DISSERTATION

TIME TO PRESENTATION AND DIAGNOSIS IN PATIENTS WITH ESOPHAGEAL CANCER AT KENYATTA NATIONAL HOSPITAL

DR. MARIAL MAJUR CIKOM MABIOR

MBBS (UoJ), MSc IH &M (Univ. of Parma)

H58/68846/2013

A DISSERTATION PRESENTED IN PARTIAL FULFILLMENT OF THE REQUIRMENT FOR DEGREE OF MASTER OF MEDICINE (INTERNAL MEDICINE) AT THE UNIVERSITY OF NAIROBI,

DECLARATION

I declare that this dissertation is my original work and has never been published or presented for a degree in any other University.

Signed: _____ Date: _____

DR. MARIAL MAJUR CIKOM MABIOR

(Resident, Department of Clinical Medicine and Therapeutics, College of Health Sciences, University of Nairobi)

APPROVAL BY SUPERVISORS

This dissertation has been submitted with our approval as Supervisors:

1. DR. ADAM SHEIKH,

   MBChB, M.Med (Nbi.), Consultant Physician and Gastroenterologist

   Lecturer,

   Department of Clinical Medicine and Therapeutics, University of Nairobi, Kenya

   Signed_____ Date_____

2. PROF. MARK D. JOSHI,

   MBChB, M.Med, Cert TropMed, MPH, Cert ClinEpid, FACC Consultant Physician and Cardiologist,

   Lecturer,

   Department of Clinical Medicine and Therapeutics, University of Nairobi, Kenya

   Signed_____ Date_____

DEDICATION

This study is dedicated to my lovely children, my beloved parents, friends and colleagues for their continuous, support and encouragement since starting this Master's program. God bless you all.

ACKNOWLEDGEMENTS

I want to thank God Almighty for giving me strength and will to carry out this project. I want to acknowledge the following persons for their support:

1. My supervisors Prof. Mark Joshi and Dr. Adam Sheikh for their guidance, advice and timely responses during the entire study period.
2. All my lecturers and colleagues for their support and encouragement.
3. The hospital administrations in Kenyatta National Hospital for their permission and co-operation, during the period of this work.

TABLE OF CONTENTS

DECLARATION ii

APPROVAL BY SUPERVISORS iii

DEDICATION iv

ACKNOWLEDGEMENTS v

TABLE OF CONTENTS vi

LIST OF TABLES ix

LIST OF FIGURES x

LIST OF ABBREVIATIONS AND ACRONYMS xi

ABSTRACT xiii

CHAPTER ONE: INTRODUCTION AND LITERATURE REVIEW 1

1.0. Introduction 1

1.1. Literature Review of Squamous Cell Esophageal Cancer 2

1.1.1. Global Esophageal Cancer Epidemiology 2

1.1.2. Epidemiology of Esophageal Cancer in Africa 3

1.2. Risk Factors for Esophageal Cancer 3

1.3. Clinical Presentations of Esophageal Cancer 4

1.4. Outcomes of Squamous Cell Esophageal Cancer 5

1.5. Approaches Shown to Improve Outcomes 5

1.6. Cancer Diagnostic Delay 6

1.6.1. Patient Delay 7

1.6.2. Health Care Provider Referral Delay 7

1.6.3. Total Diagnostic Delay 7

1.7. Factors associated with delay in cancer diagnosis 8

1.7.1. Socioeconomic status 8

1.7.2. Delay Presentation and Referral 9

1.8. Factors associated with delay in diagnosis of esophageal cancer 9
1.8.1. Patient Related Factors 9
1.8.2. Physician Related Factors 9
1.8.3. Health Care - Related Factors 9
CHAPTER TWO: JUSTIFICATION AND OBJECTIVES 11
2.1. Justification 11
2.2. Research Question 11
2.3. Objectives 11
2.3.1. Broad Objective 11
2.3.2 Specific Objectives 11
CHAPTER THREE: METHODOLOGY 12
3.1. Study Design 12
3.2. Study Site 12
3.3. Study Population. 12
3.4. Case Definition 12
3.5. Inclusion Criteria 12
3.6. Exclusion Criteria 12
3.7. Study Variables 13
3.8. Quality Assurance 16
3.9. Sampling Technique 16
3.10 Sample Size Computation 16
3.11. Patient Selection 17
3.12. Screening and Recruitment 17
3.13. Data Collection 18
3.14. Data Management and Analysis 18
3.15. Ethical Consideration 19

CHAPTER FOUR: RESULTS 20
4.1. Patients' Recruitment Flow Chart 20
4.2. Socio-Demographic Characteristics 20
4.3. Time Interval from Symptoms Onset, First Presentation and Referral to Diagnostic Facility (Patient and Referral Delay) 22
4.4. The Median Time from First Endoscopic Evaluation and Confirmed Histologic Diagnosis (Diagnostic Delay) 23
4.5. Factors Associated with Delayed First Presentation 23
4.6. Factors Associated With Delayed Referral to Diagnostic Facility (Doctor Delay) ..24
4.7. Factors Associated With Endoscopic and Histologic Results Delays in Ca-O Patients 25
4.8. Factors Associated With Overall Diagnostic Delay 26
CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS 28
5.1. Discussion 28
5.2. Conclusion 29
5.3. Recommendations 30
5.4. Limitations 30
6.0 REFERENCES 31
7.0 APPENDICES 34
Appendix I: Data Collection Proforma(English Version) 34
Appendix II: Data Collection Proforma(Kiswahili Version) 38
Appendix III: Consent Explanation 42
Appendix IV: Consent Form (English Version) 44
Appendix V: Assent Form 45
Appendix VI: Consent Explanation for the Participants (Kiswahili Version) 47
Appendix VII: Patient Consent Form (Kiswahili Version) 49
Appendix VIII: TNM Staging 50

LIST OF TABLES

Table 4. 1: Socio-demographic characteristics of the study participants.....21

Table 4. 2: Time interval from symptoms onset, first presentation and referral to diagnostic facility 22

Table 4. 3: The median time from first endoscopic evaluation and confirmed histologic diagnosis (diagnostic delay).....23

Table 4. 4: Factors associated with delayed first consultation (Patients) 24

Table 4. 5: Factors associated with delayed referral to diagnostic facility (doctor delay) 25

Table 4. 6: Factors related to delay endoscopy and histology results in of Ca-O patients 26

Table 4. 7: Factors associated with overall diagnostic delay.....27

LIST OF FIGURES

Figure 1. 1: Timelines of cancer diagnostic delay in the UK 8
Figure 3. 1: Timeline of Cancer diagnostic delay-more than 90 days……14
Figure 4. 1: Patients' recruitment flow chart 20
Figure 4. 2: Staging of cancer in patients with Ca-O at diagnosis.....22

LIST OF ABBREVIATIONS AND ACRONYMS

AC	Adenocarcinoma
ASR	age-standardized incidence rates
Ca-O	Cancer of Esophagus
CO	Clinical Officer
DCMT	Department of Clinical Medicine & Therapeutics
Eso/ESCC	Esophageal Squamous Cell Carcinoma
GERD	Gastro – Esophageal Reflux
GP	General Practitioner
HPV	Human Papilloma Virus
HCP	Health care provider
IH & M	International Health & Medicine
KNH	Kenyatta National Hospital
MSc	Master of Science
OGD	Oesophago – Gastro – Duodenoscopy
PI	Principal Investigator
SPSS	Statistical Package for Social Sciences
SCC	Squamous Cell Carcinoma
SES	Socioeconomic Status
TNM	Tumor Node Metastases Classification System
Univ	University
UoJ	University of Juba

UoN	University of Nairobi
USA	United States of America
WHO	World Health Organization

ABSTRACT

Background: Cancer of esophagus (Ca-O) is the eighth most common cancer in the world and is ranked sixth amongst the leading causes of cancer death. Ca-O is a major health problem in Sub-Saharan Africa. A high incidence rate was reported amongst men in central and western Kenya region. The identification of modifiable patient and health care system factors accounting for delayed presentation and diagnosis is critical information with potential to improve outcomes.

OBJECTIVE: To determine diagnostic time lines and factors associated with delayed health care service delivery among patients with established histological Ca-O at KNH.

Methods: This was a retrospective diagnostic cohort study was conducted at Cardiothoracic, Endoscopy and Radiotherapy unit/clinics at Kenyatta national Hospital. Eighty-five (85) participants with established histological diagnosis Ca-O consented and enrolled into the study. Data was collected using a structured questionnaire to record time intervals to presentation, referral and diagnosis and the stage at Ca-O at diagnosis. Statistical analysis was done in SPSS version 21.0. Cancer delay variables were presented as percentages and associated with independent variables using chi square and t tests.

Results: The mean age of the participants was 59.2 years (SD 14.5 years), 64.7% were males, 75.3% had attained some level of education, 47.1% were unemployed and 62.4% lived in the urban. Majority (89.4%) were diagnosed at stage III and IV. Delay to first presentation was 78.8%, referral delay was 76.5% and total diagnostic delay was 61.2%. Those who did not afford transport and consultation were more likely to delay first presentation (88.6%), OR 3.6 (95% CI 1.2-11.3), p=0.022. Referral delay was associated with residence with those living in the rural less likely to delay [OR 0.2 (95% CI 0.0-0.8), p=0.019].

Conclusion: There was a widespread delay among Ca-O patients throughout the cancer diagnostic process. More than three-quarters of the patients delayed in presenting for first consultation, referral to higher level facilities, endoscopy procedure and receiving histology results.

CHAPTER ONE: INTRODUCTION AND LITERATURE REVIEW

1.0. Introduction

Cancer esophagus (Ca-O) is the eighth most common cancer and the sixth leading cause of cancer death in the world. The hot spots of Ca-O include northern Iran, Kazakhstan, Southern Africa and northern China with annual incidence exceeding 200/100,000 per year.(1)The highly endemic regions of North-Eastern Iran to northern China have extremely high incidence of Ca-O of SCC type. The other regions with high incidence rate of Ca-O are South America, North America, Europe, India, and Southern Africa.

Ca-O is a major health problem in Sub-Saharan Africa. A high incidence rate was reported amongst men in central and western Kenya region. In a Study done at Tenwek Hospital, Bomet District, 1989-1998, Ca-O accounted for 19% of total malignancies diagnosed.(2)

In the United States of America, Blacks are 4.5 times more likely to develop Ca-O than Caucasians and men are more at risk compared to women. Amongst whites, the male to female ratio is 3:1 whilst it is 4:1 amongst blacks. In Kenya, Ca-O is the second commonest cancer in males and third in females after breast and cervical cancers.(3)The most common histological types of Ca-O are SCC and accounts for over 90% of diagnosed cancer cases. Ca-O occurs at narrow areas near the thyroid cartilage, the bifurcation of the trachea and at the level of diaphragm.

Prolonged exposure to carcinogens in tobacco is associated with majority of Ca-O SCC in Europe and North America. Adenocarcinoma (AC) arises from dysplastic mucosa secondary to Barrett's esophagus and found in the distal esophagus near the gastric cardia. AC is three times more common in whites than blacks and affects seven times more men than women.

Education of the public in Ca-O control is necessary because certain life-styles are known to be associated with the onset of cancers in various sites. Ca-O can be prevented (primary prevention) and participation in an early detection programme can lead to the discovery of a cancer while it is still curable (secondary prevention).

In Kenya, 70–80% of cancer cases are diagnosed in late stages due to lack of awareness amongst patients and healthcare workers, poor access to health facilities and insufficient diagnostic facilities.(4)

1.1. Literature Review of Squamous Cell Esophageal Cancer

1.1.1. Global Esophageal Cancer Epidemiology

The estimated new cases of Ca-O worldwide in 2008 were 482,000, accounting for 408,800 deaths.(5)A report by WHO 2009 indicated that cancer accounted for 7.9 million deaths, which is about 13% of all deaths in the world. Ca-O remains an important cancer in the Asia–Pacific region and cancer statistics shows that Asian countries have some of the highest age-standardized incidence rates (ASR) in the world with a very high concentration of cases in the Caspian littoral in Iran and several provinces in China.(6)However, the cancer incidence rates vary greatly within a diverse continent, with some countries like the Philippines, Thailand and Malaysia reporting a very low ASR.

The national cancer registry of the Malaysian Peninsula of 1991-1996 and neighboring Singapore(7)by race shows a higher incidence amongst Chinese and Indians. In Malaysia, where Malay, Chinese and Indian co-exist; marked ethnic difference in various other gastrointestinal cancers has previously been observed and reported.

The Belt of Ca-O encompasses areas of Turkey, Iran, Kazakhstan and northern and central China, with an estimated Ca-O of SCC type more than 100 cases per 100000 person-years. The South-Eastern Africa region has similarity with this Asian cancer belt with high incidence of SCC Ca-O type.

According to statistics by World Cancer Fund in December 2010, Mongolia had the highest Ca-O incidence rate- 18 cases per 100,000 in males. In the latest report by World Cancer Fund in 2012 (GLOBOCAN) and 2014 International Agency for Research on Cancer (IARC) in Sub-Saharan Africa, Malawi had the highest rate of 28.2/100,000 per year and Uganda was ranked second with a rate of 24.8/100/00 per year in males.(8)

In the same report(9), Kenya was number six with rate of 20.2/100,000 for male and was ranked third in women's prevalence in Sub Saharan Africa (SSA), with an incidence rate of 15.1/100,00 per year for women. Esophageal SCC prevalence is higher in developing countries(10) and is extremely high in many parts of Africa, especially the eastern parts of the continent, in contrast to the low frequency of Ca-O of AC type in most regions of Sub-Saharan Africa .

1.1.2. Epidemiology of Esophageal Cancer in Africa

Africa has shown an increased number of cases of Ca-O with uneven geographic distribution, with Eastern and Southern Africa as the epicenter.(11)The highest incidence rate in men was reported in South Africa, Soweto area. A study on prevalence of Ca-O in North-west Kenya between 1994 and 2004, reported Ca-O was the leading cancer- accounting for 13.8% of cases diagnosed, of which more than 90% of cases were SCC, with a male to female ratio 5:1.

A study by White et al, between 1989 and 1998, reported that Ca-O was the most common malignancy, accounting for 19% of 1499 malignancies diagnosed in Bomet District, Southwestern Kenya.(12)The study concluded that about one in five Ca-O patients (approximately 21%), were aged 30 years and below.

Patients with Ca-O have a poor prognosis due to late presentation at diagnosis and delay between symptom recognition and first medical consultation.(13)

1.2. Risk Factors for Esophageal Cancer

Risk factors play a big role in Ca-O and differ according to histological type of the cancer. In Africa, smoking and alcohol consumption are the most common risk factors for Ca-O.(14)There is increased incidence of Ca-O in areas of high tobacco and alcohol consumption. Tobacco smoking causes acid reflux, which damages esophageal mucosa. Tobacco also contains carcinogens, and concurrent smoking and alcohol consumption enhances the carcinogenic effects of chemicals in tobacco and increases the risk of Ca-O - especially SCC.(15)

Some studies have shown that nutrition also promotes or reduces the risk of Ca-O. A diet low in protein, high in fat and containing nitrosamine-laden foods increases the risk of Ca-O.(16)A diet with foods rich in antioxidants - such as vitamins A, C, E and folic acid, prevents damage to the esophagus that can lead to cancer. Selenium- mostly found in fresh vegetables, meat and eggs also has a protective role in reduction of Ca-O risk.

The AC type of Ca-O results from Barrett's esophagus, a form of metaplasia secondary to gastro-esophageal reflux (GERD).GERD causes long term irritation of esophageal mucosa. The risk of developing this type of cancer increases with age. Race is also a risk factor, with

blacks being more prone to Ca-O more than the whites. There is also a gender predilection, with men being more affected than women.

Some functional esophageal disorders, such as achalasia, increase risk of Ca-O. Both SCC and AC are ten times more common in patients with achalasia. Certain medical conditions have been implicated as risk factors for Ca-O - such as tylosis and Plummer-Vinson Syndrome. These two conditions are mostly associated with a poor prognosis subtype of SCC.

Studies also have shown an association between consumption of maize contaminated with fungi of *Fusarium verticillioides* type and the increased incidence of Ca-O (SCC) in Transkei -South Africa and Henan, China.(17)This fungus synthesizes fumonisins in the contaminated food. Fumonisins are associated with tumor promotion activity(18)and cell cycle dysregulation (19), that can lead to Ca-O.

The Human Papilloma virus (HPV) is another organism implicated in the etiology of Ca-O SCC type in South Africa.(20) Previous studies examining HPV prevalence in this type of cancer found a patient serum prevalence of 0-71%. HPV was detected in 26–71% of suspected Ca-O biopsy samples collected from South African patients.(21)

Caustic injuries of esophagus with some residual scaring and consumption of hot and spicy food are other risks for Ca-O, especially SCC type of cancer.

1.3. Clinical Presentations of Esophageal Cancer

Clinical manifestations of Ca-O are similar in both histological sub-types, but differ based on the site of initial tumor growth. Both types can present clinically with progressive dysphagia, occurring in more than 90% patients at presentation. In about 5 to 10% of these patients, dysphagia is associated with weight loss, associated with a worse prognosis.(22)

Some patients may present with chest pain, due to acid reflux or pain associated with difficulty in swallowing. Other may present with melena stool, due to upper gastro-intestinal bleed secondary to esophageal mucosal erosion. The symptoms of Ca-O usually appear three to four months prior to diagnosis and the symptoms vary depending on the segment of esophagus initially involved. Late common symptoms are hoarse voice, constant cough, hiccup, bone pain and pneumonia due to obstructive effects of the tumor mass.

1.4. Outcomes of Squamous Cell Esophageal Cancer

The poor outcomes of Ca-O SCC-subtype are mostly related to late diagnosis when advanced and their tendency to metastasize, even with small tumor bulk. The late diagnosis of this type of cancer is also attributed to ineffective screening. Lack of screening in some countries leads to in advance stage diagnosis in most patients, with high risk of recurrence. The outcome of the Ca-O is closely related to the American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) staging system.(23) A 5-year survival rates for stages I, II, III are 50-80%, 30-40%, and 10-15%, respectively. Stage IV has a median survival of less than 1 year.

1.5. Approaches Shown to Improve Outcomes

The treatment modality for Ca-O subtype of SCC, the commonest histological type in Africa and Asia is according to the stage of tumor(24. Patients with advanced stage of SCC of esophagus may be treated by endoscopic palliative means such as laser therapy, argon plasma coagulation, esophageal dilation, and esophageal stent replacement.(25)

Despite availability of a wide range of treatment options, prevention is the most effective strategy to control Ca-O SCC. Prevention of Ca-O-SCC can be via primary or secondary methods. Primary prevention focuses on prevention of esophageal dysplasia (ESD) by life style modification like smoking cessation, reducing alcohol intake, increasing physical activity, weight reduction and consumption of a healthy diet-rich in fruits and vegetables. Fruits and vegetables, especially those containing retinoid, micronutrients and trace elements have been shown to reduce Ca-O.

Secondary prevention is done by detection and elimination of ESD, preventing its progression to advanced cancer. The therapeutic options and prognosis of mucosal Ca-O SCC (carcinoma in situ) are the same as high-grade ESD9.(26)Detecting carcinoma in situ of the esophagus is therefore an appropriate target for secondary prevention of Ca-O SCC. Secondary Ca-O prevention activities include public health education on the symptoms of Ca-O, improving access to diagnostic services, raising awareness amongst primary health care workers, strengthening referral systems and improving Ca-O treatment services at secondary and tertiary levels.

The detection of Ca-O before the development of symptoms requires screening and/or pre – symptom endoscopic screens for high risk groups. This allows detection of disease at a stage when intervention may improve outcomes.(27)

1.6. Cancer Diagnostic Delay

Cancer diagnostic delay is the period from the patient's first symptoms to first healthcare provider (HCP) consultation, as well as time to initial diagnostic testing to confirm cancer diagnosis. Reduction of diagnostic delay may increase the proportion of patients with early stage cancers at diagnosis and improve survival.(28)

Diagnostic delays of Ca-O may occur at different levels of the cancer diagnostic journey and have been broadly categorized as either patient or HCP delays. These can be further categorized into patient delay, health care provider referral and system delays(OGD & Histology results). Delays are calculated on the basis of dates provided by the patients and HCPs. Each type of delay has been shown to be influenced by different conditions and characteristics related to either patients or HCPs or service delivery system

In the USA delayed cancer diagnosis is one of the most common forms of medical error and a leading cause of malpractice claims.(29)Cancer misdiagnosis is considered to be one of the most harmful and costly types of diagnostic error. According to American studies, delayed cancer diagnosis can be categorized into four areas in the cancer diagnostic pathway:

1. Patient delay — time of delay from onset of symptoms to first presentation to a health care provider.
2. Primary care delay — time of delay from first presentation to a general practitioner (GP) to referral to secondary care for further diagnostic investigations.
3. Referral delay — time of delay from referral for further diagnostic investigations to being seen in secondary care.
4. Secondary care delay — time from being seen in secondary care to confirmatory diagnosis and or treatment.

The studies investigating delays in cancer diagnosis have found that patient and primary care delays are often the longest.

1.6.1. Patient Delay

This covers time from symptom onset to first presentation to the HCP. Duration of up to 60 days was defined as a short delay and more than 60 days as a long delay. In a prospective study for 48 patients of Ca-O in National Hospital of Sri Lanka by D Subastinghe et al in Sri Lanka(30)looking at Ca-O diagnostic delay, 84% of the patients had delayed first presentation for 14 weeks. In a retrospective study conducted in China from January to July 2007 in 80 patients with Ca-O, 90% of study participants had first presentation delay.(31, 32)

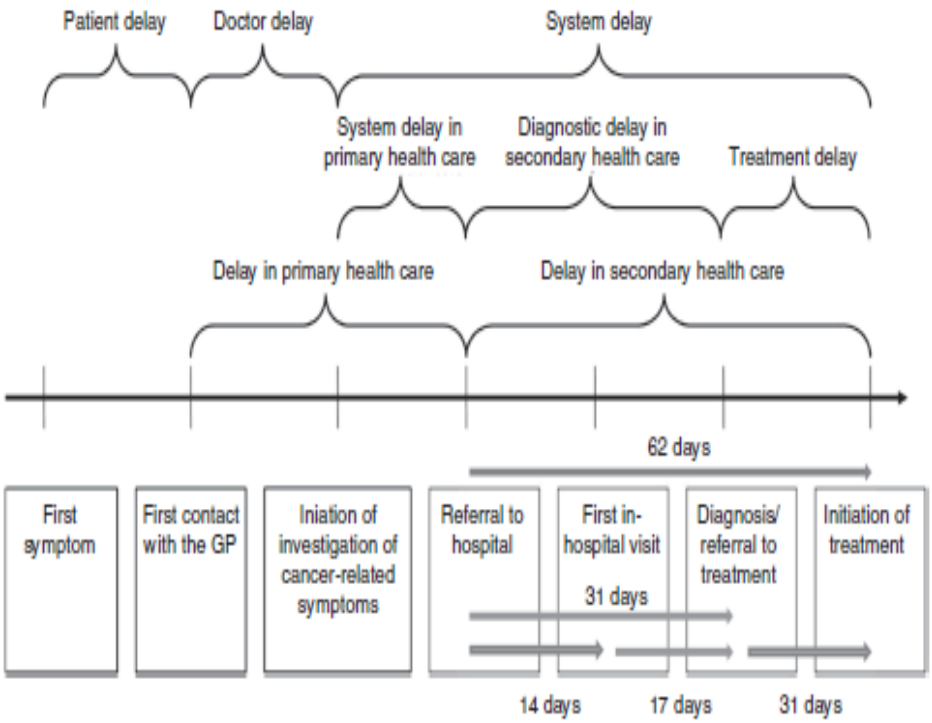
1.6.2. Health Care Provider Referral Delay

This is the time between first presentation to the HCP and the final referral to the cancer diagnostic center. A period of up to seven days was defined as a short delay and more than 7 days was a long HCP delay.(32)In the prospective study in Sri Lanka, 7% of Ca-O patients had endoscopic delay and 11% had histology delay.(32)In China, 20% of Ca-O patients had referral delay and 11% had histology report delay.(33)

1.6.3. Total Diagnostic Delay

This is the time from symptom onset to confirmed histological diagnosis. A period of up to 90 days is a short delay while 90 days or more is a long diagnostic delay.(34)

Figure 1. 1: Timelines of cancer diagnostic delay in the UK



Intervals and target times on the cancer diagnosis and treatment pathway (adapted from Hansen *et al*, 2008).

1.7. Factors associated with delay in cancer diagnosis

1.7.1. Socioeconomic status

The socioeconomic status (SES) of cancer patients in developing countries has been closely associated with various cancers, including Ca-O. Previous studies have shown SES has a big influence on delayed reporting and late stage presentation.(32) It has been reported that SES is an important factor in cancer treatment decision-making for patient and HCP choices after diagnosis.

In a study done in African American patients with breast cancer, it was found that those with higher SES underwent more appropriate treatment modalities, as compared to patients with low SES.(35)This is made worse in low-income countries by the limited access to cancer treatment services, which lead to delayed diagnosis.(36)

1.7.2. Delay Presentation and Referral

Cancer patients are more likely to delay in presenting to HCPs. This was particularly seen in breast cancer, where diagnosis was made at a more advanced stage.(32) This was found to be associated with low SES, both in developed and developing countries. In addition, a number of ethnic groups tended to present late with the disease. This could be related to multiple factors, possibly cultural, SES, lack of knowledge of cancer symptoms or inability to access diagnostic facilities.(37)Diagnostic delay can occur at different stages of the diagnostic process.

1.8. Factors associated with delay in diagnosis of esophageal cancer

1.8.1. Patient Related Factors

Most of Ca-O diagnostic delay, according to the study by Nana Wang et al in China from January to December 2007, found delay first presentation for more than 2.1 months due to low SES patients.(38)

1.8.2. Physician Related Factors

Physician delay is detrimental in cancer diagnosis and is defined as a delay from the time of first medical consultation to initiation of investigations of the cancer related symptoms and referral to diagnostic centers. This delay could be due to initial misdiagnosis,(39) insufficient medical examination and delay in referral-all attributed to health care providers. The number and accessibility of trained physicians may also have a role to play in the proportion of patients who present with advanced cancer at diagnosis.

1.8.3. Health Care - Related Factors

The health care system related factors for cancer diagnosis are important to determine diagnostic interval. Health care system determines timing of the initial referral and definite diagnosis, treatments available as well as waiting time for tests including endoscopy. In SSA, lack of screening, health care inaccessibility and poor infrastructure contributes to delay diagnosis of Ca-O. This leads to poor prognosis and limited treatment options, resulting in a high case fatality rate, despite some countries having specialized cancer centers.(39)Surprisingly, the disease has been given low priority by health care services in the

regions. This could be attributed to the fact that the health sector priorities in those regions are obscured by poverty and a massive burden of communicable diseases.(40) Unfortunately, most of the data on cancer in this region is incomplete and anecdotal. Fortunately, there is a global call to improve health information on cancer through population & health research(41). This will quantify the extent of burden in terms of morbidity and mortality caused by cancer for health policy consideration.

Table 1. 1: Summary studies on timeline diagnostic delay in patients with Ca-O and associated factors

No	Author	Type of study	Types of Ca patients	Time to presentation , referral to diagnosis & associated factors
1.	Nana Wang et al	Prospective: January–December 2007 ,China	238 Ca –O patients	- more than 2months delay presentation due to low SES
2.	Jianbo Wang et al	Retrospective: Jan-July 2007 Qilu Hospital ,Shandong , China	80 Ca–O patients	- Pt delay 90%, - System delay20% - Histology delay 11%
3	D Subastinghe et al	Prospective study for 2years National Hospital of Sri Lanka, Colombo	48 Ca-O patients	-14wks pt. 84% - Endoscopy delay7%, -Histology report 11%, -Endoscopy + histology 15%

CHAPTER TWO: JUSTIFICATION AND OBJECTIVES

2.1. Justification

According to Nairobi cancer registry Ca-O is the 2nd in male and 3rd in female in Kenya.Ca-O has high morbidity and mortality at late presentation in Eastern and Southern African regions. One of the most important prognostic factors for Ca-O is early detection of the disease which improves survival. The time of presentation and diagnosis of Ca-O and factors leading to diagnostic delay are not known in patients seen at KNH.

2.2. Research Question

What is the magnitude and the associated factors of diagnostic delay among Ca-O patients seen at KNH?

2.3. Objectives

2.3.1. Broad Objective

To determine diagnostic timelines and factors associated with timely health care service delivery among patient with Ca-O at KNH in Kenya.

2.3.2 Specific Objectives

1. To determine the median time interval from initial symptoms, first medical consultation, first referral to diagnostic facility.
2. To determine the median time interval from first endoscopic evaluation and confirmed histologic diagnosis among patient with esophagealcancer at KNH.
3. To describe factors associated with delay first consultation, referral to diagnostic facility for esophageal cancer symptoms.
4. To describe factors associated with overall diagnosis delay in patients of cancer esophagus.
5. To document the stage of cancer esophagus at diagnosis at KNH.

CHAPTER THREE: METHODOLOGY

3.1. Study Design

This was a **retrospective diagnostic cohort** study in patients with established histological diagnosis of Ca-O to determine diagnostic timelines, factors leading to delay and to document the stage of the disease at diagnosis at KNH. The information was obtained from both direct interview and from patients' files.

3.2. Study Site

This study was conducted in KNH from **September to November 2016** at Endoscopy unit, Radiotherapy and Cardiothoracic clinics.

3.3. Study Population.

This study included patients with established histological diagnosis of Ca-O who were seeking medical or surgical cancer treatment at KNH

3.4. Case Definition

Patients with complete case files with confirmed histological diagnosis of Ca-O and receiving treatment in KNH.

3.5. Inclusion Criteria

Histological diagnosis of esophageal cancer

Age more than 13years

3.6. Exclusion Criteria

Acutely ill patients who cannot give history

Patients with conditions affecting their memory

Lack of informed consent

3.7. Study Variables

3.7.1. Predictors Variables

A) Demographics

Age- was the nearest number of years from reported date of birth.

Sex- was determined by the phonotypical sexual appearance of the subjectsmale or female

Marital status – was categorized as single, married, divorced or widowed and was documented as reported by the patient

Educational Level – was the highest level of education the study participants had acquired and was reported as stated and if never attended school that was what was recorded.

B) Health Care Facility Level **–** was the level at which patient/participant first sought treatment. The Kenya HCF categorization levels are from one to six in the following these sequent: community based, Health Centre, sub-district hospital, district hospital, regional /provincial referral hospital and national referral hospital.

3.7.1. Outcome Variables

Time Points Definitions

1. Symptom onset time – was time rounded off to the nearest month of the year when patient developed initial symptoms attributable to Ca-O. The symptoms included any or combination of: difficulty in swallowing, retrosternal pain and pain on swallowing.
2. First consultation time – time rounded off to the nearest month of the year when patient first decided to make contact with health care provider (HCP), on account of concern about symptoms enumerated above. HCPs included registered nurses, clinical officers, general practitioners, gastroenterologists and oncologists in any health facility.
3. Referral Time – was time rounded off to nearest week or month of the year when HCPs referred patient to a diagnostic capable facility
4. Diagnosis time

Clinical diagnostic time –was time rounded off to the nearest month of the year when patient reported being informed of their diagnosis of Ca esophagus by HCP.

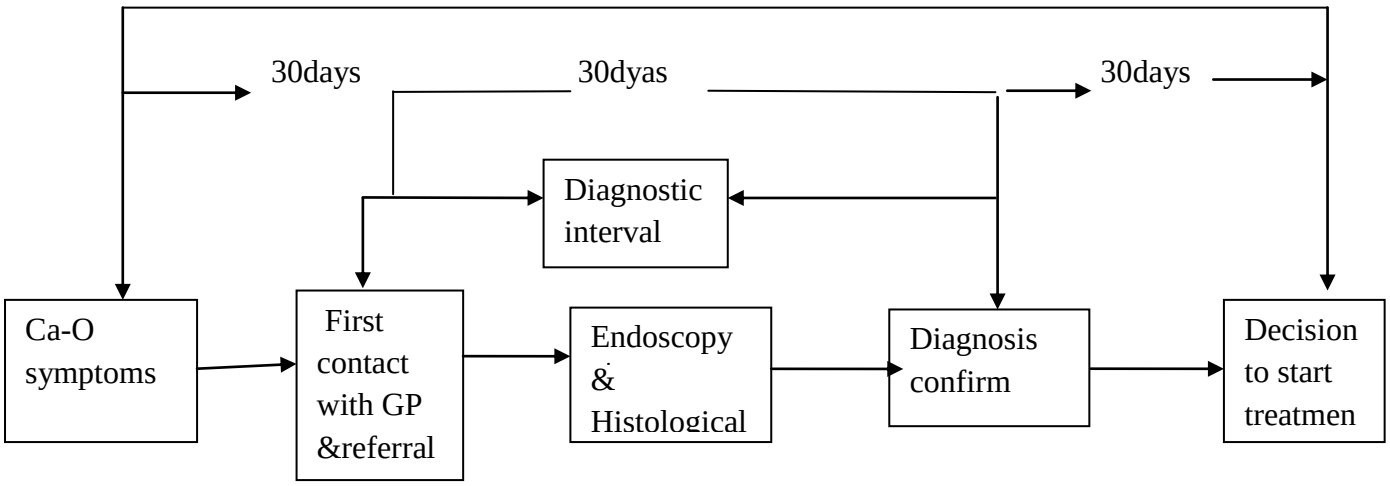
Endoscopic time – was the time the patient's first UGI endoscopy was undertaken

Histological Diagnosis Time – time when the histological diagnosis was recorded in file or date recorded on a histological report signed by recognized pathologist.

Diagnostic end Point – time at which a definite treatment plan was arrived at by the medical team.

Stage of cancer esophagus – Cancer stage is the stage as stated and recorded in the file. The TNM staging system assess tumor in three ways: extent of primary tumor (T), absence or presence of regional lymph node involvement (N) and absence or presence of distant metastases (M). When T, N, and M are known a stage can be assigned as: I, II, III and IV.

Figure 3. 1: Timeline of Cancer diagnostic delay-more than 90 days



Time Intervals

1. Time to first medical consultation – was the median interval in months between time of symptom/s onset and first HCP consultation.

2. Time to referral - median time in days between first consultation and referral to level 3,4 or 5 HCF for purposes of diagnostic investigations, such as a barium swallow and or OGD to arrive at a clinical or histological diagnosis

3. Time to endoscopy – median time in weeks from referral to when first UGI endoscopy undertaken

Total Diagnostic Delay- median time interval in months from onset of symptoms to point of confirmed histological diagnosis

Factors Associated with Delay – these are obtained from interview of patients with questionnaire

Patients delay factors

Delayed presentation time – time to HCP visit from onset of symptoms of more than 30days.Factors contributing to patient delay captured in the patient interview included:

Distance to HCF – A distance from patients' residence to the nearest HCF of twenty kilometers or more was considered a significant factor contributing to patient delay. Those residing further than twenty kilometers away from HCF with no proper means of transport are likely to experience delay to first consultation.

Income–This was assessed by how much money in Kenya shillings the patient earns per month. Patients earning less than 3000 a month are living below the poverty line, and are likely to lack money for transport and healthcare associated fees.

Educational level - the highest educational level patient had attained.

Occupation – formal employment was further categorized into skilled or unskilled, informal employment as self-employed, casual worker or unemployed.

Physician delay factors

Delay referral – This is time taken from referral to arrival in a center that can perform OGD to diagnose Ca-O. Ideally, this should not be more than 30 days. Lack of awareness of symptoms of ca esophagus at first consultation may delay referral.

Health care system delay factors

Time from booking for OGD to actual date it is performed.

Time from receipt of biopsy samples by a qualified pathologist to when the histological report was received by the clinical team/patient.

Time from receipt of the histological diagnosis to the start of cancer treatment.

3.8. Quality Assurance

Two trained research assistants with clinical background were used to aid in obtaining consent and conducting medical history interview with patients/participants. English or Kiswahili languages were used or help from selected interpreters was obtained in cases where the participants could not understand either language. The PI and the research assistants closely liaised with endoscopy, radiotherapy and cardiothoracic units. The data collected was kept safe and confidential. The PI, working closely with a qualified statistician, analyzed all information obtained.

3.9. Sampling Technique

Consecutive convenient sampling was utilized

3.10 . Sample Size Computation

Sample size calculation was obtained using the formula for finite population (Daniel, 1999). The calculation was as follows:

$$n' = \frac{NZ^2P(1-P)}{d^2(N-1)+Z^2P(1-P)}$$

Where

n' = sample size with finite population correction,

N = size of the target population = 150

Z = Z statistic for 95% level of confidence = 1.96

P = Estimated proportion of patients with late esophageal cancer disease is 50%

d = margin of error = 7

$$= 150 \frac{\text{x } 1.96^2 \text{ x } 0.5 \text{ x } 0.5}{0.07^2 \text{ (150-1)} + 1.96^2 \text{ x } 0.5 \text{ x } 0.5}$$

= 85 esophageal cancer patients will be required

3.11. Patient Selection

The participants selected were those seeking diagnostic or receiving treatment at the endoscopy, radiotherapy and cardiothoracic units in KNH, with a confirmed histological diagnosis of Ca-O, and who had given consent to participate in the study. Those who were acutely ill were excluded.

The endoscopy unit is where most participants undergo OGD and have tumor biopsies taken for histological diagnosis. Radiotherapy is an integral part in management of Ca-O both for neoadjuvant and adjuvant setting. The cardiothoracic surgery clinic plan resection surgery for those whose tumors are amenable to resection. The radiotherapy unit and cardiothoracic clinic were the two sites with a significant number of Ca-O patients and were important sites for study recruitment.

3.12. Screening and Recruitment

The principal investigator (PI) and two research assistants (qualified clinical officers) reviewed files of Ca-O patients attending the endoscopy, radiotherapy and cardiothoracic units. Cases with confirmed histological diagnosis of Ca-O documented in the files were identified. Those who met the eligibility criteria were approached and invited to participate in the study. Informed consent was obtained and participants recruited consecutively into the study.

The recruitment was done between Monday through Fridays in the endoscopy unit and Radiotherapy unit from Monday through Thursday. The recruitment from the cardiothoracic clinic was done on Fridays. Most patients were recruited from the radiotherapy clinic where enrollment was at range of 3-5 participants per day in endoscopy unit and5-6 participants per day in the cardiothoracic clinic respectively. The participants with Ca-O enrolled from the endoscopy unit were fewer than expected.

Interviews were conducted to establish their demographic characteristics, clinical history and to confirm the documented histological diagnosis in the files. Each participant was assigned a study reference number. If one declined to remain in the study after being assigned a number,

another one was selected to replace and this continued every week until the required sample size was achieved.

3.13. Data Collection

The PI and the research assistants collected data pertaining to the study participant's medical history and extracted data from their files as per the study proforma.This was then entered on a daily basis in a password-protected computer Excel sheet.

The specific data from the interview included demographics, county of residence and date of onset of the first symptoms of Ca-O experienced. Other details included when and where the participant first sought medical consultation and the diagnostic formulation before referral.

Data obtained from the medical records included dates when first OGD done and the histology result received by referring clinician and the full histological report.

Dates used for estimating diagnostic delay were dates of onset of symptoms, first consultation with Health care provider (HCP), referral to diagnostic center and date of confirmed histological diagnosis. The medical history was taken starting with the most recent event in diagnostic pathway, probing backward without interruption until the information about the type and date of symptoms experience. For patients who were unable to recall the exact date of symptoms experience and date of first consultation with HCP, the investigator approximated such dates by probing the exact week of the respective month and year when symptoms were experienced and also first consultation with HCP. The HCPs included nurses, clinical officers, general practitioners, gastroenterologists and oncologists.

3.14. Data Management and Analysis

Data from the questionnaires was entered in SPSS version 21.0 software for analysis. The study population was described using demographic characteristics, socioeconomic status and clinical data. This was done by summarizing categorical variables into percentages and continuous data into means or medians.

Time to presentation, referral, endoscopy and diagnosis was calculated and presented as medians with interquartile ranges. Categorization was done using appropriate cut offs to determine patient delay, doctor delay and health systems delay. The delays were presented as

percentages with 95% confidence interval. In addition, the stages of cancer at presentation and the reasons for delay were summarized into percentages.

Associations between delay, socio-demographic and economic factors, patients' awareness of cancer of the esophagus and physical accessibility of healthcare facility (distance) was tested using Chi square test of associations and Student's t test for categorical and continuous variables respectively. Fisher's exact test was used in cases where the numbers were small and all statistical tests were performed at 5% level of significance.

3.15. Ethical Consideration

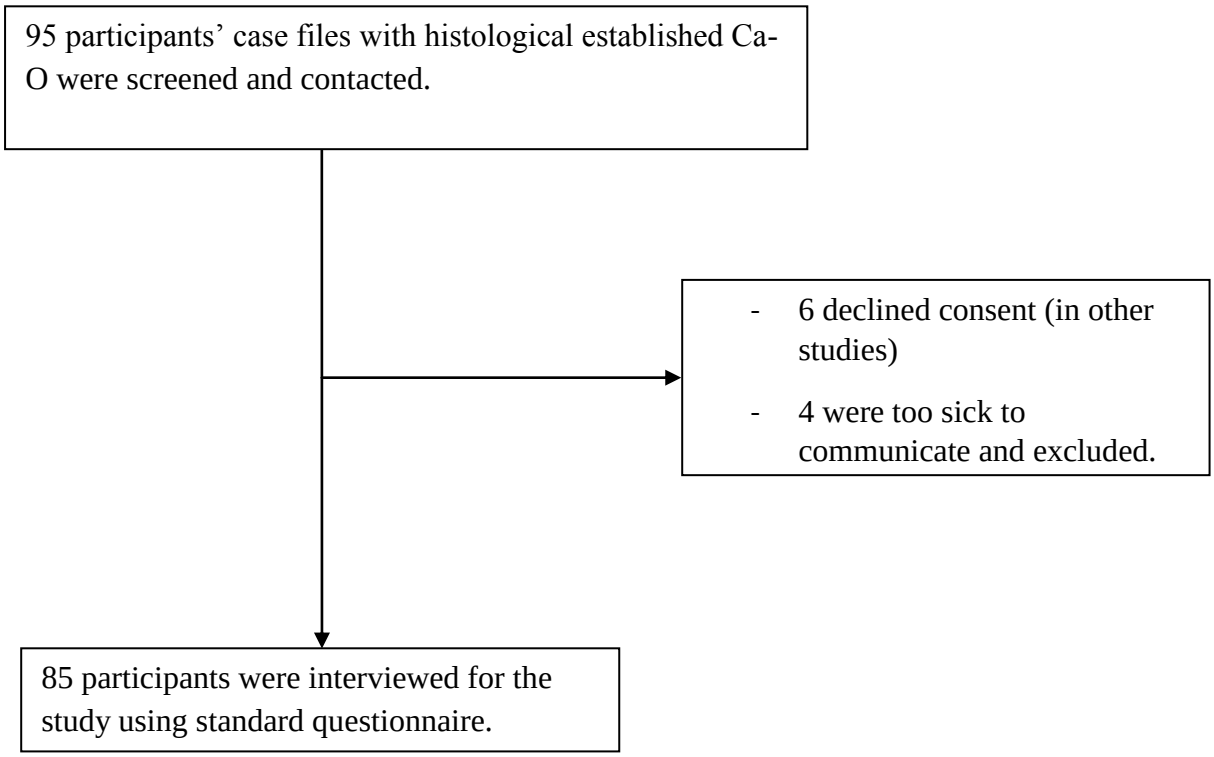
The study was conducted after the approval by DoCMT, UoN and KNH /UoN Ethic committee. Only those patients who gave consent were enrolled into the study and a strict policy of no coercion, no harm and preserving confidentiality was strictly observed

CHAPTER FOUR: RESULTS

4.1. Patients' Recruitment Flow Chart

This study was conducted from September to November 2016 with a total of 95 participants with established histological Ca-O diagnosis were screened at the cardiothoracic, endoscopy and radiotherapy units at KNH. Among eligible participants, ten were excluded, six declined to participate in the study as they were in other studies and four participants were too sick for the interview. Eventually, the study enrolled 85 patients for interview and obtained information from their files.

Figure 4. 1: Patients' recruitment flow chart



4.2. Socio-Demographic Characteristics

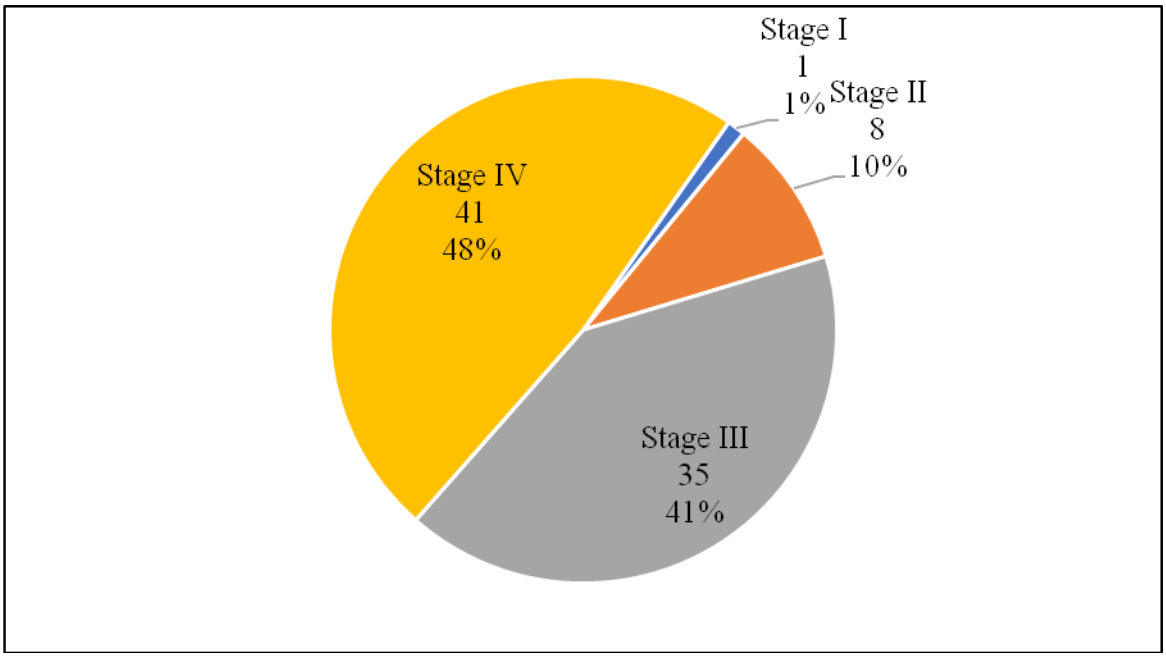
Table 4.1: illustrates the socio-demographic characteristics of the study participants. The mean age of the participants was 59.2 years (SD 14.5 years) at time of the study and 58.7 years (SD 14.6 years) at cancer diagnosis. Majority of participants (64.7%) were males, 80% were married and 62.4% living in the urban setting. About quarter (24.7%) were illiterate while 40% had completed primary education and 31.8% had attained secondary level of education. Almost a half (47.1%) were unemployed and 51.8% had a regular income.

Table 4. 1: Socio-demographic characteristics of the study participants

Variable	
Age in years (SD)	59.2 (14.5)
Age at cancer diagnosis (years)	
Mean (SD)	58.7 (14.6)
Range	20-85
Gender, n (%)	
Male	55 (64.7)
Female	30 (35.3)
Marital status, n (%)	
Single	5 (5.9)
Married	68 (80.0)
Divorced	4 (4.7)
Widowed	8 (9.4)
Residence, n (%)	
Urban city	25 (29.4)
Suburbs of the city	28 (32.9)
Rural area	32 (37.6)
Level of education, n (%)	
None	21 (24.7)
Completed primary education	34 (40.0)
Secondary	27 (31.8)
University	3 (3.5)
Occupation, n (%)	
Formally employed	23 (27.1)
Business person	22 (25.9)
Unemployed	40 (47.1)
Regular income, n (%)	
Yes	44 (51.8)
No	41 (48.2)

Figure 4.2: illustrates the stage at diagnosis of Ca-O. Majority of the patients had stage IV (48.2%) and III (41.2%) of cancer at diagnosis.

Figure 4. 2: Staging of cancer in patients with Ca-O at diagnosis



4.3. Time Interval from Symptoms Onset, First Presentation and Referral to Diagnostic Facility (Patient and Referral Delay)

Table 4.2: Shows the time interval from onset of symptoms to first presentation and then to referral to diagnostic facility. Time to first presentation was more than 30days among 78.8% of the participants with 21.2% having medical consultation in less than 30days after onset of symptoms. The median time from first consultation to referral to diagnostic-capable facility was 30 days; 76.5% having taken more than 30 days before reaching the referral facility.

Table 4. 2: Time interval from symptoms onset, first presentation and referral to diagnostic facility

Variable	Frequency (%)	95% CI
Time from initial presentation to consultation		
>=30 days (*Patient delay*)	67 (78.8)	69.4-87.1
<30 days	18 (21.2)	12.9-30.6
Time from first consultation to referral (days)		
Median days (IQR)	30 (7-30)	
Time range	1-365	
>=30 days (*Referral delay*)	65 (76.5)	67.1-84.7
<30 days	20 (23.5)	15.3-32.9

4.4. The Median Time from First Endoscopic Evaluation and Confirmed Histologic Diagnosis (Diagnostic Delay)

Table4.3: shows the time to first endoscopy (OGD) and to confirmed histology diagnosis. After presentation and evaluation in referral facility, the patients took a median time of 7 days to receive OGD with 64.7% taking 14 and more days. Similarly, OGD to histological diagnosis took a median of 7 days; 84.7% taking 14 or more days. In the overall, the median time from initial symptoms to histological diagnosis was 90 days with the total diagnostic delay (90 or more days) at 61.2%.

Table 4. 3: The median time from first endoscopic evaluation and confirmed histologic diagnosis (diagnostic delay)

Variable	Frequency (%)	95% CI
Time from referral facility evaluation to OGD		
Median days (IQR)	7 (7-30)	
Range	7-90	
Category, n (%)		
>=14 days	55 (64.7)	55.3-74.1
<14 days	30 (35.3)	25.9-44.7
Time from OGD to histological diagnosis		
Median days (IQR)	7 (7-14)	
Range	7-30	
Category, n (%)		
>=14 days	72 (84.7)	77.6-91.8
<14 days	13 (15.3)	8.2-22.4
Time from initial symptoms to histological diagnosis		
Median days (IQR)	90 (30-120)	
Range	7-120	
Category, n (%)		
Total delay(>=90 days)	52 (61.2)	50.6-71.8
No delay (<90 days)	33 (38.8)	28.2-49.4

4.5. Factors Associated with Delayed First Presentation

Table 4.4: illustrates factors associated with delay first presentation in study participants. The patients who did not afford own transport and consultation were more likely to have delayed first presentation (88.6%) than those who afforded (68.3%), OR 3.6 (95% CI 1.2-11.3), p=0.022. None of the other factors was associated with delayed first presentation (p>0.05).

Table 4. 4: Factors associated with delayed first consultation (Patients)

Variable	Patient delay		OR (95% CI)	P value
	Delayed	Not Delayed		
Sex:				
Male	43 (78.2)	12 (21.8)	0.9 (0.3-2.7)	0.845
Female	24 (80.0)	6 (20.0)	1.0	
Age at diagnosis, mean (SD)	59.1 (13.9)	57.3 (17.5)	-	0.649
Level of education:				
None	17 (81.0)	4 (19.0)	1.5 (0.4-6.0)	0.528
Primary	28 (82.4)	6 (17.6)	1.7 (0.5-5.6)	0.384
Secondary/Tertiary	22 (70.4)	8 (29.6)	1.0	
Occupation				
Unemployed	34 (85.0)	6 (15.0)	2.0 (0.6-7.1)	0.281
Employed	16 (72.9)	6 (27.3)	0.9 (0.3-3.5)	0.928
Business person	17 (73.9)	6 (26.1)	1.0	
Marital status				
Single	3 (60.0)	2 (40.0)	1.0	
Married	53 (77.9)	15 (22.1)	2.4 (0.4-15.4)	0.360
Divorced/Widowed	11 (91.7)	1 (8.3)	7.3 (0.5-111.2)	0.191
Residence				
Urban	22 (88.0)	3 (12.0)	1.0	
Urban suburbs	20 (71.4)	8 (28.6)	0.3 (0.1-1.5)	0.138
Village	25 (78.1)	7 (21.9)	0.5 (0.1-2.1)	0.331
Income				
Yes	32 (72.7)	12 (27.3)	0.5 (0.2-1.4)	0.154
No	35 (85.4)	6 (14.6)	1.0	
Distance to health facility, median (IQR)	45 (25-70)	60 (20-80)	-	0.382
Income adequate for medical cost				
Yes	22 (73.3)	8 (26.7)	0.6 (0.2-1.8)	0.360
No	45 (81.8)	10 (18.2)	1.0	
Paying for own transport and consultation				
Yes	28 (68.3)	13 (31.7)	1.0	
No	39 (88.6)	5 (11.4)	3.6 (1.2-11.3)	**0.022**
Have health insurance				
Yes	61 (78.2)	17 (21.8)	0.6 (0.1-5.3)	1.000
No	6 (85.7)	1 (14.3)	1.0	

4.6. Factors Associated With Delayed Referral to Diagnostic Facility (Doctor Delay)

Table 4.5 illustrates factors associated with referral delay to diagnostic facility. Those who lived in the rural village were less likely to experience doctor delay (65.6%) compared to those who lived in urban areas (92%), OR 0.2 (95% CI 0.0-0.8), p=0.019. None of the other factors was associated with delayed referral to diagnostic facility (p>0.05).

Table 4. 5: Factors associated with delayed referral to diagnostic facility (doctor delay)

Variable	Doctor delay		OR (95% CI)	P value
	Delayed	Not delayed		
Sex:				
Male	39 (70.9)	16 (29.1)	0.4 (0.1-1.2)	0.102
Female	26 (86.7)	4 (13.3)	1.0	
Age at diagnosis, mean (SD)	59.1 (14.8)	59.5 (14.0)	-	0.930
Level of education:				
No education	14 (66.7)	7 (33.3)	0.4 (0.1-1.5)	0.167
Primary	26 (76.5)	8 (23.5)	0.7 (0.2-2.3)	0.496
Secondary/Tertiary	25 (83.3)	5(16.6)	1.0	
Occupation				
Unemployed	18 (78.3)	5 (21.7)	1.0	
Employed	17 (77.3)	5 (22.7)	0.9 (0.2-3.9)	0.936
Business person	30 (75.0)	10 (25.0)	0.8 (0.2-2.8)	0.770
Marital status				
Single	52 (76.5)	16 (23.5)	1.0	
Married	5 (100.0)	0	-	0.579
Divorced/Widowed	8(67.0)	4(33.3)	0.6 (0.2-2.3)	0.470
Residence				
Urban	23 (92.0)	2 (8.0)	1.0	
Urban suburbs	21 (75.0)	7 (25.0)	0.3 (0.0-1.4)	0.148
Village	21 (65.6)	11 (34.4)	0.2 (0.0-0.8)	**0.019**
Income				
Yes	34 (77.3)	10 (22.7)	1.1 (0.4-3.0)	0.857
No	31 (75.6)	10 (24.4)	1.0	
Distance to HCF, median (IQR)	50 (30-75)	40 (13.5-80)	-	0.417

4.7. Factors Associated With Endoscopic and Histologic Results Delays in Ca-O Patients

Table 4.6 illustrates the factors related to endoscopy and histology results delays in Ca-O patients. The reasons for OGD delay was mainly lack of money (89.7%) while the delayed

lab results were cited to be due to inadequate tissue samples (50%) or wrong labeling of samples (12.5%).

Table 4. 6: Factors related to delay endoscopy and histology results in of Ca-O patients

Variable	Frequency (%)
Reasons for delayed OGD	
Hoping for symptoms to regress	1 (3.5)
Lack of money	26 (89.7)
Not sure	2 (6.8)
Reasons for delayed lab results	
Wrong labeling of samples	1 (12.5)
Inadequate tissue samples	4 (50.0)
Unspecified reasons	3 (37.5)

4.8. Factors Associated With Overall Diagnostic Delay

Table 4.7 illustrates the factors associated with total diagnostic delay among Ca-O patients. Neither residence nor affording transport and consultation were associated with total diagnostic delay ($p>0.05$). Total diagnostic delay for those who lived in the rural villages was 68.8% compared to 56% among those in urban areas. The patients who afforded transport and consultation had 54.5% delay compared to 68.3% delay among those who did not afford ($p=0.194$). Similarly, all the other factors were not associated with total diagnostic delay ($p>0.05$).

Table 4. 7: Factors associated with overall diagnostic delay

Variable	Diagnostic time		OR (95% CI)	P value
	Delayed	Early		
Sex:				
Male	36 (65.5)	19 (34.5)	1.7 (0.7-4.1)	0.273
Female	16 (53.3)	14 (46.7)	1.0	
Age at diagnosis, mean (SD)	59.1 (13.6)	58.2 (16.3)	-	0.804
Level of education:				
No education	16 (76.2)	5 (23.8)	2.4 (0.7-8.4)	0.151
Primary	19 (55.9)	15 (44.1)	1.0 (0.4-2.6)	0.950
Secondary/Tertiary	17(56.6)	13 (43.3)	1.0	
Occupation				
Unemployed	15 (68.2)	7 (31.8)	1.4 (0.4-4.7)	0.609
Employed	14 (60.9)	9 (39.1)	1.0	
Business person	23 (57.5)	17 (42.5)	0.9 (0.3-2.5)	0.794
Marital status				
Married	42 (61.8)	26 (38.2)	1.0	
Single/Divorced/Widowed	10 (58.8)	7 (41.2)	0.9 (0.3-2.6)	0.824
Residence				
Urban	14 (56.0)	11 (44.0)	1.0	
Urban suburbs	16 (57.1)	12 (42.9)	1.0 (0.4-3.1)	0.933
Village	22 (68.8)	10 (31.3)	1.7 (0.6-5.1)	0.322
Income				
Yes	28 (63.6)	16 (36.4)	1.2 (0.5-3.0)	0.630
No	24 (58.5)	17 (41.5)	1.0	
Distance to HCF, median (IQR)	45 (27.5-70)	50 (22.5-80)	-	0.939
Income adequate for medical cost				
Yes	19 (63.3)	11 (36.7)	1.2 (0.5-2.9)	0.763
No	33 (60.0)	22 (40.0)	1.0	
Afford transport and consultation	24(54.5)	20(45.5)	1.0	
Yes	28(68,3)	13(31.7)	1.8(0.7-4.4)	0.194
No				
Have health insurance				
Yes	2(28.6)	5(71.4)	1.0	
No	50 (64.1)	28 (35.9)	4.5 (0.8-25)	0.103

CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1. Discussion

Although not as common as cancer of other sites such as prostate, breast, and colorectal, esophageal cancer has a high mortality rate, the incidence being close to the cancer-specific mortality. One of the most important prognostic factors for Ca-O is early detection of the disease which improves survival.With these facts put into consideration it is important to note that in Kenya no other study has previously been done to determine diagnostic timelines and factors associated with timely health care service delivery among patient with Ca-Oand this study lays baseline data on the same.

These findings revealed that Ca-O was predominant in the older population with a mean age at diagnosis of 58.7 years. However, younger patients were also identified with the lowest age being 20 years. In addition, males were more affected than females with about two-thirds of the patients being males. A previous study in Kenya reported a 5 to 1 male to female ratio among patients diagnosed with Ca-O.(3) Global estimates show a higher incidence among males than females with Kenya statistics showing 20.2 cases per 100,000 males compared to 15.1 cases per 100,000 females in a year.(4) These patients had a relatively high level of illiteracy and almost a half of them were unemployed which was an indicator of a substantial degree of low socioeconomic status (SES).

This study found late presentation was widespread in this population showing about 9 in 10 patients being diagnosed at stage 3 and 4. The delay occurred at various step of diagnostic process hence allowing the cancer to progress before diagnosis was made. Patient delay which entailed the time from symptoms to initial presentation for medical consultation was recorded among 78.8% of patients. The median time from initial symptoms to histological diagnosis was 90 days with the total diagnostic delay (90 or more days) at 61.2%, and it correlated with studies in Sri Lanka which reported patient delay of 84%(30)and in China with delay of 90%.(32) These findings showed that the patients who delayed before presenting for their first medical consultation were those who did not afford paying for their transport and consultation fees. As a proxy measure of SES, this was in agreement to previous studies which have reporting economic status as an important factor associated with delay to presentation.(37)

Referral delay which was taking more than 30days from first consultation to referral to higher level facility was high at 76.5%. More than three-quarters of the patients went to health centers and sub-district hospitals at first consultation where they were done investigations and treatment before cancer diagnosis. Some of the reasons identified to have delayed referral were related alternative diagnosis and being told to return to the same facility for further review. Those patients who lived in the rural setting were at a higher risk of referral delay than the urban patients. Lower rates of referral delay have been reported in other settings. Misdiagnosis has been highlighted as one of the main reason for referral delay.(38)

Diagnostic delay in the referral facility was contributed by the time taken to endoscopy and the duration taken to get histology results. There was a substantial delay in both steps with 64.7% delay to endoscopy and 84.7% delay to histological diagnosis. Studies in Sri Lanka and China showed different results with delays in endoscopy and histology below 20% (32, 32). These findings show the regional differences in relation to efficiencies in the health care facilities. The health care system delay in our study could be attributed to shortage of endoscopy and histology facilities resulting in long bookings and delayed histology results. It has been reported in previous reviews that health care systems in sub-Saharan Africa suffer poor infrastructure hence contributing to delay in Ca-O diagnosis.(40)This delay results in patients presenting in the health facility late hence diagnosis at cancer stage III or IV which is advanced disease. This was the case in this study where most participants were diagnosed at stage III and IV due late presentation which could be attributed to the late presentation.

5.2. Conclusion

1. There is high rate of timeline diagnostic delay in patients with cancer esophagus in Kenya.
2. The bulk of the delay happens at the initial stages when there is a delay in presenting for medical consultation after patients noticed symptoms.
3. The delay to first consultation and referral to diagnostic facility were associated with inability to cover for transport and medical cost.

5.3. Recommendations

1. It is important to carry out further study on Ca-O awareness and the importance on early first presentation.
2. Improve the referral system and decentralize the endoscopic diagnostic centers
3. There were significant delays at different levels that were observed, thus a further study to determine the diagnostic delay in patients with cancer esophagus in Kenya is important.

5.4. Limitations

1. Patient recall bias may have resulted in inaccurate estimation of duration taken between the various stages of diagnostic processes.
2. Incomplete records of the medical examinations and the facilities at various hospitals attended by the patients.
3. The study was conducted in one National Referral Hospital and its findings may not be generalized to all Ca-O patients in Kenya

6.0 REFERENCES

1. Mahboubi E, Kmet J, Cook PJ, Day NE, Ghadirian P, Salmasizadeh S. Oesophageal cancer studies in the Caspian Littoral of Iran: the Caspian cancer registry. Br J Cancer. 1973 Sep;28(3):197–214.

2. White RE, Abnet CC, Mungatana CK, Dawsey SM. Oesophageal cancer: a common malignancy in young people of Bomet District, Kenya. Lancet (London, England). 2002 Aug;360(9331):462–3.

3. Korir A, Okerosi N, Ronoh V, Mutuma G, Parkin M. Incidence of cancer in Nairobi, Kenya (2004-2008). Int J Cancer. 2015 Nov;137(9):2053–9.

4. World Health Organization (WHO). GLOBOCAN 2012: Estimated Cancer incidence, Mortality and Prevalence Worldwide in 2012 [Internet]. 2012 [cited 2018 Feb 28]. Available from: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx

5. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. Cancer Incidence and Mortality Worldwide. IARC. 2012;1.1(1).

6. Rabson K. Systemic Review: Epidemiology of esophageal cancer in sub-Saharan Africa. Malawai J. 2010;22(3):65–70.

7. Warwick G., Handrrington. Some aspects of the epidemiology and etiology cancer of esophagus with particular emphasis on Transkei. South Africa Adv cancer res. 1973;17:81–229.

8. Segal I. The gastroesophageal reflux disease complex in sub-Saharan Africa. Eur J Cancer Prev. 2001;(10):209–2112.

9. Kamangar F, Malekzadeh R, Dawsey S., Saidi F. Esophageal cancer in Northeastern Iran: a review. Arch Iran Med . 2007;10:70–82.

10. Lim GC., Rampal S, Halimah Y. Cancer inceidnece in Peninsular Malaysia 2003-2005 [Internet]. Kaula Lumpur; 2008. Available from: http://www.moh.gov.my/images/gallery/Report/Cancer/CancerIncidenceinPeninsular Malaysia2003-2005x1x.pdf

11. Kamangar F, Dores G., Anderson W. Patterns of cancer incidence, mortality, and prevalence across five continents: Defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol . 2006;24:2137–50.

12. Wahhisi J, Patel K, Buzibia N. Esophageal cancer in North Rift valley of western Kenya. Afr Heal sci. 2005;5(2):157–63.

13. Marasas W. Discovery and occurrence of the fumonisins: a historical perspective. Environ Heal Perspect. 2001;109(2):239–243.

14. Cancer Research. UK. Risk and cause of esophageal cancer [Internet]. 2018. Available from: http//cancerhelp.cancer.researchuk.org/type/esophageal.cancer/about/riskand cause of esophageal-cancer

15. National Cancer Institutes. Harms of smoking and health Benefits of Quitting

[Internet]. 2018 [cited 2018 Jan 1]. Available from: http://www.cancer.gov/cancer topics/factsheet/tobacco/cessation

16. Mao W., Zheng W., Ling Z. Epidemiologic risk factors for esophageal cancer development. Asian Pac J Cancer Prev. 2011;12:2461–6.

17. Yoshizawa T, Yamashita A, Luo Y. Fumonisin occurrence in corn from high- and low-risk areas for human esophageal cancer in China. Appl Environ Microbiol. 1994;60:1626–1629.

18. Gelderblom W., Snyman S., Lebepe-Mazur S, van derWesthulzen L, Kriek N., Marasas W. The cancer-promoting potential of fumonisin B1 in rat liver using diethylnitrosamine as a cancer initiator. Cancer Lett. 1996;109:101–108.

19. Ciacci-Zanella JR, Merrill AHJ, Wang E, Jones C. Characterization of cell-cycle arrest by fumonisin B1 in CV-1 cells. Food Chem Toxicol. 1998;36:791–804.

20. Sur M, Cooper K. The role of the human papilloma virus in esophageal cancer. Pathology. 1998;30:348–354.

21. Cooper K, Taylor L, Govind S. Human papillomavirus DNA in oesophageal carcinomas in South Africa. J Pathol. 1995;175:273–277.

22. Merendino K., Mark V. An analysis of 100 cases of squamous cell carcinoma. Cancer. 1952;52–61.

23. Enzinger P., Ilson D., Kelson D. Chemotherapy in esophageal cancer. Semin Oncol. 1999;26:12–20.

24. Zhang HZ, Jin GF, Shen HB. Epidemiologic difference in esophageal cancer between Asian and western population. Chin J Cancer. 2012 Jun;31(6):281-6. doi:10.5732/cjc.011.10390. Epub 2012 Apr 13. Review.PMID:22507220

25. Yang C. Research on esophageal Cancer in China: a review. Cancer Res. 1980;40(8.1):2633–44.

26. Gerson LB, Groeneveld PW TG. Cost-effectiveness model of endoscopic screening and surveillance in patients with gastroesophageal reflux disease. Clin Gastroenterol Hepatol. 2004;2:868–879.

27. Ahmedin JM., Freddie B, Melissa M. Global cancer statistics. CA cancer J lin. 2011;61:69–90.

28. Gandhi T., Kachalia A, Thomas E. Missed and delayed diagnoses in the ambulatory setting: a study of closed malpractice claims. Ann Intern Med. 2006;145:488–96.

29. Ely J., Kaldjian LC., Alessandro D. Diagnostic errors in primary care: lessons learned. J Am Board Fam Med . 2012;25(1):87–97.

30. Subasinghe D, Samarasekera D. Delay in the diagnosis of esophageal carcinoma: Experience of a single unit from a developing country. Indian J Cancer. 2010;47:151–5.

31. Gyenwali D, Pariyar J, Onta S. Factors associated with late diagnosis of cervical cancer in Nepal. Asian Pac J Canc Prev. 2013;14(7):4189–4193.

32. JianboWang J, et al. Retrospective study Jan –July 2007 at Quilo Hospital Symptom to treatment delay and stage at the time of treatment in cancer esophagus . Japanese journal of clinical oncology volume 38, isssue 2, 1februray 2008, page 87-91.

33. Martin L., Young S, Sue-Ling H, Johnston D. Delays in the diagnosis of oesophagogastric cancer: A consecutive case series. Br Med J. 1997;314:467–71.

34. Jones RV. Time between presentation and treatment of six common cancers: a study in Devon. Br J Gnenpract. 1992;42(363):419–22.

36 Warner E., Tamimi R., Hughes M., Ottesen R., Wong Y., Edge S. Time to diagnosis and breast cancer stage by race/ethnicity. Breastcancer Res treat. 2012;136:813–21.

36. Agarwal G, Ramakant P, Sánchez Forgach E., Rendón J., Chaparro J., Basurto C. Breast cancer care in developing countries. World J Surg. 2009;33:2069–76.

37. Wang N, Cao F, Liu F, Jia Y, Wang J, Bao C, Wang X, Song Q, Tan B, Cheng Y. the effect of socioeconomic status on health care delay and treatment of esophageal cancer . J Transl Med. 2015 Jul 24;13:241. doi: 10.1186/s12967-015-0579-9. PMID: 26205792

38. Meyer H, Meyer AND, Thomas EJ. The frequency of diagnostic errors in outpatient care: Estimations from three large observational studies involving US adult populations. BMJ Qual Saf. published online first: 5 May2014:doi:10.1136/bmjqs-2013-002627.

39. Mayor S. People with esophageal & oropharyngeal cancers delay seeing their GP. BMJ. 2014;345:g1324.

40. Nevill G. Cancer of esophagus. East Afr Med J. 1961;38:515–24.

7.0 APPENDICES

Appendix I: Data Collection Proforma(English Version)

1. Sex of the patient
    - Male
    - Female
2. Date and place of birth:…….
3. Age at cancer diagnosis ……..
4. Marital status
    - Single
    - Married
    - Separated
    - Divorced
    - Others, specify…….
5. County of residence ……...
6. Type of area you live
    - Urban city
    - Suburbs of the city
    - Rural area
7. Level of education
    - None
    - Completed primary education
    - Secondary
    - university

8. Occupation:
    - employed (formal/ casual)
    - business person
    - unemployed
9. Do you have regular income?
    - Yes
    - No
    - If yes How much money in Kenya shillings do you get in a month ……
10. When did you have the first symptoms of your current disease …….
11. When did you first seek help for your symptoms ……
12. Which facility did you visit first
    - Health center
    - Sub district hospital
    - County hospital……..
13. What was done at the first facility?
    - Investigations
    - Treatment
    - Referral
    - If referral, specify to where?.....
14. When were you referred to diagnostic capable facility……
15. After doctor has seen you, were you referred immediately, if not what was the reason. :

- Given different diagnosis
- given return date to same facility
- Others specify ……

16. Which facility was you referred to:

- County hospital
- Provincial hospital
- National hospital

17. How long did it take to get referred to National hospital? ……

18. Why did you take long to be referred to National hospital:

- lack of money
- Long distance
- Hoping for symptoms to regress.

19. When first did you book for endoscopy ……

20. How long it take to get the endoscopy (OGD) done……

21. If long why did it take long to get the OGD done ……

22. How long it takes you to get the lab results confirming your cancer diagnosis after the endoscopy was done? ……

23. What delayed the lab results

- Wrong labeling
- Inadequate samples
- Others specify ……

24. How long did it take from onset of symptoms to confirmation of diagnosis of your disease ……

25. What was the stage of cancer at diagnosis :

    - I
    - II
    - II
    - IV

26. How far is your resident away from sub-district/ district hospital in kilometers …….

27. Was your monthly income in Kenya shillings enough to cover for your medical cost …….

28. Are you the one paying for the transport to HCF and for consultation?

    - Yes
    - No
    - If no specify ……

29. Do you have health insurance?

    - Yes
    - No

Appendix II: Data Collection Proforma(Kiswahili Version)

01 Jinsia ya Mgonjwa

- Mume
- Mke

02 Tarehe na mahali pa kuzaliwa? :……

03 Ulikuwa na miaka mingapi wakati saratani ilipogunduliwa ? ……

04 Hali ya ndoa?

- Sijaoa wala kuolewa
- Nimeoa/Nimeolewa
- Tumeachana
- Tumetalakana
- Nyingine, eleza …….

05 Unaishi Kaunti Gani? ……...

06 Unaishi mahaligani?

- Mjini
- Vitongoji vya mji
- Mashambani

07 Kiwango cha Masomo

- Sijasoma
- Nilimaliza shuleya Msingi
- Chuo cha Upili
- Chuo Kikuu

08 Kazi yako? :

- Nimeajiriwa (Kibarua)
- Mfanyi biashara
- Sina Kazi

09 Je una mapato ya Kawaida ? :

- Ndio
- La
- Kama ndio, unapata shilingi ngapi za Kenya kwa mwezi? ……

10 Ni lini ulipata dalili za kwanza za ugonjwa huu? ……

11 Ni lini ulitafutau saidizi kwa sababuya dalili za ugonjwa kwa maraya kwanza?

12 Ni kituo gani cha afya ulitembelea mara ya kwanza?

- Zahana
- Hospitali ya wilaya ndogo
- Hospitaliya Kaunti……..

13 Ulifanyiwa nini katika kituo cha Kwanza?

- Uchunguzi
- Matibabu
- Rufaa
- Kama ulipewa, rufaa, elezawapi? .....

14 Ni lini ulipewa rufaa ya kituo ambacho kina uwezo wa kutambua ugonjwa huu? ……

15 Baada ya kuonekanana Daktari, alikupa rufaa mara moja au la, na sababu ya kutokupa rufaa mara moja ilikuwa ipi?:

- Nilipewa utambuzi tofauti

- Nilipewa tarehe ya Kurudi
- Nyingine, Eleza ……

16 Ulipewa rufaa ya kituokipi?

- Hospitali ya Kaunti
- Hospitali ya Mkoa
- Hospitali ya Kitaifa

17 Ilichukua muda gani kupewa rufaa ya Hospitali ya Kitaifa?

18 Kwa nini ilichukua muda mrefu kupewa rufaa ya Hospitali ya Kitaifa?:

- Ukosefu wa Pesa
- Safari Ndefu
- Kutumaini Dalili za ugonjwa zitapungua

19 Ulifanyiwa *Endoscopy* maraya kwanza lini? ……

20 Ilichukua muda gani kabla kufanyiwa (OGD) *Endoscopy* ? (OGD) ……

21 Kama ilichukuamudamrefukufanyiwa (OGD) *Endoscopy*, mbona ilichukua muda mrefu hivyo? ……

22 Ilichukua muda gani kupata matokeo ya mahabara kuonyesha utambuzi wa saratani yako baada ya kufanyiwa *Endoscopy?*……

Nini kilichelewesha matokeo ya Mahabara?

- Kuchanganywa kwa matokeo
- Sampuli haba
- Mengine eleza ……

23 Ilichukua muda gani kutoka ulipopata dalili za ugonjwa, hadi kufikia utambuzi wa ugonjwa wako? ……..

24 Saratani yako ilikuwa katika hatua gani ilipofanyiwa utambuzi? :

- I
- II
- II
- IV

25 Ni umbali wakilomita ngapi kutoka unakoishi hadi kwenye hospitali ya wilayandogo? Wilaya? …….

26 Je mapato yako ya Kifedha (shilling ya Kenya) yalitosheleza matumizi yako ya kimatibabu .....

27 Wewe ndiwe unayelipia Nauli ya kwenda HCF na ada ya Uuguzi?

- La
- Ndio
- Kama La Eleza ……

29 . Je una Bima ya Afya?

- Ndio
- La

Appendix III: Consent Explanation

Introduction

My name is Dr. Marial Majur Cikom, I am a post graduate medical doctor doing masters in the internal medicine in school of medicine, college of Health sciences at University of Nairobi.

I am conducting a study on: Time to presentation and Diagnosis in patients with esophageal cancer at Kenyatta National Hospital.

Purpose of the study

To determine time to presentation and diagnosis in patients with esophageal cancer seeking medical care at Kenyatta National Hospital, to determine attributable factors in delay diagnosis of cancer esophagus and to document the stage of cancer at diagnosis.

Basis of participation

Your participation will be purely voluntary. You are free to withdraw at any time during the course of the study period. Your refusal to participate or withdrawal at any time during the study period will not in any way affect the quality of your treatment. Your participation in this study bears no cost to you but the findings will be used for benefit of cancer esophagus patients in Kenya

Confidentiality

All information obtained in the study will be treated with utmost confidentiality.

I shall NOT use your name in any of my reports.

Benefits

The results of this study may be published in a medical book or journal for teaching purposes and will be used to offer recommendations which, if implemented, may lead to reduced diagnostic timelines and improved management and quality of life of patients with cancer esophagus in Kenya

Risks and discomfort

The study will include face to face interview and there is no risk involved in being part of this study .Some of the questions asked may be personal but privacy and confidentiality will be assured at all time.

Request for information

You may ask more questions about the study at any time or at this moment.

You may contact Dr. Marial Majur Cikom, on: +254701028415

Dr. Adam Sheikh, mobile: +254722384035:

Gastroenterologist and Lecturer at University of Nairobi,

Appendix IV: Consent Form (English Version)

Having read this consent form, all my questions have been answered, my signature below indicates my willingness to participate in this study and my authorization to use and share with others.

I……the(Patient/Guardian) of……after reading and having the study purpose explained to me by Dr. Marial Majur Cikom ,do hereby give informed consent to participate in the study: Time to presentation and diagnosis in patients with esophageal cancer at Kenyatta National Hospital , Kenya .

Signed…….. Date…….

Thumb Print…….. Date……..

I confirm that I have explained to the patient the above statement.

Signature of principal Investigator (Dr.Marial Majur Cikom)…….....

For further information, you may contact any of the following:

1. Dr. Marial MajurCikom Mabior (Principal investigator)

University of Nairobi department of Clinical Medicine & Therapeutics

Kenya, Nairobi , +254701028415

Email: cikomomega1@gmail.com

Juba, South Sudan, +211955635037

2. Dr. Adam Sheikh, Kenya, Nairobi, Mobile: +254722384035

Gastroenterologist and Lecturer at University of Nairobi,

3. Kenyatta National Hospital/University of Nairobi Ethics and Research Review Committee,

P.O Box 20723 NAIROBI.

Tel 020-726300

Appendix V: Assent Form

Introduction

My name is Dr. MarialMajur Cikom. I am a post graduate medical doctor doing masters in the internal medicine in school of medicine, college of Health sciences at University of Nairobi.

I am conducting a study on: Time to presentation and Diagnosis in patients with esophageal cancer at Kenyatta National Hospital.

Purpose of the study

To determine time to presentation and diagnosis in patients with esophageal cancer seeking medical care at Kenyatta National Hospital, to determine attributable factors in delay diagnosis of cancer esophagus and to document the stage of cancer at diagnosis.

Basis of participation

Your participation will be purely voluntary. You are free to withdraw at any time during the course of the study period. Your refusal to participate or withdrawal at any time during the study period will not in any way affect the quality of your treatment.
Your participation in this study bears no cost to you but the findings will be used for benefit of cancer esophagus patients in Kenya

Confidentiality

All information obtained in the study will be treated with utmost confidentiality.

I shall NOT use your name in any of my reports.

Benefits

The results of this study may be published in a medical book or journal for teaching purposes and will be used to offer recommendations which, if implemented, may lead to reduced diagnostic timelines and improved management and quality of life of patients with cancer esophagus in Kenya.

Risks and discomfort

The study will include face to face interview and there is no risk involved in being part of this study .Some of the questions asked may be personal but privacy and confidentiality will be assured at all time.

Request for information

You may ask more questions about the study at any time or at this moment.

Voluntary Participation

You do not have to be in the study if you do not want to be in it. After we begin the study and you do not want to take part in it any further it is fine. We have informed you or your parents/guardian about the study.

If you agree to take part in the study, please sign your name.

Name of the Participant_____ Date_____

Sign your name _____

Thumb Print……. Date……..

I confirm that I have explained the details of the research to the participant.

Researcher's Name _____ Date_____

Signature of Researcher_____

1. Dr. Marial Majur Cikom Mabior (Principal investigator)

University of Nairobi department of Clinical Medicine & Therapeutics

Kenya, Nairobi , +254701028415

Email: cikomomega1@gmail.com

Juba, South Sudan, +211955635037

2. Dr. Adam Sheikh,

Kenya, Nairobi, Mobile: +254722384035

Gastroenterologist and Lecturer at University of Nairobi,

3. Kenyatta National Hospital/University of Nairobi Ethics and Research Review Committee,

P.O Box 20723 NAIROBI.

Tel 020-726300

Appendix VI: Consent Explanation for the Participants (Kiswahili Version)

Utangulizi

Jina langu ni Dkt. Marial Majur Cikom Mabior. Mimi ni mwanafunzi wa shahada ya uzamilifu katika kitengo cha Utabi buwandani, katika chuo kikuu cha Nairobi. Ninafanya utafiti juu **ya "Muda kati ya kuoneka na utambuzi wa wagonjwa wenye saratani ya Umio"** katika hospitali kuu ya Kenyatta.

Nia ya Utafiti

Kutambua muda ambao, wagonjwa wa saratani ya Umio,wanaotafuta matibabu katik a Hospitali Kuuya Kenyatta huchukua baada ya kuonekana na kutambuliwa kwa saratani ya umio,Kubaini Sababu ambazo husababisha wagonjwa, wa saratani ya Umio kuchelewa kuvumbua na kutambua ugonjwa wa Saratani ya Umio. Pia kurekodi hatua ambayo Saratani imefikia wakati wa Kutambuliwa.

Ushiriki

Ushiriki wako kwenye huu ni wa kujitolea. Uko huru kujiondoa wakati wowote unaota kakatika kipindi cha uchunguzi huu. Kukataa kushiriki au Kujiondoa kwako kwenye utafiti huu, hakutaathiri kwa vyovyote kiwango cha matibabu unayopokea. Ushirika wako kwenye utafiti huu hauna gharama yeyote kwako,lakini matokeo ya utafiti huu yatatumika kusaidia na kunufaa wagonjwa wengine humu nchini Kenya.

Usiri

Nakala na habari zote zitakazo tokana na uchunguzi huu zitahifadhiwa kwa siri.

SITAYATUMIA majina yako katika ripoti zangu za utafiti huu.

Faida ya Kushiriki

Matokeo ya Utafiti huu yatachapishwa kwenye jarida na vitabu vya Utabibu, na kutumika kwa Kufundisha. Yatatumika kupeana mwelekeo ambao ukitimizwa, unaweza kusaidia kupunguza muda wa Uvumbuzi na kuboresha matibabu na hali ya maisha ya wagonjwa wenye Saratani ya Umionchini Kenya.

Hatari

Utafiti huu utafanywa kwa njia ya kuulizwa maswali ana kwa ana,nakwa hivyo hakuna hatari yeyote kwa mgonjwa. Isipokuwa maswali yanayo ulizwa wakati mwingine ni ya Kisiri na undani,lakini usiri wako utazingatiwa wakati wote.

Kwa maswali zaidi, wakati wowote kuhusu utafiti huu

Wasiliana na:

Dkt. Marial Majur Cikom,

Simu: +254701028415

Dkt. Adam Sheikh, Kenya, Nairobi,

Simu: +254722384035

Gastroenterologist and Lecturer at University of Nairobi

Appendix VII: Patient Consent Form (Kiswahili Version)

Baada ya kusoma na kuelewa maelezo yaliotolewa kuhusu utafiti huu na Dkt. Marial Majur Cikom Mabior na pia kwa kufahamu kuwa kushiriki katika utafiti huu ni kwa hiari na niko huru kujiondoa wakati wowote bila kuadhirika, natoa idhini yangu kwa hiari, na kutia sahihi fomu hii.

Jina la mgonjwa……..

Sahihi……Tarehe……

Kwa maswali yeyote kuhusu utafiti huu, uko hurukuuliza wafuatao;

Mtafiti Mkuu:

Dkt. Marial Majur Cikom Mabior

Chuo kikuu cha Nairobi. Idaraya **Clinical Medicine & Therapeutics**

Kenya, Nairobi , +254701028415

Juba, South Sudan, +211955635037

Wasimamizi:

1. **Dkt. Adam Sheikh** , MBChB, MMed (Nbi), Fellowship Gastroenterology , Consultant Physician and Gastroenterologist, Lecturer, Department of Clinical Medicine and Therapeutics, Chuo kikuu cha Nairobi , Kenya

2. **Profesa, Mark D. Joshi**, MBChB, MMed, Cert TropMed, MPH, Cert ClinEpid, FACC Consultant Physician and Cardiologist, Department of Clinical Medicine and Therapeutics, Chuo kikuu cha Nairobi, Kenya

3. **Katibu Mkuu**,

   Kamati ya utafiti ya hospitali kuuya Kenyatta na chuo kikuu cha Nairobi

   KNH/UoN-ERC

   Hospitali kuu ya Kenyatta

   S.L.P 20723-00202, Nairobi

Nambari ya simu: 2726300-9/2716450 Ext 44102, Fax 725272

Appendix VIII: TNM Staging

Table 1: 1993 &2010 AJCC TNM Staging system for esophageal cancer

1993 Classification (Clinical)	2010 Classification (Pathologic)
Primary tumor (T)	
TIS carcinoma in situ T1 Tumor involves <5cm of esophageal length , produces no obstruction , and has no circumferential involvement T2 Tumor involves >5cm of esophageal length , causes obstruction , or involves the circumferential of the esophagus T3 Extra esophageal spread	TX primary tumor cannot be assessed T0 N no evidence of primary tumor TIS high grade dysplasia T1 tumor invades lamina propria, muscularis mucosae, or submucoa T1a tumor invades lamina propria or muscularis mucosae T1b tumor invades submucosa T2 tumor invades muscularis propria T3 tumor invades adventitia T4 tumor invades adjacent structures T4a resectable tumor involving pleura, pericardium or diaphragm T4b unresectable tumor involving other structures, such as aorta , vertebral body , trachea etc.

Regional Lymph Nodes (N)

NX regional nodes cannot be assessed N0 no nodal metastases N1 unilateral , mobile , regional nodal metastases (if clinical evaluable) N2 bilateral , mobile, regional nodal metastases (if clinically evaluable) N3 fixed nodes	Nx regional nodes cannot be assessed N0 no regional nodal metastases N1 regional LN met involving 1 to 2 nodes N2 regional LN met involving 3-6nodes N3 regional LN met involving 7 or more nodes

Distant Metastases (M)

M0 no distant metastases M1 distant met	M0 no distant met M1 distant met

Pathologic stage grouping, AJCC 2010 Squamous Cell carcinoma.

Group	T	N	M	Grade	T location
Stage 0	TIS (HGD)	N0	M0	1	Any
Stage1A	T1	N0	M0	1.x	Any
Stage1B	T1	N0	M0	2-3	Any
	T2-3	M0	M0	1.x	Lower.x