department of Radio-Diagnosis at Sri Devaraj Urs Medical College. I will be conducting a study titled "Role of magnetic resonance imaging in evaluation of carcinoma cervix" for my dissertation under the guidance of Dr. Anil Kumar Sakalecha, Professor, Department of Radio-Diagnosis. In this study, we will assess the role of MRI for accurate pretreatment staging of carcinoma cervix thereby reducing the morbidity and mortality. You would have undergone MRI pelvis before entering the study. There will be no additional expenses incurred by you for study as it is part of routine scan procedure. You will not be paid any financial compensation for participating in this research project.

All of your personal data will be kept confidential and will be used only for research purpose by this institution. You are free to participate in the study. You can also withdraw from the study at any point of time without giving any reasons whatsoever. Your refusal to participate will not prejudice you to any present or future care at this institution

Name and Signature of the Principal Investigator

Date

Phone no:

ANNEXURE – III

KEY TO MASTER CHART

AC	Adeno carcinoma
CS	Correctly staged
DM	Distant metastasis
DPV	Discharge per vagina
HD	Histopathological diagnosis
HM	Hematometra
HS	Hydrosalphynx
HUN	Hydroureteronephrosis
IMB	Intermenstrual bleed
LNI	Lymph nodal involvement
LUS	Lower uterine segment
N	No
OS	Overstaged
P	Pyometra
PA	Pelvic abscess
PCB	Post coital bleed
PI	Parametrial invasion
PM	Post-menopausal
PMB	Post-menopausal bleed
PSWI	Pelvic side wall invasion

RI	Rectal invasion
SCC	Squamous cell carcinoma
U	Upper two third
UBI	Urinary bladder infiltration
US	Understaged
UTBI	Uterine body infiltration
VI	Vaginal infiltration
Y	Yes

Master Chart – Role of Magnetic Resonance Imaging in Evaluation of Carcinoma Cervix

Sl No.	Trial ID No.	Age (in years)	Parity	PM	DPV	IMB	PCB	PMB	HD	PI	VI	UTBI	PSWI	HUN	UBI	RI	DM	Clinical FIGO staging	MRI FIGO staging	Difference in staging (by MRI)	LNI	Other findings
1	369434	51	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	P
2	370356	55	4	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	Y	IIB	IVB	OS	Y	P
3	370720	45	3	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
4	371218	55	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	Y	N	N	N	IIIB	IIIB	CS	Y	
5	375284	50	9	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	Y	N	IIIB	IVA	OS	Y	
6	376830	65	2	Y	Y	-	-	Y	SCC	Y	U	LUS	Y	Y	Y	Y	N	IIIB	IVA	OS	Y	
7	358898	50	9	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIIA	IIIA	CS	Y	HS
8	360706	40	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	
9	380256	55	3	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
10	380605	70	5	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIIA	US	Y	
11	382527	50	3	Y	N	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIB	US	Y	
12	386528	32	2	N	Y	Y	Y	-	AC	Y	U	LUS	N	Y	N	N	N	IIIB	IIIA	US	Y	
13	410264	44	2	N	Y	Y	Y	-	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	
14	410328	40	3	N	Y	Y	N	-	AC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	HS
15	412553	32	3	N	Y	Y	N	-	AC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
16	419720	67	6	Y	Y	-	-	Y	SCC	N	U	LUS	N	N	N	N	N	IIB	IIA	US	N	
17	422195	50	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	Y	N	IIIB	IVA	OS	Y	
18	422634	40	3	N	Y	N	N	-	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
19	423148	30	1	N	N	N	N	-	AC	N	U	LUS	N	N	N	N	N	IIB	IIA	US	N	
20	423340	60	6	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	Y	N	IIIB	IVA	OS	Y	

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21	424401	65	5	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	Y	IIIB	IVB	OS	Y	Hepatic metastasis
22	390419	50	4	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIB	US	Y	
23	430698	65	3	Y	Y	-	-	Y	SCC	Y	U	LUS	N	Y	Y	N	N	IIIA	IVA	OS	Y	
24	433042	60	3	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	
25	435418	60	4	Y	N	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIB	US	Y	
26	435884	65	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	Y	N	N	IIIB	IVA	OS	Y	
27	436116	45	2	N	Y	Y	Y	-	SCC	Y	U	LUS	N	N	N	N	N	IIIA	IIB	US	N	
28	436203	45	3	N	Y	N	N	-	SCC	Y	U	LUS	N	N	Y	Y	N	IIIB	IVA	OS	Y	
29	438544	45	2	N	Y	N	N	-	AC	Y	U	LUS	N	Y	Y	N	N	IIIB	IVA	OS	Y	
30	435198	60	4	Y	Y	-	-	N	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIB	US	N	
31	428994	50	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
32	437181	50	4	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIB	US	Y	
33	439981	55	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	Y	Y	Y	N	IIIB	IVA	OS	Y	
34	442363	35	3	N	Y	Y	Y	-	SCC	Y	U	LUS	N	Y	N	N	N	IIIB	IIIB	CS	Y	
35	443299	48	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
36	443723	47	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
37	445740	55	1	Y	Y	-	-	Y	SCC	Y	U	LUS	N	Y	N	N	N	IIIB	IIIB	CS	Y	
38	446332	65	3	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIB	US	Y	
39	447036	50	3	Y	N	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIIA	US	Y	
40	424939	35	2	N	Y	Y	N	-	SCC	Y	N	N	N	N	N	N	N	IIB	IIB	CS	Y	
41	439981	55	4	Y	Y	-	-	Y	SCC	Y	U	LUS	N	Y	Y	Y	N	IIIB	IVA	OS	Y	

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42	447228	55	2	Y	Y	-	-	Y	SCC	Y	U	LUS	Y	Y	Y	N	N	IIIB	IVA	OS	Y	
43	456472	68	4	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
44	462541	42	4	N	Y	Y	Y	-	SCC	Y	U	LUS	N	N	N	Y	N	IIIB	IVA	OS	Y	
45	463402	52	3	N	Y	Y	N	-	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIB	US	Y	
46	474249	42	2	N	Y	Y	N	-	SCC	N	U	LUS	N	N	N	N	N	IIB	IIA	US	Y	No DWI restriction
47	475273	45	8	N	Y	Y	Y	-	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	
48	480304	65	3	Y	Y	-	-	Y	SCC	Y	U	LUS	Y	Y	Y	Y	N	IIIB	IVA	OS	Y	
49	479728	65	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	
50	481485	50	3	N	Y	Y	N	-	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIB	US	Y	HS
51	483845	66	7	Y	Y	-	-	Y	SCC	Y	U	LUS	Y	Y	Y	Y	N	IIIB	IVA	OS	Y	P
52	484935	30	2	N	N	Y	Y	-	SCC	N	U	LUS	N	N	N	N	N	IB	IIA	OS	N	
53	492189	43	3	N	N	Y	Y	-	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	P
54	488831	55	5	Y	N	-	-	Y	SCC	Y	U	LUS	N	Y	Y	N	N	IIB	IVA	OS	N	PA
55	493423	49	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	Y	N	N	N	IIIB	IIIB	CS	Y	P
56	493721	60	5	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	HM
57	495253	50	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
58	501045	45	3	N	Y	Y	N	-	SCC	N	U	LUS	N	N	N	N	N	IIB	IIA	US	N	
59	501609	60	2	Y	Y	-	-	N	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
60	504242	75	4	Y	Y	-	-	Y	SCC	Y	U	LUS	N	Y	Y	N	N	IIIB	IVA	OS	N	
61	508851	64	2	Y	Y	-	-	N	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
62	513651	36	2	N	Y	Y	N	-	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIB	US	N	

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63	461060	45	2	N	N	Y	N	-	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	HS
64	516355	40	2	N	N	Y	N	-	SCC	Y	U	LUS	N	Y	Y	N	N	IIB	IVA	OS	N	
65	516902	52	2	Y	N	-	-	Y	SCC	Y	U	LUS	N	N	N	Y	N	IIB	IVA	OS	N	
66	519043	45	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	Y	N	N	IIIB	IVA	OS	N	HS
67	524454	30	2	N	Y	Y	N	-	SCC	N	N	N	N	N	N	N	N	IIB	IB	US	N	
68	526667	40	2	N	Y	Y	N	-	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	N	Y	
69	526752	65	3	Y	Y	-	-	-	SCC	Y	U	LUS	N	Y	Y	N	N	IIIB	IVA	OS	N	P
70	318491	38	2	N	Y	Y	N	-	SCC	Y	U	LUS	N	N	Y	N	N	IIIB	IVA	OS	Y	
71	533297	45	4	Y	Y	-	-	Y	SCC	Y	U	LUS	N	Y	N	N	N	IIB	IIIA	OS	Y	P
72	538046	51	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	
73	541261	38	2	N	Y	Y	N	-	SCC	Y	U	LUS	N	N	Y	Y	N	IVA	IVA	CS	Y	
74	544289	65	5	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	Y	Y	N	IVA	IVA	CS	Y	P
75	555594	50	4	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
76	560560	30	1	N	Y	Y	N	-	SCC	Y	U	LUS	N	N	Y	Y	N	IIIB	IVA	OS	Y	
77	560608	78	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	Y	Y	N	IVA	IVA	CS	Y	P
78	561416	45	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	Y	Y	Y	N	IVA	IVA	CS	Y	HS
79	369434	51	5	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
80	562092	48	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	Y	Y	N	IIIB	IVA	OS	Y	
81	562211	40	2	N	Y	Y	N	-	SCC	N	U	LUS	N	N	N	N	N	IIA	IIA	CS	N	
82	562317	66	7	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	Y	Y	N	IIIB	IVA	OS	N	P
83	566339	47	7	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	

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84	566511	60	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	Y	Y	N	IIIB	IVA	OS	Y	
85	566820	40	2	N	Y	Y	N	-	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	
86	580449	45	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIB	US	Y	
87	584508	40	9	N	Y	Y	N	-	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	
88	587201	35	2	N	Y	Y	N	-	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	
89	591499	75	4	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	N	HM
90	592899	70	8	Y	Y	-	-	Y	SCC	Y	U	LUS	Y	Y	Y	Y	N	IIB	IVA	OS	Y	
91	594165	65	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	
92	595556	70	5	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	P
93	595616	55	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	Y	N	N	IIIB	IVA	OS	Y	
94	597991	56	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	
95	541272	64	4	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	Y	N	N	IVA	IVA	CS	Y	
96	594578	74	5	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	HM
97	608877	45	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIB	IIB	CS	Y	
98	611518	53	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	Y	Y	Y	N	IIIB	IVA	OS	Y	HS
99	632255	70	4	Y	Y	-	-	Y	SCC	Y	U	LUS	N	Y	Y	Y	N	IIIB	IVA	OS	Y	
100	633514	55	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	Y	Y	Y	N	IIIB	IVA	OS	Y	
101	634944	65	2	Y	Y	-	-	Y	SCC	Y	U	LUS	N	N	N	N	N	IIIB	IIIB	CS	Y	
102	634967	60	2	Y	Y	-	-	Y	SCC	N	U	LUS	N	N	N	N	N	IIIB	IIA	US	Y	
103	638088	60	6	Y	Y	-	-	N	SCC	N	U	LUS	N	N	N	N	N	IIA	IIA	CS	Y	

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