UNIVERSITY OF RWANDA
COLLEGE OF MEDICINE AND HEALTH SCIENCES
SCHOOL OF MEDICINE AND PHARMACY
RADIOLOGY DEPARTMENT

CLINICAL STAGING VERSUS PELVIC MRI STAGING BEFORE AND AFTER CHEMORADIATION AMONG PATIENTS WITH CERVICAL CANCER IN RWANDA: PATIENTS SEEN AT RMH AND KFH

A Dissertation submitted in partial fulfillment of the requirements for the degree of MASTER OF MEDICINE IN DIAGNOSTIC RADIOLOGY in the college of Medicine and Health Sciences

BY

DIEUDONNE DUHORANENAYO, MD

Registration Number: 219013948

COLLEGE OF MEDICINE AND HEALTH SCIENCES SCHOOL OF MEDICINE AND PHARMACY

Master of Medicine in Diagnostic Radiology

Supervisors: Prof. RUDAKEMWA Emmanuel, MD, FCRAD (SA), Chief consultant Radiologist

Lt. Col Dr RUBONEKA Jean Paul, MD, Consultant radiologist

Dr. NYIRANEZA Sabine Esperance, MD, Consultant radiologist

September 2022

Declaration

I, Dr DUHORANENAYO Dieudonne, to the best of my knowledge hereby declare and certify that the work presented in this dissertation entitled" ***Clinical staging versus pelvic MRI staging before and after chemoradiation among patients with cervical cancer in Rwanda: Patient seen at RMH and KFH***" is entirely my own and original work except where specifically acknowledged and it has never been presented or submitted in whole or in part to the university of Rwanda or any other institution.

Dieudonne DUHORANENAYO, MD

Registration Number: 219013948

Signature: 

I here declare that this dissertation has been submitted with my approval as the supervisor Prof Emmanuel RUDAKEMWA

Signature: 

DEDICATION

To my beloved Wife NIKUZE Pacifique

To my Son IGANZE DUHORANE Arlo

To all members of my Family

This work is dedicated with great pleasure

ACKNOWLEDGMENTS

To God the Almighty, source of life, knowledge, and wisdom.
To University Teaching Hospitals in Rwanda in collaboration with the Ministry of health through Human Resources for Health (HRH) program for their input in our clinical education and research efforts.
To the College of Medicine and health sciences, University of Rwanda for endless efforts to improve healthcare in Rwanda.
To the Rwandan ministry of health for both moral and financial support throughout the radiology residency program.
I am particularly grateful to my supervisors, Prof. RUDAKEMWA Emmanuel, Lt. Col Dr RUBONEKA Jean Paul and Dr NYIRANEZA Sabine Esperance for their great dedication, invaluable support without which this work would not have been achieved.
To Dr RUGENGAMANZI Eulade for his assistance in data entry and analysis.
To all Radiologists and my teachers, they were not only my teachers, but they became my real family. Thank you for their insightful remarks, guidance during my residency program and during my research.
To my colleagues, radiology residents and medical imaging technicians for your support during my 4 years training, you were all my teachers, we worked side by side every day and I have lent much from you all.
To the whole team of Rwanda cancer center at Rwanda military hospital for your support and facilitation during my data collection.
To every member of my family for your timely support and to my friends and colleagues to stand where my family was absent.
To all care providers struggling to improve quality of life for fellow Rwandans
May all receive the expression of my sincere gratitude!

DUHORANENAYO Dieudonne

ABSTRACT

Background: Cervical cancer is among major public health concerns. Appropriate management of cervical cancer come from accurate staging. The objective of this retrospective study was to compare the performance of clinical and pelvis MRI staging before and after chemoradiation among cervical cancer patients seen at Rwanda Military Hospital (RMH)/Rwanda Cancer Centre (RCC) and at King Faisal Hospital (KFH).

Methods: From January 2020 to June 2022, 88 patients with biopsy-proven locally advanced cervical cancer who met the inclusion requirements were recruited. The patients' MRI results before and after chemoradiation were reviewed and compared with their clinical staging findings for analysis.

Results: Pre-treatment clinical and MRI staging showed a substantial agreement of 78.1% (K=0.63, P value=0.001). Invasion of the upper 2/3 vagina, parametrium and pelvic side wall all showed a fair-to-substantial agreement between clinical and pre-treatment MRI examinations by percent agreement of 70.4%,81.8% and 71.5% respectively. In pre-treatment assessment 72% patients were staged equally clinically and by MRI. 14.7% were under-staged and 12.5% were over staged by pelvis MRI compared to clinical staging. Post-treatment clinical and MRI staging showed a substantial agreement of 71.0% (K=0.71).

Conclusion: There is substantial agreement between clinical and pelvic MRI staging before and after chemoradiation in patients with cervical cancer. On further evaluation it is seen that there is concordance of seventy-two percent between clinical and pelvis MRI staging.

Keywords: Clinical staging, MRI staging, Cervical cancer, chemoradiation

Abbreviation

ADC: Apparent diffusion Coefficient

AJCC: American Joint Committee on Cancer

CIN: Cervical Intraepithelial Neoplasia

OCP: Oral Contraceptive Pills

CT: Computed Tomography

DCE: Dynamic contrast Enhancement

DNA: Deoxyribonucleic acid

DWI: Diffusion Weighted Image

EGOG: Eastern Cooperative Oncology Group

FIGO: International Federation of Gynecology and Obstetrics

HDI: Human Development Index

HIV: Human Immunodeficiency Virus

HPV: Human Papillomavirus

IRB: Institutional Review Board

KFH: King Faisal Hospital

MRI: Magnetic Resonance Imaging

NCCN: National Cancer Comprehensive Network

PACS: Picture Archiving and Communication system

PET: Positron Emission Tomography

RCC: Rwanda Cancer Centre

RMH: Rwanda Military Hospital

ROI: Region of Interest

SI: Signal Intensity

SPSS: Statistical Package for the Social Sciences

STD: Sexual Transmitted Diseases

T1W: T1 weighted

T2W: T2 weighted

Tis: Tumor in situ

TNM: Tumor Nodes and Metastases

TSI: Time-Signal Intensity

VMAT: Volumetric Modulated Arc Therapy

Definition of key terms

Cervical cancer: All malignant processes originating from the cervix (the lower constricted segment of the uterus providing the passage between the uterus proper and vagina)

Clinical staging: The clinical stage is used for cervical cancer and is based on the findings of the physical examination by the doctor, biopsies, imaging tests, and a few more procedures that are occasionally performed, such as cystoscopy and proctoscopy. It is not predicated on the results of the operation.

MRI staging: It is a useful technique for determining whether the tumor has migrated to nearby and far-off lymph nodes by using Magnetic Resonance Imaging machine

Chemoradiation: a course of therapy that includes radiation and chemotherapy in treatment of cancer. known as chemoradiotherapy as well.

Table of Contents

List of tables

List of figures

CHAPTER I. INTRODUCTION

I.1. Background and significance of the study

Cervical cancer is currently, the second largest cause of cancer-related death and the fourth most prevalent cancer in women. Around 311 000 women globally lost their lives due to cervical cancer in 2018 and about 570000 were diagnosed with the disease in the same year(1). Cervical cancer affects 22.5 percent of women in Sub-Saharan Africa who are diagnosed with cancer and the majority of these women reside in rural regions(2). With an incidence of more than 30 cases per 100,000 women annually, Eastern Africa is one of the regions most severely affected (3). The most alarming uniform increases have recently been reported in 7 of 8 sub-Saharan African countries, including the Gambia, Kenya, Malawi, the Seychelles, South Africa, Uganda, and Zimbabwe(4). With a population of 11 million, 2.72 million Rwandan women over the age of 15 are at risk of having cervical cancer(5). According to some estimates, every year close to 1000 women are diagnosed with cervical cancer, and the disease kills close to 700 of them(6). In Rwanda, cervical cancer is the most common disease among women and the most common cancer among women between the ages of 15 and 44(7). Rwanda has a substantially higher estimated incidence of cervical cancer than Eastern Africa and the rest of the globe, with 49 cases per 100,000 women year compared to 34.5 and 16 new cases per 100,000 women, respectively(8).

MRI plays important roles in cervical cancer assessment, from detection to recurrent disease evaluation(9). Cervical malignancies were previously staged clinically using the International Federation of Gynecology and Obstetrics (FIGO) classification based on the results of gynecological examinations and, if necessary, cystoscopy, proctoscopy, colposcopy, and biopsy (10). Since the FIGO staging revision 2019(11), pathological evaluations and imaging results are combined to determine stage. The overall stage and tumor size directly affect the prognosis and help to choose the best course of treatment, which may include primary (radical) surgery, chemoradiation, or palliative chemotherapy(12). It is generally well known that magnetic resonance imaging (MRI) is effective for determining cervical cancer extent such as parametrial involvement, which is crucial for initial treatment, for determining tumor volume and lymph node involvement. One study showed that the rates of recurrence, persistent disease in the pelvis, or distant metastases are significantly higher in women with stage IIIB cervical malignancies than they are in those with stage IIB cancer(13). That is why to maximize cancer evaluation and staging before any intervention is important in management.

I.2 Problem statement

In Rwanda, cervical cancer is a major public health concern. Its late detection may be related to delayed consultations, which therefore lead to poor treatment outcomes in some cases. The pelvic MRI is the best imaging modality for accurate assessment of most gynecological cancers at early stage. In regard of determining the extent of the local tumor and the spread of metastatic disease, the National Cancer Comprehensive Network (NCCN) guidelines for cervical cancer recommend MRI, chest radiography, chest/abdominal/pelvic computed tomography (CT), or whole-body positron emission tomography-CT (PET-CT) as part of the primary diagnostic work-up. The putative FIGO stage, perceived risk of metastatic disease, and local access to the various imaging modalities often influence which imaging modality each individual patient receives(12). The pelvic MRI is not usually performed before and after chemotherapy in Rwanda's cancer center in the past due to its low availability and high demanding number; instead, management decisions are frequently relied on the results of the clinical and CT-scan imaging modalities.

Only 5 MRI machines are present in Rwanda, 4 of which are in the capital city of Kigali and 1 in the western province. Despite the opening of a new cancer treatment facility in Rwanda, there is scanty of data comparing clinical and pelvic MRI staging findings among patients with cervical cancer before and after the chemoradiation.

I.3. Justification of the study

It is well known that MR is effective for determining the degree of parametrial involvement in cervical cancer, which is crucial for the initial course of treatment. In addition, it is widely known that MRI has a high degree of accuracy for determining tumor volume and lymph node involvement, therefore accurate staging may lead to proper management of cervical cancer. As sometimes in our settings, management decisions are relied on the results of the clinical and CT-scan imaging modalities due to various unclear reasons, the aim of this study is to compare the performance of clinical and pelvic MRI before and after chemoradiation. From evidences we came out with some recommendations that will help improving disease surveillance and can late improve the survival of our population with cervical cancer.

I.4. Research question

In patients with cervical cancer in Rwanda is there any agreement between the clinical and pelvic MRI staging before and after chemoradiation?

I.5. Objectives of the study

I.5.1. General Objective

To compare the performance of clinical and pelvis MRI staging before and after chemoradiation among

patients with cervical cancer seen at RMH and KFH over a period of 30 months, from January 2020 to June 2022.

I.5.2. Specific objectives

1. To determine the age, performance status and symptoms of study participants seen at RMH and KFH.
2. To assess the clinical and pelvis MRI staging before and after chemoradiation among study population seen at RMH and KFH.
3. To evaluate the degree of agreement between the clinical and pelvis MRI staging before and after chemoradiation among study population seen at RMH and KFH.

CHAPTER II. LITERATURE REVIEW

II.1. Overview of cervical cancer

II.1. 1. Definition and introduction

All malignant processes originating from the cervix (the lower constricted segment of the uterus providing the passage between the uterus proper and vagina) are referred to as cervical cancer. It is, after ovarian and endometrial cancer, the third most prevalent gynecological malignancy in the globe. In lower-income countries is one of the leading causes of cancer-related deaths in women. Squamous cell carcinoma, often known as cervical cancer, is by far the most common type (80–90%), followed by adenocarcinoma, both of which have the similar radiographic appearance. Other varieties of malignant neoplasm are much less frequent. Cervical cancer has been determined to be caused by a high-risk human papillomavirus (HPV) infection that has persisted over time(14).

II.1.2. Epidemiology

Cervical cancer is one of the major causes of cancer-related deaths among women. The percentage of young women with cervical cancer has increased over the previous 30 years, ranging from 10% to 40%(15). 529,000 new cases of cervical cancer were reported worldwide in 2008, according to estimates from the WHO and International Agency for Research on Cancer (IARC). Cervical cancer had 452,000 new cases in developing countries, placing it second among female patients' malignancies. The number of new cases of cervical cancer, on the other hand, was 77,000 in developed countries, placing it tenth among female malignancies.

Cervical cancer is the fourth most frequently diagnosed malignancy in women globally in 2018, with an expected 570,000 cases and 311,000 fatalities. However, low-income and middle-income countries have an 18 times higher death rate from cervical cancer than developed countries, with over 85% of all cervical cancer deaths occurring in developing or underdeveloped nations(16). In Sub-Saharan Africa, cervical cancer accounts for 22.5% of all instances of cancer in women, and the majority of these women reside in rural areas(17). With an incidence of more than 30 cases per 100,000 women per year, Eastern Africa is one of the regions that is most severely afflicted(3). According to some estimates, every year in Rwanda, close to 1000 women are diagnosed with cervical cancer, and the disease claims the lives of up to 700 more(6). Dr Singh et all showed that with an estimated incidence of 49 cases per 100,000 women per year, cervical cancer is the most common cancer among Rwandan women and the most common cancer in women between the ages of 15 and 44(7). In areas with a lower Human Development Index (HDI), cervical cancer trails breast cancer in terms of incidence and mortality. Numerous epidemiological studies have shown how different genetic

variables affect the likelihood of developing cervical cancer(18).

One of these is the patient contracting an HPV (human papilloma virus) oncogene type, which is the main etiological cause in the development of this malignancy. Indeed, HPV is the most widespread sexual transmitted diseases (STD) in the world and is closely linked to cervical cancer. Over the past years, HPV testing (as a screening method) and vaccination were introduced for the prevention of cervical cancer.

II.1.3. Risk factors

HPV exposure is connected to a number of cervical cancer risk factors. From the precursor lesion brought on by sexually transmitted HPV, the process of invasive cancer development could take up to 20 years. There are, however, a variety of additional risk factors (such as reproductive and sexual factors, behavioral factors....) for cervical cancers, which include having sexual relations before the age of 16, multiple partners, smoking, having a high parity, and living in a low-socioeconomic status(19,20).

II.1.3.1. Sexually transmitted diseases (STD)

II.1.3.1.1. Human Papilloma Virus (HPV)

Pre-cancerous and malignant cervical lesions are primarily caused by infection with high-risk or oncogenic HPV strains. The majority of cervical cancer cases occur due to HPV16 and 18 infections. It has been discovered that high-risk types, particularly HPV16, are very common in human populations. The infection, which results in squamous intraepithelial lesions, is typically spread through sexual contact. Due to immunological intervention, the majority of lesions disappear after 6–12 months. A small portion of these lesions, meanwhile, persist and can develop into cancer(21).

II.1.3.1.2. Human immunodeficiency virus (HIV)

Women with HIV are more likely to get high-risk HPV strains of infection. According to studies on the link between HIV and cervical cancer, those who have HIV are more likely to have persistent HPV infections with several oncogene viruses, abnormal Papanicolaou (Pap) test results, CIN, and invasive cervix carcinoma(22). HIV-positive women have a higher chance of developing cervical cancer and HPV infection at a young age (13–18 years). HIV-positive patients with cervical cancer are diagnosed earlier (15–49 years of age) than non-infected women.

II.1.3.2. Reproductive and sexual factors

II.1.3.2.1. Sexual partners

Cervical cancer has also been linked to factors related to sexual behavior. According to one study, those who have several sexual partners are at an elevated risk of developing cervical cancer. Additionally, a number of studies have found that women who have had several partners may be more likely to develop HPV and cervical cancer(23). According to the meta-analysis, those who have more sexual partners than people who have fewer partners have a much higher chance of developing cervical disorders, including both cervical cancer and non-malignant cervical disease. Even after accounting for the presence of HPV infection, a major contributor to cervical cancer, the link persisted. A further risk factor for cervical cancer is a young age at first sexual contact (14).

II.1.3.2.2. Oral contraceptive pills (OCP)

It is well known that OC tablets increase the risk of cervical cancer. A greater period of OC usage was associated with a higher relative risk for current users in an international collaborative epidemiological investigation of cervical cancer. According to several reports, using OC for at least five years and more double the risk of developing cervical cancer(24).

In a multi-center case-control study, women who tested positive for HPV DNA had a threefold greater chance of developing cervical cancer if they had taken OC tablets for five years or more. Additionally, a recent systematic review and meta-analysis revealed that using OC tablets carried a real risk of getting cervical cancer, particularly adenocarcinoma(25). This study came to the conclusion that the usage of OC tablets is an independent risk factor for developing cervical cancer.

II.1.4. Pathology.

It is believed that cervical intraepithelial neoplasia transforms into invasive cervical cancer. The principal histological types include: Squamous cell carcinoma makes up between 80 and 90 percent of instances and is linked to having been exposed to the human papilloma virus (HPV). Clear carcinoma, endometrial carcinoma, mucinous carcinoma (adenoma malignum), serous carcinoma, and mesonephric carcinoma are a few of the subtypes of adenocarcinoma, which is uncommon (5–20 percent) compared to squamous cell carcinoma type. WHO histological classification details tumors of the uterine cervix into: epithelial tumors (including squamous tumors, glandular tumors (adenocarcinoma) and precursors), mesenchymal tumors and tumor like conditions (including leiomyosarcoma, cervical angiosarcoma, …), mixed epithelial and mesenchymal tumors (including carcinosarcoma, adenocarcinoma, cervical adenofibroma,…),melanocytic

tumors (including primary cervical malignant melanoma and blue nevus of cervix) , miscellaneous tumors (including tumors of germ cell type),lymphoid and hematopoietic (including malignant lymphoma and cervical leukemia) and secondary tumors.

Cervical squamous cell carcinoma arises from the squamocolumnar junction while adenocarcinomas arise from the endocervix. In younger individuals, the squamocolumnar junction is located on the ectocervix, but as patients age, it recedes into the endocervical canal. Consequently, cervical cancers are more likely to be exophytic in younger people and endophytic in older patients.

II.1.5. Prognostic factors of cervical cancer

Planning the right course of cervical cancer treatment depends on accurately identifying the factors affecting the prognosis. Some of these factors can be clearly seen on MR imaging, while others depend on the histologic appearance. The prevalence of dissemination to lymph nodes is closely correlated with lesion volume. It is difficult to measure clinically, and even within a FIGO stage, it varies greatly. Nodal disease has a significant impact on survival despite not being part of the FIGO staging system, and the presence of metastatic lymph nodes suggests a worse prognosis within each stage. From 5% of positive pelvic nodes in stage IA2 to 55% in stage IV, show that there is an increasing incidence of unexpected metastatic lymph nodes with each stage(26). Therefore, early nodal involvement detection is essential for treatment planning. At histologic analysis, lymphatic vascular space invasion, tumor grade, and depth of invasion are all significant prognostic factors.

II.1.6. Cervical cancer staging

II.1.6.1. Purpose of staging

Cancer staging refers to determining the severity of the condition, including the size of the tumor and whether it has spread. Understanding the cancer's stage will help better grasp how bad the condition is, prospects of surviving, and how to guide treatment plans. The TNM staging system, which accurately measures local tumor depth invasion (T), regional lymph node invasion (N), and distant metastases (M), or the FIGO: International Federation of Gynecology and Obstetrics staging system, can be used to determine the stage of cervical cancer.

II.1.6.2. FIGO Staging tools

The International Federation of Gynecology and Obstetrics (Fédération Internationale de Gynécologie et d'Obstétrique) develops the FIGO staging systems. In order to "advance the welfare of women and to

increase the standard of practice in obstetrics and gynecology," FIGO staging system was established on July 26, 1954, in Geneva, Switzerland.

(FIGO) staging classification of cervical cancer was updated significantly in 2018. The exact measurement of original tumor size, abdominopelvic retroperitoneal lymphadenopathy, either with imaging alone or with pathologic examination, and improved representation of parametrial involvement are the changes made from the 2009 FIGO classification to the most recent update. The modifications were made to reflect widespread clinical practice, distinguish predictive outcomes, and direct treatment stratification(27). Depending on the stage of the disease, treatment options may include fertility-preserving and non-fertility-preserving surgical procedures, as well as chemoradiotherapy for locally advanced disease. The modality chosen depends on the technology available in the practice environment.

To determine stage and plan treatment strategy in high-resource environments, lymphadenopathy and distant metastases are evaluated using PET/CT and pelvic MRI is used to assess tumor size and central pelvic spread. Chest radiography and pelvic ultrasound are comparable modalities in settings with limited resources.

II.1.6.2.1. Revised FIGO staging of cervical carcinoma 2018

Table 1: FIGO Staging of Cervical Cancer (2018)

Adopted from “Validation of the 2018 FIGO Staging System of Cervical Cancer for Stage III Patients with a Cohort from China” (28)

Stage	Description
I	The carcinoma is strictly confined to the cervix (extension to the uterine corpus should be disregarded)
IA	Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion <5mm[a]
IA1	Measured stromal invasion <3mm in depth
IA2	Measured stromal invasion ≥3mm and <5mm in depth
IB	Invasive carcinoma with measured deepest invasion ≥5 mm (greater than Stage IA), lesion limited to the cervix uteri[b]
IB1	Invasive carcinoma ≥ 5mm depth of stromal invasion, and < 2cm in greatest dimension
IB2	Invasive carcinoma ≥ 2cm and < 4cm in greatest dimension
IB3	Invasive carcinoma ≥ 4cm in greatest dimension
II	The carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall
IIA	Involvement limited to the upper two-thirds of the vagina without parametrial involvement
IIA1	Invasive carcinoma < 4cm in greatest dimension
IIA2	Invasive carcinoma ≥ 4cm in greatest dimension
IIB	With parametrial involvement but not to the pelvic wall
III	The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or nonfunctioning kidney and/or involves pelvic and/or para-aortic lymph nodes[c]
IIIA	The carcinoma involves the lower third of the vagina, with no extension to the pelvic wall
IIIB	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney (unless known to be due to another cause)
IIIC	Involvement of pelvic and/or para-aortic lymph nodes, irrespective of tumor size and extent (with r and p notations)[c]
IIIC1	Pelvic lymph node metastasis only
IIIC2	Para-aortic lymph node metastasis
IV	The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. (A bullous edema, as such, does not permit a case to be allotted to Stage IV)
IVA	Spread to adjacent pelvic organs
IVB	Spread to distant organs

Notes: Reproduced from Bhatla N, Aoki D, Sharma DN, Sankaranarayanan R. Cancer of the cervix uteri. *Int J Gynaecol Obstet.* 2018;143(Suppl 2):22–36. Creative Commons license and disclaimer available from: http://creativecommons.org/licenses/by/4.0/legalcode.[7] When in doubt, the lower staging should be assigned. [a]Imaging and pathology can be used, where available, to supplement clinical findings with respect to tumor size and extent, in all stages. [b]The involvement of vascular/lymphatic spaces dose not change the staging. The lateral extent of the lesion is no longer considered. [c]Adding notations of r (imaging) and p (pathology) to indicate the findings that are used to allocate the case to stage IIIC. Example: If imaging indicates pelvic lymph node metastasis, the stage allocation would be Stage IIIC1r, and if confirmed by pathologic findings, it would be Stage IIIC1p. The type of imaging modality of pathology technique used should always be documented.

II.1.6.3. Radiological (MRI) TNM staging

When there is no indication of local extension in cervical cancer imaging, MRI evaluation replaces the need for invasive procedures like cystoscopy and proctoscopy(29). With the use of MR imaging, which has been demonstrated to affect treatment planning in half of patients, it is possible to determine the optimal treatment options for each patient more precisely (such as surgery or radiation therapy). The form and direction of lesion growth are evaluated using MR imaging to optimize brachytherapy and external beam therapy. Additionally, vital prognostic indicators like lesion volume and involvement of metastatic lymph nodes that influence whether a patient will receive curative or palliative care can be evaluated using MR imaging.

II.1.6.3.1. Pelvis MRI scanning Technique

Patients are advised to fast for at least 6 hours prior to the MRI to reduce bowel peristalsis, and/or they may

take antiperistaltic medications (such as 20 mg of hyoscine butyl bromide or 1 mg of glucagon by intramuscular or intravenous injection) right before the exam in dedicated centers(30). In situations of exophytic cervical cancers, endovaginal sterilized ultrasound gel may be administered for a more accurate assessment of the vaginal wall. To prevent the pelvic structure from being distorted, the urinary bladder should be mildly distended. For the staging of cervical cancer, a dedicated external phased array coil should be chosen. While endovaginal coils are more sensitive than external array coils for detecting tiny tumors, their utility is constrained in the presence of big masses due to their restricted field of view and technical difficulties. High field magnets (3T) may improve pelvic image resolution, but they do not significantly increase the overall staging accuracy for patients with cervical cancer. To prevent misleading positive results from local inflammation, an MRI should be done at least ten days after the biopsy.

II.1.6.3.2. Intravenous contrast materials

Breath-hold using spoiled gradient-echo and axial fat suppression before and after intravenous gadolinium injection as well as T1-weighted pictures are taken. T1-weighted imaging is only used to check the pelvic region. Dynamic gadolinium-enhanced imaging can be used to assess tiny, enhancing cervical lesions, find or confirm invasion of surrounding organs, and spot fistulous tracts(29).

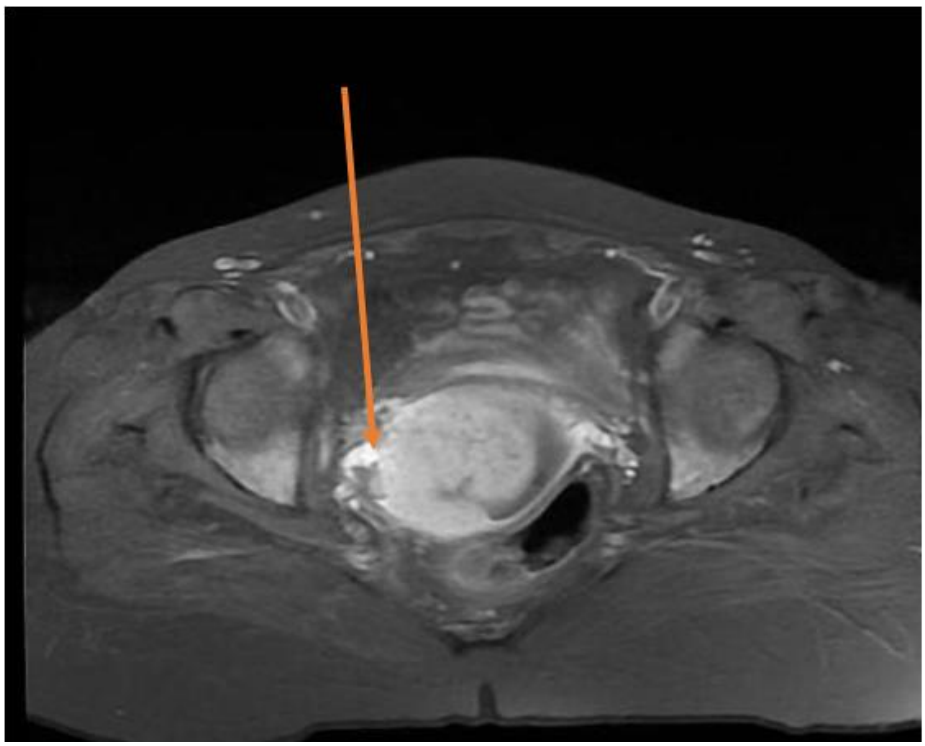


Figure 1: Cervical cancer invading the parametrium on the right side. Axial pelvis MRI T1 C+ fat sat

Above image (Figure 1) is adopted from “Radiopaedia.org ,2021”, showing a locally advanced bulky cervical mass heterogeneously enhancing that extends downward into the vagina upper third (right posterolateral aspect) and involving the parametrium on the right side (arrow on figure 1)(31).

II.1.6.3.3. Scanning Protocol

T2-W sequences are used in all imaging planes (axial, oblique sagittal, and oblique coronal) in conventional MRI study protocols for cervical cancer. T2-W mages give the best contrast between the tumor and normal cervical tissue and also allow for the detection of enlarged lymph nodes. To further assess the parametrial tissues, high-resolution pictures of the lesser pelvis are taken in an axial oblique plane, perpendicular to the long axis of the cervix. For the assessment of parametrial tissues in young individuals with prominent peri-uterine vascular plexus, as well as for the detection of fluid collections or bone marrow abnormalities, T2-W images with fat suppression may be beneficial. Bone marrow, lymph nodes, and pelvic anatomy are all revealed by T1-W pictures.

DCE-MRI is not typically used in MRI staging protocols for cervical cancer; instead, it is only useful for detecting tiny tumors, ambiguous T2-W findings, or post-treatment evaluation. Some imaging centers have added DCE-MRI to specially designed MRI protocols for staging cervical cancer and have backed its ability to distinguish between cervical and endometrial carcinomas, identify endocervical extent, and more precisely define tumor borders. DCE-MRI is a non-invasive method that may evaluate the oxygenation and perfusion of the tissue within the tumor microenvironment. Hypoxia, which is thought to be a significant influence in how tumor cells react to radiation, especially radio-resistance, can be caused by abnormalities in the tumor microvasculature and alterations in perfusion. A powerful prognostic technique for determining which patients would benefit from extra or more aggressive therapies is the capacity to assess the degree of hypoxia. DCE-MRI is widely available thanks to the use of common gadolinium-based contrast agents, the majority of commercial MRI scanners, and analysis software. Additionally, the extra sequences add only 10 minutes to the scan time, which is well tolerated by the patients. DCE measures tissue enhancement over time to examine the distribution of contrast in an indirect manner. A dynamic time-signal intensity (TSI) curve is produced using a fixed region of interest (ROI) within the organ being scanned, and the SI values are recorded prior to, during, and following the administration of contrast.

DWI has recently been incorporated into MRI staging methods for cervical cancer. The ADC values of cervical invasive carcinoma are much lower than those of the normal cervix, making it easier to identify and quantify the size of the tumor. It can also be used to distinguish between residual cancer and post-biopsy alterations; however, hemorrhage can also show restricted diffusion, which could lead to false-positive results. DWI is excellent in identifying small, even a few mm, lymph nodes; however, so far it has not been

able to discriminate between normal and malignant nodes. DWI may be especially helpful in the evaluation of pregnant patients, in whom intravenous contrast is contraindicated. Combination of DWI and T2-W images is more accurate than T2-W images alone in identifying parametrial extension or recurrent disease.

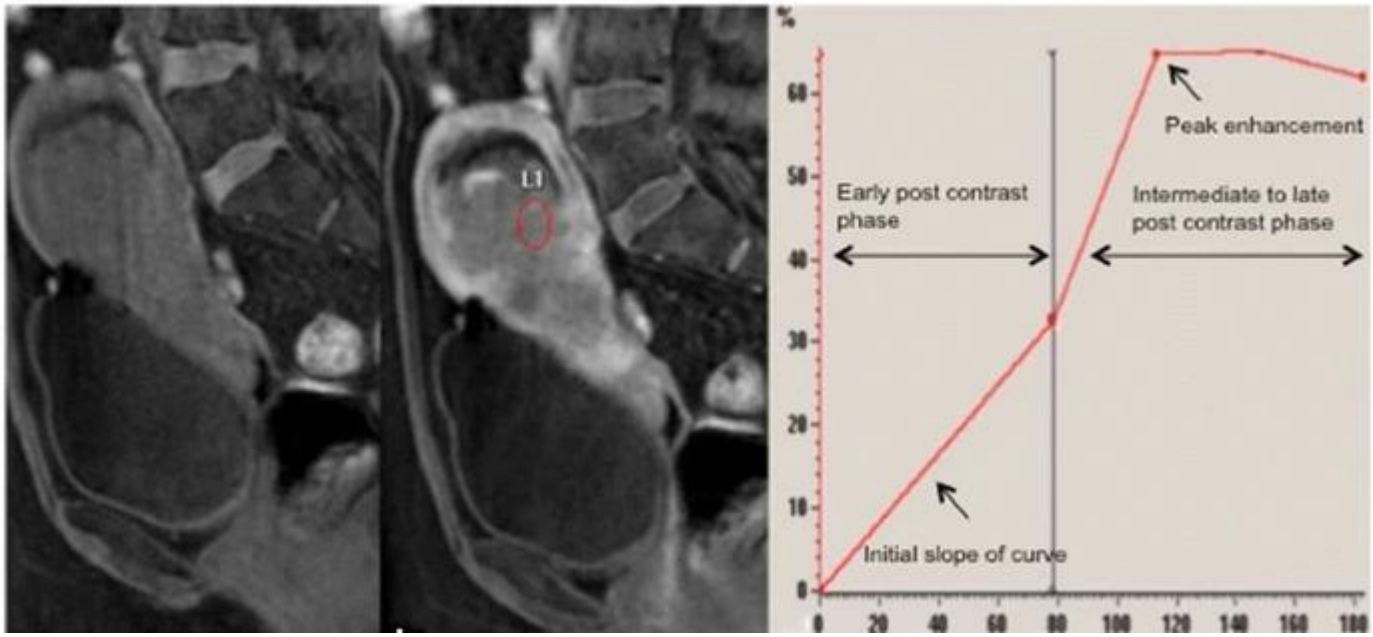


Figure 2: Enhancing endometrial carcinoma and type 3 malignant curve

Above images & graph show a pre-contrast sagittal MRI into the uterus (left image), and after contrast, at a 72 second acquisition (right image), there is augmentation of endometrial soft tissue. However, the tumor is less enhanced than the nearby myometrium, and invasion by the tumor is obviously seen. A graph with a region of interest (red circle) over the tumor and a type 3 malignant curve has been produced.

II.1.6.3.4. MR Imaging findings

II.1.6.3.4.1. Tumor size

At T2-weighted imaging, cervical cancer disrupts the low-signal-intensity fibrous stroma and exhibits intermediate signal intensity. The tumor may be exophytic, infiltrating, or endocervical with a barrel-shaped appearance and exhibit a wide range of morphologic characteristics. Cervical cancer typically begins at the squamocolumnar junction in young women and tends to be more exophytic, while it frequently begins in the endocervical canal in older women. With either protrusion into the vagina or invasion of the lower myometrium, the majority of the lesion is located at the level of the cervix. In contrast, an endometrial tumor (polyp or adenocarcinoma), which is localized in the endometrial cavity protrudes into the endocervical canal, can be distinguished by this. At T2-weighted imaging, prolapsed submucous fibroids are noticeably

more hypointense than cervical carcinomas.

Although T2-weighted imaging generally provides a clearer picture of cervical cancer, tiny tumors may be easier to spot due to their early gadolinium enhancement after dynamic injection. Stage IB or higher tumors are those that are visible. The choice of therapy is significantly influenced by the tumor's size (i.e., whether it is bigger than or less than 4 cm in diameter), and there is a strong correlation between MR imaging results and macroscopic measurements. However, due to inflammation or edema, the size of the lesion may occasionally be exaggerated at T2-weighted imaging. Because they are crucial for the planning of brachytherapy, the form and direction of growth should be observed.

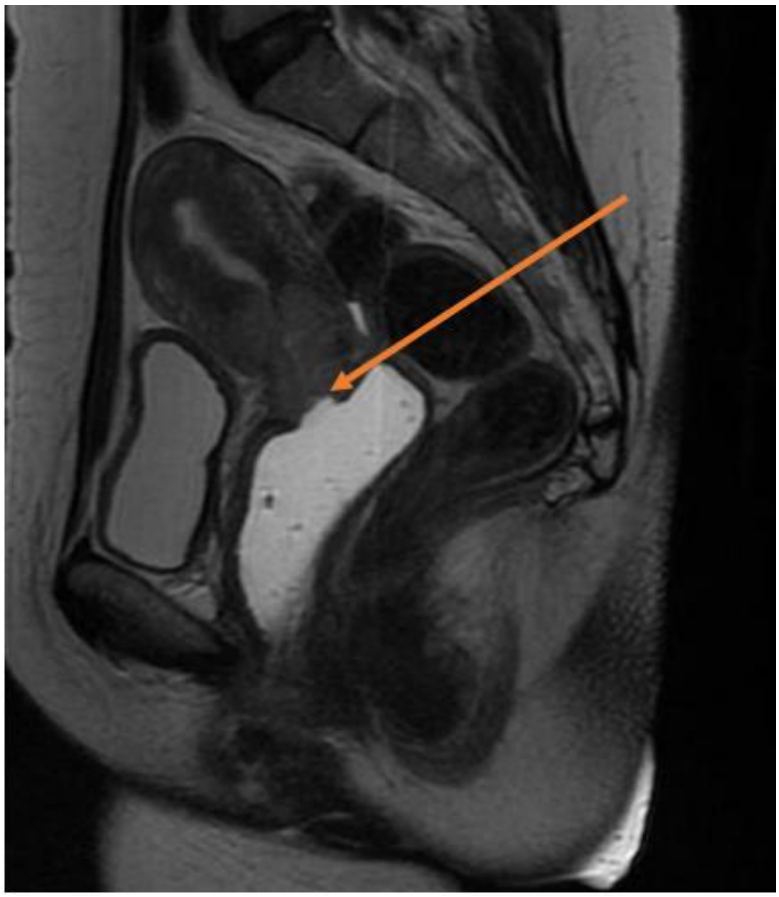


Figure 3: Cervical carcinoma extending into the upper anterior vagina. Sagittal pelvis MRI T2W

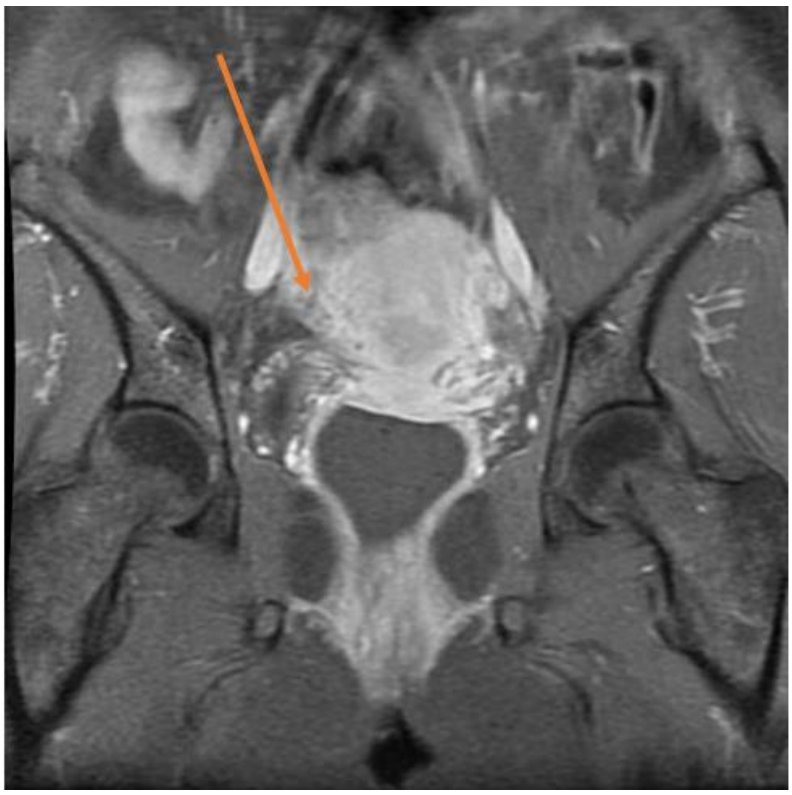


Figure 4: Cervical carcinoma that extends into the parametrium. Coronal pelvis MRI T1 C+fat sat

Images (Figure 3 & Figure 4) are adopted from "Radiopaedia.org ,2021", showing a barrel-shaped thickening and loss of normal low signal intensity of the cervix that extends into the upper anterior vagina and parametrium(arrow)(32).

II.1.6.3.4.2. Vagina involvement

Vaginal invasion is indicated by disruption of the hypointense vaginal wall with hyperintense thickening on T2-weighted imaging and contrast material enhancement on T1-weighted imaging. It is useful to rule out invasion of the lower one-third of the vagina for staging purposes because this raises the stage and necessitates changing the radiation therapy plan. Vaginal extension is, however, clinically well assessed. It could be challenging to detect invasion of the fornices on MR imaging if large lesions are present.

II.1.6.3.4.3. Parametrial involvement

At T2-weighted MR imaging, the preservation of a hypointense fibrous stromal ring has a significant negative predictive value for parametrial invasion. There might be microscopic invasion when the stromal ring is disrupted without clear parametrial mass (false-negative findings). Reliable indicators of invasion include total destruction of the ring and nodular or irregular tumor signal intensity spreading into the parametrium. Although linear stranding surrounding the cervical mass may be caused by peritumoral

inflammatory tissue (false positive findings), it is suggestive of parametrial invasion. A parametrial invasion that is unilateral or bilateral is definitely a contraindication to surgery. T2-weighted imaging has shown to be more accurate in this situation than contrast material-enhanced T1-weighted imaging.

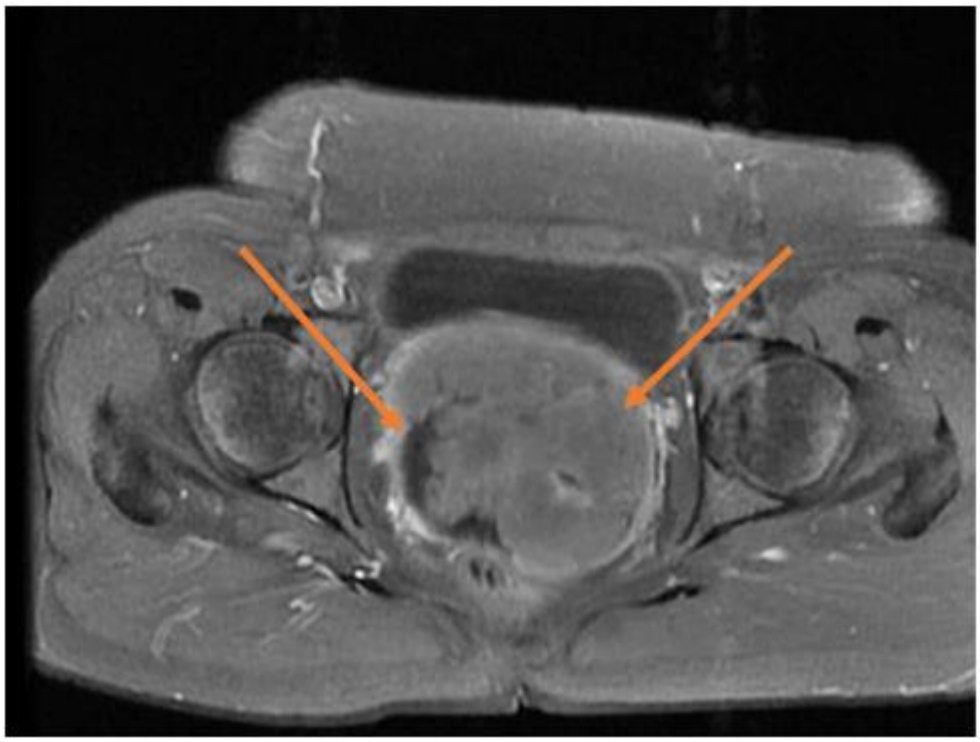


Figure 5: Cervical carcinoma with parametrial invasion. Axial T1 C+ fat sat MRI

Adopted from" MR imaging of cervical carcinoma: a practical staging approach" showing a bulky circumferential cervical mass with extensive bilateral parametrial invasion (arrow)(29).

II.1.6.3.4.4. Pelvic wall evaluation

Pelvic wall invasion is indicated by a tumor that involves the internal obturator, piriform, or levator ani muscles, whether or not the ureter is dilated. It is thought that ureteral blockage at the tumor's level is a sign of wall invasion.

II.1.6.3.4.5. Bladder and rectum assessment

When disruption of the normally hypointense walls of the bladder or the rectal cavity is shown on T2-weighted imaging, with or without a mass extending into the lumen, bladder or rectal invasion is present. Dynamic gadolinium-enhanced T1-weighted sequences are useful for finding fistulous regions and validating invasion. T2-weighted imaging's hyperintense thickening of the bladder mucosa is an indirect marker of

edema rather than an invasive sign. However, it is important to carefully examine this "bullous edema sign" of the posterior wall mucosa for any nodulation that may be present that suggests a malignancy.

II.1.6.3.4.6. Lymph Nodes

Only a size criterion, with a transverse diameter greater than 10 mm being the most frequently accepted, can be used to detect lymph node disease. T2-weighted imaging is the best method for detecting lymph nodes since it allows them to be distinguished from the hypointense muscles and blood arteries and exhibits intermediate signal intensity. It is important to distinguish adenopathy from a somewhat hyperintense ring flow artifact that is frequently found in the iliac veins. A biopsy should be carried out if treatment strategy is altered as a result of a suspicious rise in lymph node volume since the node may be mistakenly positive as a result of inflammation.

II.1.6.3.4.7. Distant metastases

Metastases with stage IVB illness typically affect the lungs, liver, adrenals, or bones. Stage IVB illness also includes peritoneal deposits. Transabdominal ultrasound, CT, or MRI are all excellent ways to evaluate the abdomen. The prevalence of lung involvement in early cervical cancer is quite low, and standard chest X-rays are typically enough to assess these patients. Chest CT should be done if there is advanced cervical cancer present. Metastases in cervical cancer with squamous cell origin could appear as cavitating lung nodules

II.1.6.3.5. TMN Staging 2021 (AJCC Version 9)

II.1.6.3.5.1. Tumor (T) Category

Table 2: Tumor (T) Category

Adopted from “The new (Version 9) American Joint Committee on Cancer tumor, node, metastasis staging for cervical cancer”(33)

T CATEGORY	FIGO STAGE	T CRITERIA
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Carcinoma is strictly confined to the cervix (extension to the corpus should be disregarded)
T1a	IA	Invasive carcinoma that can be diagnosed only by microscopy with maximum depth of invasion ≤5 mm
T1a1	IA1	Measured stromal invasion ≤3 mm in depth
T1a2	IA2	Measured stromal invasion >3 mm and ≤5 mm in depth
T1b	IB	Invasive carcinoma with measured deepest invasion >5 mm (greater than stage IA); lesion limited to the cervix uteri with size measured by maximum tumor diameter; note: the involvement of vascular/lymphatic spaces should not change the staging, and the lateral extent of the lesion is no longer considered
T1b1	IB1	Invasive carcinoma >5 mm depth of stromal invasion and ≤2 cm in greatest dimension
T1b2	IB2	Invasive carcinoma >2 cm and ≤4 cm in greatest dimension
T1b3	IB3	Invasive carcinoma >4 cm in greatest dimension
T2	II	Carcinoma invades beyond the uterus but has not extended onto the lower one-third of the vagina or to the pelvic wall
T2a	IIA	Involvement limited to the upper two-thirds of the vagina without parametrial invasion
T2a1	IIA1	Invasive carcinoma ≤4 cm in greatest dimension
T2a2	IIA2	Invasive carcinoma >4 cm in greatest dimension
T2b	IIB	With parametrial invasion but not up to the pelvic wall
T3	III	Carcinoma involves the lower one-third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or nonfunctioning kidney; note: the pelvic wall is defined as the muscle, fascia, neurovascular structures, and skeletal portions of the bony pelvis; cases with no cancer-free space between the tumor and pelvic wall by rectal examination are FIGO stage III
T3a	IIIA	Carcinoma involves the lower one-third of the vagina, with no extension to the pelvic wall
T3b	IIIB	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney (unless known to be due to another cause)
T4	IVA	Carcinoma has involved (biopsy-proven) the mucosa of the bladder or rectum or has spread to adjacent organs (bullous edema, as such, does not permit a case to be assigned to stage IVA)

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics

II.1.6.3.5.2. Lymph Node (N) category

Table 3: Lymph Node (N) Category

Adopted from “The new (Version 9) American Joint Committee on Cancer tumor, node, metastasis staging for cervical cancer”(33)

N CATEGORY[a]	FIGO STAGE	N CRITERIA
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s) ≤0.2 mm or single cells or clusters of cells ≤200 cells in a single lymph node cross-section
N1	IIIC1	Regional lymph node metastasis to pelvic lymph nodes only
N1mi	IIIC1	Regional lymph node metastasis (>0.2 mm but ≤2.0 mm in greatest dimension) to pelvic lymph nodes
N1a	IIIC1	Regional lymph node metastasis (>2.0 mm in greatest dimension) to pelvic lymph nodes
N2	IIIC2	Regional lymph node metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes
N2mi	IIIC2	Regional lymph node metastasis (>0.2 mm but ≤2.0 mm in greatest dimension) to para-aortic lymph nodes, with or without positive pelvic lymph nodes
N2a	IIIC2	Regional lymph node metastasis (>2.0 mm in greatest dimension) to para-aortic lymph nodes, with or without positive pelvic lymph nodes

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics.

The suffix (f) is added to the N category when metastasis is identified only by fine- needle aspiration or core biopsy. The suffix (sn) is added to the N category when metastasis is identified only by sentinel lymph node biopsy.

II.1.6.3.5.3. Metastasis (M) Category

Table 4: Metastasis (M) Category

Adopted from "The new (Version 9) American Joint Committee on Cancer tumor, node, metastasis staging for cervical cancer"(33)

M CATEGORY	FIGO STAGE	M CRITERIA
M0		No distant metastasis
cM1	IVB	Distant metastasis (includes metastasis to inguinal lymph nodes, intraperitoneal disease, lung, liver, or bone; excludes metastasis to pelvic or para-aortic lymph nodes or vagina)
pM1	IVB	Microscopic confirmation of distant metastasis (includes metastasis to inguinal lymph nodes, intraperitoneal disease, lung, liver, or bone; excludes metastasis to pelvic or para-aortic lymph nodes or vagina)

Abbreviations: cM, clinical metastasis category; FIGO, International Federation of Gynecology and Obstetrics; pM, pathologic metastasis category.

II. 2. Conceptual framework

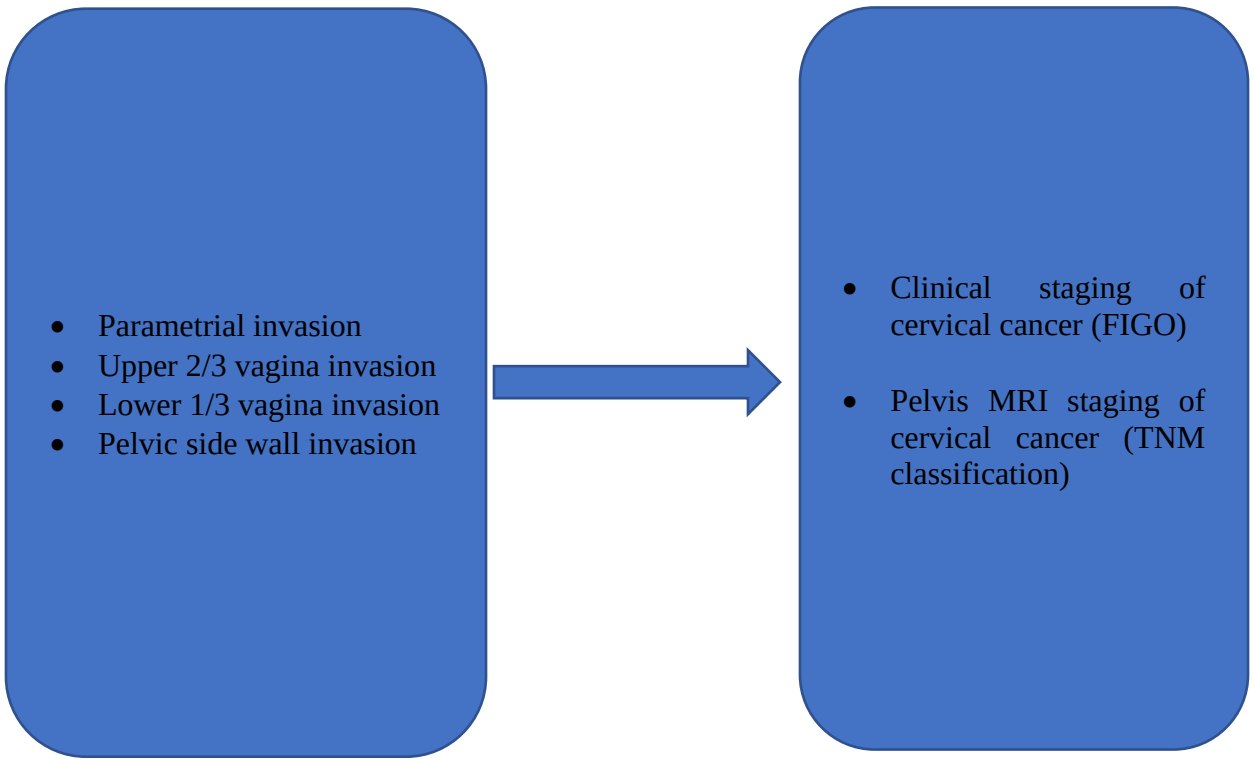


Figure 6: Conceptual framework showing independent variables and dependent variables of cervical cancer in staging

CHAPTER III. METHODS AND MATERIALS

III.1. Study design

This is a retrospective hospital-based study. A descriptive and cross-sectional analysis were used to compare pelvis MRI and clinical cervical cancer findings/patterns before and after chemotherapy in patients reviewed at RMH and scanned at KFH.

III.2. Study site and period

The study sites were: Rwanda Cancer Centre located inside Rwanda military hospital (RMH) and radiology department of King Faisal Hospital (KFH). RMH is a referral and teaching hospital located in Kicukiro district, Kigali City with bed capacity of 414. Inside has a Rwanda Cancer centre which started offering treatment from march 2019 with 2 linear accelerators machines using Volumetric Modulated Arc Therapy (VMAT), 1 CT scan for treatment planning and 20 bed capacity for chemotherapy unity. KFH is a tertial and teaching Hospital locate in Gasabo District with bed capacity of 160. The study was conducted in a retrospective fashion over a period of 30 months, from January 2020 to June 2022 based on the sample size. Data collection began after receiving IRB approvals, from January 2022 up to June 2022.

III.3. Study population

The study population was all patients who attended Rwanda Cancer Centre at RMH with confirmed primary cervical cancer clinically together with positive histology then treated with chemoradiation and had been referred at KFH in radiology department before and after chemoradiation for staging pelvis MRI.

III.4. Selection criteria

III.4. 1. Inclusion criteria

The study included all patients who attended Rwanda Cancer Centre /RMH and KFH fulfilling the following criteria:

- Have been confirmed from pathology to have cervical cancer and sent for chemoradiation at RMH.
- Who's their clinical and radiological staging (using MRI) before and after chemoradiation were available.

III.4. 2. Exclusion criteria

Patients with recurrence of cervical cancer and those who underwent surgery at the time of imaging, were excluded in this study.

III.4.3. Sample size

The Cochran's formula was used to determine the amount of ideal sample size (n) that we used in this study.

$n=z^2*p(1-p)/e^2$

Where;

n=number of sample size

z=Number of standard deviations =1.96, at confidence level of 95%

p= Known prevalence for the characteristic of interest (Cervical cancer) =5.9% from the study done by Jean Damascène Makuza, Sabin Nsanzimana et al,2015 in Rwanda (34)

e= Marginal error=5%

Thus; n=〖1.96〗^2*5.9(100-5.9)/〖5〗^2 =85 Patients

In our study 88 patients met inclusion criteria and was recruited, used as sample size.

III.5. Imaging consideration and staging

During this study the 1.5T Magnetom Amira (Siemens MRI, manufactured in 2019) available at KFH was used for pelvis MRI studies. No special patient's preparation was given like fasting or antiperistaltic agents. Axial T1W images were obtained from the kidney to perineum using 256 × 256 matrix, 32 cm field of view (FOV), 4 mm slice thickness, 1 mm interslice gap. High-resolution T2W images of pelvis were also acquired in axial, sagittal, and coronal planes using 512 × 256 matrix, 25 cm FOV, 4 mm slice thickness, 1 mm interslice gap, TE: 139ms and TR: 6840ms. With 20-40 ml iv gadolinium contrast T1W images were acquired for better characterization of tumors. In most of cases DWI/ADC map sequences were added for better characterization of lesions. No dynamic contrast studies were done. Images obtained from MRI were reviewed by experienced radiologist and stage them based on the tumor growth (T), involvement of lymph nodes (N) or metastases (M) using the new AJCC guidelines V9. Staging was done using the AJCC guidelines. During data collection the images also have been reviewed by the principal investigator and the third view from another senior radiologist was done to address interobserver variability. The conclusion was based on two consensuses (agreement) then the final staging recorded. The data were entered into a database, containing age of patient, main complaints, performance status of the patient, histological type of the tumor, tumor size and TNM staging.

III.6. Data collection

Among all the patients who received chemoradiation and underwent MRI staging before and after chemoradiation, a total number of 88 patients with cervical cancer at their initial presentation to the hospital,

were collected from the Rwanda cancer center patient's data base (Onchronos). Retrieved data such as age, main complaints, performance status of the patient (recorded by clinicians/oncologist based on EGOG performance status at the time of consultation), histological type of the tumor and clinical staging before and after chemoradiation and others were collected using a questionnaire (bellow annexed). The clinical finding records emphasize on parametrial wall invasion, upper two third vaginal involvement, lower one third vaginal involvement and pelvic side wall invasion. The clinical assessment was based on physical exam, speculum exam, colposcopy,…..didn't incorporate imaging information including MRI as the clinical notes of every patient were recorded on daily basis of consultation into Onchronos database with documentation of clinical evaluation and staging before transfer for imaging. Furthermore, radiological information was obtained from the PACS (Picture archiving and communication system) of KFH. Finally, all the collected data was recorded and summarized in an excel database.

III.7. Data Analysis

We used Stata 14 in analysis and visualization of the data. Percentages was used to describe qualitative factors, whereas means and standard deviations used to describe quantitative data. The relationship between clinical and MRI staging was demonstrated using the Kappa coefficient with percent agreement and a P value of less than 5% was considered statistically significant.

III.8. Patient Safety

All imaging were clinically indicated. No experimental studies were performed. The safety of MRI was well established and the patient's confidentiality was respected. All patient's data were anonymized and stored in a password-protected database. No patient's consent form was used because the data had been retrospectively retrieved from different data base including Onchronos at Rwanda cancer center/RMH and PACS at KFH

III.8.1. Costs to patients

All imaging studies were indicated and no additional testing or charges were requested to the patients.

III.8.2. Benefits to hospital or patients

No immediate or specific individual benefits were accrued to either the hospital or patients in this study. However, we expect that data resulted from the study will contribute significantly to the improvement of cervical cancer surveillance for patients treated in Rwanda.

CHAPTER IV. DATA PRESENTATION AND ANALYSIS

IV.1. Patients' enrollment

Entry points were Rwanda cancer centre at RMH, where patient's data base called Onchronos has been accessed and retrieved 512 patients seen in the center referred from different health facilities with confirmed cervical cancer clinically and histologically with their histology results. Each patient has been explored individually and required data were recorded. At the end 424 patients were ineligible for analysis because of different exclusion criteria meet. The most relevant exclusion criteria were unavailability of pelvis MRI study before and or after chemoradiation because many patients had pelvis CT scan for staging before and after chemoradiation. 88 patients were eligible and recruited into our study.

IV.2. Results presentation

Table 5: Age, performance status, histopathology evaluation and staging.

Variables	Categories	Frequency	Percent
Age(years)			
Mean (Standard deviation)	57.7(±10.6)		
Age group			
	<50	19	21.3
	>50	69	78.7
ECOG			
	0	37	41.3
	1	42	48.3
	2	7	8.1
	3	2	2.3
Histology grade			
	Grade I	11	12.5
	Grade II	50	56.8
	Grade III	7	7.9
	Grade IV	1	1.1
	Unknown	19	21.5

Histopathological subtypes			
	SCC	85	96.6
	Adenocarcinoma	3	3.4
Pretreatment Clinical Staging			
	IB	10	11.4
	IIA	18	20.4
	IIB	25	28.4
	IIIA	15	17.0
	IIIB	16	18.1
	IVA	4	4.6
Nodal Involvement	Yes	22	25
	No	66	75
Pretreatment MRI Staging			
	IB	8	9.1
	IIA	22	25.0
	IIB	18	20.5
	IIIA	14	15.9
	IIIB	13	14.7
	IIIC	2	2.3
	IVA	10	11.4
	IVB	1	1.1

The mean age was 57.7 ± 10.6 years, ranging from 24 -78 years. Majority were in age group of more than 50 years old (78.7%). The majority (48.3%) of the patients had ECOG, 1. 96.6% of all cervical cancers were squamous cell carcinoma and most of the patients had grade II (56.8%).

Most of the patients were clinically staged IIB (28.4%), while MRI staging showed that most of the patients were in stage IIA (25%).

Eastern Cooperative Oncology Group (ECOG) performance status

Table 6: ECOG performance status

Adopted from "Performance Status Assessment by Using ECOG (Eastern Cooperative Oncology Group) Score for Cancer Patients by Oncology Healthcare Professionals"

GRADE	ECOG PERFORMANCE STATUS
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
5	Dead

Abbreviation: EGOG, Eastern Cooperative Oncology Group

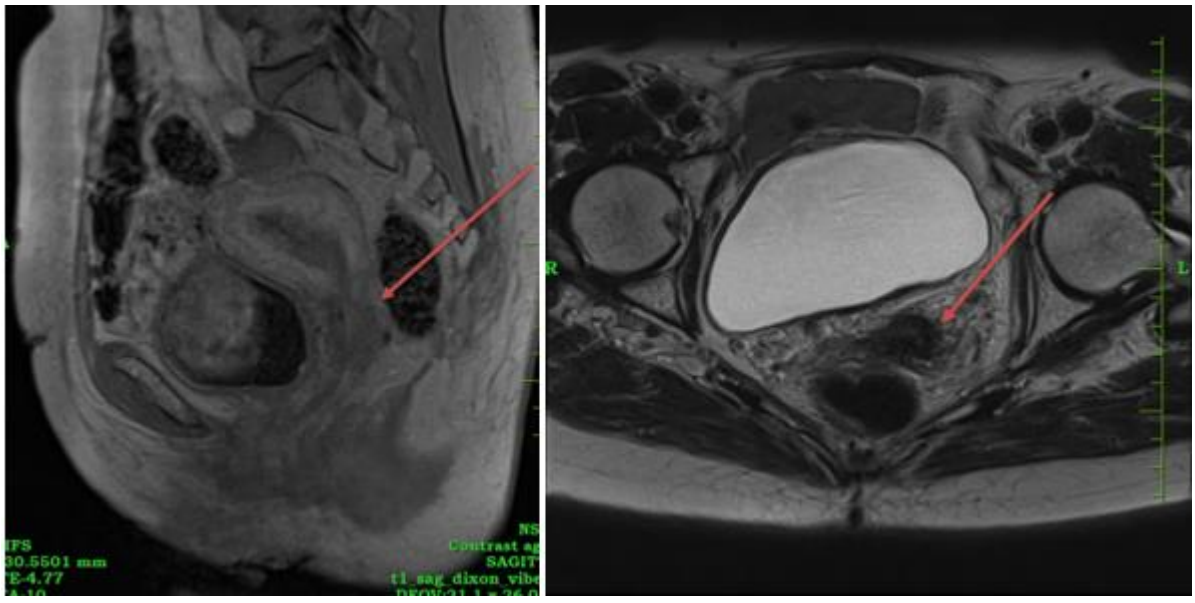


Figure 7: Cervical cancer, T2aN0M0

Images of 69 patient presented with vaginal bleeding, recently diagnosed of cervical cancer
Sagittal (left) T1W +C shows heterogeneously enhancing cervical mass (arrow)with extension into the upper third vagina, axial (right) T2W shows cervical mass (arrow)without parametrial invasion.

Figure 7: In courtesy of the radiology head of department of KFH

Prevalence of symptoms

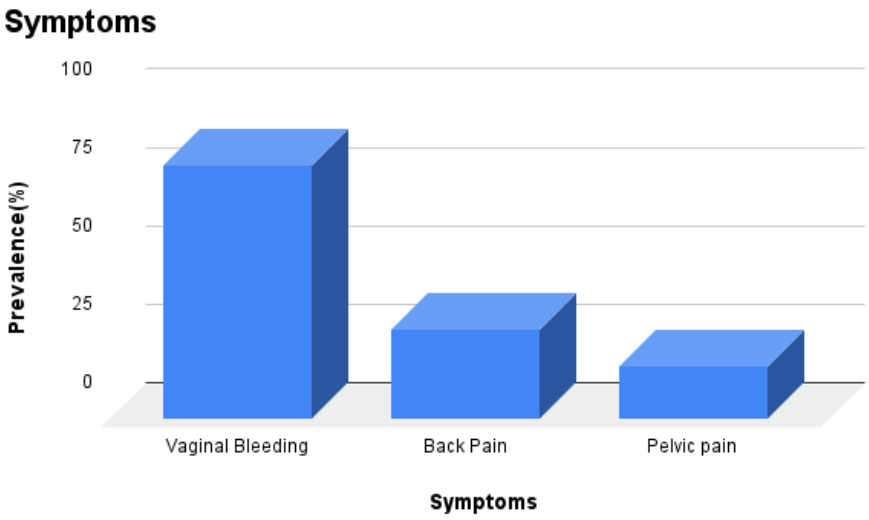


Figure 8: Prevalence of cervical cancer symptoms

Prevalent symptom reported by patients was vaginal bleeding with 80.6% followed by back pain with 28.4% then Pelvic pain which counted 17%.

Table 7: Concordance between pretreatment clinical staging and MRI staging

	MRI								
Clinical Staging	**IB**	**IIA**	**IIB**	**IIIA**	**IIIB**	**IIIC**	**IVA**	**IVB**	**Total**
IB	7	2	1	-	-	-	-	-	10(11.6)
IIA	1	16	1	-	-	-	-	-	18(20.4)
IIB	-	2	14	2	1	-	1	-	20(22.7)
IIIA	-	-	1	9	-	-	3	1	14(16.8)
IIIB	-	2	1	3	10	1	4	-	20(23.0)
IVA	-	-	-	-	2	1	2	-	4(4.5)
IVB	-	-	-	-	-	-	-	-	0(0)
Total	8(9)	22(25)	18(20.5)	14(15.9)	14(16.8)	2(2)	10(11)	1(1)	88

Sixty-four (72%) patients were staged equally by MRI and clinical findings, thirteen patients (14.7%) were under-staged and eleven patients (12.5%) were over staged.

Table 8: Pre-treatment agreement between clinical staging and pelvis MRI staging in cervical cancer patients

Site	Agreement (%)	Kappa	P
Parametrial invasion	81.8%	0.69	0.001
Upper vaginal 2/3 invasion	70.4%	0.26	0.023
Lower 1/3 Invasion	75.0%	0.52	0.046
Pelvic Side wall Invasion	71.5%	0.44	0.001
Overall	78.1%	0.63	0.001

Overall pre-treatment clinical and MRI staging's showed a substantial agreement of 78.1% (K=0.63). Clinical and pelvis MRI evaluation showed 75.0% agreement (K=0.52) in lower vaginal one third invasion, 70.4% agreement (K=0.26) in upper vaginal two third invasion, 71.5% agreement (k=0.44) in pelvic sidewall invasion. According to kappa coefficient, clinical and MRI evaluation for parametrial invasion showed a statistically significant substantial correlation (K = 0.69, P value < 0.001).

Table 9: Pre-treatment Tumor invasions

Site	Clinical Examination	MRI findings
Parametrial invasion		
No	48(54%)	48(54%)
Yes	40(46%)	40(46%)
Upper 2/3 vaginal Invasion		
No	10(12%)	8(9%)
Yes	78(88%)	80(91%)
Lower 1/3 vaginal Invasion		
No	48(54%)	56(64%)
Yes	40(46%)	32(36%)

Pelvic Side wall invasion		
No	60(68%)	50(57%)
Yes	28(32%)	38(43%)

46% of study population showed parametrial invasion by both MRI and clinical assessment. MRI and clinical assessments detected upper 2/3 vaginal involvement in 91% and 88% respectively. Pelvic side wall invasion was seen in 32% clinically and 43% in MRI assessment.

Table 10: Post-treatment agreement between clinical staging and pelvis MRI staging in cervical cancer patients

Site	Agreement (%)	Kappa	P
Parametrial invasion	79.8%	0.61	0.001
Vaginal 2/3 invasion	78.4%	0.52	0.001
Lower 1/3 Invasion	76.0%	0.62	0.001
Pelvic side wall Invasion	76.5%	0.53	0.001
Overall	71.0%	0.71	0.001

Overall, post-treatment clinical and MRI staging showed a substantial agreement of 71.0% (K=0.71). Clinical and pelvis MRI evaluation showed 76.0% agreement (K=0.62) in lower vaginal one third invasion, 78.4% agreement (K=0.52) in upper vaginal two third invasion, 76.5% agreement (k=0.53) in pelvic sidewall invasion. According to kappa coefficient, clinical and MRI evaluation for parametrial invasion showed a statistically significant substantial correlation (K = 0.61, P value < 0.001).

Table 11: Post-treatment tumor invasions

Site	Clinical Examination	MRI findings
Parametrial invasion		
No	74(83%)	74(83%)
Yes	14(17%)	14(17%)
Upper 2/3 vagina invasion		
No	70(80%)	68(77%)

Yes	18(20%)	20(23%)
Lower 1/3 vagina invasion		
No	80(91%)	80(91%)
Yes	8(9%)	8(9%)
Pelvic side wall invasion		
No	81(92%)	80(91%)
Yes	7(8%)	8(9%)

14% of study population showed parametrial invasion by both MRI and clinical assessment. MRI and clinical assessments detected upper 2/3 vaginal involvement in 23% and 20% respectively. Pelvic side wall invasion was seen in 8% clinically and 9% in MRI assessment.

CHAPTER V. DISCUSSION, CONCLUSION AND RECOMMENDATIONS

V.1. Discussion

V.1.1. Mean age of cervical cancer

In our study, the mean age was 57.7 ± 10.6 years. Majority (78.7%) were in age group of more than 50 years old. This increased number of patients having above50 years is because with increased age HPV infection, which is important risk factors get long time to colonize the epithelium with high risk of malignancy transformation. In the study conducted by Rebecca J. DeBoer et al. at Butaro cancer center (in Rwanda) found that the median age was 54 years among 379 patients newly diagnosed cervical cancer(36).This is explained by the fact that the Rwandan population sharing same risk factors are considered in those both studies. Our findings are slightly higher to what Mazvita SM et al. found in their retrospective study conducted in 11 sub-Saharan African countries. For them the mean age was 53.4 years (standard deviation ±14.5), ranging from 44.9 years in Kampala, Uganda to 56.1 years in the Eastern Cape, South Africa(37). That small difference can be explained by the factors that large sample size with different risk factors has been used in the later study compared to our study. Worldwide, the incidence and mortality of cervical cancer, has been found in the range of 44 years (Vanuatu) to 68 years (Singapore), the average age at cervical cancer diagnosis worldwide was 53 years (38). Our findings are almost similar to those found in one prospective study conducted in India, where the mean age was 56 years among cervical patients assessed clinically and radiologically before and after chemoradiation(39). The mean age found in our study is slightly lower of what has been found in the study conducted in Norway, where the mean age at diagnosis of cervical cancer was 60 years (standard deviation 17) and ranged from 22 to 99 years(40).A higher life expectancy and rarer HPV infections in Norwegian compared to Rwandese people may explain this slight difference in mean age of cervical cancer occurrence which is higher in Norwegians.

V.1.2. Performance status in cervical cancer

Our results demonstrated that majority (48.3%) of the patients had ECOG 1 performance status and only 2.3% of the patient had been seen confined to chair or bed (ECOG 3). The previously published study in Rwanda at Butaro Cancer Center of Excellence showed that 79% of population had a normal performance status (ECOG 0) at presentation with 13% and 2 % having ECOG 1 and ECOG 3 performance status respectively(36). In comparison to our study, these small differences in performance status score, may be justified by that Butaro cancer center was providing the chemotherapy only as treatment option without radiotherapy, so many patients may consult when they still presenting full performance status. A prospective study conducted in India revealed almost similar findings with our study where the majority of

population (45%) had ECOG 1 performance status(39).

V.1.3. Symptoms in patient with cervical cancer

In our study the prevalent symptom reported by patients was vaginal bleeding with 80.6% followed by back pain 28.4% then Pelvic pain counted 17%. Our findings are similar to those Ahmad SS et al found in their study where during assessment of diagnostic accuracy of MRI versus clinical staging in cervical cancer, all patients recruited presented abnormal uterine bleeding as their chief complaint(42). These findings are also identical to what Aravindh SA et al found in their study the most frequent presenting complaint, seen in 68% of patients with cervical cancer, was vaginal hemorrhage, which was followed by dyspareunia, growth in the introitus, and abnormal vaginal discharge(39).

V.1.4. Pre-treatment Clinical Staging

Most of our patients were clinically staged in IIB (28.4%). These findings are slightly different to those found in the study conducted at Butaro cancer center, where physical examination, ultrasonography and chest X-ray were used to stage the majority of cases then majority of individuals were documented in stage III clinically with 46% of patients. In the study conducted in Tanzania, Ramadhani ML et al. saw that majority of patients were staged clinically in IB (28.2%) and II (20.4%)(43). In 2008, Damar O et al. showed that almost similar findings as our study, where the majority of patient treated at Kenyatta National Hospital was in stage IIIB (21.9%) and IIB (27.2%)(44). All those similarities could be explained by the above study sites and population are not far different to ours, where they share in common most of the characteristics. Our findings are not far different to what has been found in the study conducted in India where the most common stage in the set of their patients was stage IIB (26.6%)(39).The same as in Turkey Gülgün E et al. showed that most of cervical cancer patients presented in stage II and III with equal percentages (45.2%), when staged before radiotherapy(45). Some small differences are present when comparing different studies, this may be due to some changes which has been occurring in the past, updating the clinical staging of cervical cancer(46).

V.1.5. Pre-treatment MRI Staging

With Pelvis MR staging before chemoradiation, in our study we found that most patients were in stage IIA (n=22, 25%). Our findings look slightly different to what had been found by Supajit N et al in 2021 when conducted their study where, MRI staging showed multiple stages as follows: (10.8%) of stage IIB, 2.7%) of stage IIIA, (10.8%) of stage IIIB, (48.7 %) of stage IIIC1, (5.4%) of stage IIIC2, (13.5%) of stage IVA and

(8.1%) of stage IVB(46). Our findings are not far different to what had been found in the study conducted in one of Indian cancer treatment center where the most stage in their recruited patients with cervical cancer was stage IIB with 39.1% followed by stage IIIB (23.4%) and IIIA (17.2%)(39).

Nodal disease has a significant impact on survival and the presence of metastatic nodes suggests a worse prognosis within each stage. Our study showed that MRI detected nodal involvement in 22 patients (25%). The study of Aravindh SA et al showed that there were no loco regional lymph nodes involved in 40% of the patients. 15.6% of patients showed lymph node involvement that was limited to the para cervical region. 12.5% of patients had internal iliac involvement, 25% had external iliac involvement, and 6.3% had common iliac involvement(39). Nawapun et al conducted a study and saw that MRI was used to assess lymphadenopathy in 27 (73.0%) out of 37 individuals. Six patients (16.2%) had para-aortic lymphadenopathy, while 21 patients (56.8%) had pelvic lymphadenopathy. Both pelvic and para-aortic lymphadenopathy affects three patients(46).

V.1.6. Pre-treatment agreement between clinical staging and pelvis MRI staging in cervical cancer patients

In our study, we found that Sixty-four (72%) patients were staged equally by MRI and clinical findings, thirteen patients (14.7%) were under-staged and eleven patients (12.5%) were over staged. Ahmad SS et al.in their study conducted on 27 patients showed that 9 individuals (33%) were found to be at stage 1 based on clinical staging. In eight of them, MRI staging and clinical staging were coordinated, and for one patient, MRI showed stage 2B (88% concordance)(42) .

In our study, overall pretreatment clinical and MRI staging's showed a substantial agreement of 78.1%. Clinical and pelvis MRI evaluation showed 75.0% agreement in lower vaginal one third invasion, 70.4% agreement in upper vaginal two third invasion and 71.5% agreement in pelvic sidewall invasion. According to kappa coefficient, clinical and MRI evaluation for parametrial invasion showed a statistically significant substantial correlation.

Our findings appear not far different to the findings conducted in Thailand, where there was a good correlation between clinical and MRI staging, with 78.4% agreement. Clinical and MRI evaluation revealed a correlation between the invasion of the vagina (77.0% agreement, K = 0.128w), the pelvic sidewall (67.6% agreement, K = 0.098), the nearby pelvic organ (78.4% agreement, K = 0.000), and the spreading to distant organ (91.9% agreement, K = 0.000)(46). This is similarities are may be explained by the fact the sample size used appear almost equal in terms of numbers.

Gülgün E et al found that the pre-treatment correlations for diagnoses without parametrial invasion, with parametrial invasion, and with pelvic sidewall invasion between MRI and clinical findings were 71.0%,

64.7%, and 15.8%, respectively. The parametrial invasion correlation scored poorly (r = 0.410, P 0.01) in the Spearman's rho (rank correlation) test(45).

V.1.7. Post-treatment agreement between clinical staging and pelvis MRI staging in cervical cancer patients

In the present study, Overall, post treatment clinical and MRI staging showed substantial agreement of 71.0% Clinical and pelvis MRI evaluation showed 76.0% agreement in lower vaginal one third invasion, 78.4% agreement in upper vaginal two third invasion, 76.5% agreement in pelvic sidewall invasion. According to kappa coefficient, clinical and MRI evaluation for parametrial invasion showed a statistically significant substantial correlation. Engin et al. saw that the clinical and MRI data had an 88.9% (32/36) correlation in the evaluation of a local response to treatment. The correlation between clinical and MRI results was 75.8% in post-chemoradiation. Similarly, there was a 75.0% concordance between clinical and MRI findings regarding sacro-uterine thickness and tension after treatment (45). Aravindh SA et al showed that that the hazard ratio of recurrence between non responders and responders was 8.667 times higher. The p value (p=0.001.95% confidence interval 2.82 to 35.1) was determined to be significant. Clinical evaluation of the response revealed a hazard ratio between non responders and responders of 1.667, although this result was not statistically significant (p=0.438) (39).

V.2. Limitations of the study

The Rwanda cancer Centre started to be operational and providing chemoradiation in 2019, with relatively limited patients' access, this led to the small sample size for our study.

There is no MRI at RMH/ Rwanda Cancer Centre, this led to majority of patients undergoing CT abdomen/pelvis for both loco-regional & distant staging.

The retrospective nature of the study with its inherent weaknesses (low level of confidence, prone to recall/misclassification bias, sample size not representing the general population) was a limitation.

V.3. Conclusion

Our study found that sixty-nine out of eighty-eight women recruited were above of fifty years. About ninety-seven percent of our patients were ambulatory and capable of all selfcare. Twenty-eight percent of our study participants were found to have stage IIB disease clinically and twenty-five percent had stage IIA disease by pelvis MRI. The study analysis revealed a substantial agreement between clinical and pelvis MRI before and after chemoradiation with about seventy-two percent of our study population staged equally clinically and by

pelvic MRI.

Therefore, our alternative hypothesis is kept and null hypothesis is rejected.

V.4. Recommendations

V.4.1. To Researchers

A prospective clinical and pelvic MRI study on cervical cancer patients is recommended to mitigate for the limitations of the retrospective study findings.

V.4.2. To all health care providers

All health care providers in general: Adequate recording of patient's information to facilitate retrospective studies in the future.

To clinicians/oncologists: To always incorporate pelvis MRI in cervical cancer staging

V.4.3. To the Ministry of Health

To carry out a comprehensive screening, diagnostic, treatment and follow-up study to assess the true extend of the burden of cervical cancer and its outcomes.

Bibliography

1. Cervical cancer [Internet]. [cited 2021 Jul 22]. Available from: https://www.who.int/health-topics/cervical-cancer?__cf_chl_captcha_tk__=pmd_0ee35b96a525adc0e2bd0b1874b9f38038bb2a81-1626973695-0-gqNtZGzNAs2jcnBszQji#tab=tab_1
2. Ntekim A. Cervical Cancer in Sub Sahara Africa. Topics on Cervical Cancer With an Advocacy for Prevention. 2012;(March 2012).
3. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin [Internet]. 2011 Mar 1 [cited 2021 Jul 22];61(2):69–90. Available from: https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.20107
4. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May;71(3):209–49.
5. Makuza JD, Nsanzimana S, Muhimpundu MA, Pace LE, Ntaganira J, Riedel DJ. Prevalence and risk factors for cervical cancer and pre-cancerous lesions in Rwanda. PAMJ 2015; 22:26 [Internet]. 2015 [cited 2021 Jul 22];22(26). Available from: https://www.panafrican-med-journal.com/content/article/22/26/full
6. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer [Internet]. 2010 Dec 15 [cited 2021 Jul 22];127(12):2893–917. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/ijc.25516
7. Singh DK, Anastos K, Hoover DR, Burk RD, Shi Q, Ngendahayo L, et al. Human Papillomavirus Infection and Cervical Cytology in HIV-Infected and HIV-Uninfected Rwandan Women. J Infect Dis [Internet]. 2009 Jun 15 [cited 2021 Jul 22];199(12):1851–61. Available from: https://academic.oup.com/jid/article/199/12/1851/881994
8. S de S, B S, X C, M B, J M, L B, et al. Human papillomavirus (HPV) and related cancers in the Global Alliance for Vaccines and Immunization (GAVI) countries. A WHO/ICO HPV Information Centre Report. Vaccine [Internet]. 2012 Nov 20 [cited 2021 Jul 22];30 Suppl 4. Available from: https://pubmed.ncbi.nlm.nih.gov/23510764/
9. Otero-García MM, Mesa-Álvarez A, Nikolic O, Blanco-Lobato P, Basta-Nikolic M, Llano-Ortega RM de, et al. Role of MRI in staging and follow-up of endometrial and cervical cancer: pitfalls and mimickers. Insights Imaging [Internet]. 2019 Dec 1 [cited 2021 Jul 22];10(1). Available from: /pmc/articles/PMC6375059/
10. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. International

Journal of Gynecology & Obstetrics [Internet]. 2009 May 1 [cited 2021 Jul 22];105(2):103–4. Available from: https://obgyn.onlinelibrary.wiley.com/doi/full/10.1016/j.ijgo.2009.02.012

11. Corrigendum to: Revised FIGO staging for carcinoma of the cervix uteri (International Journal of Gynecology & Obstetrics, (2019), 145, 1, (129-135), 10.1002/ijgo.12749). International Journal of Gynecology and Obstetrics. 2019 Nov 1;147(2):279–80.
12. Haldorsen IS, Lura N, Blaakær J, Fischerova D, Werner HMJ. What Is the Role of Imaging at Primary Diagnostic Work-Up in Uterine Cervical Cancer? Current Oncology Reports 2019 21:9 [Internet]. 2019 Jul 29 [cited 2021 Jul 22];21(9):1–15. Available from: https://link.springer.com/article/10.1007/s11912-019-0824-0
13. T K, N F, T T, Y N, K K, K T, et al. Clinical evaluation using magnetic resonance imaging for patients with stage III cervical carcinoma treated by radiation alone in multicenter analysis: its usefulness and limitations in clinical practice. Am J Clin Oncol [Internet]. 2003 Dec [cited 2021 Jul 26];26(6):574–83. Available from: https://pubmed.ncbi.nlm.nih.gov/14663375/
14. Zhang S, Xu H, Zhang L, Qiao Y. Cervical cancer: Epidemiology, risk factors and screening. Chinese Journal of Cancer Research [Internet]. 2020 [cited 2021 Sep 2];32(6):720. Available from: /pmc/articles/PMC7797226/
15. Song B, Ding C, Chen W, Sun H, Zhang M, Chen W. Incidence and mortality of cervical cancer in China, 2013. Chinese Journal of Cancer Research. 2017 Dec 1;29(6):471–6.
16. Prabhu M, Eckert LO. Development of World Health Organization (WHO) recommendations for appropriate clinical trial endpoints for next-generation Human Papillomavirus (HPV) vaccines. Papillomavirus Research. 2016 Dec 1;2:185–9.
17. Topics on Cervical Cancer With an Advocacy for Prevention - Google Books [Internet]. [cited 2021 Jul 22]. Available from: https://books.google.co.ke/books?hl=en&lr=&id=9DiaDwAAQBAJ&oi=fnd&pg=PA51&ots=F9ArzD9iq3&sig=ExvDrLpARnxiKQq5g09rn2yRYM8&redir_esc=y#v=onepage&q&f=false
18. la Vecchia C, Boccia S. Oral contraceptives, human papillomavirus and cervical cancer. European Journal of Cancer Prevention [Internet]. 2014 Mar [cited 2021 Sep 2];23(2):110–2. Available from: https://journals.lww.com/eurjcancerprev/Fulltext/2014/03000/Oral_contraceptives,_human_papillomavirus_and.6.aspx
19. RG G, S G, MJ X, LT C, H S. Cervical cancer control in HIV-infected women: Past, present and future. Gynecol Oncol Rep [Internet]. 2017 Aug 1 [cited 2021 Sep 2];21:101–8. Available from: https://pubmed.ncbi.nlm.nih.gov/28819634/
20. E R, X C, M P, N T, T W, N M, et al. Smoking as a major risk factor for cervical cancer and pre-

cancer: results from the EPIC cohort. Int J Cancer [Internet]. 2014 Jul 15 [cited 2021 Sep 2];135(2):453–66. Available from: https://pubmed.ncbi.nlm.nih.gov/24338632/

21. Burd EM. Human papillomavirus and cervical cancer. Clin Microbiol Rev [Internet]. 2003 Jan [cited 2022 Jul 27];16(1):1–17. Available from: https://journals.asm.org/journal/cmr
22. Y Y, X C, F S, F M. HPV post-infection microenvironment and cervical cancer. Cancer Lett [Internet]. 2021 Jan 28 [cited 2021 Sep 2];497:243–54. Available from: https://pubmed.ncbi.nlm.nih.gov/33122098/
23. Liu ZC, Liu WD, Liu YH, Ye XH, Chen SD. Multiple Sexual Partners as a Potential Independent Risk Factor for Cervical Cancer: a Meta-analysis of Epidemiological Studies. Asian Pac J Cancer Prev [Internet]. 2015 [cited 2022 Jul 27];16(9):3893–900. Available from: https://pubmed.ncbi.nlm.nih.gov/25987056/
24. Cervical cancer and hormonal contraceptives: collaborative reanalysis of individual data for 16 573 women with cervical cancer and 35 509 women without cervical cancer from 24 epidemiological studies. Lancet. 2007 Nov 10;370(9599):1609–21.
25. Muñoz N, Franceschi S, Bosetti C, Moreno V, Herrero R, Smith JS, et al. Role of parity and human papillomavirus in cervical cancer: the IARC multicentric case-control study. The Lancet. 2002 Mar 30;359(9312):1093–101.
26. Nicolet V, Carignan L, Bourdon F, Prosmanne O. MR imaging of cervical carcinoma: A practical staging approach. Radiographics. 2000;20(6):1539–49.
27. Salib MY, Russell JHB, Stewart VR, Sudderuddin SA, Barwick TD, Rockall AG, et al. 2018 figo staging classification for cervical cancer: Added benefits of imaging. Radiographics [Internet]. 2020 Oct 1 [cited 2022 Jul 27];40(6):1807–22. Available from: https://pubs.rsna.org/doi/10.1148/rg.2020200013
28. Liu X, Wang J, Hu K, Zhang F, Meng Q, Wang W, et al. Validation of the 2018 FIGO Staging System of Cervical Cancer for Stage III Patients with a Cohort from China. 2020 [cited 2022 Jul 27]; Available from: http://doi.org/10.2147/CMAR.S239624
29. Nicolet V, Carignan L, Bourdon F, Prosmanne O. MR Imaging of Cervical Carcinoma: A Practical Staging Approach1. https://doi.org/101148/radiographics206.g00nv111539 [Internet]. 2000 Nov 1 [cited 2022 Jul 28];20(6):1539–49. Available from: https://pubs.rsna.org/doi/10.1148/radiographics.20.6.g00nv111539
30. Bourgioti C, Chatoupis K, Moulopoulos LA. Current imaging strategies for the evaluation of uterine cervical cancer. World J Radiol [Internet]. 2016 Apr 4 [cited 2022 Jul 28];8(4):342. Available from: /pmc/articles/PMC4840192/

31. Goel A, Rasuli B. Cervical carcinoma. Radiopaedia.org [Internet]. 2021 Mar 27 [cited 2022 Sep 12]; Available from: http://radiopaedia.org/cases/cervical-carcinoma-5
32. Haouimi A, Rasuli B. Cervical cancer. Radiopaedia.org [Internet]. 2018 Sep 13 [cited 2022 Sep 12]; Available from: http://radiopaedia.org/cases/cervical-cancer-5
33. The new (Version 9) American Joint Committee on Cancer tumor, node, metastasis staging for cervical cancer | Enhanced Reader.
34. Makuza JD, Nsanzimana S, Muhimpundu MA, Pace LE, Ntaganira J, Riedel DJ. Prevalence and risk factors for cervical cancer and pre-cancerous lesions in Rwanda. Pan Afr Med J [Internet]. 2015 [cited 2022 Aug 18];22. Available from: /pmc/articles/PMC4662515/
35. Fontham ETH, Wolf AMD, Church TR, Etzioni R, Flowers CR, Herzig A, et al. Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society. CA Cancer J Clin [Internet]. 2020 Sep [cited 2022 Aug 18];70(5):321–46. Available from: https://www.cancer.org/cancer/cervical-cancer/about/key-statistics.html
36. DeBoer RJ, Umutoni V, Bazzett-Matabele L, Katznelson E, Nguyen C, Umwizerwa A, et al. Cervical cancer treatment in Rwanda: Resource-driven adaptations, quality indicators, and patient outcomes. Gynecol Oncol [Internet]. 2022;164(2):370–8. Available from: https://doi.org/10.1016/j.ygyno.2021.12.002
37. Sengayi-Muchengeti M, Walburga |, Joko-Fru Y, Miranda-Filho A, Singh E, Eva |, et al. Anne Korir 10 | Shyam Manraj 11 | Cesaltina Lorenzoni 12 | Carla Carrilho 12 | Rolf Hansen 13 | Anne Finesse 14 | Nontuthuzelo I. M. Somdyala 15 | Henry Wabinga 16 | Tatenda Chingonzoh 17 | Margaret Borok 18 | Eric Chokunonga 18. 2020;
38. Arbyn M, Weiderpass E, Bruni L, de Sanjosé S, Saraiya M, Ferlay J, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. Lancet Glob Health [Internet]. 2020 Feb 1 [cited 2022 Aug 18];8(2):e191. Available from: /pmc/articles/PMC7025157/
39. Anand AS, Abraham MM, Kuriakose VG. MRI versus clinical assessment in staging and response evaluation in locally advanced cervix cancer patients treated with concurrent chemo-radiation in a tertiary cancer center: a prospective study. Int J Reprod Contracept Obstet Gynecol. 2017;6(2):392.
40. Baasland I, Vie G, Romundstad PR, Lönnberg S. Cervical cancer mortality in Norway according to screening attendance and age. Acta Obstet Gynecol Scand [Internet]. 2022 Sep 1 [cited 2022 Aug 18];101(9):952–9. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/aogs.14402
41. Noegroho BS, Kurniawan AP, Wijayanti Z, Mustafa A. Factors Affecting Survival Outcome After Percutaneous Nephrostomy as Palliative Urinary Diversion in Obstructive Uropathy due to Advance Cervical Cancer Patients. Asian Pacific Journal of Cancer Prevention. 2021;22(4):1211–6.

42. Shirazi AS, Razi T, Cheraghi F, Rahim F, Ehsani S, Davoodi M. Diagnostic accuracy of magnetic resonance imaging versus clinical staging in cervical cancer. Asian Pacific Journal of Cancer Prevention. 2014;15(14):5729–32.
43. Mlange R, Matovelo D, Rambau P, Kidenya B. Patient and disease characteristics associated with late tumour stage at presentation of cervical cancer in northwestern Tanzania. BMC Womens Health [Internet]. 2016;16(1):1–7. Available from: http://dx.doi.org/10.1186/s12905-016-0285-7
44. Osok D, Karanja S, Kombe Y, Njuguna E, Todd J. Assessing Factors Associated With Survival Among Cervical Cancer Patients in Kenya: A Retrospective Follow-up Study. East Afr Health Res J [Internet]. 2018 [cited 2022 Aug 19];2(2):118. Available from: /pmc/articles/PMC8279180/
45. Engin G, Küçücük S, Ölmez H, Haşiloğlu ZI, Dişçi R, Aslay I. Correlation of clinical and MRI staging in cervical carcinoma treated with radiation therapy: A single-center experience. Diagnostic and Interventional Radiology. 2011;17(1):44–51.
46. Nawapun S, Aphinives C, Srisitthiprapha W, Thamronganantasakul K, Temtanakitpaisan A. Correlation of clinical staging and MRI staging for cervical cancer. Egyptian Journal of Radiology and Nuclear Medicine [Internet]. 2021 Dec 1 [cited 2022 Aug 19];52(1):1–7. Available from: https://ejrnm.springeropen.com/articles/10.1186/s43055-021-00544-8

CHAPTER VI: ANNEXES

VI.1. Data collection form

Section I: Demographic:

1. Age of the patient:
2. District:
3. Province:

Section II: Clinical note

1. Symptoms:
   - Abnormal vaginal bleeding
   - Bleeding after intercourse or a pelvic examination
   - Vaginal discharge
   - Pain during sexual intercourse
   - Bleeding after menopause
   - Unexplained, persistent pelvic and/or back pain

2. Performance status (ECOG):

3. Histopathology type/grading :

4. Clinical assessment before chemoradiation
   - upper 2/3 vaginal wall: Y(yes)/N(No)
   - Parametrial invasion: Y/N
   - Lower third vagina: Y/N
   - Pelvic sidewall invasion : Y/N
   - Hydroureter and hydronephrosis : Y/N
   - Nodes: Y/N
   - Metastases: Y/N
   - FIGO staging:

5. Clinical assessment after chemoradiation
   - upper 2/3 vaginal wall: Y(yes)/N(No)

- Parametrial invasion: Y/N
- Lower third vagina: Y/N
- Pelvic sidewall invasion : Y/N
- Hydroureter and hydronephrosis : Y/N
- Nodes: Y/N
- Metastases: Y/N
- FIGO staging:

Section III: Imaging

1) Technique:
   - Anti-peristaltic agent given: Y/N
   - IV contrast: Y/N

2) Radiological findings before chemoradiation
   - upper 2/3 vaginal wall: Y(yes)/N(No)
   - Parametrial invasion: Y/N
   - Lower third vagina: Y/N
   - Pelvic sidewall invasion : Y/N
   - Hydroureter and hydronephrosis : Y/N
   - Nodes: Y/N
   - Metastases: Y/N
   - Tumor size:
   - TNM staging:

3) Technique after chemoradiation:
   - Anti-peristaltic agent given: Y/N
   - IV contrast: Y/N

4) Radiological findings after chemoradiation
   - upper 2/3 vaginal wall: Y(yes)/N(No)
   - Parametrial invasion: Y/N

- Lower third vagina: Y/N
- Pelvic sidewall invasion : Y/N
- Hydroureter and hydronephrosis : Y/N
- Nodes: Y/N
- Metastases: Y/N
- Tumor size:
- TNM staging:

5) Disease response (RECIST criteria) evaluation:

IV. Treatment

Type of chemotherapy:

Radiotherapy doses:

All sections: information was extracted from Rwanda cancer centre patients' data storage (Onchronos) at RMH.

Section III: information was obtained from the PACS (Picture archiving and communication system) at KFH

VI.2. Budget

	Item	Quantity	Unit price(Frws)	Total price (Frws)
1.	Fuel for weekly visit of study sites	24 visits (all sites visited the same day)	15.000	360000
2	Communication (both air time & internet).	-	-	150.000
3	Statistical data analysis by a Consultant Statistician	1	300.000	300000
4.	Printed copies of the draft / dissertation, 60 pages each	10x2copies	1.200	24.000
5.	Final printed copies of the dissertation, 60 pages each	10x2 copies	1.200	24.000
6.	Book binding	5x2 copies	5.000	50.000
	S/Total			908.000
	Miscellaneous 20%			181.600
	Total			**1.089.600**

VI.3. Time frame for study activities

	November 2021 - January 2022	January - June 2022	June - July 2022	July - August 2022	September-October 2022
-Proposal writing -Approval -Fundraising	✓				
Data collection		✓			
Data analysis			✓		
Paper writing				✓	
Manuscript ready					✓

VI.4. Copy of CMHS – IRB approval, University of Rwanda

UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 31st /January /2022

Dr DUHORANENAYO Dieudonne
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 048/CMHS IRB/2022

Your Project Title *"Correlation of clinical and pelvic MRI staging before and after chemoradiation in determining prognostic factors in patient with cervical cancer at RMH &KFH. "Cross-sectional Study among patients with confirmed cervical cancer who underwent chemoradiation and pelvic"* has been evaluated by CMHS Institutional Review Board.

Name of Members	Institute	Involved in the decision		
		Yes	No (Reason)	
			Absent	Withdrawn from the proceeding
Prof Kato J. Njunwa	UR-CMHS	X		
Prof Stefan Jansen	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Prof Gishoma Darius	UR-CMHS	X		
Prof Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 31st January 2022, **Approval has been granted to your study.**
Please note that approval of the protocol and consent form is valid for **12 months**.

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

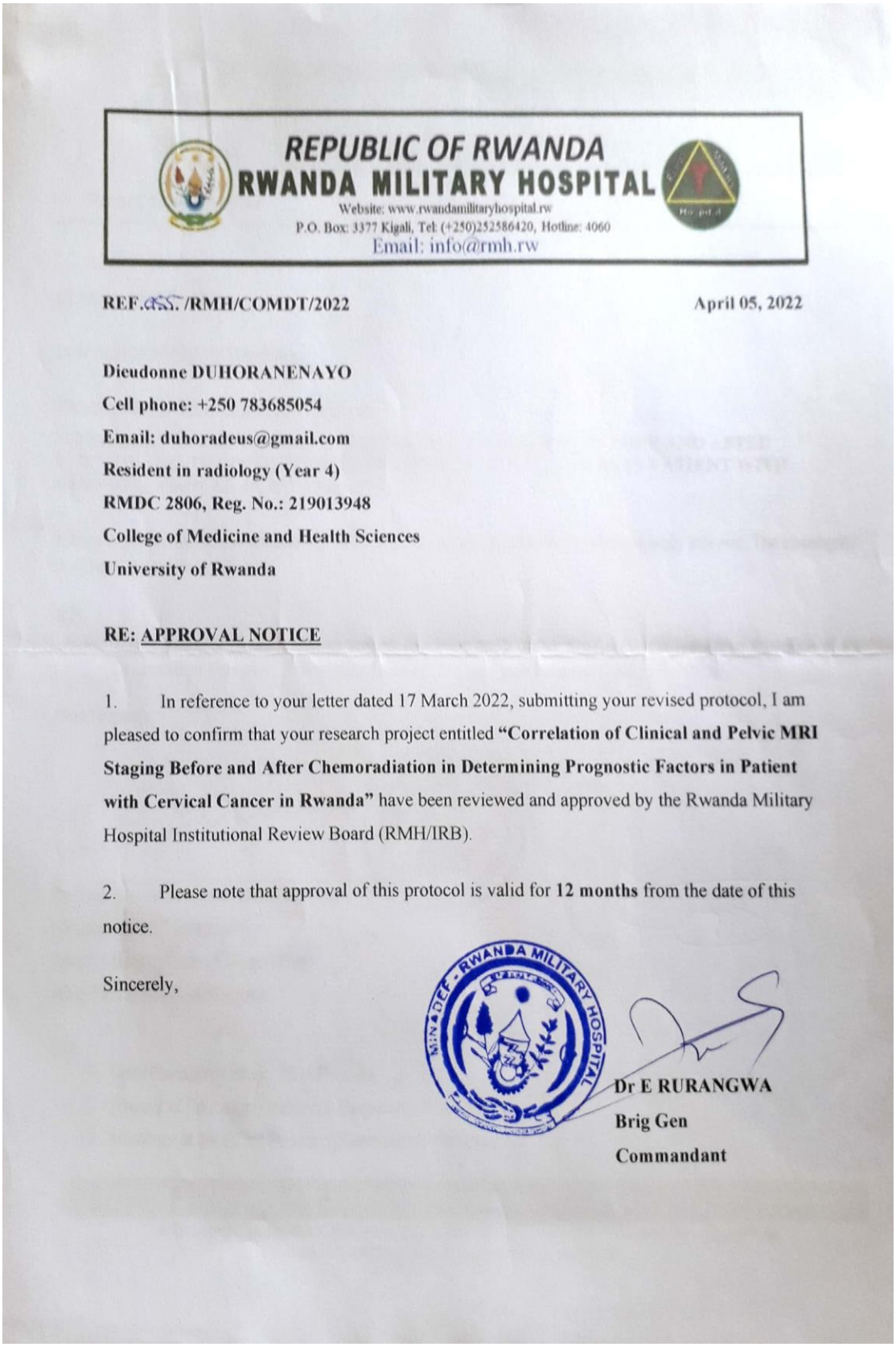
Date of Approval: The 31st January 2022

Expiration date: The 31st January 2023

Assoc. Prof. Stefan Jansen
Ag. Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

VI.5. Copy of Rwanda Military Hospital – IRB approval



REPUBLIC OF RWANDA
RWANDA MILITARY HOSPITAL
Website: www.rwandamilitaryhospital.rw
P.O. Box: 3377 Kigali, Tel: (+250)252586420, Hotline: 4060
Email: info@rmh.rw

REF.055 /RMH/COMDT/2022 April 05, 2022

Dieudonne DUHORANENAYO
Cell phone: +250 783685054
Email: duhoradeus@gmail.com
Resident in radiology (Year 4)
RMDC 2806, Reg. No.: 219013948
College of Medicine and Health Sciences
University of Rwanda

RE: APPROVAL NOTICE

1. In reference to your letter dated 17 March 2022, submitting your revised protocol, I am pleased to confirm that your research project entitled **"Correlation of Clinical and Pelvic MRI Staging Before and After Chemoradiation in Determining Prognostic Factors in Patient with Cervical Cancer in Rwanda"** have been reviewed and approved by the Rwanda Military Hospital Institutional Review Board (RMH/IRB).

2. Please note that approval of this protocol is valid for **12 months** from the date of this notice.

Sincerely,

MINADEF - RWANDA MILITARY HOSPITAL

Dr E RURANGWA
Brig Gen
Commandant

VI.6. Copy of King Faisal Hospital (KFH) – IRB approval

KING FAISAL HOSPITAL, RWANDA
ETHICS RESEARCH COMMITTEE

Patient Centered Care

6th, MAY 2022

ETHICAL APPROVAL

Dear DUHORANENAYO Dieudonne,

We acknowledge receipt of your study protocol:

"CORRELATION OF CLINICAL AND PELVIC MRI STAGING BEFORE AND AFTER CHEMORADIATION IN DETERMINING PROGNOSTIC FACTORS IN PATIENT WITH CERVICAL CANCER IN RWANDA."

After a thorough review, the reviewers of KFH Ethics Research Committee consider this study relevant. The investigator is allowed to start data collection.

N.B.

- The investigator is ***requested to submit one hard copy of his final research results*** in the office of the Directorate of Education, Training and Research at King Faisal Hospital, Kigali

Best Regards

Dr. Dushimiyimana Jean Marie Vianney
Consultant ENT surgeon
Chair, Ethics Research Committee
King Faisal Hospital, Rwanda.

CC:

1. Chief Executive Officer_ KFH-Rwanda
2. Director of Education, Training & Research_KFH- Rwanda
3. Members of the Ethics Research Committee, KFH- Rwanda