UNIVERSITY of RWANDA

PATHOLOGY CHARACTERISTICS, PROGNOSTIC DETERMINANTS AND THE OUTCOME OF PATIENTS DIAGNOSED WITH COLORECTAL ADENOCARCINOMA AT UNIVERSITY TEACHING HOSPITAL OF KIGALI

Delphine Uwamariya, MD

Master of Medicine (Anatomical Pathology) Dissertation

University of Rwanda

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by

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A Dissertation Submitted in Partial Fulfilment of the requirements for the Degree of Master of Medicine (Anatomical Pathology) of the

University of Rwanda.

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University of Rwanda

December 2021

CERTIFICATION FOR AWARD

The undersigned certify that they have read and hereby recommend for examination by the University of Rwanda a dissertation entitled "**Pathology characteristics, prognostic determinants and the outcome of patients diagnosed with colorectal adenocarcinoma at University Teaching Hospital of Kigali**" in partial fulfillment of the requirements for the Degree of Master of Medicine (Anatomical Pathology) of the University of Rwanda.

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(Co-Supervisor)

Date: 2021-12-20

DECLARATION AND COPYRIGHT

This thesis is my original work and has not been presented in any institution leading to the award of a degree or any other award.

Signature 

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Last but not definitely least I thank my almighty God for the grace and forgiveness to me.

Delphine Uwamariya

DEDICATION

To my husband Mr Augustin Nzitakera

To lovely mother Mrs Venantie Musomandera

To my son Plaisir Junior Ndamukunda and

To my daughter Precious Liana Ndamukunda

I dedicate this dissertation

ABSTRACT

Colorectal cancer (CRC) is the second most diagnosed cancer in female and the third in men worldwide, arising from the epithelium of the colon and the rectum. It is known that colorectal cancer is common in developed countries than in developing countries, the latter being mainly located in Africa. However, this may be due to inaccurate data on the existence of the disease in that region combined with embracing western lifestyle expressed by the current trend of changes in cultural, social, and lifestyle practices playing a major part in the etiology of the cancer.

The present study was conducted document the epidemiological and pathological characteristics and prognostics determinants of patients diagnosed with colorectal adenocarcinoma in Rwanda. This data would be used in deferent sectors to improve diagnostic, preventive and therapeutic interventions and reduce the CRC-associated morbidity and mortality.

Ethical approval from the Institutional Review Board (IRB) of the University of Rwanda (UR) College of Medicine and Health Sciences (CMHS) and study permission from the study-hosting hospital were obtained prior to data collection. From the records in histopathology unity at University Teaching Hospital of Kigali (CHUK), 101 resection colorectal specimen were retrieved and all Hematoxylin and Eosin (H&E-stained) glass-slides were reviewed for diagnosis confirmation, tumor grading, tumor staging and other prognostic determinants including, margins status, inflammatory reaction, lympho-vascular and perineural invasion. Patients' files were consulted for epidemiologic and clinical information.

The mean age of participants was 54.26 (range 17–89) years. There was a slight female predominance (52.5%). Kigali City was over-represented (32.7% of participants). The main symptom was rectal bleeding (n=47 or 46.5%); the duration of symptoms was <6 months in 53 (52.5%) cases. The rectal adenocarcinoma NOS represented 40.6% of all CRC cases. The majority (n=56; 55.4%) of CRC diagnosed at CHUK showed microscopic tumor border with irregular infiltrating pattern and the conventional adenocarcinoma was the most frequent (n=61; 60.4%) histologic type. In addition, most tumors were of Grade II (n=55; 54.5%) while the most common stage was pT3N0 with a frequency of 21 (20.8%). Resection margins were free of tumor in 72 (71.3%) cases. Lympho-vascular invasion was present in 51 (49.5%) cases, while perineural invasion was seen in 29 (28.7%) cases. There was a high immune response in 72

(71.3%) cases. Of 101 patients diagnosed with CRC from the year 2014 to 2020, 56 (55.4%) were still alive at the end of the data collection, and 29.3% have overall survival of 5 years.

The results of this study give a broad picture of colorectal adenocarcinoma patients in in Rwanda in terms of clinical pathologic characteristic and prognostic determinants and most of colorectal adenocarcinoma Rwandan patients are older (>50years). Inflammatory response, lympho-vascular invasion, perineural invasion and tumor border are some of prognostic determinants which have strong association with tumor differentiation which also affect the outcome of CRC patients.

Key words

Colorectal adenocarcinoma; pathologic characteristics; prognostic determinant; outcome.

LIST OF ABBREVIATIONS

AJCC: American Joint Committee on Cancer

ASCO: American Society of Clinical Oncology

CDX2: Codal type homeobox transcription factor 2

CHUK: Centre Hospitalier Universitaire de Kigali

CRC: Colorectal Cancer

CT: Computer Tomography

DNA: Deoxyribonucleic Acid

FAP: Familiar Adenomatous Polyposis

FIT: Fecal Immunochemical Test

gFOBT: guaiac based Fecal Occult Blood Test

GI: Gastro Intestinal

GLOBOCAN: Global Cancer Observatory

hMLH1: MutL homolog 1

hMSH2: MutS protein homolog 2

hMSH6: MutS homolog 6

HNPCC: Hereditary non-Polyposis Colorectal Cancer

hPMS2: Human Postmeiotic Segregation Increased, S. Cerevisiae 2

IHC: Immunohistochemistry

LN: Lymph node

LVI: Lympho-vascular invasion

MMR: Mismatch Repair

NOS: Not otherwise specified

PNI: Perineural invasion

TNM: Tumor, Node, Metastasis

UICC: Union for International Cancer Control

U.R: University of Rwanda

WHO: World Health Organization

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CHAPTER I. INTRODUCTION

1.1 Background

Worldwide, CRC is at 3rd position after breast and lung cancer (1). There is a perception that colorectal cancer is more frequent in developed countries due to their western diet and may be an uncommon disease in Sub-Saharan Africa (1). However, this may be related to poor epidemiological data on cancer in general in that region. African countries are embracing the civilization which may play a big role in the increase of colorectal cancer incidence and also raise the burden of the disease in the region (2).

Colorectal carcinoma occupies 90-95% of all colorectal malignancies and more than 90% of colorectal carcinomas are adenocarcinomas originating from epithelial cells of the colorectal mucosa (3,4). Other rare types of colorectal carcinomas include neuroendocrine, squamous cell, adeno-squamous, spindle cell and undifferentiated carcinomas. The present study focused on adenocarcinoma category in which the main subtype is conventional adenocarcinoma and is characterized by glandular formation which also plays the major role on the concept of histologic tumor grading .

Data related to colorectal adenocarcinomas in Rwanda are scanty except few epidemiological information from our national cancer registry. The purpose of this study is to provide basic clinico-pathological information, available prognostic determinants and the outcome of patients diagnosed with colorectal adenocarcinomas in Rwanda which can help to develop strong measures in terms of prevention and control of the disease in the country.

1.2 Problem statement

Data concerning colorectal cancer rates and pathology prognostic information are scanty in Rwanda, yet it is known that these data are very important in guiding policy makers to plan for interventions (In terms of prophylactic, diagnostic, therapeutic and research). Therefore, there is a need of having a broad picture of data on colorectal cancer in our settings in regard to pathology prognostic determinants, staging in order to use those data in planning patient's management.

1.3 Study rationale

This study will bring a great contribution about knowledge on colorectal cancer in our health institutions. We hope that data from this study will be used by oncology and pathology services when needed to enrich their knowledge about epidemiology, pathology, prognostic determinants, and the outcome for colorectal cancer patients and also guide policy makers and health administrators in their planning. As a resident in pathology, this study has contributed a lot in increasing my capacity in regard to microscopic diagnosis of colorectal cancer as I had to review many glass slides which increased my practical exposure to this type of cancer.

1.4 Study objectives

1.4.1 Main objective

To describe pathology characteristics and prognostic determinants of colorectal adenocarcinomas at CHUK in 2014-2020.

1.4.2 Specific objectives

1)To determine the clinical and epidemiological characteristics of patients with colorectal adenocarcinoma attending CHUK in 2014-2020.

2) To describe the histopathological characteristics of colorectal adenocarcinomas diagnosed at CHUK in 2014-2020.

3)To determine the available pathologic prognostic determinants of colorectal adenocarcinomas diagnosed at CHUK in 2014-2020.

CHAPTER II. LITERATURE REVIEW

2.1 Epidemiology, risk factors and protective factors of colorectal cancer

2.1.1 Incidence and mortality

Colorectal cancer (CRC) incidence and mortality varies around the world. It is estimated as third most common cancer diagnosed in males and the second in females, with the recent GLOBOCAN database of 2020 giving a number of 1.14 million new cases in 2020 (1). In Africa, CRC occupies the 5th position after breast, cervix, prostate, and liver with around 70,000 new cases in 2018 making around 6% of all cancers. Globally, the mortality reported by GLOBOCAN 2020 was 576,858 deaths. Higher incidence rates are found in Europe, North America, New Zealand and Australia while lower incidences are found in Africa and South Central Asia (5). In the East African region, a study conducted in Tanzania in 2015 found a 2% increase of colon cancer every year from 2005 to 2015 (2).

In Rwanda, preliminary data from Rwanda National Cancer Registry showed that CRC is at 6th position after breast, cervix, stomach, prostate and hematological malignancies, with 4% in 2018 data (6). Age is considered a major risk for CRC. It is not common to see CRC before 40 years of age and the incidence increases between 40 years and 50 years. There is a tendency of increase of colorectal cancer among under 50 years aged patients (7). Studies have also identified low socioeconomic status as a risk factor, with a 30% increase risk of CRC compared with higher socioeconomic status, all other risk factors accounted (8). The overall trend of incidence of CRC shows an increase of incidence in low- and middle-income countries while a decrease is observed in high income countries. This may reflect adoption of western lifestyles by populations in low-income countries (9).

The mortality of CRC has been stable or decreasing between 1.4%-1.8% in western countries mainly due to improvements in detection and removal of colonic polyps, detection of tumors at early stage, best primary and adjuvant treatments and well-established screening programs (10). However, the mortality of CRC in more limited resources countries continues to increase (11).

2.1.2 Risk factors

Concerning the risk factors associated with CRC, the inherited susceptibility is the most striking factor with increased high risk of developing CRC. However, majority of CRC are sporadic, rather than familial, giving a weight to environmental factors (12). Risk factors can be subdivided in two groups: those that can have power to influence screening recommendation and those which have low or uncertain risk. The following paragraphs discuss the factors influencing the screening of CRC.

-*Hereditary syndromes*: There are several genetic abnormalities that can be inherited in autosomal dominant form, but the most common are Familial adenomatous polyposis (FAP) and Lynch syndrome (hereditary nonpolyposis colorectal cancer, HNPCC). However, together these two conditions account for only approximately 5 percent of CRC cases, the majority of which are Lynch syndrome (13). Lynch Syndrome is more common than FAP and accounts for approximately 3 percent of all colorectal adenocarcinomas. The syndrome is caused by a defect in one of the DNA mismatch-repair (MMR) genes, most commonly *hMLH1*, *hMSH2*, *hMSH6*, or *hPMS2*. Patients have a germline mutation in one of the two alleles and the second allele will undergo a somatic inactivation mutation. As a result, these types of CRC have impaired DNA MMR and microsatellite unstable. Patients in this category develop tumors at younger age, with predominance of right-sided tumors (14).

-*Personal and family history of sporadic CRC and adenomatous polyps*: patients in this category are at risk of developing CRC in the future. Adenomatous polyps of more than 1 cm, and polyps with villous or tubulo-villous histology or with high-grade dysplasia also increase the risk of CRC, n particularly if multiple (15). Family history of CRC in a first degree relative (parent, sibling or child) has also been reported to increase the risk of developing CRC by twofold over that of general population (16).

-*Inflammatory bowel diseases*: Ulcerative colitis has been described among factors that increase the risk of developing CRC up to 5-15fold increase in risk compared to general population. Extent, duration and activity of colitis are also known as key determinants (17). A similar relative risk has also been reported with Crohn disease.

-*Abdomino-pelvic radiation*: Patients who underwent this type of radiation in the setting of cancer treatment in the past were reported to be at increased risk for other GI tumors, the most

common being CRC. This has mainly been observed in pediatric patients where the Children Oncology Group recommends a follow up colonoscopy every 5 years for children's survivors of cancer who received abdomino-pelvic radiation in the past (18).

-*Risk factors that do not alter screening recommendation:* These include obesity, frequently eating red and processed meat, alcohol consumption and cigarette smoking. They have been reported in several meta-analysis studies.

2.1.3 Protective Factors

-*Physical activity*: Several studies have reported the benefit of physical activity in preventing CRC and other different types of cancer (19). The mechanism underlying this is not yet fully understood and there are no trials for physical activities and CRC has been reported.

-*Diet*: A dietary fiber and consumption of fruits and vegetables on daily basis have also been reported in protecting against CRC in several systematic meta-analysis studies (20).

2.2 Screening for colorectal cancer

Screening for CRC can identify premalignant lesions or detect early-stage asymptomatic small tumors. The natural history of CRC allows it to be screened as it is commonly starting as small adenomatous colon polyps of < 8mm that evolve into larger polyps, followed by dysplasia and carcinoma. The progression from adenoma to carcinoma can approximately take at least 10 years (20). Well established screening programs have helped developed countries to lower the incidence and mortality of CRC (21). Many guidelines recommend initiating screening at age of 50 years and discontinue the process at 75 years of age for average risk persons. Most CRC occur over 50 years and choosing this age was important in balancing between the benefits of detection and prevention and potential burden of screening process (22). Members of families with high risk may be screened earlier as the disease tends to occur before the age of 50 years.

Different screening tests have been developed from stool-based tests (FIT=fecal immunochemical test; FIT-DNA=multitargeted stool DNA test; gFOBT=guaiac-based fecal occult blood test) to direct visualization tests based on colonoscopy (Colonoscopy, CT colonography, Flexible sigmoidoscopy, Flexible sigmoidoscopy with FIT). The choice of the test will be guided by comfort, cost, availability, test safety, effectiveness and preferences of the patient and should be a shared decision making. Colonoscopy every 10 years is preferred but in

setting where it is not possible, a stool-based test can be done annually but keeping in mind that when a stool-based test is positive, a colonoscopy should be performed.

2.3 Clinical presentation, Diagnosis and Staging of Colorectal cancer

2.3.1 Clinical presentation

Majority of patients at early stage do not have symptoms and are detected during screening process. However, 70-90% of patients are symptomatic at time of diagnosis. Typical symptoms may be hematochezia or melena, otherwise unexplained iron deficiency anemia, abdominal pain or a change in bowel habits. In resource limited setting, patients have tendency to present at advanced stage with signs of intestinal obstruction, peritonitis or GI bleeding (23). Symptoms may also differ according to the tumor location: Change in bowel habits is more common with left-sided tumors than right-sided CRCs because the stool is more liquid when still on right side, with a larger diameter on right colon, hence less likely to cause obstruction. Hematochezia is common with rectosigmoid tumors and iron deficiency anemia of unexplained blood loss is common with right-sided CRCs (24). CRC can spread through hematogenous, or lymphatic ways and patients can present signs according to the location of metastatic deposits at time of diagnosis. The most common metastatic sites are the regional lymph nodes, liver, lungs, and peritoneum. Considering the portal system as the venous drainage of colorectum, the most common hematogenous spread is the liver, followed by the lung, bones and other sites including the brain.

2.3.2 Diagnosis and Pathology of CRCs

Colonoscopy is the most accurate diagnostic procedure as it is followed by a biopsy which will confirm the histology diagnosis. Pathology will provide diagnosis as well a full range of information of prognostic value:

-*Gross appearance*: Tumors in the right colon are mainly polypoid, fungating, exophytic masses. In contrast, tumors in the left or distal colon are more commonly annular or encircling lesions with a classical napkin-ring picture, causing narrowing of the lumen and associated with constipation, diarrhea, and bowel obstruction.

-*Histology of CRC*: the vast majority are Carcinomas. Table 1 is a WHO classification of colorectal carcinomas.

Table 1. WHO (5th Edition, 2019), classification of colorectal carcinomas.

Adenoma like Adenocarcinoma
Medullary carcinoma
Micropapillary carcinoma
Mucinous (colloid) adenocarcinoma (>50%mucinous)
Serrated adenocarcinoma
Signet-ring cell carcinoma (>50% signet-ring cells)
Adeno-squamous carcinoma
Poorly cohesive carcinoma
Carcinoma with sarcomatous component
Carcinoma, undifferentiated, NOS

NOS: not otherwise specified; WHO: World Health Organization

Some of the morphologic variants carry a prognostic significance: the signet ring morphology is aggressive with an overall poor prognosis, while the medullary type is associated with deficiency in MMR proteins and has a relatively favorable prognosis (25).

-*Immunohistochemistry:* Although IHC is not commonly used for primary diagnosis of CRCs, Cytokeratin 20 and CDX2 are two of the most used markers of intestinal differentiation and are useful in identifying adenocarcinomas of colorectal origin (26) as well as SATB2 which is more specific for cancer originating from the colon (27).

-*TNM* staging: It is now recommended to use the tumor, node, metastasis (TNM) staging system of the American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) and the older Duke's classification is no longer used. The following is the recent 8th edition of CRC TNM staging:

Table 2: Pathologic Stage Classification of CRC (AJCC Staging manual, The 8th edition, 2020).

Parameters	Representation	Explanations
Primary tumor	Tx	Primary tumor cannot be assessed
	T0	There is no evidence of primary tumor
	Tis	The tumor is within the mucosa
	T1	Primary tumor invades up to the submucosa
	T2	The tumor invades up to muscularis propria
	T3	Tumor invades up to the subserosa
	T4	There is evidence of invasion of peritoneal visceral or adjacent organs
Assessment of LN	Nx	LN cannot be assessed
	N0	No Regional LN metastasis
	N1	1-3 LN are positive with the tumor
	N2	4 or more LN positive with the tumor
Assessment of distant Metastasis	M1	Metastasis to distant site or organ also with peritoneal metastasis
	M1a	Metastasis to one site without peritoneal metastasis
	M1b	Metastasis to 2 or more sites without peritoneal metastasis
	M1c	Peritoneal metastasis with or without metastasis to another site

CRC: Colorectal Cancer, AJCC: American Joint Committee on Cancer, T: Tumor, LN: Lymph-node, M: metastasis

2.4 Prognostic determinants of CRCs

The most common indicator of outcome after resection of CRCs is the pathologic stage. We can highlight the following prognostic determinants that make the staging classification:

-***Local extent of the tumor***: The depth of invasion in the colonic wall has independent prognostic information and influences survival (28).

-***Residual tumor***: The presence of a residual tumor is also another feature of poor prognosis. The residual disease is coded as following in the TNM system:

- R0= Completely resected tumor with uninvolved margins

- R1= Incomplete resection with microscopic tumor involving resection margins (but no gross involvement of margins)
- R2= Incomplete tumor resection with grossly present unresected tumor on the margins

-***Regional nodes****:* Regional lymph nodes involvement is among strongest predictors of outcome after CRC resection and comes at the second position after presence of distant metastases. The presence of involved nodes is an indication for adjuvant therapy. Some studies have even found that the presence of involved lymph nodes is a factor of intrinsic metastatic potential of the tumor (29). The number of positive nodes is a strong predictor of outcome. N1 and N2 status can influence the outcome regardless of the T status in CRC (30). Pathologists should also remember that the total number of harvested nodes in the resection specimen of CRC has an influence on the prognosis in the node negative disease as well as in the node positive disease. This is why it is recommended to harvest at least 12 lymph nodes to increase the likelihood of a proper staging (31). If fewer than 12 lymph nodes are found in the specimen, techniques like fat clearing and methylene blue staining have been described to increase their number (32).

-Lymphovascular invasion and perineural invasion*:* The lympho-vascular and perineural invasions also provide important prognostic information. Both veins and lymphatic invasion carry independent prognostic factors. It is one of clinico-pathological factors to classify "high risk tumors" of stage II category by American Society of Clinical Oncology (33).

- ***Signet ring, mucinous, poorly differentiated, or undifferentiated tumors***: Poorly differentiated tumors carry an inferior prognosis and are criteria to be classified in "high risk stage II CRC in the ASCO guidelines as described above when tumors are mismatch repair stable. Mucinous carcinomas are those with 50% or above amount of mucin production. Some data suggest that the presence of mucin carry an inferior prognosis in rectal but not colonic tumors (34).

-***Tumor border***: An irregular, infiltrating pattern of growth at the advancing edge of the tumor carries prognostic significance, independently from tumor stage, compared to a smooth pushing expansile border (34).

-***Tumor infiltrating lymphocytes*****:** The presence of tumor infiltrating lymphocytes is a sign of host immune response and carries a better prognosis in many types of cancer including CRC. It indicates that the defensive host mechanisms were functioning (35,36).

-***Tumor budding***: This is an independent prognostic factor in colorectal carcinoma which is associated with lympho-vascular invasion, perineural invasion, lymph node and distant metastasis and also, research has shown that tumor budding is associated with high TNM stage (37).

***-Presence of bowel obstruction or perforation at presentation*:** Bowel obstruction or perforation has been described as factors associated with poor survival in many studies. They are both in factors that define "high risk stage II patients" by ASCO as described above (38).

2.5 Treatment of colorectal cancer

CRC is treated according to the stage of the disease as well presence or absence of features of high risk as described above. Surgical resection of tumor by colectomy is the preferred choice for early and locally advanced disease. Neoadjuvant chemotherapy can be administered for big unresectable tumors, followed by surgery. Stage I CRC is treated with surgery alone. Stage II without features of high risk (also called stage II low risk) can be treated with surgery and observation. Stage II with features of high risk (Poorly differentiated (except in MMR deficiency), less than 12 nodes examined, extensive lympho-vascular invasion, extensive perineural invasion, bowel obstruction, perforation, positive surgical margins) will be treated with surgery followed by adjuvant chemotherapy (39).

CHAPTER III. RESEARCH METHODS

3.1 Research setting

The present study was conducted at the University teaching hospital of Kigali (CHUK) histopathology laboratory unit. University Teaching Hospital of Kigali is a tertiary referral hospital and the largest university teaching hospital in the country with 519 beds. The Histopathology unit has started its activities in October 2013 and perform analysis of approximately 3203 surgical pathology specimens (biopsies and resections) and 975 cytology specimens per year. It has only 5 general pathologists and it is one of main centers for anatomic pathology training in Rwanda. No sub specialization available for the whole country.

3.2 Research design

This was a retrospective descriptive study extending from 1st January 2014 to 31st December 2020. This was an observational study that reviewed tissue biopsies whose diagnosis was consistent with colorectal adenocarcinoma. On top of histological re-examination, this study was also done by looking backwards to clinical data from the patients' files during the above period, and this type of study was done in order to determine the pathology characteristics, prognostic determinants and the outcome of patients diagnosed with colorectal adenocarcinoma at the University Teaching Hospital of Kigali (CHUK). This study design was very important because it covered a wider period of seven years, which would have been almost impossible prospectively for a student whose program runs for 4 years.

3.3 Study population

This study targeted all cases with confirmed colorectal adenocarcinoma diagnosed at the University Teaching Hospital of Kigali during the year 2014 to 2020.

3.4 Inclusion and exclusion criteria

Biopsies and files whose patients underwent surgical resection were included in the study. Biopsies and files from non-operated patients were excluded as they could not provide most pathology/prognostic data to be collected.

3.5 Sample size

The study sample was calculated using the formula for single proportion as following:

$$n = \frac{Z^2 \times P(1-P)}{d^2} = \frac{1.96^2 \times 0.065(1-0.065)}{0.05^2} = 93.4 \approx 94$$

Where, **n** is the sample size; **z** is the confidence interval, **p** is the estimated proportion and **d** the desired precision.

3.6 Data collection and analysis

Patient's files from the CHUK main archive and accession books were used to retrieve clinical information and accession number of colorectal specimens respectively and slides were retrieved together with specimen submission form for collection of additional clinical information. Slides were retrieved from CHUK archives to review all above mentioned pathology information and tissue blocks for some missing or damaged glass-slides were retrieved to be recut. A data collection tool was designed with all variables to be collected.

Patient characteristics are described as mean for quantitative variables, and as frequency (percentage) for categorical variables. Comparisons were performed using Chi square tests, Fisher 'exact test and Odd ratio with 95% confidence interval (CI) as appropriate. We measured survival as the time from the date of diagnosis until the date of death, regardless of the cause, or loss to follow-up, or censoring on 31st December 2020. Survival curves were plotted using the Kaplan–Meier method. The log-rank test was used to assess the statistical differences in the observed survival curves by each categorical variable. For all analyses, a *P* value <0.05 was considered statistically significant. Statistical analyses were performed using Statistical Product and Service Solutions (SPSS) version 26 (IBM Corporation, New York 10504-1722, USA), GraphPad Prism (GraphPad Software, Inc., CA 92037 USA) version 9, accordingly and MedCalc (MedCalc Software, Mariakerke, Belgium) v.10.2.0.0.

3.7 Pathology characteristics definitions

For the grading, we used the WHO 5th Edition grading system. For inflammatory reaction, we graded it according to Klintrup–Mäkinen (KM) system. Stage Grouping were done according to WHO (5th Edition) TNM classification of tumors of the colon and rectum.

3.8 Reliability and validity of the results

Data that were extracted from patients' archives were double checked by both the researcher and the research assistant. During histopathological review, the researcher, in this case the resident pathologist reviewed the tissue slides under the supervision of a senior pathologist. Where possible a second opinion would be sought from the third party.

3.9 Ethical considerations

Ethical clearance was requested from the Hospital research and Institutional Review Board. Once granted, the permission to carry out the study was sought from the Hospital administration as well as IRB. Considering that no additional sample, procedure or any interview was required to patients and a consent form was not necessary.

All patients' data were anonymous and were kept with confidentiality. With that, patients' personal identifiers were not appearing on the data collection form to assure patients' confidentiality, each case was identified by a given code corresponding to (but different from) the accession number and all identified patient information was stored on an encrypted flash drive and a personal password protected computer.

CHAPTER IV. RESULTS

4.1 Clinical and epidemiological characteristics of the study participants

Table 3 is showing clinical and epidemiologic data. During the study period a total number of 101 colorectal resection specimens were collected for the study.

Table 3. Distribution of age, sex, residence, main symptoms, duration of the symptoms and biopsy site for the study participants

Characteristics	n	Percent
Age (n=101)		
≤ 24	2	2
25 - 34	11	10.9
35 - 49	27	26.7
50 - 64	29	28.7
65 - 79	29	28.7
≥ 80	3	3
Sex (n=101)		
Male	48	47.5
Female	53	52.5
Residence (n=101)		
Eastern	17	16.8
Kigali City	33	32.7
Northern	13	12.9
Southern	25	24.8
Western	13	12.9
Main Symptom (n=101)		
Abdominal pain	25	24.8
Constipation	1	1
Obstruction	19	18.8
Perforation	9	8.9
Rectal bleeding	47	46.5
Duration of symptoms (n=101)		
< 6 months	52	51.5
> 24 months	4	4
13-24 months	7	6.9
7-12 months	38	37.6
Anatomic site (n=101)		
Ascending colon	28	27.7
Descending colon	27	26.7
Rectum	41	40.6
Transverse colon	5	5

N= number

Patients' demographic and clinical information were retrieved from the archive of the University Teaching Hospital of Kigali (CHUK). The age of participants ranges between 17 to 89 years with a mean age of 54.26. Female were 53 (52.5%), males were 48 (47.5%) and the predominating age group were 51-75 which comprises 54 patients. Many of the attendees were coming from Kigali city with a number of 33 (32.7%) and West and North provinces were the residences providing a small number of patients, each of them provided 13 (12.9%) cases. The main symptom was rectal bleeding with a frequency of 47 (46.5%) and the duration of symptoms was less than 6 months with a frequency of 53 (52.5%). A high number of tumors was found to arise in the rectum 41 (40.6%).

4.2 Gross appearance and histopathological characteristics of colorectal carcinomas

Table 4 is showing information about the gross appearance of the tumor which was found in the archived reports of patients in CHUK Laboratory and all glass slides for each case were retrieved and re-examined for diagnosis confirmation. The majority of CRC diagnosed at CHUK showed infiltrating pattern with a frequency of 69 (68.3%) and the conventional adenocarcinoma was the main histologic type, it accounted for 61 (60.4%) cases.

Table 4. Gross appearance and histopathological characteristics of colorectal carcinomas.

Characteristics	Number	Percent
Gross appearance (n=101)		
Infiltrating	69	68.3
Polypoid	32	31.7
Histologic type (n=101)		
Adenocarcinoma	61	60.4
Mucinous adenocarcinoma	40	39.6

N= number

4.3 Pathologic prognostic determinants of colorectal carcinomas

Table 5 is showing the distribution of prognostic determinant where many tumors were of Grade II with a frequency of 55 (54.5%) and the most common staging group was stage III with a frequency of 22 (21.8%) however most of the patients 31(30.7%) were not staged due to lack of their clinical stage. A total number of 72 (71.3%) specimen were having radial margins which are free from the tumor and no case was found with proximal or distal margins positive.

Most of tumor border was irregular infiltrating in 56 (55.4%); there was no lymph vascular invasion in 52 (51.5%) specimens and no perineural invasion in 72 (71.3%) specimens. There was a high immune response in 72(71.3%) cases.

Table 5. Pathologic prognostic determinants of colorectal carcinomas

Characteristics	**Number**	**Percent**
Tumor grade (n=101)		
Grade I	28	27.7
Grade II	55	54.5
Grade III	18	17.8
Tumor stage (n=101)		
Stage I	10	9.9
Stage II	21	20.8
Stage III	22	21.8
Stage IV	17	16.8
No stage	31	30.7
Margin status (n=101)		
Negative radial margin	72	71.3
Positive radial margin	29	28.7
Lympho-vascular invasion (n=101)		
Not present	52	51.5
Present	49	48.5
Perineural invasion (n=101)		
Not present	72	71.3
Present	29	28.7
Tumor border (n=101)		
Expansile	45	44.6
Irregular infiltrating	56	55.4
Immune response (n=101)		
High	72	71.3
Low	29	28.7

N= number

4.4 Inflammatory response

Figure 1 is showing immune cell infiltrates characterization where most of CRC specimen (72,71.3%) were considered to have high immune response.

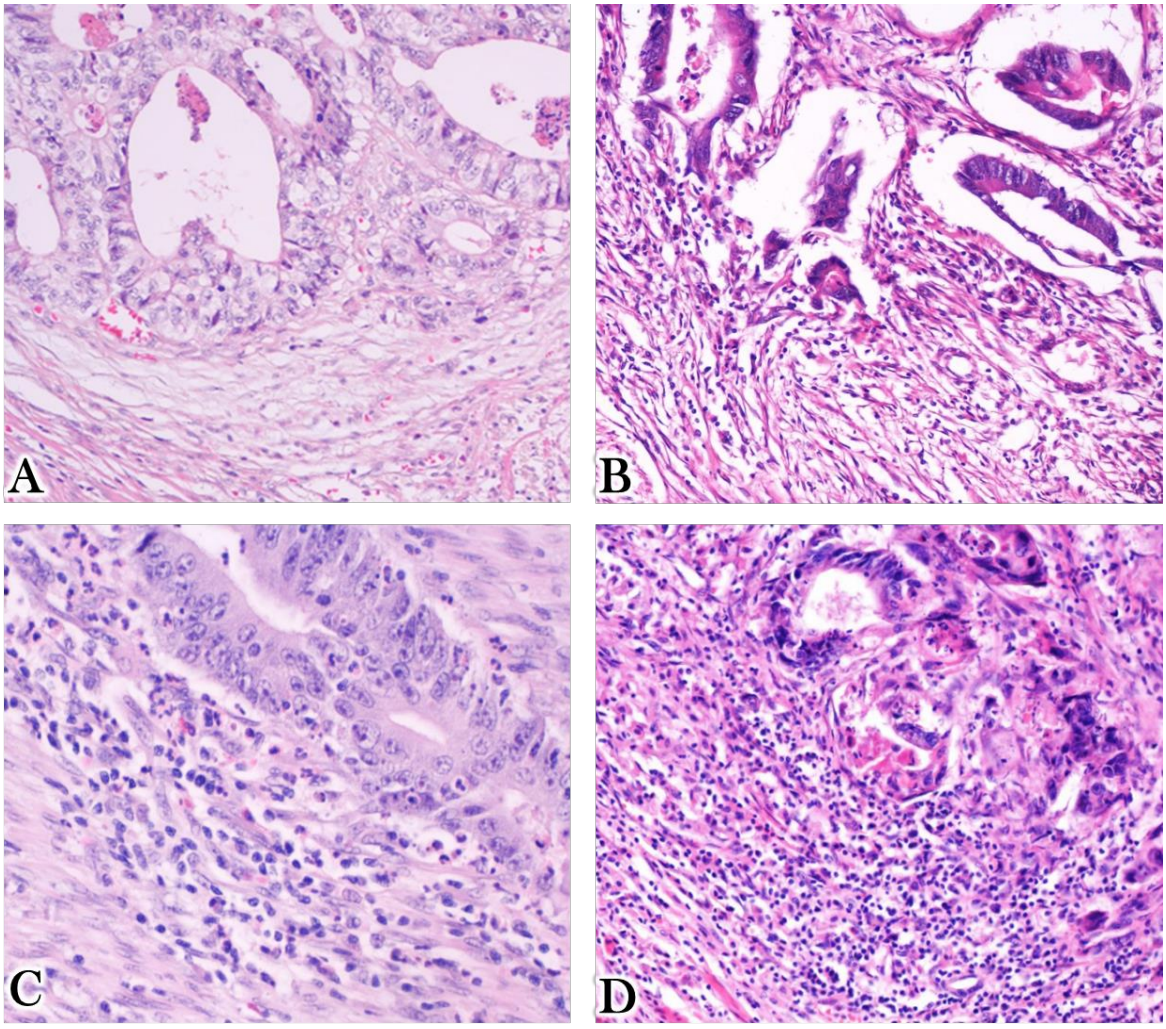

Figure 1. Microphotographs illustrating inflammatory response

***A**: Score 0, **B**: Score 1, **C**: Score 2, **D**: Score 3. For interpretation, scores 0 and score 1 are considered low immune reaction while scores 2 and score denote high immune reaction.*

4.5 Microscopic tumor border

Figure 2 is showing what means infiltrating tumor border or expansile tumor border where most of study participants (56 = 55.4%) were having irregular infiltrating tumor border.

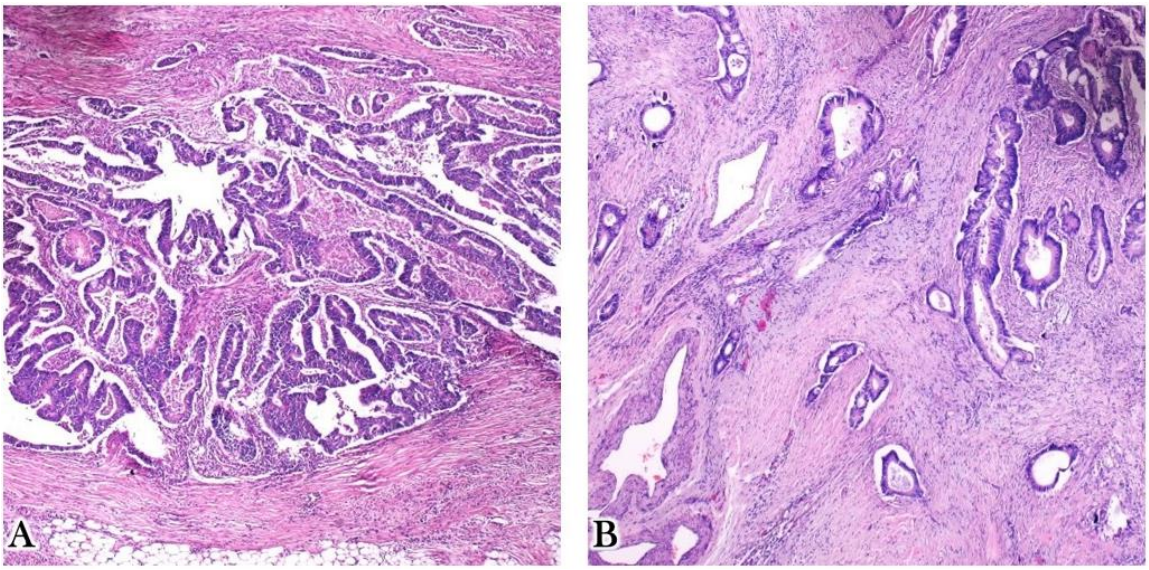

Figure 2. Microphotographs illustrating tumor borders

A*: Expansile tumor border;* ***B****: Infiltrating tumor border.*

4.6 Association between different variables.

Table 6 is showing correlation between sex and age groups where it shows that being male by gender prone someone to develop CRC at younger age 2.7 times more than female and this is statistically significant with an OR= 2.7 (95%CI = 1.2 – 6.2) and *P*-value= 0.01.

Table 6. Correlation between sex and age group

	Age group		*OR (95% CI)*	*P*
	<50	>50		
Sex (n=101)				
Male	26	22	2.7 (1.2 – 6.2)	0.01
Female	16	37		

P value by Fisher's exact test, N= number, OR: Odd ratio, CI: Confidence interval

Table 7 is showing correlation between some prognostic determinants and tumor grade & stage. From the table, it is shown that all prognostic determinants studied are associated with tumor grading and it is statistically significant for all.

Table 7 Correlation between prognostic determinants and tumor grade & stage

Characteristics	*Tumor grade*		*OR (95% CI)*	*P**	*Tumor stage*		*OR (95% CI)*	*P*
	Low	*High*			*Low*	*High*		
Immune response	*(n=101)*				*(n=70)*			
High	42	30	2.6 (1.1 – 6.5)	0.03	27	27	2.2 (0.7 – 7.2)	0.19
Low	10	19			*5*	*11*		
Lymphovascular invasion	*(n=101)*				*(n=70)*			
Not present	38	14	6.7 (2.8 – 16.2)	<0.0001	19	21	1.18 (0.4 – 3.0)	0.7
Present	14	35			13	17		
Perineural invasion	*(n=101)*				*(n=70)*			
Not present	43	29	3.29 (1.3 – 8.24)	0.01	20	26	0.76 (0.3 – 2.0)	0.6
Present	9	20			12	12		
Tumor border	*(n=101)*				*(n=70)*			
Expansile	30	15	3.1 (1.4 – 7.0)	0.007	17	13	2.17 (0.8 – 5.7)	0.11
Irreg. infiltrating	22	34			15	25		
Margin status	*(n=101)*				*(n=70)*			
Neg radial marg.	46	26	6,7 (2.4 – 18.7)	0.0002	23	28	0.91 (0.3 – 2.6)	0.8
Pos radial marg.	6	23			9	10		
Histologic type	*(n=101)*				*(n=70)*			
Carcinoma, NOS	40	21	4.4 (1.8 – 10.4)	0.0007	22	23	1.43 (0.5 – 3.8)	0.47
Carcinoma, mucinous	12	28			10	15		

**P value by Fisher's exact test; NOS: not otherwise specified; OR: odds ratio; CI: confidence interval*

Figure 3 is showing the association between anatomical location and histologic type, where it is shown that conventional adenocarcinomas are mainly found in rectum and mucinous adenocarcinomas are mainly found in ascending colon. This is statistically significant with a *P*-value =0.003 (Chi-square test for trend).

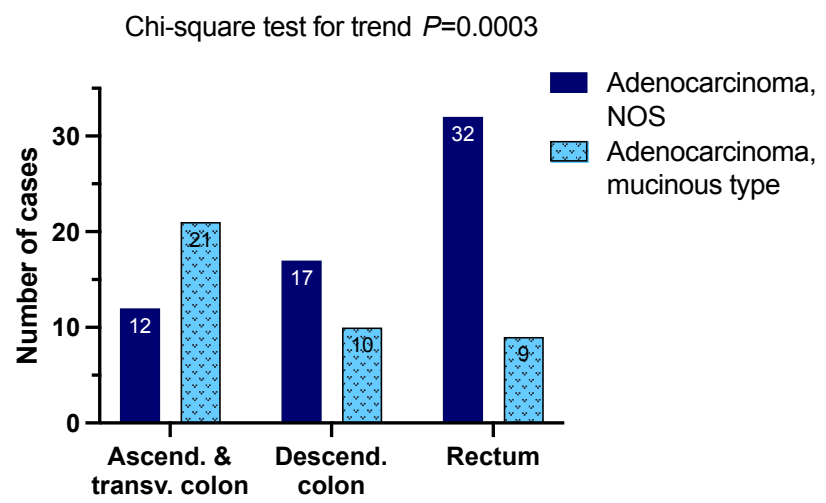

Figure 3. Correlation between anatomical location of the tumor and histologic type

NOS: not otherwise specified

4.7 The outcome of patients diagnosed with colorectal carcinoma operated on at CHUK

Table 8 shows that the years 2017 and 2020 were the ones in which 20 and 22 cases were respectively diagnosed. Of 101 patients diagnosed with CRC from the year 2014 to 2020, 56 (55.4%) were still alive up to the time of this study, and 23/56 have a diagnostic period which is less than or equal to 1 year.

Table 8. The outcome of patients diagnosed with colorectal carcinoma operated on at CHUK

Characteristics	Number	Percent
Deceased	36	35.6
Alive	56	55.4
Loss of follow up	9	8.9
Total	**101**	**100**

4.8 Survival time according to different factors

The figure 4 shows the survival trend after the diagnosis of colorectal carcinoma, each step down represents a patient dying from the disease, at least 73.1% of the patients diagnosed with colorectal carcinoma lived for 1 year after the diagnosis. And only 29.3% could live between 5 to 6 years.

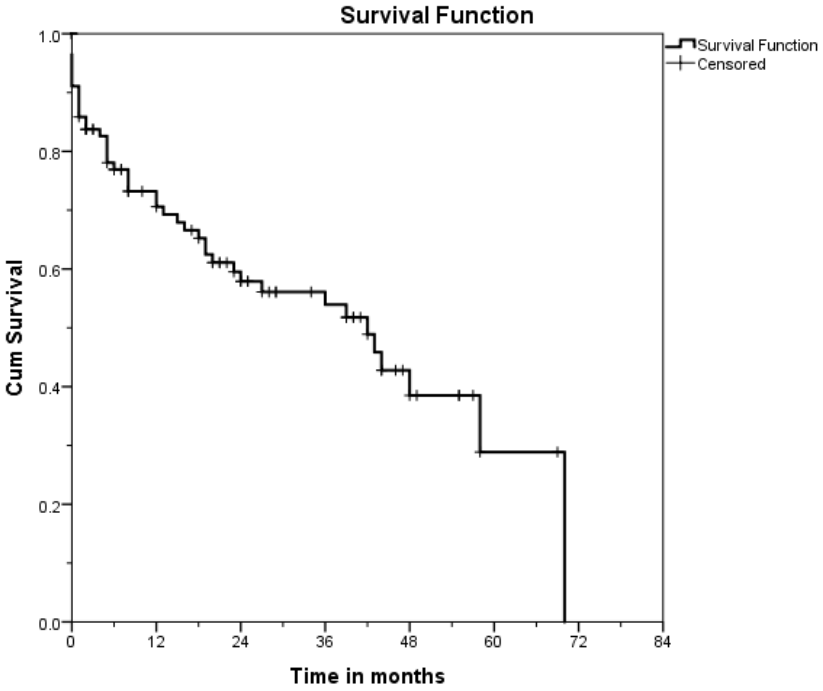

Figure 4. Kaplan–Meier overall survival curve

Figures 5-8 are showing survival time of patients with CRC according to the following prognostic factors: age groups, sex, tumor grade, tumor stage, margin status, lympho-vascular invasion, perineural invasion, tumor border and immune response. Only few of these factors showed a statistically significant association. Age group <50 years survived longer than other age groups with a mean of 45 months period. Patients whose biopsies were not having lympho-vascular invasion also have an improved survival with a mean of 50 months period, patients who have high inflammatory response also live longer with a mean of 51 months period and these are statistically significant with a P value <0.05.

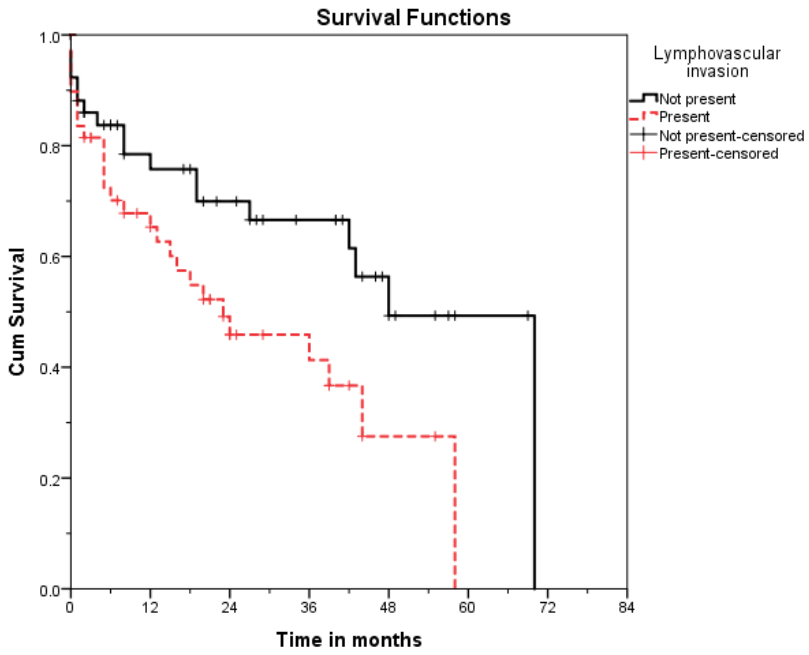

Figure 5. Kaplan-Meier survival according to lympho-vascular invasion

Log-rank test P value=0.018

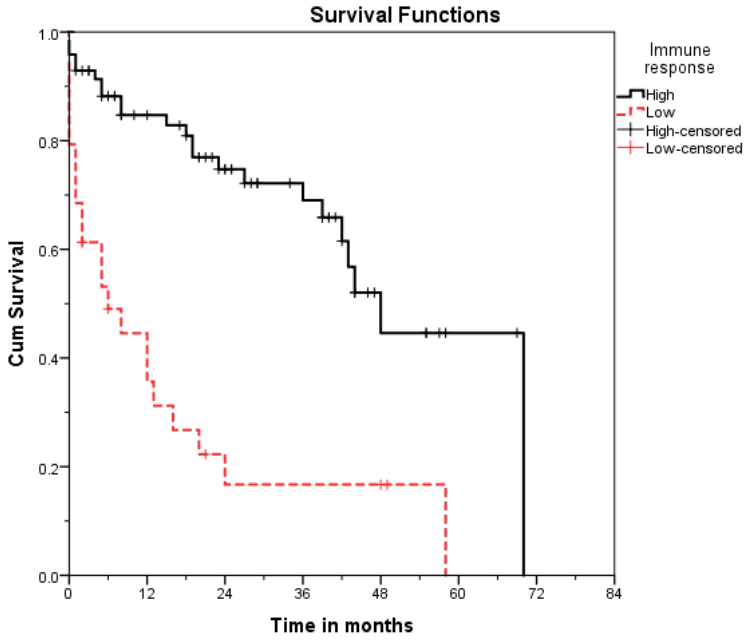

Figure 6. Kaplan-Meier survival according to immune response status

Log-rank test P value =0.001

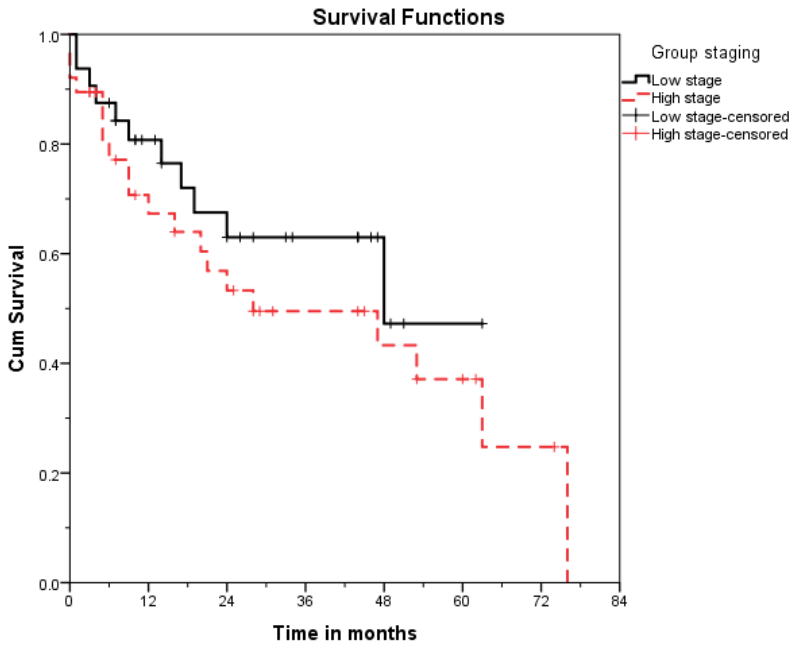

Figure 7. Kaplan-Meier survival according to stage groups

Log-rank test P value=0.227

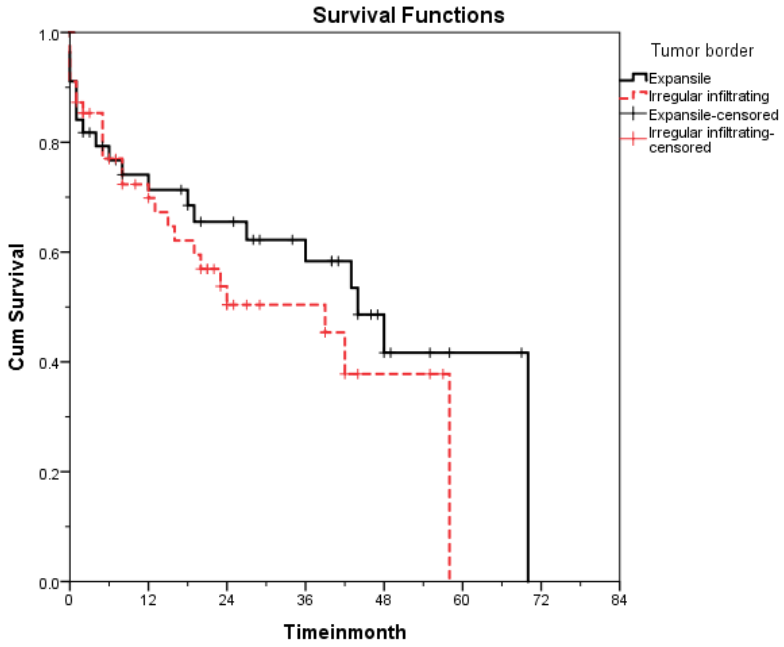

Figure 8. Kaplan-Meier survival according to tumor border

Log-rank test P value= 0.321

CHAPTER V. DISCUSSIONS

The aim of this study was to describe demographic and pathology characteristics, prognostic determinants and outcome of patients diagnosed with colorectal adenocarcinoma at University Teaching Hospital of Kigali (CHUK). In this study, the age of participants at presentation ranges between 17 to 89 years with a mean age of 54.26, in general, it is known that CRC is a disease of old people in their fifties and sixties, however the present study has shown a considerable number of patients under 50 years old with 2 patients ≤ 24 years, 11 patients in 25-34 years and 27 patients in 35-49 years (cfr table 3). This finding is of great value as it highlighting the ear onset of the disease in Rwandan population. The finding about the age range is comparable to the one found in the study done in Zambia where the range was 11 to 82 years of age. In the same study, the mean age was 48.6 a finding which lower than the one presented in the current study (38). Female were 53 (52.5%) and males were 48 (47.5%), this means that women tend to seek health care than men (40), it can also be due a natural phenomenon where female are much more presented in the general population than men. This finding is similar to the one found in the study which was conducted in Uganda where the percentage of female was 53.4 % (41).

With five regions of Rwanda represented, most of the specimens were provided by patients coming from the capital city of Rwanda, Kigali, with 32.7% and the southern region accounting for 24.8%. This is no surprising since many of health facilities where cancer diagnosis is done, are in the capital, and people who live in the capital city in one way or the other can afford the diagnosis or are more educated with a higher awareness about cancer, which makes them to consult. The southern region is also bordering the Kigali city. This finding is similar to others conducted in Tanzania and Zambia, whereby the majority of patients would also come from the respective capital cities (2,38). The main symptom was rectal bleeding with a frequency of 46.5%, this was similar the study published in Zambia (38). A high number of tumors was found to arise in the rectum with 40.6% of cases which is also similar to the one published in Zambia by Akwi Wasi Asombang1 et al (38).

The majority of CRC showed gross appearance of infiltrating pattern with occurrence of 68.3%, this is similar to what have been found within another study conducted in Europe/Greece by PAPAGIORGIS et al where infiltrative growth pattern was seen in 38 =32% of the patients in contrast to patients (23=20%) with exophytic or polypoid growth pattern (42). Conventional

adenocarcinoma or adenocarcinoma NOS was the main histologic type, it accounted for 60 =60.4% of cases. This was also similar to the one from Zambia (38).

The present study reveals that many tumors were of Grade II accounting for 54.5% and the most common stage group was stage III with 21.8%. With regard to stage, previous studies have reported similar finding, in the study of Saidi et al.,2011; stage III was most prevalent with 40.1% (43), while a percentage of 43.8% was also reported for Stage III elsewhere in Korea (44). In their study, Papagiorgis et al., also found Grade II to be the commonest grade (42). Most tumors were also found to be of moderate tumor differentiation in another study done in China with 76.5% of cases. In the same study, tumors with T3 were (40%), whereas tumors with N0 were (48%) (45).

The incidence of lymph vascular, margins status and perineural invasion were 48.5%, 28.7%, 28.7% respectively and it has been noted that all proximal and distal margins were all negative however the radial margin was not well evaluated where the serosal surface were mainly evaluated as radial margin instead of true surgical margin on the mesocolon. In a retrospective review which was performed in the USA on the National Cancer Data Base (NCDB), 2004-2011, positive margins were 39.7 % (46). In their study, Yahyazadeh et al., found that lymph vascular invasion was present in 16.4%, whereas perineural invasion was 30.7%, the study was conducted in Iran (47). The results about perineural invasion and margins status from those two studies are comparable with the results of the present study. Considering lymphocytic infiltration on H&E staining, there was a high immune response in 71.3% cases, though IHC (CD8 and CD3) were not performed for the characterization of those lymphocytes, but previous researches have indicated that local lymphocytosis is associated with a favorable prognosis as it has been demonstrated by Klintrup and Mäkinen (36,47–49).

The present study demonstrates a positive correlation between male gender and below 50 years age group where being male will expose you to develop colorectal carcinoma in the younger age than female in the same age group and this is statistically significant with a *P*-value =0.01, OR:2.7 (95%CI=1.2 – 6.2); this was also found by Leonard K. Katalambula et all in their study done in Tanzanian hospitals (2).

This study has shown that having high immune response expose someone to have a low-grade tumor which is statistically significant with a *P*-value: 0.03, OR 2.6 (95%CI=1.1 – 6.5). This finding is similar to what have been found by Klintrup et all (36).

The study shows that absence of lympho-vascular invasion goes with having a well differentiated tumor which is statistically significant with a *P*-value <0.0001, OR= 6.7 (95%CI=2.8 – 16.2) and shows that absence of perineural invasion also, goes with having low grade tumor and it is statistically significant with a *P*-value 0.01, OR= 3.3(95%CI=1.3 – 8.24). These associations were also found in the study done by Eisar Al-Sukhni et all where they found a strong association between presence of LVI/PNI and poorly differentiated tumor (46).

Within this study, it is showing that the more you have an expansile tumor border the more you have a low-grade tumor, which is statistically significant with a *P*-value= 0.007, OR= 3.1 (95%CI=1.36 – 7.0) and also, it shows that having negative radial margin goes with low grade tumor, and also, this is statistically significant with a *P*-value= 0.0002, OR= 6.7 (95%CI=2.4 – 18.7). This is inversely similar to the findings of the study done by M. Ashraf Balbaa et all in Egypt, for them they have demonstrated that having infiltrating tumor pattern and positive circumferential margin is associated with having a high grade tumor or grade III tumor (50).

From the present study, it is shown that many conventional adenocarcinomas come from the rectum by anatomical site followed by descending colon then after, ascending colon and that many mucinous adenocarcinomas come from the ascending colon by anatomical location followed by descending colon and rectum comes after, so it means if anyone has a rectal disease it is more likely to be conventional adenocarcinoma and when anybody has an ascending colon disease, it is more likely to be mucinous adenocarcinoma which is statistically significant with a *P*-value= 0.003 (chi-square test for trend). It is similar to what have been described by Michelle McCabe et all. in their study where they found conventional adenocarcinoma to arise mainly in the rectum (51).

While it is early to ascertain with confidence the survival outcome, 55.4% of patients diagnosed with CRC at CHUK are still alive. For all patients who survived, the average survival period is 46 months (3 years).

Overall, the results of the present study show not statistically significant (*P*-value=0.253) relationship between histologic staging group and the CRC outcome where lower stage group I and II live longer with a mean of 51months period, a finding which is similar to the one found by Bardakhchyan S et al, in their 9 years retrospective study conducted in Armenian oncology center, where they found a 3- and 5-year OS rates were 62.9% and 51.8% for all stages combined and 79.7% and 68.5% for stages I-II, 62.5% and 48.4% for stage III, and 24.4% and 17% for

stage IV respectively (52). The results of the study show that Grade I survived longer than others with a mean of 47months period. Though, not statistically significant (*P* value=0.255*)*, it appears that patients with low grades tend to survive longer than high grades. And this is similar to what was demonstrated by Bardakhchyan S et al, 2020; where tumor grade was considered as the most influential prognostic factor together with tumor stage (52).

Also, though it is not statistically significant, the current study shows an influence of tumor borders to the outcome of patient with CRC where, having an expansile smooth border goes with having a better outcome comparing to irregular infiltrating tumor border. This is similar to what have been demonstrated by Viktor H. Koelzer and Alessandro Lugli,2014; for them, they also found an ameliorated outcome to patients with pushing border or expansile tumor growth pattern in contrast to those with infiltrating tumor border with 92.9% and 81.8% chance of 5 years survival rate, respectively (53).

CHAPTER VI. CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

To the best of our knowledge this is the 1st study done in Rwanda on histomorphology characteristics and prognostic determinants on colorectal adenocarcinoma. Among 101 colorectal resection specimens, most of patients were female accounting 53 (52.5%) and patients presented with wide age range 17-85years with a mean of 54.26. Also, it has been shown that among 48 male patients presented, all 27 are below 50 years which is a big number of Rwandan males and it can be taken as a public health problem to deal with, with possible implementation of screening measures at early.

Most of patients were coming from Kigali city comparing to other region of the country with a number of 33 patients followed by Southern province with a number of 25patients this is explained by the reason that Kigali city is where getting health facilities is easy and also, surrounded by a good number of southern districts where came enough patients.

The most presenting symptom was rectal bleeding which was found in 47 cases, followed by abdominal pain which was found in 25 cases. There was a significant number of cases whose patients presented with complications like obstruction and perforation accounting 9 and 19 cases respectively and most of these are associated with poor outcome or immediate death during intervention or few days after intervention.

Conventional Adenocarcinoma was the most common histologic type diagnosed and most of prognostic determinants studied have shown that they affect the outcome of the patient, stage group being among them although many cases were not staged due to lack of information about distant metastasis which can be attributed to inadequate pre-surgical investigations and peri-intervention death.

Also, it has been shown that there is a considerable overall survival period of 46 months and with this (58%) survived 2 years and (56%) survived 3 years.

6.2 Recommendations

With the study's findings and results, we came up with the following recommendations:

1) Sensitize to the population about risk factors that are associated with colorectal cancer development, hence changing life style can play a major role in CRC prevention.
2) To promote available screening methods and establish screening flow as it has been shown that there is a good number of young populations with CRC.
3) Promote early healthcare-seeking behavior, to be emphasized in sensitization by healthcare providers, health administrators, local and central government leaders and other stake-holders as we all know that the earlier diagnosis the better treatment and prognosis.
4) To enrich Rwandan laboratories in terms of infrastructures with advanced technologies in performance of molecular studies as it plays a role in CRC development.
5) Healthcare providers should use properly established protocols for better management of patients and research purposes.
6) A large research project to look for major risk factors of CRC and probable confound factors interfering with prognosis.
7) To everyone: to read this work, mainly its part of result presentation as it shows a broad picture of colorectal adenocarcinoma in Rwanda.

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APPENDICES

Data collection form

Pathology characteristics, prognostic determinants and the outcome of patients diagnosed with colorectal adenocarcinoma at University Teaching Hospital of Kigali (CHUK)

Form number: ☐ Histopathology number: ☐

Demographic data

1. Age: ☐ 2. Sex: ☐
3. Residence:

Kigali City ☐ East ☐ West ☐

North ☐ South ☐ Foreigner ☐

Clinical data

1. Main symptom

Obstruction ☐ Perforation ☐

Bleeding ☐ Other(specify) ☐

2. Duration of symptoms:

< 6months ☐ 7-12 months ☐

13-24 months ☐ >24 months ☐

3. Biopsy site:

Ascending colon ☐ Transverse colon ☐

Descending colon ☐ Rectum ☐

4. Vital status:

Alive: ☐

Deceased, date of death: ☐

Loss of follow-up, date: ☐

Histopathology result

1. Gross appearance:

   Polypoid ☐ Infiltrative ☐

2. Histologic type
3. Tumor grade
4. Tumor stage
5. Margin's status:

   Positive ☐ Negative ☐

6. Lymph-nodes status:

   Number of LN found ☐ Number of LN with tumor ☐

7. Lympho-vascular invasion:

   Present ☐ Not present ☐

8. Perineural invasion:

   Present ☐ Not present ☐

9. Tumor borer:

   Irregular infiltrating ☐ Smooth expansile border ☐

10. Host Immune response, score:

    Score 0 ☐ Score 1 ☐

    Score 2 ☐ Score 3 ☐

11. Host Immune response, overall

    High ☐ Low ☐

12. Date of diagnosis: ☐

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 20th May 2020

Dr. Delphine UWAMARIYA
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 074/CMHS IRB/2020

Your Project Title ***"Pathology Characteristics and Prognostic Determinants of Colorectal Carcinoma Diagnosed at University Teaching Hospital of Kigali."*** has been evaluated by CMHS Institutional Review Board.

		Involved in the decision		
		Yes	No (Reason)	
Name of Members	**Institute**		**Absent**	**Withdrawn from the proceeding**
Prof Kato J. Njunwa	UR-CMHS		X	
Prof Jean Bosco Gahutu	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	
Dr Gishoma Darius	UR-CMHS		X	
Dr 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 20th May 2020. **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 20th May 2020

Expiration date: The 20th May 2021

Professor GAHUTU Jean Bosco
Chairperson Institutional Review Board
University of Rwanda College of Medicine and Health Sciences

Cc:

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

CENTRE HOSPITALIER UNIVERSITAIRE
UNIVERSITY TEACHING HOSPITAL

Quality Health Care
Training & Research

Ethics Committee / Comité d'éthique

16, Jun, 2020 Ref.:EC/CHUK/043/2020

Review Approval Notice

Dear Delphine UWAMARIYA,

Your research project: ***"PATHOLOGY CHARACTERISTICS AND PROGNOSTIC DETERMINANTS OF COLORECTAL CARCINOMA DIAGNOSED AT UNIVERSITY TEACHING HOSPITAL OF KIGALI. "***

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 16,Jun,2020 to evaluate your request for ethical approval of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your research project.

You are required to present the results of your study to CHUK Ethics Committee before publication by using this link:www.chuk.rw/research/fullreport/?appid=122&&chuk.

PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

Dr Emmanuel Rusingiza Kamanzi
The Chairperson, Ethics Committee,
University Teaching Hospital of Kigali