

DECLARATION

I, Dr KARENZI Irénée David, hereby declare that this dissertation: "FACTORS AFFECTING DELAY IN COLORECTAL CANCER DIAGNOSIS AND SHORT TERM SURGICAL OUTCOMES IN KUTH" and all its contents have never been submitted to any other institution of higher learning for any academic award.

Signature: Date: May 31st, 2019

Dr. KARENZI Irénée David General Surgery Resident University of Rwanda

SUPERVISORS

We hereby declare that this dissertation: "FACTORS AFFECTING DELAY IN COLORECTAL CANCER DIAGNOSIS AND SHORT TERM SURGICAL OUTCOMES IN KUTH" was submitted by Dr. KARENZI Irénée David with our approval.

Signatures:

Dr NIFASHA Antoine

Senior consultant General Surgeon

University teaching hospital, Kigali

Dr RUHUNGANDE Landouald

Consultant General Surgeon

University of Rwanda

П

DEDICATION

To Almighty God, through his grace we had this opportunity to study;

To my parents, my beloved wife **UWITONZE Médiatrice**, my daughters **GIRANEZA UMUHIRE Linda** and **INEZA CYUZUZO Nicole** for their moral support and patience; my sisters and all my family members, my friends and all who participated in my studies.

To all my Lecturers, for their inspirations, all friends and fellow Residents and classmates we shared experiences in different areas.

To late **Dr BISETSA Aphrodice**, the senior resident who died in theatre saving life, for his encouragement and unforgettable technical support he provided to me,

I dedicate this memoir.

TABLE OF CONTENTS

DECLARATION	Error! Bookmark not defined.
DEDICATION	iii
LIST OF TABLES	vi
ACKNOWLEDGEMENTS	vii
LIST OF ABBREVIATIONS	ix
ABSTRUCT	xi
BACKGROUND	xi
1. INTRODUCTION	1
1.1 BACKGROUND	1
1.2 LITERATURE REVIEW	2
1.2.1 Clinical presentation	2
1.2.2 Etiology	2
1.2.3 Pathology and staging	4
1.2.4 Treatment	5
1.3 PROBLEM STATEMENT	7
1.4 Research questions	8
1.5 Hypothesis	8
1.6 Aim and Objectives	8
Objectives	8
2 METHODOLOGY	8
2.1 Study description	8
2.2 Study design	8
2.3 Study site	9
2.4 Study population	9
2.5 Main exposure and outcome to be measured	9
2.6 Inclusion criteria:	
2.7 Exclusion criteria:	
2.8 Study procedures	
2.9 Sample size	
2.10 Data management	
2.11 Study limitations	

2.12 Ethical consideration14
2.13 Confidentiality14
2.14 Benefit of the Study
2.14.1 To the investigator
2.14.2 To the community
2.14.3 Conflict of interest
3. RESULTS
3.1 Descriptive Data characteristics15
4. DISCUSSION AND CONCLUSION
5. CONCLUSION
6. RECOMMENDATIONS
6.1 To Rwanda Biomedical Center: Non communicable disease division
6.2 To University teaching hospital of Kigali29
6.3 To other health care facilities
6.4 To the community
6. REFERENCES
APPENDIX A: STUDY COORDINATION
APPENDIX B: INFORMED AGREEMENT FOR CHILDREN BETWEEN 15-20YEARS OF AGE B
APPENDIX C: INFORMED CONSENTD
DATA COLLECTION FORMF

LIST OF TABLES

Table 1: TNM classification of CRC (seventh edition).	4
Table 2: SOCIODEMOGRAPHIC CHARACTERISTIC	15
Table 3: Characteristics of first consultation	16
Table 4: Diagnosis at first health facility	17
Table 5: Clinical characteristics at referral hospital	17
Table 6: Histopathology and staging	19
Table 7: Histopathology and staging	20
Table 8: Factors affecting delays	22
Table 9: Clinical characteristics and delayed diagnosis	23
Table 10: Description of surgical management options and related outcomes	24
Table 11: Comparison among different procedures performed	25

ACKNOWLEDGEMENTS

I would like to thank the government of Rwanda through the Ministry Of Health for sponsoring my studies at the University of Rwanda.

We remain acknowledging all those who contributed to the realization of this work. We first acknowledge project supervisors **Dr NIFASHA Antoine** and **Dr RUHUNGANDE Landouald**, for their supervision, guidance, and great support to make this work possible.

My gratitude extends to **Dr Jean Marie Vianney KAGIMBANGABO**, for his inestimable support during this project.

To the Director of research department at CHUK, Dr Jean Claude BYIRINGIRO who granted me a permission to access patients' data

To all the team: Doctors, nurses and anaesthesia providers working in Endoscopy unity at CHUK

To all Resident Doctors who helped me in all teaching hospitals

To the University of Rwanda through the department of Surgery, for the effort to make this training more effective

We also give thanks to fellow colleagues, all my family members and my friends for their financial and moral support during the preparation of this work.

LIST OF ABBREVIATIONS

CRC	: Colorectal cancer
LAR	: Low anterior resection
CHUK	: University teaching Hospital of Kigali
Subtotal C	: Subtotal colectomy
GI	: Gastrointestinal
Sigmoid C	: Sigmoid colectomy
HNPCC	: Hereditary non polyposis colon cancer
UK	: United Kingdom
APC	: Antigen presenting cells
LHC	: Left hemicolectomy
WHO	: World health organization
APR	: Abdominal perineal Resection
TNM	: Tumor Node Metastasis
NCCN	: National comprehension cancer network
AJCC	: American joint committee on cancer
IRB	: Institutional review board
CRT	: Chemotherapy and radiotherapy
MUSA	: Mutuelle de sante
RSSB	: Rwanda Social Security Board

MMI	: Military Medical Insurance
SORAS	: Société Rwandaise d'Assurance
GIST	: Gastrointestinal stromal tumor
1 st H F	: First Health facility
DH	: District Hospital
RDV	: Rendez-vous
R Colon	: Right Colon
L Colon	: Left colon
P stoma	: Palliative stoma
SPSS	: Statistical Package for Social Sciences
SSI	: Surgical Site infection
СТ	: Computed Tomography
MRI	: Magnetic Resonance Imaging
U/S	: Ultrasound
Na	: Sodium
Cl	: Chloride
K	: Potassium
FBC	: Full Blood Count
Hb	: Hemoglobin
Referral H	: Referral Hospital
НC	: Health center

ABSTRACT

BACKGROUND: Colorectal cancer is the third most common leading cause of cancer related death worldwide. It is also a major cause of morbidity and mortality. Surgery is the mainstay of the treatment. Delay in diagnosis can affect outcomes of patients and it can be related to the health care personnel or to patients. This study described the factors that affect delay in CRC cancer diagnosis and it described early postoperative outcomes for operated patients.

METHODS: This was a descriptive prospective observational hospital based study that evaluated patterns of diagnosis delay in patients with CRC. Information from the patients was collected on questionnaire on their arrival at CHUK and operated ones were followed within 30 days. Outcomes were measured in hospital and after discharge from the day of operation till day 30 and pathology results were recorded.

RESULTS: 72 patients were recruited with confirmed CRC and 2 of them were missed for follow up; of the 70 remained, 39 (55.7%)were males and 31(44.3%) females, the mean age was 56.09 from 21 years to 85 years. The most frequent symptoms were rectal bleeding; abdominal pain and change in bowel habits with 74.2%, 45.7%, and 42.9% respectively. The patients' majority presented with one or more symptoms. The mean duration of symptoms at presentation was 14.6 months and 50% of patients presented with symptoms lasting for >12 months. The patterns of delays were: delay to consult (5.7 month), referral delay and delay (delay at 1st health care facility: mean =3 months and delay at district hospital mean= 3.1 months) at CHUK (mean = 4.3 months). Health insurance and clinical presentation of CRC were significantly associated with diagnostic delay. 58 (82.8%) of patients were operated. Abdominal perineal resection and low anterior resection were popular in 41.4% with 4% mortality rate. Other procedures were polypectomy, right hemicolectomy, left hemicolectomy and palliative stoma. There was no significant difference in outcomes for all procedure performed in this study.

CONCLUSION: CRC prevalence is increasing in Rwandan population; more often its diagnosis is delayed by several factors, related to patients and health care personnel or health system. The surgical management is associated with good outcomes.

1. INTRODUCTION

Colorectal cancer is prevalent worldwide and is the 3rd leading cause of cancer related death in men and the second in women. Early detection and treatment is associated with good surgical outcomes. Rwandan population also presents with colon and rectal cancers and many are treated in CHUK; more often they delay to come for treatment. Little is known about the causes of delay and surgical outcomes for these conditions. This is a prospective descriptive study assessing factors affecting delay in colorectal cancer diagnosis and its short term outcomes after surgery, at a referral hospital in Rwanda.

1.1 BACKGROUND

Colorectal cancers are mainly common in high income countries. Colorectal cancer is the third most common form of cancer in general. CRC is a disease of high prevalence, which has a long pre-malignant, asymptomatic course and can be detected by screening¹.

Colorectal cancer (CRC) is a growing public health concern with increasing rates in countries with, previously known, low incidence².

There is an increase in prevalence in CRC with tendency to develop at slightly lower age than that reported from higher incidence countries, which has important implications for the etiology and pathogenesis of this disease among black Africans³.

Urgent colorectal operations are still associated with higher mortality and morbidity than elective surgery even though perioperative care and operative techniques are getting advanced⁴.

In Nigeria CRC was found prevalent in rural dwellers with often late presentations. The right colon was the dominant site affected⁵.

Even if the incidence of CRC is low in Nigeria and other developing countries, outcomes of treatment remains poor due to late presentation, ignorance, poverty and superstition⁶.

A study done in Kenya showed that from 2005-2010, CRC presented mostly at young age and advanced stage with a peak age of 41-50 years⁷.

A retrospective study done in CHUK showed that in 2015, colorectal cancer was found in 23.5% of all GI tumors, 91.6 % of them presented for Surgery at advanced stage (T3 and T4); and 65% of those CRC were diagnosed at colonoscopy⁸.

In Rwanda CRC was found to be common in female and was counting 4.5% of female cancer related deaths, yet there is no prevention strategies in place⁹.

In symptomatic CRC patients, a longer diagnostic and therapeutic delay in routine clinical practice was not associated with an adverse effect on survival¹⁰.

Delayed diagnosis for rectal cancer remains a significant problem, with instances of delay attributable to both patient and physician¹¹.

1.2 LITERATURE REVIEW

1.2.1 Clinical presentation

Patients with CRC may be asymptomatic and are diagnosed during screening colonoscopy, others present with suspicious symptoms and/or signs and there are some who present as emergence with intestinal obstruction or peritonitis.

In the majority of cases they are no symptoms or signs of early stage colorectal cancer. 70 to 90 % of patients present after onset of symptoms and they relatively have advanced CRC¹².

Symptoms associated with CRC are rectal bleeding or melena, constipation, abdominal pain, unexplained iron deficiency anemia and weight loss and change in bowel habit¹³. The most frequent symptoms that prompt colonoscopy were found to be: rectal bleeding (37%), abdominal pain, anemia and change in bowel habits¹².

1.2.2 Etiology

Heredity and environmental factors have a considerable role in development of CRC. Up to 15 % of all CRC are hereditary so the family history is a strong risk factor for development of CRC. Lifetime risk for developing CRC is double among people with first degree relative with CRC and the risk increases 4-fold if the diagnosis is set before 45 years of age¹⁴. The most known inherited CRC syndromes are Lynch syndrome(1-3% of all CRC), also called hereditary non polyposis colorectal cancer (HNPCC) and familial adenomatous polyposis in less than 1% of all CRC, both are inherited as autosomal dominant¹⁵. The majority of colorectal cancers are sporadic; approximately three-quarters of patients have a negative family history¹⁶.

Migration studies have shown that persons, who migrate from low CRC incidence place to one with high incidence, ultimately develop the disease or their descendants do¹⁷.

Environmental exposures, personal and family history of colorectal polyps and cancer are both risk factors for CRC development¹⁸.

Diet factor contributes to 30% to 50% of all CRC incidences. Diet may also act as risk modifier for the CRC development process, like tumor initiation, promotion, and progression¹⁹.

Smoke from cigarettes contains around 60 carcinogens and free radicals that can affect colorectal mucosa; this potentiates the alteration of cancer related genes. The association between cigarette smoking and CRC has been shown to be dose dependent and duration of exposure²⁰.

1.2.3 Pathology and staging

CRC is histologically divided into several types, suggested by World Health Organization (WHO), with adenocarcinoma, mucinous adenocarcinoma and signet ring cell cancer. CRC is classified according to the tumor- lymph node -metastasis (TNM) staging system, which is most widely used and it provides information about local infiltration of primary tumor, spread to regional lymph node or distant organs²¹. Other different staging systems are based on architectural and/or cytology features; they describe the level of cell differentiation within the tumor: well differentiated (grade 1), moderately differentiated (grade 2), poorly differentiated (grade 3) and undifferentiated (grade 4)²².

Stage	Т	Ν	Μ
I	T1-2	0	0
ПА	T3	0	0
IIB	T4	0	0
IIIA	T1-2	N1	0
ШВ	T3-4	N1	0
шс	Any	N2	0
IV	Any	Any	1

 Table 1: TNM classification of CRC (seventh edition)

Тх	Primary tumor cannot assessed
Tis	Carcinoma in situ
T1	Tumor invades sub mucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through muscularis propria into sub serosa or
	into non-peritonealized pericolonic or perirectal tissue
T4	Tumor directly invades other organs or structures and/or
	perforates visceral peritoneum
T4a	Perforates visceral peritoneum
T4b	Directly invades other organ or structures

Nx	Regional lymph nodes cannot be assessed
NO	No regional lymph node metastasis
N1a	Metastasis in 1 regional lymph node
N1b	Metastasis in 2-3 regional lymph nodes
N1c	Satellites in sub serosa, without regional lymph nodes
N2a	Metastasis in 4 or more regional lymph nodes
N2b	Metastasis in 4-6 lymph nodes
N2c	Metastasis in 7 or more lymph nodes

I	MO	No distant metastases
I	M1a	Distant metastases in one organ
I	M1b	Distant metastases in more than one organ or peritoneum

Colonoscopy and biopsy is the diagnostic modality that can be used to confirm the CRC and imaging completes diagnosis by staging. CT colonography can be an alternative in elderly people with vague symptoms like abdominal pain and weight loss²³.

Endoscopic examination provides the most accurate about the intestinal mucosa morphology and surrounding tissues are evaluated by cross sectional imaging modalities like CT scan, MRI and these imaging modalities complete each other in the diagnostic process of the colorectal cancers²⁴.

70% of rectal cancer and 30% of CRCs can be detected by rectal examination during consultation but the most effective is colonoscopy that also permits to localize the tumor and obtain tissue for histological evaluation²⁵.

1.2.4 Treatment

Surgery is the mainstay curative treatment in colorectal cancer and the overall management should be discussed in multidiscipline approach. The surgical option depends on the site of the tumor, stage and general health of the patient. In early stage of the disease the radical character of surgical procedure is assured^{26,27}.

The tumor resection follows embryonic plan; the segment is resected with its mesentery, vascular supply and lymphatic drainage with free margins of least 5 cm from the tumor and the vessels are ligated from their bases to harvest all the lymph nodes and complete mesocolon (mesorectum) excision in mandatory for oncological resection²⁸.

In the surgical treatment of colorectal cancer, a lymphadenectomy is considered adequate when at least 12 lymph nodes are removed, and the number of lymph nodes surgically removed is directly correlated with patient survival. National Comprehensive Cancer Network (NCCN), the College of American Pathologists, and the American Joint Committee on Cancer (AJCC) suggest a minimum of 12 lymph nodes to establish the N stage; patient with stage II cancer with less than 12 lymph nodes removed is considered high risk and should receive adjuvant chemotherapy²⁷.

Total mesorectal excision, en-bloc resection of T4c colon carcinomas, avoiding tears or incisions of the tumor have been previously accepted as common principles and recently the significance of the circumferential resection margin is also considered in surgical treatment of colorectal cancers²⁹.

For cancers that are limited on mucosa or sub mucosa without lymph node invasion, endoscopic resection can be done with complete removal of the cancer³⁰.

Surgical resection may be contraindicated in advanced rectal cancer when there is involvement of other structures like ureters, sacrum (tumor reaching S2), sciatic nerve pain, lymphedema and peritoneal carcinomatosis. These patients may undergo chemotherapy and/or radiotherapy, as palliation. For obstructing tumors with metastasis, a diverting colostomy should be an option³¹.

The 5 year survival rate after resection for colorectal cancer is 90% in stage I, 70-80% for stage II and 40 -65% in stage III; the recurrence risk also depends on the pathological stage of the primary tumor: 30% for stage II and 50% in stage III and it is higher within the first 2 years after surgical resection³². Previous randomized controlled trials showed that postoperative radiation therapy decreases local recurrence but recently, neo adjuvant chemo radiation was found to decrease local recurrence compared to surgery alone³³. Surgery can be done after short course radiotherapy with 2 to 5 days or delayed beyond 4 weeks (4 to 12 weeks) to minimize complications³⁴.

The palliative approach for incurable stage IV CRC is currently a multidiscipline approach with a pivotal role played by chemotherapy and the survival rate has been increased with good selection of patients³⁵.

Many randomized controlled trials have established the role of radiotherapy in the management of CRC. It reduces local recurrence and improves survival in stage II and III of the disease, it is better tolerated and efficient when it is given preoperatively and it can be combined with chemotherapy for better enhancement and down staging the tumor³⁶.

1.3 PROBLEM STATEMENT

Colorectal cancer is prevalent worldwide and is the third leading cause of death among the cancer patients; early detection and treatment is associated with good surgical outcomes. Rwandan population also presents with CRC and many are treated in CHUK; more often they delay to come for treatment. Recent retrospective survey for gastrointestinal cancers, have revealed that colorectal cancer was prevalent in 23.5% of cases; and more than 90% of them presented at CHUK with advanced disease. Little is known about the causes of delays and surgical outcomes for these conditions. So far there is no common protocol that can be used to help practitioners in early diagnosis and treatment of the patients with colorectal cancers. This study will help to identify gaps in Rwandan health system that may affect delays in diagnosis and early treatment of colorectal cancers. It is understood that more information is needed on delay in CRC care. Factors affecting diagnostic delay are not well understood whether are patients or health care related.

1.4 Research questions

Which factors are affecting the delay in colorectal cancer surgery at CHUK?

What are the short term outcomes after surgery at CHUK?

1.5 Hypothesis

We hypothesize that:

Socio-economic status and referring system are the cause of delay in the management of colorectal cancer.

There is a high postoperative morbidity and mortality in the patients with colorectal cancer

1.6 Aim and Objectives

Aim: To describe the factors affecting delay in diagnosis of colorectal cancer in patients when they present at the referral hospital considering the referring health facility.

Objectives:

- Describe characteristics of patients with colorectal cancer presenting to CHUK.
- Identify the delays faced by patients with colorectal cancer to access medical care.
- Identify the factors affecting the patients' delay.
- Describe the surgical management options and related short term outcomes.
- To determine the rate of intraoperative decisions change, curative vs palliative surgery.

2 METHODOLOGY

2.1 Study description

This is a prospective, descriptive study of factors affecting delay in colorectal cancer diagnosis and short term outcomes after surgery at CHUK. We assessed the patterns of presentation of colon and rectal cancer, delays of patients to have diagnosis and short term outcomes of operations done for the patients who were operated in the study period.

2.2 Study design

This was a prospective, descriptive observational study of all patients who presented to CHUK with colorectal cancer over a period of one year (February 2018- January 2019).

2.3 Study site

This study was conducted in University Teaching Hospital of Kigali, departments of surgery (unit of General Surgery), Internal Medicine and Pathology laboratory.

2.4 Study population

All adult patients (>15 years of age) who were consulted in CHUK with suspicion of colorectal cancer, to whom the pathology results confirmed colorectal cancer during a one year period from February 2018- January 2019

2.5 Main exposure and outcome to be measured

The collected information included admission details including demographics, nutritional status, duration of the condition, and time of first consultation to health care facility, time of referral for surgical consultation, duration of investigations and type of operation if done, history and duration of weight loss, admission diagnosis and planned procedure, paraclinical investigations. On the hospital course we collected information including operation performed, intraoperative events, and pathology results for the specimen and post operative complications.

Delay in diagnosis and surgical care, were patient related or health care (Health Center, District Hospital and Referral Hospital) related. Patient's delays were evaluated as the estimated time between first onset of symptom and first consultation to health care facility. Health care delay was the time between the first consultation to the health care facility and date of final diagnosis. We also assessed referral delay (from first consulting health care provider to surgeon consultation plus the time of getting diagnosis) and hospital diagnostic/ treatment delay (time between the diagnosis and date of treatment).

After the diagnosis of CRC, patients were interviewed regarding economic status and delays faced to access health care. These questions focused on patient related delay and primary health care delay; we included the waiting time of first rendezvous to see the surgeon.

For each patient, we evaluated the total delay from onset of symptoms to the date of final diagnosis and treatment plan that was curative or palliative.

Primary outcome: delay to diagnose CRC. Patients were followed from the confirmation of the cancer, imaging and staging up to the surgical plan for the condition according to its extent. The

duration of preoperative follow up depended on the hospital system. Secondary outcomes: inhospital mortality, tumor resectability, intra operative management changes and postoperative complications, operated patients were followed for a maximum of 30 days which was maximum time to have biopsy results after surgery at CHUK. Intra operative information was pooled from operative notes in the patients' files.

2.6 Inclusion criteria:

All adult patients with confirmed colorectal cancer were recruited in this study.

2.7 Exclusion criteria:

Patient who would not consent to participate in the study would be excluded.

Patients who consulted for recurrence of CRC were excluded.

2.8 Study procedures

Recruitment procedure

All patients who presented in General Surgery service within the above mentioned period with colorectal cancer were recruited. We also included all patients who were sent in Colonoscopy unit of Internal Medicine and found to have confirmed CRC. Patients were pooled from outpatient services, Emergency department, Endoscopy unit and those who came in radiology service for diagnosis and staging from other center than CHUK. We also included patients from other centers whose histology samples were analyzed at CHUK laboratory.

Informed consent was obtained and signed by patients before enrolling them in this study and they were allowed to decline the recruitment without consequences at any time.

For all patients suspected to have CRC, a full history was asked to have necessary information regarding all the details on the delays to receive health care and we only enrolled ones with confirmed CRC.

Follow up

All operated patients were followed up within one month for post operative complications until 30th day after surgery. After surgery all the specimens were sent in laboratory for histology analysis. In hospital they were followed on daily basis for post operative infection, anastomosis

leak and wound dehiscence and in hospital mortality. After discharge they came back on post operative day 30 for follow up and post operative biopsy results were recorded. Addresses and contacts were kept for follow up after discharge; in any case that a patient fails to come back on day 30 he/she would be called to complete follow up, but all of the discharged patients came for follow up. In this study, patients who stayed more than 30 days in hospital were not followed after discharge. The surgical outcomes were measured within 30 days. Every patient found to have colorectal cancer was communicated the results by the attending Doctor (Surgeon or Internist); the patients were managed in multidisciplinary approach including the nurses, psychologists for counseling ,especially for ones with advanced stage disease and poor prognosis, nutritionist, Oncologists, Internists, Radiologists and Surgeons.

Measurement of exposures

Data were collected on admission, details included demographics, duration of symptoms on arrival at referral hospital, and duration of waiting the first visit to the health facility, duration before referral to surgical consult or endoscopic evaluation/ biopsy, duration between final diagnosis and operation, admission plan and all investigations done.

Intra operative details included: tumor location, resectability, extension, duration of the operation and intra operative complications.

Measurement of outcomes

Primary outcome was delayed colorectal cancer diagnosis. Delays were divided the in two groups: patients related delay and healthcare related delay; the second delay were sub divided in transfer (referral) delay and hospital diagnostic delay. Secondary outcomes were in-hospital mortality, postoperative complications including surgical site infection, intra abdominal abscess, pneumonia, anastomosis leak and wound dehiscence. Laboratory results were collected from the patient files (electronic or manuscript files). Laboratory studies were processed according to standard hospital laboratory protocol. For the pathology, results were gathered from the results registry in the hospital laboratory.

Definitions:

Diagnostic delay: estimated time between first onset of symptom (s) and last date of final diagnosis.

Referral delay: estimated time between first consultation and last date of final diagnosis.

Patient delay: estimated time between first onset of symptom (s) and first consultation to health care facility.

The socioeconomic status was evaluated based on UBUDEHE categories which are also the measurement of economic status of Rwandan population and are based on for government planning for the population³⁷. Category 1 and 2 were classified as low economic status, category 3 as moderate and category 4 and 5 were classified as good economic status.

2.9 Sample size

Data from the registry estimates that the prevalence of CRC in Endoscopy unity and outpatient clinic is 1% for the previous consultations, the acceptable precision for this research is 0.05. With these values the sample size will be

Calculated by the formula: $SS = \frac{Z^2(p)(1-p)}{d^2}$

Z: z value (at p value <0.05 is =1.96), p: percentage picking a choice, d: precision. We found 72

2.10 Data management

Data were collected on a paper form and entered into an Excel-based spreadsheet for security. Follow up data were collected on regular basis in hospital for those who were operated and laboratory results were pooled from the patient files or Laboratory records and pathologist written reports, patients were interviewed to complete information not recorded in their files.

Data collection was carried out by the investigator in all the areas mentioned above; Surgeon, Internist and pathologist were generating and tracking data during evaluation and management of patients. Internists were doing colonoscopy and biopsy; pathologists were analyzing samples taken and were the ones to confirm cancer, Surgeons proceeded with the rest of management after confirmation of the disease involving also Oncologists, nutritionists and nurses.

Analysis was done using SPSS 16th version; Descriptive statistics was used to describe variables, Categorical variables were reported as frequencies and percentages. Continuous variables were reported as medians and means. Tables were made in Microsoft Word and Excel.

2.11 Study limitations

The primary limitation of this study was a long time taken for one patient to have final diagnosis and surgical management plan, though around 20% of recruited were still pending for surgery and for them the post operative outcomes were not studied. Some of the patients were financially limited to afford materials for minimal invasive procedures and others (2.9%) did not cope with permanent colostomies and refused surgery. The study center was not having chemotherapy and radiotherapy available, patients were sent to other remote centers.

The delay in referring systems was another limitation to obtain many patients for the study. Sometimes CT scan was not functioning and thus patients had to wait longer to have metastasis screening done before surgery is planned.

Many patients with rectal cancer could not afford MRI as it is a modality of choice for staging and CT was used with some uncertainty about sphincter complex involvement; that was a challenge for Surgeons to choose the appropriate management plan.

Surgeons had a long list of patients waiting for operations including other malignancies so that ones for colorectal cancers have to wait before they are operated and there was luck of materials like circular staples for bowel anastomosis and rectal resection; this led to longer operations and it was not possible to operate more than one case per operating day which means that only two cases could be operated in a week for the patients who were ready for Surgery.

The laboratory was not able to analyze cancer biology and chemotherapy was given empirically.

2.12 Ethical consideration

Consent form was signed before enrollment of the patients in this study and IRB approval was obtained before data collection. Minors even if not enrolled during the study, they would be informed and give their verbal consent and ascent documents were prepared before data collection.

2.13 Confidentiality

All patients information was kept in a password protected electronic devices. Investigator used codes for patients' identification not their names.

2.14 Benefit of the Study

2.14.1 To the investigator

This study will be submitted for fulfillment of the requirement for award of Masters of Medicine in Surgery/General Surgery of the University of Rwanda.

It will be used as reference for further studies in colorectal cancer in Rwanda or in the region.

Data will be available for any project in future that will be supporting CRC surgery in Rwanda.

2.14.2 To the community

It will help the improvement in the management of CRC in Rwanda as well as increasing awareness of the condition to the health care personnel.

2.14.3 Conflict of interest

There are no conflicts of interest for this study.

3. RESULTS

3.1 Descriptive Data characteristics

Seventy two (72) patients were recruited in the study, 2 of them were missed for follow up and discontinued the study; the total of 70 patients were followed until the end of the study period.

Of the 70 remaining, 39 (55.7%) were female and 31 (44.3%) male. The mean age was 56.09 years minimum 21 years, maximum 85 years. The majority of the patients were below 60 years of age, 57.1% with peak age of 41 years. The patients were coming from all the province of the country including a small proportion from Burundi: 2 (2.85%); Kigali 21, North: 15, South: 13, west: 12, East: 7.

The majority of patients presented with low economic status 48.57%; the remaining had good and moderate economic status 14.28% and 37.14 respectively. The nutritional status was evaluated by normal weight 36 (51.43%), weight loss 33 (47.14%) and cachectic 1(1.43%).

58 (82.86%) were operated, 12 (17.14%) were not; among non operated patients, two of them refused surgery because they did not accept to bear with permanent colostomy; 4 patients were sent for neo adjuvant CRT, 3 patients died before investigations were completed and 3 were still pending for surgery. Among all operated patients, 12 (20.7%) of them were emergency cases and 46(79.3%) were electives ones.

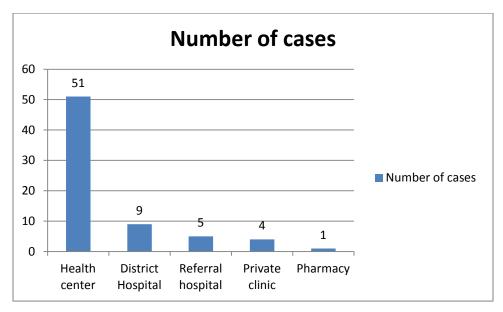
Variable	Categories	Frequencies n (%)
Age	<40	10(14.3)
	40-50	18(25.7)
	50-60	12(17.1)
	>60	30(42.9)
Gender	Female	39(55.7)
	Male	31(44.3)
Province	Kigali	21(30.0)
	North	15(21.4)
	South	13(18.6)
	West	12(17.1)

Table 2: Sociodemographic characteristics

	East	7(10.0)
	Abroad	2(2.9)
Socioeconomic status	Low	34(48.6)
	Moderate	26(37.1)
	Good	10(14.3)
Insurance	MUSA	63(90)
	RSSB/MMI/SORAS	4(5.7)
	None	3(4.3)

CRC was found to be more prevalent in patients below 60 years of age 57.1%; most predominantly in female than male, 30% of all were residents of Kigali but all the provinces of the country were represented in this study. Low economic status counted 48.6% of the patients and only 14.3% were found to have good economic status. 90% of all were using community health insurance known as Mutuelle.

Table 3: Characteristics of first consultation



The majority of the patients with colorectal cancer 72.3%, consulted at health center for their first visit; this means that they were consulted by non physician health personnel. Only 25.7% of recruited patients were seen by a Doctor (private clinic, district hospital and referral hospital) on their first consultation.

			First health facility			
Diagnosis	Frequency	Pharmacy	Health	Private	District	Referral
	N (%)		center	clinic	hospital	hospital
Amebiasis	36 (51.4)	1(2.7)	31(86.1)	2 (5.6)	2 (5.6)	0 (0.0)
Hemorrhoids	4 (5.7)	0 (0.0)	1 (25)	3 (75)	0 (0.0)	0 (0.0)
Intestinal	3 (4.3)	0 (0.0)	2 (66.7)	0 (0.0)	1 (33.3)	0 (0.0)
obstruction						
Peritonitis	1 (1.4)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal	1 (1.4)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)
mass						
Colorectal	5 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (100)
tumor						
Unknown	20 (28.6)	0 (0.0)	16(80.0)	1 (5.0)	3 (15.0)	0 (0.0)
Total	70	1 (1.4)	51(72.9)	4 (5.7)	9 (12.9)	5 (7.1)

 Table 4: Diagnosis at first health facility

The majority of patients with CRC (60.7%) at health center were delayed being treated for amebiasis before referral to next level. For 28.6% of the patients, the diagnosis was unknown at first consultation and they were referred to the next level.

Variable	Categories	frequencies	
nutrition	Normal	36(51.4)	
	Wasted	34(48.1)	
Weight loss	<5 months	42(60)	
	>5 months	28(40)	
constipation	Yes	32(45.7)	
	No	38(54.3)	
Rectal bleeding	Yes	52(74.3)	
	No	18(25.7)	
Rectal prolapse	Yes	2(2.9)	

 Table 5: Clinical characteristics at referral hospital

	No	68(97.1)
Abdominal pain	Yes	30(42.9)
	No	40(57.1)
Bowel obstruction	Yes	12(17.1)
	No	58(82.9)
Peritonitis	Yes	3(4.3)
	No	67(95.7)
Anemia	Yes	13(18.6)
	No	57(81.4)
Tumor site	R Colon	12(17.1)
	L colon	12(17.1)
	Rectum	46(65.7)

CRC patients presented at referral hospital with rectal bleeding, weight loss, constipation and abdominal pain in 74.3%, 48.6%, 45.7% and 42.9% respectively. Other 21.4% were received as emergency having bowel obstruction or peritonitis. Rectum was the most affected site and counted 65.7% CRCs.

Variable	Categories	Frequencies n(%)
Histopathology	Grade I	28(40.0)
	Grade II	37(52.8)
	Grade III	3(4.3)
	Grade IV	1(1.4)
	GIST	1(1.4)
Stage	0	6(8.6)
	Ι	8(11.4)
	II	11(15.7)
	III	32(45.7)
	IV	12(17.1)
	Not staged	1(1.4)
Туре	Adenocarcinoma	64(91.4)
	Mucinous adenocarcinoma	5(7.1)
	GIST	1(1.4)

 Table 6: Histopathology and staging

The majority of cancers were adenocarcinoma (91.4%) and others were mucinous adenocarcinoma and gastrointestinal stromal tumors (GIST). Among the group of adenocarcinoma the most frequent pathological grade was grade 2 (moderately differentiated adenocarcinoma) counted for 52.8%, others were grade 1 (well differentiated adenocarcinoma), poorly differentiated (grade 3) and undifferentiated (grade 4).

Measure	Value	95% CI
	(months)	Lower & Upper limit
Mean duration of	14.6	12.0-17.5*
symptom		
Median duration of	12.0	9.0-12.0*
symptom		
Mean delay to consult	5.7	4.3-7.1*
Median delay to consult	3	3.0-4.5*
Mean delay, 1 st HF	3.0	1.9-4.2
Median delay, 1 st HF	3	0-2.5
Mean delay, DH	3.1	1.9-4.3
Median delay, DH	1.5	1.0-2.0
Mean delay, RDV CHUK	1.4	0.9-2.2
Median delay, RDV CHUK	1.0	0.5-1.0
Mean delay, biopsy	0.9	0.76-1.05
• • •		
Median delay, biopsy	1.0	0.75-1
Mean delay, Imaging	1.1	0.8-1.0
Median delay, Imaging	1.0	0.5-1.0
Moon dolog CIUIV	4.3	2 4 5 5*
Mean delay CHUK		3.4-5.5*
Median delay CHUK	3.5	3.0-4.2*

Patient with CRC presented at CHUK with a mean duration of symptoms of 14.6 months and 50% of them were having symptoms for more than 12 months. Patterns of delays were: delay to

consult health facility (mean: 5.7 months), delay in referral system; comprising delay at first health facility that was mainly health center (mean: 3 months), delay to second health facility which district hospital (mean: 3.1 months) and delay at CHUK (mean: 4.3 months). At CHUK, they had rendezvous (mean: 1.4 months) for Surgeon or gastroenterologist consultation, imaging (mean: 1.1 months), colonoscopy and biopsy (mean: 0.9 months) and treatment plan. 50% of the patient delayed at referral hospital for more than 3.5 months to have the final diagnosis.

Variable	Delay <12 months	Delay >12 months	p-value	
	N (%)	N (%)		
Gender			0.148	
Male	6(19.4)	25(80.6)		
Female	3(7.7)	36(92.3)		
Age			0.482	
<40	1(10)	9(90.9)		
40-50	3(16.7)	15(83.3)		
50-60	0(0)	12(100)		
>60	5(16.7)	25(83.3)		
Province			0.487	
Kigali	4(19.0)	17(81)		
North	1(6.7)	14(93.3)		
South	1(7.7)	12(92.3)		
West	3(25.0)	9(75.0)		
East	0(0)	7(100)		
Abroad	0(0)	2(100)		
Socioeconomic			0.643	
Low	6(17.7)	28(82.3)		
Moderate	2(7.7)	24(92.3)		
Good	9(12.9)	61(87.1)		
Insurance			0.022*	
MUSA	8(12.7)	55(87.3)		
RSSB/MMI/P/SORAS	0(0)	6(100)		
None	1(100)	1(100)		

 Table 8: Factors affecting delays

There was association with delayed diagnosis and health insurance (p=0.022) but socio economic status did not affect delay in CRC diagnosis and treatment. There was no association between age and delay.

variable	Delay <12 months	Delay >12 months	p-value
Nutritional status			0.327
Normal	6(16.7)	30(83.3)	
Wasted	3(8.8)	31(91.2)	
Constipation			
Yes	2(6.3)	30(93.8)	0.130
No	7(18.4)	31(81.6)	
Rectal bleeding			<0.001*
Yes	2(3.8)	50(96.2)	
No	7(38.9)	11(61.1)	
Rectal prolapse			0.582
Yes	0(0)	2(100)	
No	9(13.2)	59(86.8)	
Abdominal pain			0.122
Yes	6(20.0)	24(80.0)	
No	3(7.5)	37(92.5)	
Bowel obstruction			<0.001*
Yes	6(50)	6(50)	
No	3(5.2)	55(94.8)	
Pertonitis			0.279
Yes	1(33.3)	2(66.7)	
No	8(11.9)	59(88.1)	
Anemia			0.538
Yes	1(7.7)	12(92.3)	
No	8(14.0)	49(86)	
Tumor site			<0.001*
R colon	4(33.3)	8(66.7)	
L colon	5(41.1)	7(58.3)	
Rectum	0(0)	46(100)	

 Table 9: Clinical characteristics and delayed diagnosis

Weight loss			0.244
<5 months	7(16.7)	35(83.3)	
>5 months	2(7.1)	26(92.9)	

Delayed CRC diagnosis was significantly associated with clinical presentation of the disease such as rectal bleeding, bowel obstruction and tumor site (p value <0.001). Patient delayed in health system before the final diagnosis is made or others delayed to consult until they develop symptoms of advanced disease.

Table 10: Description of surgical management options and related outcomes

Procedure	N (%)	death	SSI	Absces	pneu	Leak	dehiscen	improve
				S	moni		ce	d
					a			
APR	16(28)	0(0.0)	2(12.5)	0	0	0	1(6.3)	14(87.5)
Bypass	1(2)	1(100)	0	0	0	0	0	0(0.0)
LAR	8(14)	1(12.5)	1(12.5)	1(12.5)	0	2(25)	0	6(75)
LHC	5(9)	0	0	0	0	0	0	5(100)
P. Stoma	6(10)	1(16)	0	0	0	0	0	5(84)
polypectomy	9(16)	0	0	0	0	0	0	9(100)
RHC	9(16)	1(11)	0	0	0	0	0	8(89)
Sigmoid C	2(4)	1(50)	0	0	0	0	0	1(50)
Subtotal C	2(2)	0	0	0	0	0	0	2(100)
Total	58(100)	5(9)	3(5)	1(2)	0	2(4)	1(2)	50(86)

The management options were curative (86.2%) or palliative surgery (13.8%). Abdominal perineal resection (APR) was the most frequent operation performed (27%) with postoperative complications in 12.5%; 1 case had both SSI and wound dehiscence. Other surgical procedures were: low anterior resection (14%) with 12.5% mortality from anastomosis leak. Polypectomy (16%), Right hemicolectomy (16%), left hemicolectomy (9%), sigmoidectomy (4%), palliative

colostomy, subtotal colectomy and ileocolic by pass. Overall hospital mortality was 9% and 60% of death was observed in patients with palliative surgery. Surgical site infection was observed in 5% of operated cases and other post operative complications were less frequent: intra abdominal abscess 2%, anastomosis leak 4% and surgical wound dehiscence 2%.

Procedures	Improved	Not	Chi-square	P value
	N (%)	improved		
		N (%)		
APR	14(87.5%)	2(12.5)	1.750	0.186
LAR	5(62.5)	3(37.5)	0.490	0.484
Sigmoid C	1(50)	1(50)	5.526	0.019
Subtotal C	1(100)	0(0)	0.378	0.539
polypectomy	9(100)	0(0)	3.575	0.059
LHC	4(80)	4(20)	0.139	0.709
RHC	9(100)	0(0)	3.848	0.050
P stoma	0(0)	4(100)	1.581	0.209
bypass	0(0)	1(100)	2.723	0.099

 Table 11: Comparison among different procedures performed

There was no statistic significance in terms of outcomes related to the procedures done; but the group of abdominal perineal resection (APR) the mortality was 0%. There were no complications observed in patients who underwent polypectomy.

4. DISCUSSION AND CONCLUSION

In this prospective, hospital based, descriptive observational study; all patients with symptomatic CRC were included in elective and emergencies provided that all information on diagnostic delay was given. In Rwanda there is no known screening program for colorectal cancers, though all the cases presented at CHUK with clinical symptoms and it explains the delay in diagnosis for patients, because early diagnosis is made in screening for asymptomatic patients. Four provinces and Kigali were represented in this group and many people were coming from Kigali as the referral hospital is located in the same city. This can be a reliable picture representing CRC diagnosis in Rwanda. The purpose of this study was document and report areas of delay in diagnosis of colorectal cancer in the largest referral hospital in the Country.

The results of the current one year study have showed that CRC mostly affected people with young age (<60 years) lowest age 21 highest 85 and the majority of patients (62.8%) were found to have advanced stage of disease (Stage III and IV). Rectum was the most common site of CRC in 65.7%. Jochim et al found rectal cancer in 37% of all cases in Northern Holland; this difference may be due to the fact that our sample was smaller than theirs (70 vs 272)¹⁰. Similar results were found in local study done in Kenya, Tanzania and South Africa and Tunisia^{2,7,38 39}⁴⁰. The finding of late presentation (advanced disease) is consistent with another study done in Nigeria by Madubogwu et al where 65.6% of patients presented with intestinal obstruction. Laura et al also found similar results where 65.1% of patients were having stage III and IV CRC^{6,41}.

Our results found that patients with CRC were delayed at health center, district hospital being treated for other benign conditions like intestinal parasites (most commonly amebiasis), hemorrhoids others were delayed without known diagnosis; others consulted as emergence either for intestinal obstruction or peritonitis and were directly referred to the surgeon. This is consistent with the findings from the study done in Western Pennsylvania Hospital over 50% of cases, their symptoms were attributed to hemorrhoids¹¹; it may also be explained by the fact that the majority of our patients presented at young age with normal nutritional state, though primary health care providers did not consider malignant conditions in first position; the reason why delayed referral was observed. Total health care related delay (delay in referral system plus delay at referral hospital) was superior to patient delay alone. This may be related to the existing

referral system where the majority of the patients passed through a long channel from health center to district hospital; and later they were sent to referral hospital to be seen by a Surgeon after several visits at different levels.

At referral hospital, the patients delayed (mean duration: 4.3 months) waiting for rendezvous to be seen by surgeon (mean duration: 1.4 months), and waiting for the final diagnosis and staging provided by colonoscopy, biopsy and imaging; these investigations took time to have results. This was due to the long waiting list of outpatients for consultation, many other patients waiting for imaging also contributed much to the delayed diagnosis for CRC patients because they have to wait for long time to have results and bring them back to the primary physician (Surgeon or Gastroenterologist) for the final plan.

On bivariate analysis there was association with rectal bleeding, intestinal obstruction and delayed diagnosis (p<0.001). This may be explained by the fact that patients were before treated for benign diseases like amebiasis, hemorrhoids long time before they develop complications or before are referred to surgeon, while they were having colorectal cancer. Health insurance was also associated with delay; the majority of our patients were using public health insurance (mutuelle) and for them to arrive at referral they had to pass through a long channel from health center to district hospital and then to be referred at tertiary level in order to be covered by mutuelle this took longtime for the patients and they delayed to present in our settings.

The surgical management options were curative resection and palliative procedures including mainly diverting colostomies. Abdominal perineal resection and low anterior resection were mostly performed (41%) of all operated cases these results are consistent with another study done in Nigeria and in Kenya^{7,42}. It can also be due to the fact that rectal cancer was most common finding in our study population (74.3%) and these procedures are performed in rectal cancers. Our findings were different from results seen by Sheik et al where right hemicolectomy was the most frequent (around 27%) procedure and this was probably because the right side of the colon was mostly affected by cancer⁴³.

Among the 58 patients who were operated, in hospital mortality was 9% different from the result observed in United Kingdom $(0.04\%)^{43}$ this difference can be explained by the advances in perioperative, postoperative management and high level critical care settings in UK compared to

Rwanda. Postoperative complications were observed in 14% of the total group. This results are not similar to other studies: Bruno et al found 38% of post operative complications⁴⁴, in Tunisia they found 27%⁴⁵ this difference may be explained by a narrow sample in our study and relatively short period of the study compared to the above mentioned studies. Polypectomy was done without complications. Over all perineal wound complications after abdominal perineal resection was12.5% it is similar to the findings of Prytz et al where they found 12.0% of perineal wound infection⁴⁶. Muster et al found 29%⁴⁷, this difference from our finding may be due to difference in sample sizes and our results were from a single center. In Abdominal perineal resection group we observed less postoperative complications 2 cases (12.5%) and no mortality.

5. CONCLUSION

Although it was previously thought to be a less prevalent condition, colorectal cancer prevalence is increasing in Rwanda and in general, the diagnosis of colorectal cancer is delayed for all patients because they consulted when they have developed symptoms, and the management delayed. This study has found that major causes of delay were patients related and health care related; where they delayed to seek for medical care and when they consulted, they also delayed in the referral system, which is a long channel from the health center to the referral hospital, at the referral hospital patients delayed by the process of an appointment to consult a Specialist and waiting for investigations before the final diagnosis is made; yet there is no existing local guidelines for diagnosis and management of patients with CRC. All these prolong the waiting time and the majority of the patients are operated when they have advanced stages of the disease. Early post operative outcomes in our settings were acceptable with less mortality and morbidity and were comparable to other centers' data. Early detection for this condition could be made possible by screening program and the outcomes would be improved if the patients are treated timely.

6. RECOMMENDATIONS

6.1 To Rwanda Biomedical Center: Non communicable disease division

To install a strategy for early detection of colorectal cancer by rising awareness of CRC in the community and health care facilities, so that all practitioners do the same for the patients

Screening program for colorectal cancer could be availed so that patients at risk start to consult before they have symptoms.

To put in place guidelines for colorectal cancer management in multidiscipline approach, in order to have all patients treated in the same way at any center in Rwanda; this will prevent gaps and discrepancy in health system.

Education of the population to raise awareness of colorectal cancer in Rwandans

6.2 To University teaching hospital of Kigali (CHUK)

To establish a cancer registry where all the information on CRC patients are recorded for follow up and data for quality improvement researches.

To create a network where Physician/Oncologist- Surgeon- Radiologist-Pathologist can work and communicate jointly to decrease the delay in the process of investigations.

To conduct another study of long term outcomes and survival after treatment of CRC

6.3 To other health care facilities

To rule out CRC in patients presenting with rectal bleeding and change in bowel habits by early referral for colonoscopy, before treatment of other benign conditions

6.4 To the community

To consult early when they notice rectal bleeding or change in bowel habits for timely detection and treatment of CRC when it is found.

6. REFERENCES

- Coetzee E. Early detection of colorectal cancer of individuals who sporadic disease, up Colonoscopy visualises the mucosa of the Colorectal cancer Of the familial CRC. 2013;31(6):210-212.
- Katalambula LK, Ntwenya JE, Ngoma T, et al. Pattern and Distribution of Colorectal Cancer in Tanzania: A Retrospective Chart Audit at Two National Hospitals. *J Cancer Epidemiol.* 2016;2016:1-13. doi:10.1155/2016/3769829
- Duduyemi B, Akang E, Adegboyega P, Thomas J. Significance of Dna Mismatch Repair Genes and Microsatellite Instability in Colorectal Carcinoma in Ibadan, Nigeria. Am J Med Biol Res. 2013;1(4):145-148. doi:10.12691/ajmbr-1-4-7
- Abdel-Razek AH. Challenge in diagnosis and treatment of colonic carcinoma emergencies. *Alexandria J Med.* 2012;48(2):109-113. doi:10.1016/j.ajme.2011.12.006
- Oribabor FO, Adebayo BO, Aladesanmi T, Akinola DO. Anatomical Sites of Colorectal Cancer in a Semi-Urban Nigerian Hospital: Is There a True Rightward Shift. *East Afr Med* J. 2013;90(8):248-252.
- 6. Ci M. Colorectal Cancer : Late Presentation and Outcome of Treatment. :1-3.
- Saidi H, Abdihakin M, Njihia B, et al. Clinical Outcomes of Colorectal Cancer in Kenya. Ann African Surg. 2011;7(1):2009-2012. doi:10.4314/aas.v7i1.67029
- 8. CLINICOPATHOLOGICAL CHARACTERISTICS OF GASTROINTESTINAL LESIONS DIAGNOSED AT THE ANATOMICAL PATHOLOGY UNIT OF UNIVERSITY TEACHING HOSPITAL OF KIGALI. 2107.
- 9. Profile CM, Trends ACM, Incidence C. Rwanda. 2014.
- Terhaar sive Droste JS, Oort FA, van der Hulst RWM, et al. Does delay in diagnosing colorectal cancer in symptomatic patients affect tumor stage and survival? A populationbased observational study. *BMC Cancer*. 2010;10(1). doi:10.1186/1471-2407-10-332
- Ristvedt S.L., Birnbaum E.H., Dietz D.W., Fleshman J.W., Kodner I.J., Read T.E. Delayed treatment for rectal cancer. *Dis Colon Rectum*. 1736;48(9):1736-1741. doi:http://dx.doi.org/10.1007/s10350-005-0069-x
- Macrae FA, Bendell J. Clinical presentation, diagnosis, and staging of colorectal cancer Clinical presentation, diagnosis, and staging of colorectal cancer Page 2 of 22. 2014:1-22.

- Majumdar SR, Fletcher RH, Sc M, Evans AT. How Does Colorectal Cancer Present? Symptoms, Duration, and Clues to Location. 1999;94(10).
- Johns LE, Houlston RS. A systematic review and meta-analysis of familial colorectal cancer risk. *Am J Gastroenterol*. 2001;96(10):2992-3003. doi:10.1016/S0002-9270(01)03239-7
- Mai P. Hereditary Colorectal Cancer Colorectal Cancer. 2014:919-932. doi:10.1056/NEJMra012242
- Kuipers EJ, Grady WM, Lieberman D, et al. Colorectal cancer. *Nat Publ Gr.* 2015;1:1-25. doi:10.1038/nrdp.2015.65
- Hawaz Y, Admassie D, Kebede T, Ababa A. 9990 East Cent . Afr . J . surg . (Online) e text] 9990 East Cent . Afr . J . surg . (Online). 2012;17(1):2010-2013.
- Bohorquez M, Sahasrabudhe R, Criollo A, et al. Clinical manifestations of colorectal cancer patients from a large multicenter study in Colombia. *Med (United States)*. 2016;95(40). doi:10.1097/MD.00000000004883
- Presentation C. GASTROENTEROLOGY CLINICS. 2008;37:1-24. doi:10.1016/j.gtc.2007.12.002
- Parajuli R, Bjerkaas E, Tverdal A, Selmer R, Marchand L Le. The Increased Risk of Colon Cancer Due to Cigarette Smoking May Be Greater in Women than Men. 2013;22(May):862-872. doi:10.1158/1055-9965.EPI-12-1351
- Edge SB, Compton CC. The American Joint Committee on Cancer : the 7th Edition of the AJCC Cancer Staging Manual and the Future of TNM. 2010:1471-1474. doi:10.1245/s10434-010-0985-4
- 22. Ueno H, Kajiwara Y, Shimazaki H, et al. New criteria for histologic grading of colorectal cancer. *Am J Surg Pathol*. 2012;36(2):193-201. doi:10.1097/PAS.0b013e318235edee
- Vega P, Valentín F, Cubiella J. Colorectal cancer diagnosis: Pitfalls and opportunities. World J Gastrointest Oncol. 2015;7(12):422. doi:10.4251/wjgo.v7.i12.422
- Bor R, Fábián A, Szepes Z. Role of ultrasound in colorectal diseases. 2016;22(43):9477-9487. doi:10.3748/wjg.v22.i43.9477
- Świderska M, Choromańska B, Dąbrowska E, et al. The diagnostics of colorectal cancer. Wspolczesna Onkol. 2014;18(1):1-6. doi:10.5114/wo.2013.39995
- 26. Mastalier B, Tihon C, Ghiță B, et al. Surgical treatment of colon cancer: Colentina

surgical clinic experience. J Med Life. 2012;5(3):348-353.

http://www.ncbi.nlm.nih.gov/pubmed/23144667%0Ahttp://www.pubmedcentral.nih.gov/a rticlerender.fcgi?artid=PMC3493968.

- BATISTA VL, IGLESIAS ACRG, MADUREIRA FAV, BERGMANN A, DUARTE RP, FONSECA BFS da. Adequate lymphadenectomy for colorectal cancer: a comparative analysis between open and laparoscopic surgery. *ABCD Arq Bras Cir Dig (São Paulo)*. 2015;28(2):105-108. doi:10.1590/s0102-67202015000200005
- West NP, Hohenberger W, Weber K, Perrakis A, Finan PJ, Quirke P. Complete mesocolic excision with central vascular ligation produces an oncologically superior specimen compared with standard surgery for carcinoma of the colon. *J Clin Oncol.* 2010;28(2):272-278. doi:10.1200/JCO.2009.24.1448
- Kessler H, Hohenberger W. Extended lymphadenectomy in colon cancer is crucial. World J Surg. 2013;37(8):1789-1798. doi:10.1007/s00268-013-2130-6
- Watanabe T, Itabashi M, Shimada Y, et al. Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2014 for treatment of colorectal cancer. *Int J Clin Oncol*. 2015;20(2):207-239. doi:10.1007/s10147-015-0801-z
- 31. Ronnekleiv-Kelly SM, Kennedy GD. Management of stage IV rectal cancer: Palliative options. *World J Gastroenterol*. 2011;17(7):835-847. doi:10.3748/wjg.v17.i7.835
- Brandi G, Lorenzo S De, Nannini M, et al. 2016 Colorectal Cancer : Global view Adjuvant chemotherapy for resected colorectal cancer metastases : literature review and meta-analysis. 2016;22(2):519-533. doi:10.3748/wjg.v22.i2.519
- Murphy CC, Harlan LC, Lund JL, Lynch CF, Geiger AM. Patterns of Colorectal Cancer Care in the United States: 1990-2010. *J Natl Cancer Inst.* 2015;107(10):1-11. doi:10.1093/jnci/djv198
- Glimelius B. Optimal Time Intervals between Pre-Operative Radiotherapy or Chemoradiotherapy and Surgery in Rectal Cancer? *Front Oncol.* 2014;4(April):1-10. doi:10.3389/fonc.2014.00050
- Costi R, Leonardi F, Zanoni D, et al. palliative care and end-stage colorectal cancer management : The surgeon meets the oncologist. 2014;20(24):7602-7621. doi:10.3748/wjg.v20.i24.7602
- 36. Rivera S, Villa J, Quero L, Hennequin C. Adjuvant radiotherapy for rectal cancer : Recent

results, new questions La radiothérapie adjuvante pour le cancer du rectum : résultats récents, nouvelles questions. 2011. doi:10.1016/j.gcb.2010.07.017

- 37. Amabwiriza_y_Ubudehe_2016.pdf.
- Wentink MQ, Räkers M, Stupart DA, Algar U, Ramesar R, Goldberg RA. Incidence and histological features of colorectal cancer in the Northern Cape province, South Africa. *South African J Surg.* 2010;48(4):109-113.
- Limaiem F, Azzabi S, Sassi A, Mzabi S, Bouraoui S. Colorectal cancer in young adults: A retrospective study of 32 tunisian patients. *Pan Afr Med J*. 2018;31:1-9. doi:10.11604/pamj.2018.31.62.11043
- Asombang AW, Madsen R, Simuyandi M, et al. Descriptive analysis of colorectal cancer in Zambia, Southern Africa using the National Cancer Disease Hospital Database. *Pan Afr Med J.* 2018;30:1-8. doi:10.11604/pamj.2018.30.248.12464
- 41. Siminoff L, Thomson M, Dumenci L. Factors associated with delayed patient appraisal of colorectal cancer symptoms. *Psychooncology*. 2014;23(9):981-988. doi:10.1002/pon.3506
- 42. Irabor DO, Afuwape OO, Ayandipo OO. The Present Status of the Management of Colon and Rectal Cancer in Nigeria. *J Cancer Res*. 2014;2014:1-7. doi:10.1155/2014/267190
- Sheikh AA, Joel AS, Johnson MA, Vimalachandran D. Outcome of colorectal cancer resection in octogenarians. *South African J Surg.* 2013;51(2):68-72. doi:10.7196/SAJS.1535
- Andreoni B, Chiappa A, Bertani E, et al. Surgical outcomes for colon and rectal cancer over a decade: Results from a consecutive monocentric experience in 902 unselected patients. *World J Surg Oncol.* 2007;5:1-10. doi:10.1186/1477-7819-5-73
- 45. Bouassida M, Feidi B, Mroua B, et al. Histopathologic characteristics and short-term outcomes of colorectal cancer in young tunisian patients: One center's experience. *Pan Afr Med J*. 2012;12(1):1-7.
- Prytz M, Angenete E, Ekelund J, Haglind E. Extralevator abdominoperineal excision (ELAPE) for rectal cancer - Short-term results from the Swedish Colorectal Cancer Registry. Selective use of ELAPE warranted. *Int J Colorectal Dis*. 2014;29(8):981-987. doi:10.1007/s00384-014-1932-9
- 47. Musters GD, Sloothaak DAM, Roodbeen S, Van Geloven AAW, Bemelman WA, Tanis PJ. Perineal wound healing after abdominoperineal resection for rectal cancer: A two-

centre experience in the era of intensified oncological treatment. *Int J Colorectal Dis*. 2014;29(9):1151-1157. doi:10.1007/s00384-014-1967-y

APPENDIX A: STUDY COORDINATION

RESEARCHERS:

- Dr KARENZI Irénée David, investigator, study coordinator
- Dr NIFASHA Antoine, Supervisor
- Dr RUHUNGANDE Landouald, Co-supervisor

APPENDIX B: INFORMED AGREEMENT FOR CHILDREN BETWEEN 15-20YEARS OF AGE

Research title:" COLORECTAL CANCERS: FACTORS AFFECTING DELAY IN COLORECTAL CANCER DIAGNOSIS AND SHORT TERM SURGICAL OUTCOMES IN CHUK"

INVESTIGATOR: Dr KARENZI Irénée David

Tel: 0788868136, email: karenzi.david@gmail.com

INFORMATION SHEET & CONSENT/ IBISOBANURO NO KWEMERA KUJYA MU BUSHAKASHATSI

Please read carefully before deciding on participation

Purpose of the study: to determine the factors affecting delay in colorectal cancer diagnosis and short term outcomes after surgery in Rwanda

What you will do in the study: to give information about the progression of your condition by answering some related questions

Time required being included in the study: You will be included in the study from the time of admission in colonoscopy unity until the final treatment and day 30 post operation it will not interfere with your own program or usual life.

Risks related to the study: There are no anticipated risks for anyone who will be included in the study

Benefits from the study: there is no financial benefit to participate in this study, but later it may help patients with this condition to be managed earlier.

Confidentiality: All information will be kept confidential there will be no access for anyone else than the researcher or the patient.

Right to withdraw from the study: Any participant is free to withdraw from the study at any time without consequences either for him or his life.

В

Results from the study may be published in scientific conferences or medical journals for better understanding and management of this condition by many health care workers.

If you have concern about the study, contact

Dr KARENZI Irénée David, University of Rwanda, Resident in Surgery; tel: + (250)788868136 E-mail: <u>karenzi@gmail.come</u>

If you have questions about your rights in the study, contact:

Professor Kato J. Njunwa, Chair person, Institutional Review Board, tel: +250788490522

Dr Brenda Asiimwe-Kateera, Secretary, Institutional review Board

College of Medicine and Health Sciences, University of Rwanda/ P.O.Box 3286 Kigali/Rwanda Email: <u>researchcenter@ur.ac.rw</u>; website: http//chms.ur/ac/rw/

Agreement:

I agree to participate in the research study described above, I have been explained all about the purpose and usefulness of the study before signing.

Verbal assent given?	Yes	Date
----------------------	-----	------

APPENDIX C: INFORMED CONSENT

Research title:" COLORECTAL CANCERS: FACTORS AFFECTING DELAY IN COLORECTAL CANCER DIAGNOSIS AND SHORT TERM SURGICAL OUTCOMES IN CHUK"

INVESTIGATOR: Dr KARENZI Irénée David

Tel: 0788868136, email: karenzi.david"gmail.com

INFORMATION SHEET & CONSENT

Please read carefully before deciding on participation

Purpose of the study: to determine the factors affecting delay in colorectal cancer diagnosis and short term outcomes after surgery in Rwanda

What you will do in the study: to give information about the progression of your condition by answering some related questions

Time required being included in the study: You will be included in the study from the time of admission in colonoscopy unity until the final treatment and day 30 post operation it will not interfere with your own program or usual life.

Risks related to the study: There are no anticipated risks for anyone who will be included in the study

Benefits from the study: there is no financial benefit to participate in this study, but later it may help patients with this condition to be managed earlier.

Confidentiality: All information will be kept confidential there will be no access for anyone else than the researcher or the patient.

Right to withdraw from the study: Any participant is free to withdraw from the study at any time without consequences either for him or his life.

Results from the study may be published in scientific conferences or medical journals for better understanding and management of this condition by many health care workers.

If you have concern about the study, contact

Dr KARENZI Irénée David, University of Rwanda, Resident in Surgery; tel: + (250)788868136 E-mail: <u>karenzi@gmail.come</u>

If you have questions about your rights in the study, contact:

Professor Kato J. Njunwa, Chair person, Institutional Review Board, tel: +250788490522

Dr Brenda Asiimwe-Kateera, Secretary, Institutional review Board

College of Medicine and Health Sciences, University of Rwanda/ P.O.Box 3286 Kigali/Rwanda Email: <u>researchcenter@ur.ac.rw</u>; website : http//chms.ur/ac/rw/

Agreement: I

agree to participate in the

research study described above

Signature:

Date

DATA COLLECTION FORM

"Colorectal cancer" Factors affecting the delay in CRC management and short term surgical outcomes in CHUK.

Names and/or Initials		Hospital ID			Number:			
Age:	Years	Sex: M/F	District	Р	Province			tal
Econom	nic status	(ubudehe)	Insurance: MUSA	RSSB	PRIVATE	OTHER		
Clinica	l present	tation						
Nutritic	onal statu	s: Normal,	weight loss	(duration?) cach	nectic		
Present	ting com	plaints: chr	onic constipation, re	ctal bleedin	g, prolapse or	mass, bov	vel	
obstruct	tion, peri	tonitis, abdo	ominal pain, anemia,	hernias, oth	ner:			
Investi	gations: 1	FBC (Hb:) electrolytes (Na:	K:	Cl:	mol/L)		
Imagin	g done: 1	U/S, Fluoro	scopy, CT scan, MR	I, other:				
colonos	scopy/bio	opsy:						
Duratio	on of syn	nptoms: 1-3	3months, 3-6 months	s, 6- 12 mon	ths, 1-2 years,	>2 years (?)
Decisio	n to seek	for Health	care: in 1month, 1-3	months, 3-6	6 months, 6-12	2, >1 year (?)
First co	nsultation	n: Health C	enter (HC), District	Hospital (D	H), Private cli	nic, Referral	hospi	ital
At HC	(Dg knov	wn Y/N if Y	:) refe	rred opd? Y	//N if Y after l	now long ()
Duratio	n from H	IC to DH () (Dg known	at DH ? Y/	N if Y:)
referred	l opd? Y	/ N if yes a	fter how long?					
Duratio	n to reac	h Surgeon f	rom referring health	facility: imr	nediate, RDV	(weeks,	moi	nths)
Duration to find results: colonoscopy/ biopsy (), i), imaging (), oth			
Total dı	uration of	f investigati	ons:					
Duratio	n to get I	Diagnosis a	nd plan by Surgeon (days,	weeks,	months)		
Duratio	n to be o	perated afte	r diagnosis:					
Preope	rative in	formation:						
Admiss	sion diag	nosis:		planned	procedure:			
Elective	e operati	ion		Emerger	nce operation			

Operative finding: tumor characteristics:resectableYes/Notumor site: Right colonLeft colon (descending, sigmoidRectum)

Cancer extension: only colon, Lymph nodes other organs: bladder liver other

procedure done: curative palliative

Right hemicolectomy Left hemicolectomy total colectomy anterior resection palliative colostomy, duration of procedure (hours), intra op complications: (bleeding, iatrogenic injury, other:

Early surgical Outcomes: died in hospital post op infection (SSI, intra abdominal abscess) anastomosis leak, wound dehiscence, improved on discharge, prolonged hospital stay ()

Post operative histology results:

Total duration from onset of symptoms to definitive treatment: