EVALUATION OF DRUG-RELATED PROBLEMS, HEALTH-RELATED QUALITY OF LIFE AND SURVIVAL OUTCOMES AMONG PATIENTS WITH GASTROINTESTINAL CANCERS AT KENYATTA NATIONAL HOSPITAL

BY

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DEDICATION

This thesis is dedicated to my wife for her constant support and encouragement throughout my study.

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TABLE OF CONTENTS

ABBREVIATIONS AND ACRONYMS

ADR	Adverse drug reaction
DRPs	Drug-related problems
ECOG	Eastern Cooperative Oncology Group
EORTC QLQ–CR29	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Colorectal Cancer Module 29
EORTC QLQ	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
EORTC QLQ–OES18	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Esophageal Cancer Module 18
EORTC QLQ–STO22	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Gastric Cancer Module 22
HRQoL	Health-related quality of life
KNH	Kenyatta National Hospital
SPSS	Statistical Package for the Social Sciences

LIST OF TABLES

LIST OF FIGURES

LIST OF EQUATIONS

OPERATIONAL DEFINITION OF TERMS

Cancer-specific survival: is defined as the time interval from the date of primary cancer diagnosis to the date of cancer related-death or last follow-up.

Cancer-specific survival after metastasis: defined as the time interval from the date of the first radiographic metastasis to the date of cancer-related death or last follow-up.

Censored observations: Consequences to cancer patients whose statuses were unknown or patients who did not develop the outcome of interest (death) at the end of the follow-up period or patients who were lost to follow-up.

Complete response: defined as no evidence of disease on repeat scanning after treatment.

Definite adverse drug reaction: The total score of the Naranjo Causality Assessment Scale of ≥ 9.

Doubtful adverse drug reaction: The total score of the Naranjo Causality Assessment Scale of ≤ 0.

Drug-drug interaction: An effect where the administration of one drug alters the clinical results of another drug when both are administered together.

Good health-related quality of life: A high mean score (≥60) on a global scale and the functional domains of quality of life and a low mean score (<60) on the symptom domains of quality of life as per the European Organization for Research and Treatment of Cancer Quality of Life questionnaire Scale.

High score for a functional scale: This represents a high/healthy level of functioning (Score ≥ 60) in the functional domains of health-related quality of life.

High score for the global health status: This represents a high (good) quality of life (Score ≥ 60) in the global health domains of health-related quality of life.

High score for symptom scale/items: A severe or high level of symptoms (Score ≥ 60) in the symptoms domains of health-related quality of life.

Ineffective drug therapy: A drug inappropriate for a patient suffering from a particular disease or medical condition is refractory to the drug product.

Mean survival time: A period between the diagnosis of disease and death, recurrence or progression of the disease, or the end of patient follow-up.

Metastasis-free survival: defined as the time interval from the date of primary cancer diagnosis to the first radiographic metastasis.

Naranjo algorithm score: is a method to assess whether there is a causal relationship between an identified untoward clinical event and a drug.

Need for additional drug therapy: Need to add drug(s) missing to achieve the desired treatment goals for a patient.

Selected gastrointestinal cancers: Malignant conditions of the gastrointestinal tract, including the esophagus, stomach, colon and rectum, after histological confirmation.

Serious drug interaction: Undesired drug-drug interactions that necessitate the use of alternative medications in the treatment regimen.

Survival outcome: will be defined in terms of mortality, cancer-specific survival, metastasis-free survival, cancer-specific survival after metastasis, progression of the disease, non-response, complete response and partial responses.

Partial response: defined as a reduction in tumour volume of at least 50% compared with pretreatment imaging.

Poor health-related quality of life: Represented by a low mean score (<60) on the global and functional scale and a high mean score (≥60) on the symptom scale of health-related quality of life.

Possible adverse drug reaction: The Naranjo Causality Assessment Scale total scores of 1 to 4.

Probable adverse drug reaction: The total Naranjo Causality Assessment Scale score of 5 to 8.

Progressive disease: defined as increased size of the tumour despite therapy.

Unnecessary drug therapy: There is no valid medical indication for the drug therapy; multiple drug products are being used for a condition requiring single-drug therapy, or the medical condition is more appropriately treated with non-drug therapy.

PUBLICATIONS FROM THE THESIS WORK

Degu, A., Karimi, P. N., Opanga, S. A., & Nyamu, D. G. (2023). Determinants of survival outcomes among esophageal cancer patients at a national referral hospital in Kenya. Chronic Diseases and Translational Medicine, 9(1), 20–28. https://doi.org/10.1002/cdt3.52. ISSN:2589-0514.

Degu, A., Karimi, P. N., Opanga, S. A., & Nyamu, D. G. (2023). Predictors of survival outcomes among patients with gastric cancer in a leading tertiary, teaching and referral hospital in Kenya. Cancer Medicine, 12(4), 4147–4160. https://doi.org/10.1002/cam4.5275. ISSN:2045-7634.

Degu, A., Karimi, P. N., Opanga, S. A., & Nyamu, D. G. (2023). Survival outcomes among colorectal cancer patients at Kenyatta National Hospital: A retrospective cohort study. Cancer Reports, 6(3), e1743. https://doi.org/10.1002/cnr2.1743. ISSN:2573-8348.

Degu, A., Karimi, P. N., Opanga, S. A., & Nyamu, D. G. (2023). Drug-related problems among esophageal, gastric and colorectal cancer patients at the National and referral hospital in Kenya. Journal of Oncology Pharmacy Practice, 107815522311782. https://doi.org/10.1177/10781552231178297. ISSN: 1078-1552.

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ABSTRACT

Background

The prevalence of gastrointestinal cancers is increasing in Kenya. Most of the cases are diagnosed late since the initial symptoms are vague. Patients are subjected to different treatment modalities, including radiotherapy, surgery or chemotherapy. The drugs used exhibit adverse effects that impact patient health-related quality of life and survival outcomes. In spite of this, there is insufficient data on drug-related problems, health-related quality of life and survival outcomes among gastrointestinal cancer patients in Kenya.

Objective

To evaluate drug-related problems, health-related quality of life and survival outcomes among adult gastrointestinal cancer patients at Kenyatta National Hospital.

Methods

Multimodal studies comprising cross-sectional and retrospective one-arm cohort designs were used to assess drug-related problems, health-related quality of life and survival outcomes. The cross-sectional arm comprised 160 esophageal, 103 gastric and 96 colorectal cancer patients, while the retrospective cohort had 299 esophageal, 247 gastric and 232 colorectal cancer patients. The study participants were selected using simple random sampling. The Data were collected with an investigator-administered questionnaire and data abstraction tool. Patient-specific clinical characteristics and treatment regimens were recorded after reviewing patient medical records and conducting patient interviews. The Cipolle *et al* classifications were used to determine the categories of drug-related problems. The quality of life was assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaires. Survival outcomes were reported using mortality, median and mean cancer-specific survival, metastasis-free survival, and cancer-specific survival after metastasis. The data entry and analysis were carried out using Statistical Package for the Social Sciences version 26.0 software. The Kaplan-Meier analysis was used to compute the median survival time. Cox regression analysis was utilized to examine the determinants of survival outcomes. The determinants of health-related quality of life and drug-related problems were assessed using binary logistic

regression analysis. The results were presented in tables, graphs, and charts. Statistical significance was considered when the p-value was less than 0.05.

Results

The mean age of esophageal, gastric and colorectal cancer patients was 60.5± 12.7 years, 59.8 ± 1.3 years and 53±1.5 years, respectively. More than half of the esophageal (97, 60.6%), gastric (64, 62.1%) and colorectal (64.6%) cancer patients were males. The prevalence of drug-related problems among the patients was 51.9% (esophageal cancer), 59.2% (gastric cancer) and 62.5% (colorectal cancer). The need for additional drug therapy was the predominant (39, 33.9%) category of drug-related problems in esophageal cancer patients, while adverse drug reactions were predominant in gastric (40, 51.3%) and colorectal (41, 46.1%) cancer patients. Most of the identified adverse drug reactions had possible causality scores, mild severity levels and were preventable. The study found that patients with comorbidities who had esophageal (AOR=2.4, 95% CI=1.6, 2.9, p=0.03), gastric (AOR=2.0, 95% CI=1.8-5.3, p=0.02), and colorectal (AOR=4.4, 95% CI=1.6-12.8, p=0.01) cancer were more likely to experience drug-related problems compared to those without comorbidities. Similarly, advanced-stage esophageal (AOR=2.8, 95% CI=1.4-3.6, p=0.03), gastric (AOR=2.2, 95% CI=1.4-3.7, p=0.03) and colorectal (AOR=2.1, 95% CI=1.2-5.3, p=0.03) cancer patients had higher odds of experiencing drug-related problems.

The overall health-related quality of life was poor in most esophageal (118, 73.7%), gastric (118, 72.8%), and colorectal (72, 75%) cancer patients. However, most gastrointestinal cancer patients did not have significant problems in the symptoms domain of health-related quality of life. Co-morbid esophageal (AOR=3.9, 95% CI= 2.4-5.8, p=0.02), gastric (AOR=2.3, 95% CI= 2.2-4.6, p=0.01) and colorectal (AOR=2.5, 95% CI= 1.3-4.5, p=0.03) cancer patients were more likely to have a poor health-related quality of life. Furthermore, advanced-stage (stages III & IV) esophageal (AOR=2.8, 95% CI= 1.3-3.7, p=0.03), gastric (AOR=1.8, 95% CI= 1.5-5.3, p=0.04) and colorectal (AOR=10.3, 95% CI= 1.8-13.4, p=0.03) cancer patients had a higher odds of having a poor health-related quality of life.

Patients with esophageal cancer had high mortality (129, 43.1%), disease progression (60, 20.1%), non-response (39, 13%) and distant metastases (29, 11.1%). The study revealed that 64

(33.3%) patients had new distant organ metastases, 104 (42.1%) experienced disease progression and a 33.6% (83) mortality among gastric cancer patients. Almost one-third (79, 34.1%) of patients showed disease progression and 41 (23.6%) had new distant metastases in colorectal cancer patients. The five-year survival was 25.0%, 32.7% and 45.4% among esophageal, gastric and colorectal cancer patients, respectively. In advanced-stage esophageal cancer patients, co-morbidities (AHR= 7.5, 95% CI =2.2-12, p=0.001), chemotherapy (AHR= 3.9, 95% CI= 1.2-6.1, p=0.020), chemoradiation (AHR= 5.6, 95% CI=1.6-10.2, p=0.006) and radiotherapy (AHR=3.3, 95% CI= 1.4-7.8, p=0.007) were the significant determinants of survival. Gastrectomy (AHR=4.2, 95% CI=1.7-10.4, p=0.002), radiotherapy (AHR=3.2, 95% CI= 0.4-24.2, p=0.01) and chemotherapy (AHR=16.6, 95% CI=4.5-20.2, p<0.001) and co-morbidity (AHR= 2.7, 95% CI= 1.3-7.9, p=0.04) were the significant determinants of survival in advanced gastric cancer patients. Older age (AHR=2.7, 95% CI=1.5-4.8, p=0.001), co-morbidity (AHR=2.7, 95% CI= 1.1-6.3, p=0.03), surgery (AHR= 1.5, 95% CI= 1.1-1.9, p=0.01) and radiotherapy (AHR=4.7, 95% CI= 1.7-5.5, p=0.04) were significant determinants of survival in advanced-stage colorectal cancer patients. Surgery was the only determinant of survival in early-stage esophageal (AHR= 1.9, 95% CI=1.2-3.6, p=0.049) and gastric (AHR=2.5, 95% CI= 0.5-13.2, p=0.02) cancer patients. However, none of the variables had a significant association with survival among early-stage colorectal cancer patients.

Conclusions

The prevalence of drug-related problems was high among gastrointestinal cancer patients due to comorbidities and advanced-stage disease. The need for additional drug therapy and adverse drug reactions were the most prevalent categories of drug-related problems. Therefore, close monitoring is required to manage patients with advanced-stage and multiple illnesses. There was generally poor overall health-related quality of life due to advanced stages of disease at presentation and comorbidity. This suggests that early screening among patients with comorbidities is necessary to initiate treatment to avert the progression to the advanced stages of the disease. Mortality, disease progression, non-response and distant metastasis were high in patients with gastrointestinal cancer due to advanced-stage disease at diagnosis. Hence, screening at early stages is required for early initiation of optimal treatment to mitigate survival outcomes.

THESIS PRESENTATION AND LAYOUT

This thesis is presented in different chapters with different subsections under each chapter. The preliminary page of the thesis contains the title of the study, declaration of originality, supervisor approval, dedication, acknowledgement, table of contents, list of abbreviations, the definition of terms, list of tables, list of figures, list of equations, and abstract sections.

Chapter one of this thesis entails the background of the study, a statement of the problem, justification, research questions, objectives, and significance of the study with their relevant descriptions.

Chapter two of the thesis consists of a literature review with different subsections, such as a theoretical literature review, an empirical review and a summary of the current gaps in the literature.

Chapter three is about the methods section of the thesis. This section consists of detailed descriptions of methods used in this study, such as study design, setting, data collection period, target population, eligibility criteria, sample size determination, sampling techniques, research instruments, data collection techniques, study variables, data quality control procedure, data management, data analysis, and ethical consideration.

Chapters four, five, six, seven and eight consist of the details of the findings of the study. Chapter nine is about the summary, conclusions, recommendations, strengths and limitations of the study, new knowledge generated from the study and dissemination plans of the study's main findings.

The appendices consist of participant information, a consent form, data collection tools, an ethical approval letter, a study registration certificate, a copy of the National Commission for Science, Technology & Innovation research permit and copies of the published articles and Turnitin plagiarism report.

CHAPTER ONE: INTRODUCTION

1.1 Background

The estimated global burden of cancer is 9.9 million deaths and 18.1 million new cases annually (Ferlay et al., 2021; Sung et al., 2021; International Agency for Research on Cancer, 2020). Developing countries accounted for about 70% of cancer mortality in 2020 (World Health Organization, 2018). An estimated 23.6 million cancer cases will be diagnosed annually by 2030 (Cancer Research UK, 2018). This rising cancer incidence has prompted more advanced research into cancer treatment and prevention (Gavhane et al., 2011). The economic burden of cancer-associated care is substantially high and requires a significant expenditure on diagnosis, screening, and treatment. It also substantially decreases productivity due to sickness and premature mortality (Garaszczuk et al., 2022; Yabroff et al., 2021).

Cancer incidence and mortality are increasing at an alarming rate in Africa, necessitating a comprehensive strategy for cancer therapy and control (Olaleye & Ekrikpo, 2017; Sharma et al., 2022). The cumulative burden of all neoplasms in Africa is expected to rise to 2.1 million new cases and 1.4 million deaths per year by 2040 (Sharma et al., 2022). Even though remarkable progress has been made in cancer care over the past few decades, there is a vast disparity between developed and underdeveloped countries in diagnosis, treatment, and outcomes. Despite this, there has been little investment in capacity building to combat the current cancer problem in African countries (Boyle et al., 2019). In Kenya, cancer ranks as the third highest cause of mortality (Ministry of Health Kenya, 2022).

1.1.1 Burden of gastrointestinal cancers

Globally, one in four cancer incidences and one in three cancer deaths are attributable to gastrointestinal tract malignancies. Nonetheless, incidence and fatality rates vary considerably across the globe (Arnold et al., 2020a). Esophageal, gastric, liver and colorectal cancers are the most prevalent gastrointestinal malignancies worldwide (Somi et al., 2019). Digestive tract cancers accounted for more than a quarter of all malignancies (Jardim et al., 2023). Furthermore, 26% of all new cases of cancer and 35% of all cancer fatalities are caused by gastrointestinal malignancies, and therefore, they remain significant public health problems (Arnold et al., 2020b). Esophageal cancer has a higher incidence and mortality in African nations, with a larger preponderance in men (Asombang et al., 2019). Studies in Africa have

shown a rise in the burden of colorectal cancer owing to the increasing of preventable risk factors (Awedew et al., 2022). Even though most reported stomach cancer incidence rates were declining, only a few African countries have a promising reduction (Shokouhi et al., 2021). According to The Global Cancer Observatory 2018 report, esophageal and colorectal cancers were the third and fourth leading types of cancer in Kenya (International Agency for Research on Cancer, 2018).

1.1.2 Drug-related problems among gastrointestinal cancers

Previous studies have shown a high burden of possible drug-related problems (DRPs) among cancer patients (Ismail et al., 2020; Lund et al., 2018). As the disease progresses, they are more likely to have organ failure and metabolic changes (Bulsink et al., 2013). DRPs account for 15% of hospital-related admissions, with a high incidence in older and multiple medications-treated patients (Ayalew et al., 2019; Očovská et al., 2022). Around 12.4% of hospitalisations in cancer patients were due to DRPs, yet 50% of these occurrences were preventable (Chan et al., 2014). Drug-related hospitalization cost of care is very high in cancer patients (Ko et al., 2014). Although chemotherapy is the frontline treatment in managing colorectal cancer, it is associated with various limitations, such as systemic toxicity, unsatisfactory response rate, unpredictable resistance, and lack of targeted tumour selectivity (Xie et al., 2020). About 60% of drug-related problems are associated with targeted chemotherapy (Kucuk et al., 2020).

Even though chemotherapy is the main treatment approach for gastric cancer treatment, chemo-resistance limits chemotherapy's effectiveness and results in treatment failure (Shi & Gao, 2016). Monoclonal antibody therapy is the recent advancement in gastrointestinal cancers, in addition to chemotherapy, to improve patients' overall survival. However, they have been associated with some adverse effects, such as hypertension, proteinuria, thromboembolism, bleeding and slow wound healing (Arora et al., 2017).

1.1.3 Survival outcomes of gastrointestinal cancers

Despite the fact that metastatic gastric cancer treatment outcomes have changed as surgery and chemotherapy have evolved, there are still areas for improvement to enhance patients' survival (Leiting & Grotz, 2019). Even though stomach cancer has consistently decreased over the last 50 years in developed countries, treatment outcomes remain dismal, owing primarily to the late-stage presentation. Consequently, due to their genetic complexity, successful treatment for

gastric cancer is minimal. Furthermore, despite considerable efforts to enhance treatment, including introducing new drugs, advanced gastrointestinal cancer still has a poor prognosis. As a result, optimal management is required to ensure patients receive the best possible care (Lordick et al., 2014).

Colorectal cancer has a significant burden in African countries and their survival is still poor (Awedew et al., 2022; Gullickson et al., 2021). Population growth, ageing, and unfavourable patterns in key risk factors such as physical inactivity, overweight and obesity, and Western eating habits are likely to increase colorectal cancer incidence. Consequently, the number of cases and deaths is expected to rise in the coming decades unless successful preventive measures are implemented globally (Brenner & Chen, 2018). Approximately 25% of patients have metastatic colorectal cancer at diagnosis, which is much harder to treat than the localized stage. In addition, 40-50% of patients initially diagnosed with localized colorectal cancer ultimately develop metastatic disease (Moriarity et al., 2016). A study in Tanzania indicated that most colorectal cancer patients presented with advanced diseases that adversely affected the desired treatment outcomes (Chalya et al., 2013). Most patients with colorectal cancer in the early stages are often asymptomatic. In the advanced stages of the disease, the risk of an inadequate response to treatment is higher (Dekker et al., 2019). Prior history of a leukemic type of malignancy significantly reduces the survival of colorectal cancer patients (Al-Husseini et al., 2019).

Due to inadequate treatment and diagnostic facilities, sub-Saharan African countries have worse treatment outcomes for cancer patients than other regions (Olaleye & Ekrikpo, 2017). Despite the fact that early identification may lead to long-term survival (Basaran et al., 2015), there is substantial inconsistent data regarding the survival outcome of gastrointestinal malignancies worldwide. Furthermore, younger populations have a higher prevalence of gastric cancer in certain regions (Wong et al., 2021). Nevertheless, only a handful of studies were available in East African countries to evaluate survival outcomes in gastrointestinal cancer patients.

1.1.4 Health-related quality of life among gastrointestinal cancers

Health-related quality of life (HRQoL) is indispensable in various aspects of patient care in cancer patients, including overall survival. Hence, HRQoL needs to be addressed regularly to

ensure that cancer patients obtain optimum care and experience the best possible outcomes (Sitlinger & Zafar, 2018). Generally, cancer patients often have lower HRQoL than the general population (Quinten et al., 2015). Besides, despite an individualized and increasingly tolerable treatment, there is still a significant decline in the HRQoL of cancer patients (Peters et al., 2016).

In summary, there is inconclusive evidence about DRPs, HRQoL, and survival outcomes of patients with esophageal, gastric and colorectal cancer. Moreover, the available studies in East African countries are minimal and non-comprehensive. Hence, this study purposed to investigate drug-related problems, HRQoL and survival outcomes among selected gastrointestinal cancer patients at Kenyatta National Hospital (KNH).

1.2 Statement of the problem

Globally, cancer is a major threat to developing countries with ill-equipped healthcare systems to deal with complicated and expensive cancer treatments (van den Bemt et al., 2015). The prevalence of gastrointestinal cancers is growing rapidly in the Western world (Keum & Giovannucci, 2019). In addition, several comorbidities are associated with these cancers (Danese et al., 2014). Therefore, patients with gastrointestinal malignancies generally receive other treatments apart from cancer chemotherapy, which carries an intrinsic risk of drug-related problems, ultimately influencing the favourable treatment outcome (Cehajic et al., 2015).

Drug interactions, adverse drug events, and non-compliance are the main drug-related problems among patients diagnosed with cancer (Yeoh et al., 2015). Furthermore, the emergence of secondary malignancies after long-term usage of chemotherapy and radiation is a new challenge for healthcare providers (Travis, 2002).

Patients with advanced solid cancer often experience severe toxicity associated with cancer treatment, which may negatively impact HRQoL (Tykodi et al., 2018).

Good clinical responses have been obtained by treating single molecular abnormalities, and the mean survival time has partially increased in some cancers. Nonetheless, this approach to cancer treatment is still inadequate, and more issues need to be resolved to mitigate treatment outcomes in cancer patients (Zugazagoitia et al., 2016). Early treatment and detection of cancer have a significant impact on improving survival and mortality reduction of patients with cancer (Neal, 2009). Nonetheless, there is a lack of adequate resources for diagnosing and treating cancer in underdeveloped countries, especially in sub-Saharan African countries (Neal, 2009). This can

substantially affect the desired survival outcomes in patients with cancer in African countries. Anti-cancer drugs have considerable inter-individual pharmacokinetic variability, resulting in unpredictable treatment outcomes (Undevia et al., 2005). Cancer therapeutics currently have the lowest clinical trial success rates of all major diseases, which might be linked to the lack of successful anti-cancer drugs (Cagan & Meyer, 2017). Cancer therapy has immense potential for poor patient outcomes due to the toxicity of most anticancer drugs. Patients with esophageal cancer have low survival, despite many advances in diagnosis and therapy (Mao, 2016).

A review report revealed that patients with colorectal cancer in sub-Saharan Africa had a lower survival rate than in Western countries. However, slight improvements have been observed in recent decades (Hassen et al., 2022). Hence, there is an urgent need to identify the significant barriers to poor survival. Despite many advances in the treatment of gastric cancer, the prognosis of advanced disease is still poor (Dahdaleh & Turaga, 2018; Digklia, 2016). There are gaps at many levels of society, and not every cancer patient can access these modern improvements on the African continent (Boyle et al., 2019; Stefan, 2015). Despite a few reports, there is a lack of comprehensive evidence about the survival outcome and drug-related problems of gastrointestinal malignancies in Kenya. In addition, early detection of drug-related problems and the provision of appropriate management would improve outcomes in cancer patients.

Approximately 42% of patients face a substantial economic burden due to cancer diagnosis and treatment, which eventually adversely impacts the HRQoL (Sitlinger & Zafar, 2018). Hence, these facets of quality of life need to be addressed to ensure that patients with cancer receive appropriate treatment and achieve the best possible treatment outcome.

There are many symptoms for cancer patients that can influence their HRQoL, so there is a need to establish successful symptom management strategies that enable patients to have a greater sense of control over their disease (Nayak et al., 2017).

Most cases of gastrointestinal malignancies are diagnosed at advanced stages. These patients are subjected to chemotherapeutic agents, among other interventions. These drugs are given in combinations and have adverse effects that increase morbidity and mortality in patients who are often debilitated. Patients with gastrointestinal malignancies often have poor HRQoL and the benefits of treatment on HRQoL are not comprehensively assessed. Many of these patients are on palliative care and therefore require regular evaluation of HRQoL. This study unravels the interrelationship between HRQoL, DRPs, and survival outcomes at KNH.

1.3 Research questions

1. What is the prevalence of DRPs among adult patients with esophageal, gastric and colorectal cancer?
2. What are the types of DRPs among adult patients with esophageal, gastric and colorectal cancer?
3. What is the HRQoL among adult esophageal, gastric and colorectal cancer patients?
4. What are the survival outcomes among adult esophageal, gastric and colorectal cancer patients?
5. What are the determinants of DRPs, HRQoL and survival outcomes among adult esophageal, gastric and colorectal cancer patients?

1.4 Objectives of the study

1.4.1 General objective

To evaluate drug-related problems, health-related quality of life and survival outcomes among patients with gastrointestinal cancers at Kenyatta National Hospital.

1.4.2 Specific objectives

1. To determine the prevalence and types of drug-related problems among esophageal, gastric and colorectal cancer patients at Kenyatta National Hospital.
2. To assess the health-related quality of life of esophageal, gastric and colorectal cancer patients at Kenyatta National Hospital.
3. To evaluate the survival outcomes of esophageal, gastric and colorectal cancer patients at Kenyatta National Hospital.
4. To assess the determinants of drug-related problems, health-related quality of life and survival outcomes among esophageal, gastric and colorectal cancer patients at Kenyatta National Hospital.

1.5 Research hypotheses

Null hypothesis

Clinical characteristics of patients and their treatment regimens may not affect the occurrence of DRPs among gastrointestinal cancer patients.

Clinical characteristics of patients and their treatment regimens may not affect the HRQoL of gastrointestinal cancer patients.

Clinical characteristics of patients and their treatment regimens may not affect the survival outcomes of gastrointestinal cancer patients.

Alternative hypothesis

Clinical characteristics of patients and their treatment regimens may affect the occurrence of DRPs among gastrointestinal cancer patients.

Clinical characteristics of patients and their treatment regimens can affect the HRQoL of gastrointestinal cancer patients.

Clinical characteristics of patients and their treatment regimens can affect the survival outcomes of gastrointestinal cancer patients.

1.6 Justification of the study

The cytotoxic nature of chemotherapeutic agents has been linked to a diverse array of drug-related toxicities in cancer treatments. Furthermore, several studies reported the high prevalence of drug-related hospitalization in patients with cancer, which can also increase the cost and complexity of cancer treatment. Despite these problems being reported in developed countries, many investigations were not conducted in African settings, whereby cancer screening, diagnosis and treatment are still in the infancy stage. In addition, the studies reported in the African settings mainly reported the prevalence of DRPs and data about the significant contributing factors for the considerable prevalence of DRPs in patients with gastrointestinal cancer were inadequate to make further interventions.

Chronic diseases, including cancer and the associated treatments, can also affect the HRQoL of patients. Data on the extent to which they affect the HRQoL among Kenyan gastrointestinal cancer patients is scarce. Although epidemiological studies reported a rising burden of gastrointestinal cancers in Africa, including Kenya, adequate information was unavailable about the extent of survival and its potential determinants in patients with these malignancies.

Moreover, the best treatment modalities giving the optimal outcome are yet to be characterized in these malignancies. In addition, there is a lack of sufficient objective evidence about the long-term impacts of various treatment modalities on the survival outcomes of gastrointestinal cancer patients. The available investigations in DRPs, HRQoL and survival were minimal and had conflicting data. Hence, the study was purposed to investigate DRPs, HRQoL and survival outcomes among patients with gastrointestinal cancer. The study findings will give direction about the potential determinants of DRPs, HRQoL and survival outcomes to suggest appropriate interventions to improve cancer patients' survival and HRQoL. The study findings also unearth the long-term impacts of various treatment modalities on the survival and HRQoL of gastrointestinal cancer patients. Besides, the clinician will be guided to the appropriate treatment modalities that can improve HRQoL and survival in those patients. The output of this investigation may be used as baseline data for further investigations.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This chapter entails an overview of the epidemiology of gastrointestinal cancers, DRPs, survival outcomes, and HRQoL among esophageal, colorectal, and gastric cancer patients. It also covers the significant impacts of various cancer treatment modalities on HRQoL and survival outcomes. At the end of each subheading, the gaps identified were indicated after a rigorous review of previous studies.

2.2 Epidemiology of gastrointestinal cancers

According to global estimates, there were nearly ten million deaths and 19.3 million new cancer cases in 2020 globally (International Agency for Research on Cancer, 2020). The disease is a significant cause of morbidity and mortality in every region, regardless of human development level (Sung et al., 2021). Breast cancer is the most common cancer, followed by lung, colorectal, prostate and stomach cancer. With an estimated 1.8 million deaths, lung cancer remained the primary cause of cancer-related mortality, followed by colorectal, liver, stomach and breast cancer (Sung et al., 2021).

Cancer was estimated to cause 1.1 million new cases and 700,00 deaths in Africa every year (World Health Organization, 2023). Sub-Saharan African regions were estimated to have had 801,392 new cancer cases and 520,158 cancer deaths (Bray et al., 2022). Cancer-related mortality will rise to one million deaths per year by 2030 unless immediate interventions are implemented in the region. Therefore, urgent action is required to address the growing cancer incidence and mortality crisis in Sub-Saharan African countries (Ngwa et al., 2022).

Globally, 4.8 million cases and 3.4 million mortalities were reported in gastrointestinal cancers. Twenty-six percent of cases and 35% of cancer-related deaths worldwide were related to gastrointestinal malignancies (International Agency for Research on Cancer, 2022). Gastrointestinal cancers such as esophageal, gastric and colorectal cancers are emerging gastrointestinal malignancies. Currently, it is an emerging cause of cancer-related morbidity and mortality (Cai et al., 2022; Keum & Giovannucci, 2019; Morgan et al., 2022; Xi & Xu, 2021). By 2040, the annual burden of gastric cancer is expected to rise to 1.8 million new cases and 1.3 million deaths (Morgan et al., 2022). In 2020, 604,100 cases and 544,100 deaths were reported

as a result of esophageal cancer. If current trends continue, 957,000 new cases and 880,000 deaths from esophageal cancer are expected in 2040 (Morgan et al., 2022). Although 1.93 million cases and 0.94 million deaths were attributed to colorectal cancer in 2020, the global projection for the incidence of new cases of colorectal cancer will increase to 3.2 million by 2040 (Xi & Xu, 2021).

Although cancer is among the lowest public health priorities in the sub-Saharan African regions, gastrointestinal cancers are expected to increase by 73%. Over 90% of all gastrointestinal cancers in sub-Saharan Africa have late presentation compared to the Western countries (Singh et al., 2017). Therefore, gastrointestinal cancers such as esophageal, gastric and colorectal cancer cause significant morbidity and mortality in the African regions, particularly in sub-Saharan African countries.

Cancer is the third leading cause of death in Kenya, following infectious and cardiovascular diseases (Ministry of Health Kenya., 2017). In addition, a previous study also reported that cancer was causing a significant health problem in Kenya (Macharia et al., 2019). Access to cancer screening and treatment has been shown to be one of the most significant barriers in the local setting. Furthermore, most cancer centres have limited capacity in terms of diagnostic and treatment services (Wambalaba et al., 2019). A study in Kenya showed that esophageal, gastric and colorectal cancer patients accounted for 5.0%, 5.2% and 6.4% of cases, respectively (Macharia et al., 2019).

2.3 Drug-related problems

Drug-related problems are incidents encompassing drug therapy that can deter attaining the desired treatment goals (Ruths et al., 2007). Drug-related problems are estimated to account for 5-10% of hospital admissions, 50% of which are preventable (Nelson & Talbert, 1996). A previous study demonstrated that 12.4% of hospital admissions were associated with DRPs. Out of these, the majority of DRP-related hospitalizations were due to adverse drug reactions (Chan et al., 2014). A systematic review revealed that chemotherapy-related neutropenia was responsible for more than 50% of emergency visits and hospital admissions (Vandyk et al., 2012). The United States-based systematic review also reported that the percentage of patients experiencing readmission within 30 days ranged from 3%–34% among cancer patients (Bell et al., 2017). Drug-related problems have a substantial negative impact on patients' health in terms

of extended hospitalization and higher healthcare costs in the absence of effective intervention (Cipolle et al., 2012).

A systemic review showed that the intervention of clinical pharmacists had a significant improvement in medication-related outcomes in patients receiving anti-cancer therapies (Maleki et al., 2019). Another systematic review indicated that pharmacist interventions could improve outcome measures in outpatients with cancer (Colombo et al., 2017). An Australian study showed a high cost of treatment in chemotherapy-related adverse drug reactions (Livingston et al., 2012). Similarly, the expense of drug-related hospitalisation in cancer patients was high owing to longer hospital stays (Ko et al., 2014).

Drug-related problems are categorized as ineffective drug therapy, need for additional drug therapy, unnecessary drug therapy, dose too high or too low, adverse drug reactions (ADRs), drug-drug interactions and medication non-adherence (Cipolle et al., 2012). A study in Singapore demonstrated that drug-drug interactions, ADRs and non-adherence were the commonest DRPs in patients with cancer (Yeoh et al., 2015). A similar study depicted that drug-drug interactions and ADRs were the predominant DRPs in cancer patients (Vantard et al., 2015). Due to the complexity of cancer therapy and the greater likelihood of organ failure with disease progression, patients with cancer are at heightened risk for drug-drug interactions (Bulsink et al., 2013). Potential drug-drug interaction was highly prevalent among cancer patients (Stoll & Kopittke, 2015). According to a Netherlands study, 49.8% of DRPs were detected among patients with cancer. Most of the identified DRPs were mostly drug-drug interactions and contraindications (Bulsink et al., 2013). Despite drug-drug interactions comprising a critical issue in cancer patients, there is a scarcity of data on their clinical consequences (Riechelmann & Saad, 2006).

In general, cancer pharmacological treatments are complicated and carry a potential risk of drug-related problems (Cehajic et al., 2015). Similarly, problems associated with anti-cancer medications are more prevalent in cancer patients, which poses a substantial challenge for healthcare workers (Iftikhar et al., 2015). A study on Ethiopian cancer patients showed a high prevalence of ADRs (52.86%) (Belachew et al., 2016). Similarly, an Indian study reported that more than half (58.6%) of patients had chemotherapy-induced ADRs (Chopra et al., 2016). A systematic review showed that the majority of patients with solid cancers (64%) suffer from toxicities arising from anti-cancer drugs (Versteeg et al., 2014). The rate of adverse drug

reactions encountered per patient was about 1.18, secondary to antineoplastic agents (Behera et al., 2017). Cancer treatment has potential DRPs owing to the cytotoxic nature of antineoplastic regimens (Jaehde et al., 2008). An Ethiopian study reported that DRPs were found in 74.7% of cancer patients (Sisay et al., 2015) and 48.7% of colorectal cancer patients (Kefale et al., 2022). In contrast, a 93.8% prevalence of DRPs was reported in Kenya among cervical cancer patients (Degu et al., 2017). A Ugandan study demonstrated that at least one clinically significant drug-drug interaction was found in more than half of cancer patients (Luzze et al., 2022).

Similarly, a study in Turkey reported that 53.9% of patients had drug-related problems after two chemotherapy cycles (Boşnak et al., 2019). Another study also showed that 32.1% of DRPs were associated with dosing errors of anti-cancer agents (Aguiar et al., 2018). A comprehensive DRPs study may provide healthcare professionals with useful insight into reducing the occurrence of DRPs in cancer patients (Koh et al., 2005). Nonetheless, extensive studies are scarce on DRPs among gastrointestinal cancer patients at the leading tertiary and teaching hospital in Kenya.

According to the World Health Organization, adverse drug reactions are the undesired response to a medication used for prophylaxis, diagnosis, or disease treatment at standard doses (World Health Organization, 1972). Adverse drug reactions are prevalent and often serious, causing substantial morbidity and death. ADRs cause a major economic burden on society in addition to human costs, as they frequently contribute to emergency visits, hospital admission and prolonged hospital stays (Lundkvist & Jonsson, 2004; Singer & Khong, 2002). Anti-cancer drugs are the most common drugs associated with adverse drug incidents that involve admission to the intensive care unit (Nazer et al., 2013). Over 80% of ADRs requiring hospital admission are type A adverse drug reactions. Thus, from the known pharmacology of the drug, it is predictable and possibly avoidable. Geriatric patients tend to be especially at risk for ADRs since several medications are also expected to be given because of co-current comorbidities in this population (Routledge et al., 2003).

There is an immense opportunity for ADRs in systemic cancer treatment as a result of the high toxicity of most therapeutic regimens. Pharmacists can play a vital role in identifying and managing ADRs in systemic cancer therapy to assure the quality and safety of the patients and other healthcare providers (Jaehde et al., 2008). All-encompassing ADR research could provide valuable insights for health workers to minimize ADRs in cancer patients (Koh et al., 2005). However, an extensive study on DRPs among patients with gastrointestinal cancer at KNH is

lacking. Hence, this investigation aimed to determine the prevalence of DRPs and their determinants in gastrointestinal cancer patients in the study setting.

Previous studies show that the significant predictors associated with DRPs in cancer patients were the female gender, number of medications, body mass index, and extreme age. Early detection and intervention are crucial to ensure better treatment outcomes (Singh et al., 2016). Another study reported that female gender, age, polypharmacy, and potential drug interactions were independent predictors, which increased the likelihood of getting DRPs (Tigabu et al., 2014). The number of drugs used, comorbidity and duration of hospital stay in cancer patients are risk factors for DRPs (Sisay et al., 2015). A Nigerian study reported that comorbidities and the number of drugs in cervical cancer patients were significant predictors of DRPs (Mustapha et al., 2018).

2.4 Determinants of survival outcomes in patients with esophageal cancer

Cancer treatment has been transformed by molecular and immune therapies, which have improved patient outcomes and survival. However, as the cost of cancer care continues to rise, the pricing of these drugs has become an issue (Tran & Zafar, 2018). Esophageal cancer is a prevalent gastrointestinal cancer with a low survival rate, particularly in those with advanced disease (Jaffe et al., 2022).

Despite advancements in esophageal cancer management, the overall outcome remains poor after esophagectomy (Huang & Yu, 2018). Further, review reports have shown that surgical intervention is linked to increased morbidity and mortality among elderly esophageal cancer patients (Mantziari et al., 2021). A Dutch study revealed higher one-year mortality (36.0%) in curable esophageal cancer patients regardless of treatment modality (van Holstein et al., 2022). According to a single-centre study in China, chemoradiotherapy and esophagectomy combination therapy resulted in the longest overall survival time compared to the other treatment modalities (Yang et al., 2022). Furthermore, another study found that chemoradiotherapy and surgically treated patients have a higher overall survival rate than chemoradiotherapy alone treated esophageal cancer patients (Lee et al., 2022). Following the administration of multimodal treatment approaches, including surgery, the overall three-year survival rate for patients with metastatic esophageal cancer was 23% (Bardol et al., 2022). The overall pooled five-year survival rate was 26.6% following primary surgical treatment in esophageal cancer patients (De Virgilio et al., 2023). The overall five-year survival in locally advanced esophageal cancer was

27% (Sio et al., 2016). In developing countries, esophagectomy was associated with higher mortality (Kamarajah et al., 2021). Studies in developing countries revealed higher mortality rates due to late diagnosis (Hull et al., 2020). A systematic review in Africa demonstrated that patients with esophageal cancer had a higher mortality rate, although modifiable risk factors are commonly associated with these conditions (Asombang et al., 2019). Esophageal cancer is still deadly in Africa, with high morbidity and mortality (Kamarajah et al., 2021; Sharma et al., 2022).

An Ethiopian study reported a very low overall survival in esophageal cancer patients despite a slight improvement observed among patients treated with surgery, radiotherapy and chemotherapy. From the cox-regression analysis, surgery, radiotherapy and chemotherapy were the significant factors influencing survival in esophageal cancer patients (Hassen et al., 2021). Previous investigations depicted that men and people aged 70 years and above had the highest mortality rates from esophageal cancer (Fan et al., 2020).

2.5 Determinants of survival outcomes in patients with gastric cancer

Although studies have suggested that surgical resection is curative for an early stage of gastric cancer, most patients still have a recurrence. Hence, combined treatment approaches are the standard in managing this condition (Smyth et al., 2016). A previous study on gastric cancer patients revealed a median survival of 18 months after undergoing adjuvant chemotherapy. The study also reported the possibility of achieving long-term survival from gastric cancer with early diagnosis (Basaran et al., 2015). Contrastingly, the overall survival of early-stage (T1-T2) older gastric cancer patients was generally poor and had a higher prevalence of postoperative mortality after surgical resection (Bausys et al., 2018). According to a study done in Korea, mortality was 15.5% in gastric cancer patients, although adequate chemotherapy was given after surgery (Hong et al., 2017). A study in Oman showed that the overall five-year survival was 16.7% among patients with gastric adenocarcinoma after surgical and medical treatments (Al-Moundhri et al., 2006). Another investigation showed that the five-year overall survival was 62% after adjuvant chemoradiotherapy in advanced gastric cancer patients (Kim et al., 2011). A Korean study revealed that the 2-year and 5-year disease-free survival was 77.5% and 74.2%, respectively, in gastric cancer patients after surgery (Gwak & Park, 2018). A retrospective study in gastric patients showed that the mean disease-free survival was 93.6±1.5 months in elderly patients after surgical intervention (Kim & Kim, 2016). In addition, the 5-year relative survival of patients

with gastric cancer was 40% and 23% for the youngest (< 50 years) and oldest (≥80 years) age groups, respectively (Schlesinger-Raab et al., 2016). After surgical resection of early-stage gastric cancer patients, the overall five and eight-year survival rate was 100 % and 95.2%, respectively (Yang et al., 2021). Despite advances in treatment, the overall prognosis of advanced gastric cancer is still poor (Dahdaleh & Turaga, 2018; Digklia, 2016). A study in Brazil found that advanced gastric cancer patients' survival was generally poor after first-line chemotherapy (Vieira et al., 2019). Contrastingly, a recent meta-analysis showed that the combination of targeted therapy with chemotherapy significantly improved overall and disease progression-free survival in patients with advanced gastric cancer (Zhao et al., 2018). Iranian study depicted that the five-year survival probability for patients with gastric cancer was 28 %, with a median survival time of 25.69 months (Zeraati & Amiri, 2016). Another study suggested that 5-fluorouracil-based adjuvant chemoradiotherapy improves relapse-free and overall survival (Jácome et al., 2015). Similarly, neoadjuvant (Farhan et al., 2019) and adjuvant chemoradiotherapy (Andreollo et al., 2019) improved survival in locally advanced and advanced gastric cancer, respectively. Furthermore, the overall one, two and three (71%, 56% and 49%) year survival rates of gastric patients were significantly reduced after surgical resection of the tumour (van der Werf et al., 2019). Another study also reported that the overall 1, 2 and 3-year survival rates (91.7%, 79.4% and 63.2%, respectively) gradually declined after gastrectomy (Kato et al., 2019). The overall disease-free and 5-year survival rates in advanced gastric cancer after gastrectomy were 47.20 % and 43.6%, respectively (Zhang et al., 2019). A systematic review depicted that triplet chemotherapy regimens were superior to the doublet chemotherapy regimens in advanced gastric cancer in terms of improving overall survival time (Guo et al., 2019). Furthermore, combination chemotherapy significantly improved survival compared to monotherapy in older gastric cancer patients (Hayashi et al., 2019).

A clinical trial revealed that the median survival rate among patients in the modified docetaxel, cisplatin and 5-fluorouracil regimen (14 months) was slightly shorter than the epirubicin, oxaliplatin, and capecitabine (15 months) regimen among advanced gastric cancer patients (Ahmadzadeh et al., 2020).

A Taiwan study showed that high pathological grading was a significant determinant of poor survival outcomes in gastric cancer patients (Lin et al., 2014). Another study showed that age (Age > 60 years), the presence of less than 15 lymph nodes at the time of surgery, and gastric

adenocarcinoma at the cardia and fundus were significant predictors of poor overall survival in gastric cancer patients (Alnimer et al., 2019).

A systematic review demonstrated that blood groups A and AB were linked with an augmented threat of gastric cancer (Mao et al., 2019). A retrospective study on early-stage gastric cancer revealed that total gastrectomy and severe postoperative complications were the major determinants of poor overall survival in older patients (Bausys et al., 2018).

In the African setting, a Cameroonian study demonstrated lower three-year (10.1%) and five-year (4.6%) survival rates in gastric cancer patients (Bang et al., 2020). In addition, a Zambian study revealed 142 days of median survival in gastric cancer patients (Asombang et al., 2014).

Studies reported that the advanced stage of gastric cancer is the most prominent factor for poor survival in gastric cancer patients (Al-Moundhri et al., 2006; Guardiario & Dy, 2022). Besides, a pooled meta-analysis showed that high pretreatment neutrophil to lymphocyte ratio was a significant determinant of poor outcomes in gastric cancer patients (Sun et al., 2016). Besides, a lower Eastern Cooperative Oncology Group (ECOG) score was a determinant of progression-free survival in advanced gastric cancer patients (Abdel-Rahman, 2019).

Although younger patients had lower disease-free survival, age was not a major prognostic factor in gastric cancer patients (Ramos et al., 2019). Besides, the presence of more than one type of metastasis was the most important predictor of the overall survival of stage IV gastric cancer patients (Solaini et al., 2019).

2.6 Determinants of survival outcomes in patients with colorectal cancer

The findings in the Caucasian population showed relatively higher (65.0%) five-year survival rates in patients with colorectal cancer (Rawla et al., 2019). A study from nine European countries reported a higher (89.2%) fiver-year cancer-specific survival (Cardoso et al., 2022). Developing countries experienced low five years survival rates (43.5%) (Gullickson et al., 2021) than developed countries such as Korea (76.2%), the United States (66.1%), Canada (60.9%) and Europe (53.9%) (Jiang et al., 2021. The Netherlands study demonstrated that five-year survival substantially improved from 53 to 62% for colon cancer and 51 to 65% for rectal cancer (Brouwer et al., 2018). Previous systematic reviews demonstrated that colorectal cancer patients had a 1-year, 3-year and 5-year survival rate of 88.1%, 70.7% and 57.3%, respectively (Nikbakht et al., 2020). A systematic review and meta-analysis of the Iranian population reported a 54.0% five-year survival rate in colorectal cancer patients (Maajani et al., 2019). Compared to

other treatment modalities, adjuvant chemotherapy has been linked with long-term survival benefits in stage IV colon cancer patients (Xu et al., 2019). An Indonesian study showed that colorectal cancer patients had low (8.7%) overall survival rates (Dharmaji et al., 2021).

Despite advances in managing colorectal cancer, patients in sub-Saharan African countries still have poor survival (Gullickson et al., 2021). Studies from Ghana (16.0%) also showed that the stage of cancer, chemotherapy, chemoradiation and body mass index were the significant predictors of survival in colorectal cancer patients (Agyemang-Yeboah et al., 2018). A study in 11 sub-Saharan African countries reported a lower five-year (43.5%) survival rate in colorectal cancer patients. In addition, the study also demonstrated that low human development index, late-stage diagnosis and young or old age at diagnosis were poor determinants of survival. (Gullickson et al., 2021). An Egyptian study reported that the median survival time among colon cancer patients was two years, with the shortest time in stage IV disease (8 months) (Metwally et al., 2018).

A clinical outcome study in Kenya reported that the overall recurrence (37.5%) and mortality rates (29.4%) were high among colorectal cancer patients (Saidi et al., 2011). Over six years follow period, the cumulative incidence of death in colorectal cancer patients was 34.8% in Ethiopia. In addition, male gender, late diagnosis, carcinoembryonic antigen level, age (≥ 60 years), recurrence, stage of cancer and co-morbidity were the significant determinants of mortality in colorectal cancer patients (Atinafu et al., 2022; Tiruneh et al., 2022). In Uganda, colorectal cancer patients were reported to have low (33.3%) three years survival. Further, stage II, stage III and stage IV disease were associated with increased mortality, while surgery alone, surgery and chemotherapy had improved survival in colorectal cancer patients (Wismayer et al., 2022).

Kenyan study reported that the male gender, presence of comorbidity, cancer recurrence, disease stage and receipt of chemotherapy were significant determinants of mortality among patients with colorectal cancer (Saidi et al., 2011). Pre-existing diabetes mellitus is significantly associated with poor survival in patients with colorectal cancer (Li et al., 2017).

2.7 Health-related quality of life in esophageal cancer patients

The concept of HRQoL refers to an individual's state of health and subjective evaluation of their physical, mental, and social well-being (Karimi & Brazier, 2016). It includes all aspects of the

overall HRQoL that can be clearly shown to impact physical or mental health (Centers for Disease Control and Prevention, 2018). Cancer survivors have a significantly lower HRQoL (Tay et al., 2022).

A Chinese study reported a significant impairment of HRQoL in esophageal cancer patients following treatment, with a maximum reduction in advanced stages (Liu et al., 2018). There is usually a high prevalence of physical and cognitive disability, depression, and social isolation among esophageal cancer patients (van Deudekom et al., 2018). A different study showed that most patients (66%) have a favourable HRQoL after chemotherapy (Heydarnejad et al., 2011). Despite this, no statistically significant association was observed between HRQoL and curative treatments in esophageal cancer (van den Boorn et al., 2020). Similarly, no significant change in HRQoL trends after systemic palliative therapy in esophageal cancer patients was observed (Ter Veer et al., 2018). A previous study showed no substantial differences in mean scores in the global HRQoL and physical function between esophagectomy and gastrectomy among patients with gastroesophageal junction adenocarcinoma (Kauppila et al., 2018).

Esophagectomy is the cornerstone of esophageal cancer curative therapy; however, it is related to considerable morbidity and mortality, with a substantial adverse effect on HRQoL (Alghamedi et al., 2018). After esophagectomy, a substantial problem was observed in the symptom and physical domains of HRQoL in esophageal cancer patients (Kauppila et al., 2020a). Similarly, a Swedish study showed long-term digestive tract problems in esophageal cancer patients following surgery (Schandl et al., 2023). This procedure has been associated with reduced HRQoL in various domains and persistent gastrointestinal symptoms in esophageal cancer patients (Boshier et al., 2022; Mariette et al., 2020). There was a substantially reduced HRQoL in patients with esophageal cancer for more than one year following esophageal surgery (Markar et al., 2022). Chemoradiotherapy can reduce the incidence of dysphagia and boost the HRQoL for inoperable patients with esophageal cancer (Forootan et al., 2019). The overall HRQoL decreases considerably in patients with esophageal cancer following the completion of neoadjuvant chemoradiotherapy (Noordman et al., 2019). In patients with resectable esophageal cancer, chemoradiotherapy with cisplatin and 5-fluorouracil have a significant detrimental long-term impact on overall HRQoL (Hurmuzlu et al., 2011). Another cross-sectional multicenter study showed that the HRQoL score among patients with esophageal cancer was surprisingly declining (Wang et al., 2020). Medical complications are associated with long-term illness and a

decline in the HRQoL in esophageal cancer patients (Kauppila et al., 2020b). Those with three or more comorbidities at the time of surgery have reduced overall HRQoL and physical activity compared to patients without comorbidity (Backemar et al., 2020).

No disparity in HRQoL between treatments for 12 months among esophageal cancer patients exists (van den Boorn et al., 2020). Low functional scores and severe symptoms in curative and palliative care-treated esophageal cancer patients have been reported (Sunde et al., 2021). Esophagectomy is significantly linked to a decline in esophageal cancer patients' HRQoL (van den Boorn et al., 2020). The advanced stage of the disease significantly impacted the reduction of HRQoL (Liu et al., 2018).

Generally, most of the available evidence demonstrates that the HRQoL of esophageal cancer patients is significantly impaired following surgical resection of the tumour. Nonetheless, there were many disparities among the studies regarding the substantial impacts of various treatments on HRQoL in esophageal cancer patients.

2.8 Health-related quality of life in gastric cancer patients

Patients with advanced gastric cancer showed that disease progression and deterioration of performance status are associated with a worse HRQoL in all functional, global and symptom scales of HRQoL (Chau et al., 2019). A multicenter study in China showed that the overall HRQoL among gastric cancer patients was significantly impaired after treatment during the advanced stages of the disease (Xia et al., 2020)**.** In addition, gastrectomy declines the HRQoL with more problems in symptom domains among long-term gastric cancer survivors (Kwon et al., 2020). In contrast, patients with early gastric cancer had a better (86.7) physical functional and symptom score after gastrectomy (Eom et al., 2019). Patients subjected to chemotherapy and gastrectomy-treated patients have a worse HRQoL in most functional and symptom domains (C. J. Wang et al., 2022). Adjuvant chemotherapy-treated patients portray a better HRQoL in the physical functioning score (van Amelsfoort et al., 2022). The global HRQoL is significantly impaired compared to functional scales in patients with advanced gastric cancer (Chau et al., 2019). Those with metastatic gastric cancer depict a high prevalence of the symptom burden when reaching the end of life (Bubis et al., 2021). A Vietnamese study found that the quality of life in patients with gastric cancer was higher, except in the sexual activity domain (Ngoc Thi Dang et al., 2019). Cancer type, pain intensity and fatigue are significant determinants of the HRQoL life among cancer patients undergoing chemotherapy (Chau et al., 2019).

Age, occupation, comorbidity, duration of illness and treatment regimens significantly influence different functional domains of HRQoL in patients with gastric cancer (Xia et al., 2020). A similar study also showed that the most important determinants of HRQoL in gastric cancer patients were age, occupation, education, disease stage and treatment regimens (Ngoc Thi Dang et al., 2019). The advanced stage of gastric cancer is associated with a substantial decrement in HRQoL (Xia et al., 2020). In most functional and symptom scales, gastrectomy is the most important poor predictor of HRQoL (Brenkman et al., 2018).

In summary, despite numerous studies demonstrating poor overall HRQoL among gastric cancer patients following treatment, there is a lack of conclusive evidence regarding the significant impact of various treatment modalities on the HRQoL in gastric cancer patients.

2.9 Health-related quality of life in patients with colorectal cancer

A systematic review report showed low overall HRQoL among colorectal cancer patients with palliative treatment (Flyum et al., 2021). Iranian study showed the HRQoL of colorectal cancer patients was inferior in the physical, social and financial domains of HRQoL (Akhondi-Meybodi et al., 2016). A Chinese study also revealed low HRQoL in the symptoms scales of HRQoL. (Huang et al., 2018). Generally, colon and rectal cancer survivors diagnosed at a younger age (< 50 years of age) have lower functioning and more significant symptom burden than those diagnosed at an older age (Thong et al., 2019). The high incidence of malnutrition in older gastrointestinal cancer patients ultimately diminishes the HRQoL (Williams et al., 2020).

Lower anterior surgical resection of the colon significantly affects HRQoL (Heinsbergen et al., 2020). The progression of the disease is associated with worsening HRQoL for patients with colorectal cancer (Marschner et al., 2020). A Chinese study demonstrated that HRQoL was reduced significantly in patients with colorectal cancer (Huang et al., 2021). A systematic review showed that survivors of colorectal cancer experienced persistent symptoms and functional impairments for more than one year following the completion of treatment (Rutherford et al., 2020).

Patients with rectal cancer undergoing long-term chemoradiotherapy show substantially improved bowel functions than those undergoing short-term radiation therapy (Downing et al., 2019). The overall HRQoL improves after three months of treatment in non-metastatic rectal cancer patients despite the complexity of their treatment regimens (De Souza et al., 2018).

Treatment of locally advanced rectal cancer with chemoradiation affects numerous HRQoL domains with substantial impairment in cognitive and role functioning (Lim et al., 2019). Rectal cancer treatment (neoadjuvant therapy or rectal surgery) within the first six months after diagnosis is associated with a substantial decline in HRQoL (Couwenberg et al., 2018). Sexual dysfunction is a frequently encountered long-term treatment-related complication in rectal cancer (Sun et al., 2016), and the overall HRQoL worsens after chemotherapy (van der Valk et al., 2019). Contrastingly, the overall HRQoL remains stable after chemoradiation in the early stage of the disease (Lynn et al., 2017). However, physical and social functioning scores have been significantly lower after chemotherapy (Kinoshita et al., 2017), but the global HRQoL score was high (Qedair et al., 2022). Likewise, colorectal cancer survivors reported satisfactory HRQoL though men experience more anxiety and sexual issues (Al-Shandudi et al., 2022). A study in Jordan also showed a good HRQoL among colorectal cancer patients (Sharour et al., 2020). A Malaysian study also revealed a good HRQoL in functional, global and symptoms domains of HRQoL in colorectal cancer patients. However, most patients had reduced sexual functioning (Magaji et al., 2019). Older age, lower level of education, tumour location in both the colon and the rectum, distant metastasis and a combination of chemotherapy and radiation therapy are statistically significant determinants of poor HRQoL (Ratjen et al., 2018). Advanced-stage and surgical interventions are significant predictors of poor HRQoL among colorectal cancer patients (Tran et al., 2020).

2.10 Summary of the literature review

Most studies reported a high prevalence of DRPs and hospitalization due to DRPs in cancer patients. In addition, most studies indicated that the prevalence of ADRs due to cancer chemotherapy was high in cancer patients, although only a few studies were available in gastrointestinal cancer patients. However, most studies did not examine the outcomes of DRPs, causality, severity and preventability of the identified ADRs (Table 2.1).

Globally, there are conflicting data on the survival rate of patients diagnosed with gastrointestinal cancer. A poor overall survival with the highest mortality rate in African settings was reported in most available studies despite the fact that studies in East African settings are marginal in determining survival outcomes in gastrointestinal malignancies. Nonetheless, most studies did not examine survival outcomes based on different cancer stages and treatment modalities (Table 2.2-Table 2.4).

Several studies have shown that cancer treatment has adverse effects on the HRQoL of patients. However, there is a substantial heterogeneity of outcomes between the studies in various domains of HRQoL. Most studies reported a low overall HRQoL in multiple domains in gastrointestinal cancer patients after therapy. Studies in African settings that examine HRQoL in gastrointestinal cancer patients are very scarce. However, most studies did not examine different domains of HRQoL and HRQoL disparities based on the cancer stage and various treatments (Table 2.5).

Table 2.1: Summary of literature review on drug-related problems and research gaps

Author (s)	Topic	Methods (study setting, population & design)	Main findings	Research Gap (s)
(Livingston et al., 2012)	cost of treatment among chemotherapy-related ADRs	A retrospective audit of cancer patients in Australia	High cost of treatment due to ADRs of chemotherapy	The study did not assess major ADRs of chemotherapy
(Chan et al., 2014)	Unplanned admission due to DRPs	A prospective cohort study in cancer patients in Singapore	12.4% of admissions were due to DRPs, and most were due to ADRs (94.5%).	The study did not examine DRPs and its associated factors in gastrointestinal cancers
(Yeoh et al., 2015)	DRPs in patients with cancer	A retrospective study of cancer patients in Singapore	ADRs, drug-drug interactions & non-adherence were the most common DRPs	The study did not assess DRP prevalence in the young adult population
(Vantard et al., 2015)	DRPs in patients with cancer	A retrospective study of cancer patients in France	ADRs & drug-drug interactions were the most prevalent DRPs	The study did not indicate the type of ADRs identified
(Sisay et al., 2015)	DRPs in patients with cancer	A cross-sectional study of cancer patients in Ethiopia	The prevalence of DRPs was 74.7% in cancer patients	Causality, severity and preventability assessment was not done for the identified ADRs
(Belachew et al., 2016).	The pattern of ADRs in cancer patients	A cross-sectional study of cancer patients in Ethiopia	A high prevalence of ADRs (52.86%)	The study did not address the outcomes of the identified ADRs. Causality, severity and preventability assessment was not done
(Chopra et al., 2016)	The pattern of ADRs in cancer patients	A retrospective cohort study of cancer patients in India	more than half (58.6%) of cancer patients had chemotherapy-induced ADRs	Causality, severity and preventability assessment was not done
(Bell et al., 2017)	Readmission in cancer patients	A systematic review of cancer patients in the United States	3-34% readmission rate in cancer patients	The study did not examine drug-related problems
(Colombo et al., 2017)	The impact of pharmacist interventions on cancer patients	A systematic review of cancer patients in Brazil	Pharmacist interventions improved outcomes in outpatient cancer patients	The study did not examine DRPs
(Degu et al., 2017)	DRPs in cervical cancer patients	A cross-sectional study of colorectal patients in Kenya	93.8% DRPs in patients with cervical cancer	Causality, severity and preventability assessment was not done
(Aguiar et al., 2018)	DRPs in cancer patients	A retrospective study of cancer patients in Brazil	32.1% of DRPs were associated with dosing errors of anti-cancer agents	The study did not clearly indicate the categories DRPs identified
(Maleki et al., 2019)	Impact of Pharmacists on medication outcomes	A systematic review of cancer patients in Australia	a significant improvement in medication-related outcomes	The study did not examine ADRs
(Boşnak et al., 2019)	Role of Pharmacist in Preventing DRPs	A prospective interventional study of cancer patients in Turkey	53.9% of patients had DRPs, 86.4% DRPs resolved with pharmacists intervention	The study did not clearly indicate the proportion of DRPs due to cancer chemotherapy
(Kefale et al., 2022)	DRPs in colorectal cancer patients	A cross-sectional study of colorectal patients in Ethiopia	48.7% DRPs in patients with colorectal cancer	Causality, severity and preventability assessment was not done for the identified ADRs
(Luzze et al., 2022)	drug-drug interaction in cancer patients	A cross-sectional study of cancer patients in Uganda	At least significant drug-drug interaction was found in >50% of patients with cancer	The study did not examine other categories of DRPs

DRPs: Drug-related problems, ADRs: Adverse drug reactions

Table 2.2: Summary of literature review on survival outcomes of patients with esophageal cancer and research gaps

Author (s)	Topic	Methods (study setting, population and design)	Main findings	Research Gap (s)
(Huang & Yu, 2018)	Treatment outcomes in esophageal cancer	A review study in esophageal cancer patients in Taiwan	15-40% 5-year survival rate after surgery	The outcomes of survival based on different stages were not clearly examined in this study
(Asombang et al., 2019)	Mortality in esophageal cancer patients	A systematic review of esophageal cancer treatment outcomes in Africa	The mortality rate was high	The study did not examine mean and median survival time after treatment
(Kamarajah et al., 2021)	Mortality after surgery in esophageal cancer patients	A multicenter prospective cohort studies in developing and developed countries of esophageal cancer patients	Esophagectomy was associated with higher postoperative mortality	The study did not assess the outcome in other treatment modalities
(Hassen et al., 2021)	Survival outcomes in esophageal cancer patients	A retrospective cohort study of esophageal cancer in Ethiopia	Low 1-year (14.4%), 2-year (6.3%) and 3-year (2.4%) survival rate	The study did not assess survival rates in these patients based on stages
(Mantziari et al., 2021)	Treatment outcomes in elderly esophageal cancer patients	A systematic review of elderly esophageal cancer patients	Surgical intervention is associated with a higher morbidity and mortality rate in elderly patients	The overall impact on the survival time of other treatment modalities was addressed in this study
(Jaffe et al., 2022)	Treatment outcomes in Advanced esophageal cancer	A retrospective cohort study in esophageal cancer patients in Asian and Western Countries	31.1% of patients had a complete or partial response, 32.0% disease progression, 15.6% death and 20.9% stable disease	Overall five-year survival was not assessed in the study
(van Holstein et al., 2022)	Treatment outcomes in elderly curable esophageal cancer patients	A cohort study in curable esophageal cancer patients in Dutch	36.0% one-year all-cause mortality rate	Esophageal cancer-specific mortality and long-term survival were not examined in this study
(Yang et al., 2022)	Treatment outcomes in elderly curable esophageal cancer patients	A retrospective cohort study in elderly curable esophageal cancer patients in China	Trimodality treatment was associated with the longest survival time	The study did not examine the impact of triple therapy on the incurable patients
(Bardol et al., 2022)	Survival of metastatic esophageal cancer patients	A systematic review of survival in metastatic esophageal cancer patients after multiple therapies	Overall three-year survival rate was 23%	The study did not assess the five-year survival rates in these patients
(De Virgilio et al., 2023)	Treatment outcomes in esophageal cancer patients after surgery	A systematic review and meta-analysis of esophageal cancer patients after surgery	The pooled five-year survival rate was 26.6%	The study did not assess the outcome in other treatment modalities

Table 2.3: Summary of literature review on survival outcomes of patients with gastric cancer and research gaps

Author (s)	Topic	Methods (study setting, population and design)	Main findings	Research Gap (s)
(Asombang et al., 2014)	Survival outcomes in gastric cancer patients	A retrospective audit in gastric cancer patients in Zambia	The median survival time was 142 days	The study did not assess five year survival rate and mortality rate
(Hong et al., 2017)	Survival outcomes in gastric cancer patients after surgery	A retrospective cohort study in gastric cancer patients in Korea	Mortality was 15.5%	The study did not assess the outcome in other treatment modalities
(Bausys et al., 2018).	Treatment outcomes after surgery	A retrospective cohort study in gastric cancer patients in the United States	a higher prevalence of postoperative mortality after surgical resection	The study did not assess the outcome in other treatment modalities
(Gwak & Park, 2018)	Survival outcomes in gastric cancer patients after surgery	A retrospective cohort study in gastric cancer patients in Korea	2-year and 5-year disease-free survival was 77.5% and 74.2%, respectively.	The study did not assess the outcome in other treatment modalities
(Vieira et al., 2019)	Survival outcomes in metastatic gastric cancer patients after chemotherapy	A retrospective cohort multicenter study in metastatic gastric cancer patients in Brazil	Poor survival after first-line chemotherapy	The study did not assess the impacts of second-line chemotherapy on the survival outcomes of these patients
(van der Werf et al., 2019)	Survival outcomes in gastric cancer patients after surgery	A retrospective cohort study in gastric cancer patients in the Netherlands	The overall one, two, and three (71%, 56% and 49%) year survival rates significantly reduced after surgery	The study did not assess the outcome in other treatment modalities
(Kato et al., 2019)	Survival outcomes in gastric cancer patients after surgery	A retrospective cohort study in gastric cancer patients in Japan	The overall 1, 2, and 3-year survival rates (91.7%, 79.4% and 63.2%) gradually declined after gastrectomy	The study did not assess the outcome in other treatment modalities
(Bang et al., 2020)	Survival outcomes in gastric cancer patients	A retrospective cohort multicenter study in gastric cancer patients in Cameroon	lower three-year (10.1%) and five-year (4.6%) survival rates	The study did not assess survival differences among different stages of gastric cancer
(Yang et al., 2021)	Survival outcomes in early-stage gastric cancer patients after surgery	A retrospective cohort multicenter study in gastric cancer patients in Korea	The overall five and eight-year survival rate was 100 % and 95.2%, respectively	The median or mean survival time was not assessed in this study

Table 2.4: Summary of literature review on survival outcomes of patients with colorectal cancer and research gaps

Author (s)	Topic	Methods (study setting, population and design)	Main findings	Research Gap (s)
(Agyemang-Yeboah et al., 2018)	Survival of colorectal cancer patients	A retrospective study in colorectal cancer patients in Ghana	Low (16.0%) overall survival rates	The study did not quantitatively estimate the survival rates based on different cancer stages
(Maajani et al., 2019)	Survival of colorectal cancer patients	A systematic review and meta-analysis of colorectal cancer patients in Iran	54.0% 5-year survival rate	The study missed assessing the outcomes based on different cancer stages
(Nikbakht et al., 2020)	Survival of colorectal cancer patients	A systematic review of colorectal cancer patients in Eastern Mediterranean regions	1-year, 3-year, and 5-year survival rate of 88.1%, 70.7%, and 57.3%, respectively	The study missed assessing the outcomes based on different cancer stages
(Jiang et al., 2021)	The global trend of survival in colorectal cancer patients	A systematic review of colorectal cancer patients across the globe	Five-year survival rates in Korea at 76.2%, the United States at 66.1%, Canada at 60.9%, and Europe at 53.9%	The study missed assessing the outcomes based on different cancer stages
(Gullickson et al., 2021)	Survival of colorectal cancer patients	A retrospective cohort study in colorectal cancer patients in 11 sub-Sharan African countries	Low five-year survival rate (43.5%)	The study did not address the survival rates in all sub-Sharan African countries
(Atinafu et al., 2022)	Mortality in colorectal cancer patients	A retrospective cohort study in colorectal cancer patients in Ethiopia	80.1% mortality rate at six-year follow-up	The study missed assessing the mortality rate based on different cancer stages
(Tiruneh et al., 2022)	Mortality in colorectal cancer patients	A retrospective cohort study in colorectal cancer patients in Ethiopia	27.2% mortality rate during the follow-up	The study missed assessing the mortality rate based on different cancer stages
(Wismayer et al., 2022)	Survival of colorectal cancer patients	A retrospective cohort study in colorectal cancer patients in Uganda	low (33.3%) three years survival	The study did not examine five-year survival rates

Table 2.5: Summary of literature review on health-related quality of life of patients with gastrointestinal cancer and research gaps

Author (s)	Topic	Methods (study setting, population and design)	Main findings	Research Gap (s)
(Akhondi-Meybodi et al., 2016)	HRQoL in colorectal cancer	Prospective study among colorectal cancer patients in Iran	Low physical, social and financial domains of HRQoL	The study did not assess HRQoL based on different stages of cancer
(Liu et al., 2018)	HRQoL in esophageal cancer	A multi-setting cross-sectional study in esophageal cancer patients in China	Significant impairment of HRQoL following treatment	The study did not examine different domains of HRQoL
(van Deudekom et al., 2018)	HRQoL in esophageal cancer	A systematic review of HRQoL of esophageal cancer patients	Significant impairment in the physical and cognitive domains of HRQoL	The study did not assess all domains of HRQoL
(Ter Veer et al., 2018)	HRQoL in esophageal cancer	A systematic review of HRQoL of in advanced esophageal cancer patients	No significant change in HRQoL after palliative therapy	The study did not assess HRQoL in all stages of cancer
(Huang et al., 2018)	HRQoL in colorectal cancer	A cross-sectional study among colorectal cancer patients in China	Low HRQoL in symptom domains	The study did not assess HRQoL based on the standard tools
(Chau et al., 2019)	HRQoL in advanced gastric cancer	Randomized control trial among advanced gastric cancer patients in the United States	Worse HRQoL in all functional, global and symptom scales of HRQoL	The study did not assess HRQoL based on different stages of cancer and treatment modalities
(Magaji et al., 2019)	HRQoL in colorectal cancer	A cross-sectional study among colorectal cancer patients in Malaysia	Good HRQoL in physical, global and symptoms domains of HRQoL	The study did not assess the HRQoL across different treatments
(Eom et al., 2019)	HRQoL in early-stage gastric cancer after surgery	Retrospective study among gastric cancer patients in Korea	Better HRQoL in physical and symptom domains	The study did not examine the HRQoL of other treatments
(van den Boorn et al., 2020).	HRQoL in esophageal cancer	A systematic review of HRQoL of esophageal cancer patients	No change in HRQoL after curative treatment	The study did not assess HRQoL based on different stages of cancer
(Xia et al., 2020)	HRQoL in gastric cancer	A cross-sectional study among gastric cancer patients in China	Impaired overall HRQoL	The study did not assess HRQoL based on the standard tools
(Kwon et al., 2020)	HRQoL in gastric cancer after surgery	Prospective cohort study among gastric cancer patients in Korea	Reduced HRQoL with major concern in symptom scales	The study did not examine the HRQoL of other treatments
(Kauppila et al., 2020a)	HRQoL in esophageal cancer after surgery	A prospective cohort study in esophageal cancer patients in Sweden	a substantial problem in the symptom and physical domains HRQoL	The study did not assess HRQoL based on different stages of cancer
(Rutherford et al., 2020)	HRQoL in colorectal cancer	A meta-analysis of colorectal cancer patients	Persistent symptoms and functional impairments after treatment	The study did not assess all domains of HRQoL
(Flyum et al., 2021)	HRQoL in colorectal cancer	A systemic review and meta-analysis of colorectal cancer patients in palliative care	Low overall HRQoL after palliative treatment	The study did not assess all domains of HRQoL
(Huang et al., 2021)	HRQoL in colorectal cancer	A cross-sectional study among colorectal cancer patients in China	Low overall HRQoL	The study did not assess HRQoL based on the standard tools
(Markar et al., 2022).	HRQoL in esophageal cancer	A cross-sectional study in a multicenter setting in esophageal cancer patients in European countries	Substantially reduced HRQoL in patients with esophageal following surgery	The study did not examine different domains of HRQoL
(Wang et al., 2022)	HRQoL in gastric cancer	Prospective cohort study among gastric cancer patients in Korea	A worse HRQoL in most functional and symptom domains after chemotherapy and surgery	The study did not assess HRQoL based on different stages of cancer
(Boshier et al., 2022)	HRQoL in esophageal cancer after surgery	A prospective cohort study in esophageal cancer patients	a substantial problem in the symptom and various domains of HRQoL	The study did not assess HRQoL based on different stages of cancer and treatment

HRQoL: Health-related quality of life

2.11 Conceptual/ theoretical framework

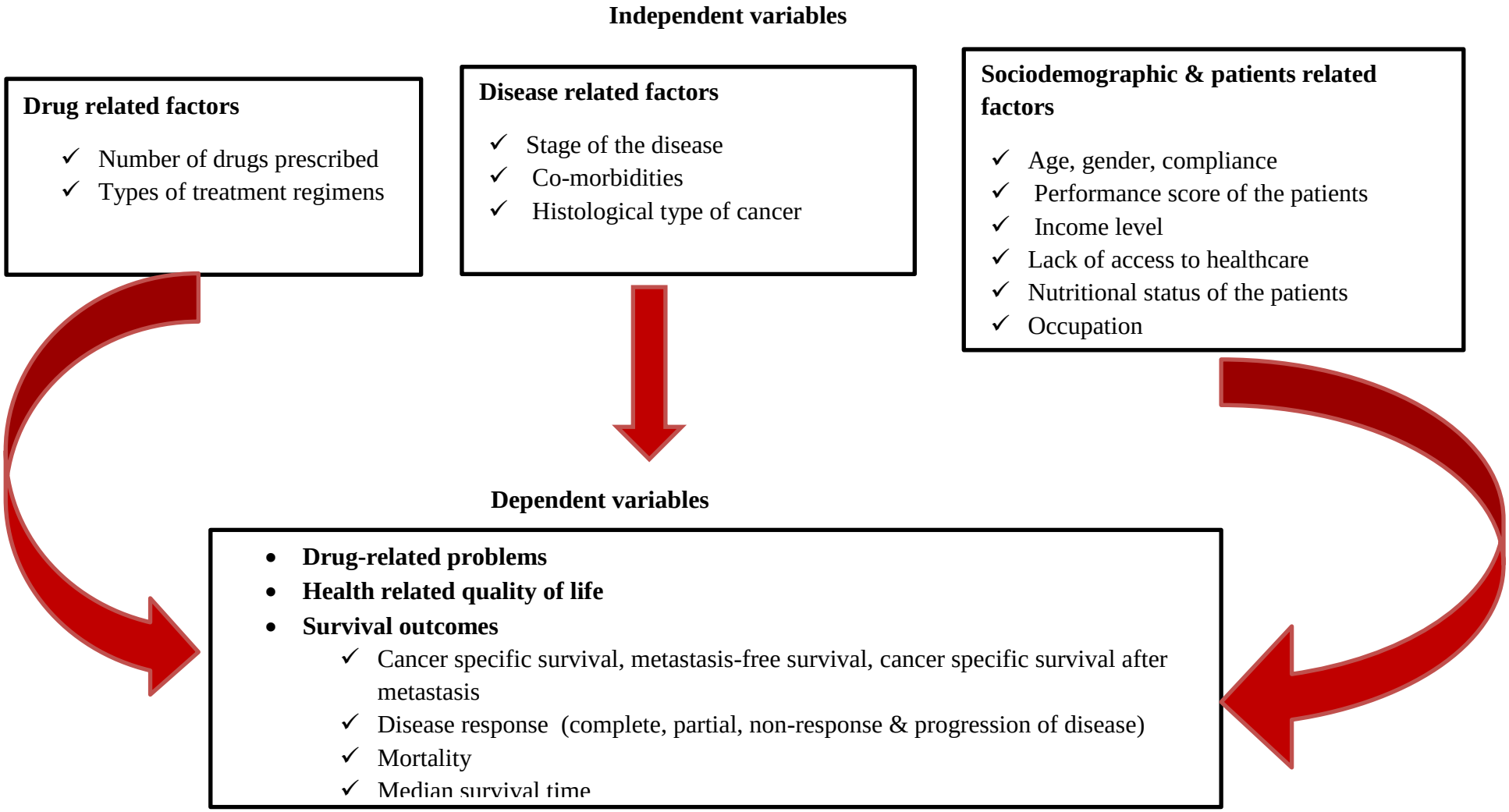


Figure 2.1: Conceptual framework of the study

The overall goals of treating patients with gastrointestinal cancers are to improve survival and HRQoL and minimize drug-related problems. These outcomes are dependent on the patient sociodemographic characteristics, types of drugs used as well as disease-related factors, as shown in Figure 2.1.

The number of drugs prescribed, and types of treatment regimens, influence the above-indicated outcomes. Drugs used to treat cancer have many adverse effects. This is because both the cancerous and normal cells are destroyed by these drugs, although to different extents. The consequences are both physiological and pathological. These effects are dependent on the number and types of drugs used. Their influence affects the survival and HRQoL of patients.

The presence of comorbidities, stage of the disease, and histological type of cancer are independent variables that can influence DRPs, HRQoL and survival outcomes in patients with gastrointestinal cancer. Comorbidities weaken the body, and therefore the patients are not able to withstand the chemotherapy appropriately. On their own, they weaken the body and reduce the HRQoL. Patients with advanced diseases are usually weak and their systems deranged, predisposing them to more adverse drug effects compared to those with less advanced diseases. Generally, patients with advanced cancer and comorbidities have poor HRQoL.

Owing to the cytotoxic nature of anticancer medications, they have a great potential to increase the risk of developing DRPs. This will prolong the duration of hospitalization and increase economic costs and expenditure on drug-related complications. They can also affect HRQoL and survival time in patients with gastrointestinal cancer.

Sociodemographic characteristics such as age, gender, performance status, education level, occupation, income level and lack of access to healthcare are additional variables that influence DRPs, HRQoL and survival outcomes. Aging can cause pharmacodynamic and pharmacokinetic changes, such as reduced hepatic and renal functions and prolonged elimination time of cytotoxic drugs in older patients. Therefore, older patients are more likely to develop drug-related problems. As a result of the high burden of DRPs due to aging, the patients can have deranged HRQoL and low survival outcomes. Gender is also another factor that can affect survival and drug-related problems. Generally, females have reduced hepatic clearance compared to males, which can increase the risk of ADRs due to anticancer medications. In addition, female cancer

patients have a better prognosis than male cancer patients suggesting gender disparities in the survival outcomes of cancer patients. ECOG Performance score is another factor influencing DRPs, HRQoL and survival outcomes. The ECOG score measures the patients' physical functioning level to care for them and do daily activities. Hence, a low ECOG score can suggest poor physical functioning. This low score can adversely affect survival outcomes and HRQoL. In addition, the risk of having DRPs will be higher in patients with low ECOG scores. Income level and lack of healthcare access will affect the patient's capability to get optimal cancer care. These two parameters can influence the HRQoL and survival of gastrointestinal cancer patients.

CHAPTER THREE: METHODOLOGY

3.1 Introduction

This chapter entails a thorough overview of the methods employed in this study. Two types of study design (cross-sectional and retrospective cohort) were used to achieve the study objectives. Each study design had a specific target population, sample size, eligibility criteria, and sampling techniques. This chapter also outlines the study setting, study period, target population of the study, eligibility criteria, sampling, research instrument, data collection techniques, study variables, data quality control procedure, reliability, validity, ethical consideration, and statistical analysis.

3.2 Study design

A multimodal quantitative study design was employed due to the nature of the outcomes in this study. A cross-sectional study was used to evaluate DRPs and HRQoL and their determinants in adult patients with esophageal, gastric and colorectal cancer. This study design was chosen since the strength of the association of the determinants of HRQoL and DRPs was quantitatively estimated in terms of odds ratio using binary logistic regression analysis. A one-arm retrospective cohort study was carried out to evaluate the survival outcomes among adult patients with esophageal, gastric and colorectal cancers. In this study design, the exposure was the various cancer treatment modalities for the selected gastrointestinal cancers. Survival outcomes for the respective cancer types were measured at the completion of the follow-up period. The non-exposed comparative group was not considered since this study focuses on assessing the outcome of the various treatment regimens for exposed cancer patients. This study design was chosen since the outcomes of interest (survival outcome) take a long time to occur after introducing various treatment modalities of cancer and require intensive follow-up. Accordingly, reliable determination of the outcomes of interest can be achieved after several years of following retrospectively, starting from treatment commencement.

3.3 Study setting and period

The study was carried out at the Department of Oncology of KNH. The hospital is the biggest referral facility in East and Central Africa, with 1800 bed capacity. Of the total bed size of 1800, the private wings have 209 beds. The hospital was designed to serve as a national referral, teaching, and research centre. The hospital is the leading referral system for the health sector and

occupies 45.7 hectares. Within the hospital premises, it encompasses the National Laboratory Service, Kenya Medical Training College, and the Faculty of Health Sciences of the University of Nairobi. It has 22 outpatient clinics, 24 theatres, 50 wards and the Accident and Emergency Department. As the largest tertiary public facility, the institution has a diverse patient population across the nation (Kenyatta National Hospital, 2017). The data collection was conducted for one year and six months (1st October 2021-30th March 2023).

3.4 Study population

3.4.1 Study population for the cross-sectional study

The study comprised all adult (18 years and above) patients with esophageal, gastric and colorectal who were hospitalised and receiving outpatient treatment in the study setting.

3.4.2 Study population for the retrospective cohort study

The study population consisted of medical records pertaining to adult patients aged 18 years and older who received treatment for esophageal, gastric, and colorectal cancers at the Department of Oncology of KNH from 1st January 2016 and 31st December 2020. This period was selected since five years follow-up period is required to determine the five-year survival rates of each of the selected gastrointestinal cancers. These cancers were selected for investigation because of their emerging prevalence and the availability of survival outcome-measuring parameters in the context of the study setting.

3.5 Eligibility criteria

3.5.1 Inclusion criteria for the cross-sectional study

- ✓ Adult patients (≥18 years) with gastric cancer, esophageal cancer and colorectal cancer who received treatment at KNH during the study period.
- ✓ Gastrointestinal cancer patients (gastric cancer, esophageal cancer and colorectal cancer) who had been treated with at least one course of chemotherapy with complete documentation of diagnosis, stage of disease and treatment regimen.
- ✓ Patients who signed the informed written consent.

3.5.2 Exclusion criteria for the cross-sectional study

- ✓ Patients with incomplete documentation of diagnosis, stage of disease and treatment.
- ✓ Patients who refused to take part in the study.

- ✓ Patients who were comatose and unable to provide information at the time of data collection.

3.5.3 Inclusion criteria for the retrospective cohort study

- ✓ All medical records of adult patients (18 years and older) with gastric cancer, esophageal cancer, and colorectal cancer who underwent treatment from 1st January 2016 to 31st December 2020.
- ✓ All medical records of adult patients 18 years and older with complete documentation of diagnosis, treatment and stage of disease.
- ✓ Gastric, esophageal, and colorectal cancer patients who had received at least one treatment modality from 1st January 2016 to 31st December 2020.

3.5.4 Exclusion criteria for the retrospective cohort study

- ✓ All adult patients (18 years and older) with incomplete documentation of diagnosis, treatment regimens and cancer stage from 1st January 2016 to 31st December 2020.

3.6 Sample

3.6.1 Sample size for the cross-sectional study

The sample size for all three gastrointestinal malignancies was estimated using a single population proportion formula (Hajian-Tilaki, 2011).

Equation 3.1: Sample size estimation for the cross-sectional study

$$\mathbf{n= \frac{Z^2_{\alpha/2} \quad x\, P(1-P)}{d^2}}$$

Where: n is the smallest required sample size for a large population (≥10,000)

- $Z_{\alpha/2}$ is the critical value at a 95% confidence interval (= 1.96)
- P is the proportion of DRPs and HRQoL in the selected gastrointestinal cancer patients. Since no prior studies have been performed in Kenya, P was considered 50% (0.5).
- d is the margin of error (5%).

Therefore, the required sample size for all three gastrointestinal cancers (n) = $\frac{(1.96)^2 \times 0.5(1-0.5)}{(0.05)^2} = 384$ for each of the cancers to be studied.

However, for all three cancers, the population was less than 10,000. Hence, the final sample size was determined using the reduction formula.

Corrected sample size $= \frac{\mathbf{n \times N}}{\mathbf{n+N}}$ Where N= source population and n= the estimated sample size for a larger population (N≥10,000). As per the data provided by the Health Information Department of KNH, the average number of patients undergoing active treatment was 234 esophageal, 125 gastric, and 113 colorectal cancer patients. After computing the sample size using this reduction formula and a 10% adjustment for the incomplete documentation, the final adjusted sample size was 160 esophageal, 103 gastric and 96 colorectal cancer patients (Table 3.1).

Table 3.1: Sample size estimation for the cross-sectional study design

Cancer types	Source population	Corrected sample size with the reduction formula	Adjusted final sample size with 10% contingency
Esophageal cancer	234	145	160
Gastric cancer	125	94	103
Colorectal cancer	113	87	96

3.6.2 Sample size for the retrospective single-arm cohort study

For the retrospective cohort study design, Yamane's formula was used to determine the sample size (Yamane, 1967).

Equation 3.2: Sample size estimation for the retrospective cohort study

$$n = \frac{N}{1 + N * (e^2)}$$

Where N= Population, n= the estimated sample size and e= the significance level at a 95% confidence level (0.05).

The Department of Health Information of KNH data showed that around 849 (esophageal cancer), 508 (gastric cancer), and 445 (colorectal cancer) patients were treated from 1st January 2016 to 31st December 2020. Therefore, the sample size was determined as follows for this study design.

The estimated sample size for esophageal cancer $(n) = \frac{849}{1+849\,(0.05^2)} = \frac{849}{3.1225}$ = 272. Thus, 299 esophageal cancer patients comprised the final sample size with a 10% contingency to account for patients with missing records.

The estimated sample size for gastric cancer $(n) = \frac{508}{1+508\,(0.05^2)} = \frac{508}{2.27}$ = 224. So, the final sample consisted of 247 gastric cancer patients with a 10% contingency for missing records.

The estimated sample size for colorectal cancer $(n) = \frac{445}{1+445\,(0.05^2)} = \frac{445}{2.1125} = 211.$

Therefore, the final sample comprised 232 colorectal cancer patients after adding a 10% adjustment for incomplete documentation.

3.6.3 Sampling techniques

3.6.3.1 Sampling techniques for the cross-sectional study

The study participants were selected using a simple random sampling technique. This sampling technique was selected since it gave an equal probability of being chosen in the study. Hence, it can enhance the statistical power and generalizability of the findings of the study.

In this study design, the list of hospitalized and ambulatory esophageal, gastric, and colorectal cancer patients was sourced from the records using their unique hospital identification numbers. The research assistants examined the records of the patients to determine their suitability for inclusion using the study's specified eligibility criteria. Then, a list of their unique identification numbers was written individually on pieces of paper identical in size, shape, and appearance. The papers that contained the unique identification numbers were placed in a basket and thoroughly mixed to ensure they were well-shuffled and randomly distributed within the container. After that individual papers that contained the hospital identifying numbers were randomly selected using a lottery method by picking one paper at a time until the desired sample size was obtained. As each piece of paper was drawn from the container, the unique identification numbers on the paper were recorded to keep track of which members of the population had been selected for the sample.

3.6.3.2 Sampling techniques for the retrospective single-arm cohort study

In this study design, simple random sampling with a lottery method was employed to select the study participants to ensure every individual in the population has an equal chance of being selected for the study. The list of all patient records with esophageal, gastric and colorectal cancer patients who received treatment within the study setting from 1st January 2016 to 31st December 2020 was also obtained from the Department of Health Information. The patient identification numbers were inscribed on paper, subsequently creased and deposited in a basket. The papers with the unique patient identification numbers were mixed thoroughly to ensure randomness. Then, the research assistants used a lottery method to select patient identification numbers from the pool. The procedure was repeated until the desired sample size was attained. Patients with the chosen identification numbers were enrolled in the retrospective cohort study. Throughout the data collection period, the research assistants conducted a daily examination of the patient records to assess their suitability using the retrospective cohort study design criteria.

3.7 Research instruments

3.7.1 Informed consent information and consent form

The informed consent information and consent form (Appendix I) contained the study's title, the purpose of the study, benefits, risks, participant selection, voluntary participation/ withdrawal from the study, confidentiality, and contact information. The last section contained a statement of consent for the participants and a statement by the researcher/person taking consent to ensure that the study participants voluntarily consent to be involved in the study. This form was used for the cross-sectional study design to get written consent for the study.

3.7.2 Questionnaire for the cross-sectional study

Data were collected from patients and medical records using a structured interviewer-guided questionnaire and data abstraction form (Appendix II). The tools comprised socio-demographics, clinical characteristics and Cipolle *et al* DRPs identification instruments (Cipolle et al., 2012). The drug-related problem tools were also composed of Naranjo's Causality Assessment Scale (Naranjo et al., 1981), the modified Hartwig and Siegel's ADR severity assessment scale (Hartwig et al., 1992), and the modified Schumock and Thornton scale (Schumock & Thornton, 1992).

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-30 (EORTC QLQ-30) (Appendix III), EORTC QLQ–CR29 (colorectal module) (Appendix IV), EORTC QLQ–OES18 (esophageal cancer module) (Appendix V), EORTC QLQ–STO22 (gastric cancer module) (Appendix VI) were employed to assess the HRQoL of patients (Cocks et al., 2008). The QLQ-C30 consists of 30 questions, both single and multi-item scales. Each raw score was standardized (0 to 100) by undergoing a linear transformation of the individual score as per the Scoring Manual of EORTC QLQ-C30 (Fayers et al., 2001). The scoring of EORTC QLQ–CR29, EORTC QLQ–OES18 and EORTC QLQ–STO22 was computed as per the EORTC QLQ-CR29 (Whistance et al., 2009), EORTC QLQ-OES18 (Blazeby et al., 2003) and EORTC QLQ–STO22 scoring manual, respectively (Blazeby et al., 2004). The scoring methods for the QLQ-CR29 were identical to the function and symptom scales of the EORTC QLQ-30. The scoring principles of EORTC QLQ–OES18 and EORTC QLQ–STO22 were similar to the symptom scales of the QLQ-C30. If items I_1, I_2, ... I_n were included in a scale, and the raw scores were calculated for each scale.

Equation 3.3: Raw score calculation of health-related quality of life

Raw Score = $(I_1+I_2 \ldots +I_n)/n$, where n is the number of items on each scale. Then linear transformation was applied to obtain the score (S) in the range of 0 to 100.

Equation 3.4: Functional scales calculation of health-related quality of life

Functional scales: Raw Score= $\left\{\mathbf{1}-\frac{\boldsymbol{Row\ score-1}}{\boldsymbol{Range}}\right\}*\mathbf{100}$

Equation 3.5: Symptom scales/items calculation of health-related quality of life

Symptom scales/items: Raw Score = $\left\{\frac{(\boldsymbol{Raw\ score-1})}{\boldsymbol{Range}}\right\}*\mathbf{100}$

Equation 3.6: Global health status calculation of health-related quality of life

Global health status/quality of life: Raw Score =$\left\{\frac{(\boldsymbol{Raw\ score-1})}{\boldsymbol{Range}}\right\}*\mathbf{100}$

The range was the difference between the maximum possible raw score value and the minimum possible value. The QLQ-C30 had been developed such that all items have the same set of ranges on any scale. Hence, the raw score range is identical to the item values range. Most items were ranked from 1 to 4, with a range of 3. The exceptions were the items that relate to the global

health/quality of life status, which were 7-point questions with a range of 6. After standardization, all scales and single-item measures varied from 0 to 100. A high score in the functional domain and global health status (score ≥ 60) and a low score in symptom scales (score <60) were considered healthy functioning and high HRQoL. A high rating for a symptom scale/item (score ≥ 60) and low values in global health scales and functional domains (score <60) indicated a low HRQoL.

3.7.3 Data abstraction form for a retrospective cohort study

For this study design, the data abstraction format consisted of socio-demographics, clinical characteristics of patients, and survival outcome measuring parameters. The data collection tools were developed based on previous studies (Basaran et al., 2015; Bausys et al., 2018; Gullickson et al., 2021; Hassen et al., 2021; Kim et al., 2011) and the revised Response Evaluation Criteria in Solid Tumors (RECIST) guideline with slight modification (Eisenhauer et al., 2009). A pretest was conducted in the data collection tools, and all the changes required were adopted before the data collection.

3.8 Data collection techniques

3.8.1 Data collection techniques for the cross-sectional study

The principal investigator, along with two pharmacists and two oncology nurses, conducted the data collection. Those stakeholders were selected based on their previous experience with cancer patients. The research assistants underwent pertinent training on the proper use of the data collection instruments. Following a random selection based on patient identification numbers, the research assistants described the study objective and clarified any ambiguity to the enrolled study participants. Then, the research assistants obtained written informed consent before collecting the data. After that, an interview was conducted with each participant in the facility's private doctor’s office. In the interview, socio-demographics, HRQoL and DRPs were examined. Nevertheless, the medical records were reviewed to record comorbidities, histological types, stage of disease, tumour size and treatment regimens.

Drug-related problems were assessed by comparing the Kenya cancer treatment guideline (Ministry of Health, 2013), the European Society for Medical Oncology practice guidelines, and the National Compressive Cancer Network (Ajani et al., 2016, 2019; Benson et al., 2017, 2018). Medscape, Lexicomp, and Stockley's drug Interactions were used to identify potential

drug interactions. The categories of DRPs were organised using the Cipolle DRPs classification system, which includes the need for additional drug therapy, drug-drug interaction, ADRs, unnecessary drug therapy, ineffective drug therapy and dosing problems (Cipolle et al., 2012). The Naranjo causality assessment scale (Naranjo et al., 1981), the modified Hartwig and Siegel ADR Severity Assessment Scale (Hartwig et al., 1992) and Schumock and Thornton Criteria (Schumock & Thornton, 1992) were used to assess the causality, severity and preventability of the identified ADRs, respectively.

3.8.2 Data collection techniques for the retrospective cohort study

The list of patient identification numbers of esophageal, gastric and colorectal cancer patients treated from 1st January 2016 to 31st December 2020 was acquired from the Department of Health Information. Using their unique hospital identification numbers, the medical records were evaluated based on the eligibility criteria of the study. The research assistants reshuffled the eligible medical records list in a basket to select the study participants. The research assistants randomly chose the medical records using the lottery method for each type of gastrointestinal cancer. Then, each data collector assessed the survival outcomes of the selected cancer types using the structured data abstraction format. During the process of data abstraction, pertinent clinical characteristics, sociodemographic variables, histological classifications, and time to either mortality or last follow-up were recorded. The time between the initial cancer diagnosis and the appearance of the first metastasis and the time between the appearance of the first metastasis and the occurrence of cancer related-mortality or last follow-up was also documented. The calculation of the survival year involved determining the ratio of patients who survived in a given period to the number of patients who were at risk during that same period. Treatment response was evaluated based on the RECIST guideline with slight modifications (Eisenhauer et al., 2009). Results from interval computed tomography (CT) scans were used to categorise treatment response as complete response (eradication of all lesions), partial response (≥30% shrinkage in the tumour size from the baseline), stable disease (no significant increase or decrease in tumour size) and progression of the disease (≥20% increase in tumour size or growth of new lesions). A comparison of the tumour size was made from the baseline CT scan findings of the tumour size.

3.9 Pretest study

Before beginning the study, a pre-test was administered to 5% of the samples for each type of cancer to ascertain the reliability of the data collection tools. For the retrospective cohort study, 15 esophageal, 13 gastric and 12 colorectal cancer patients were enrolled in the pretest study. Eight esophageal, six gastric, and five colorectal cancer patients were pretested in the cross-sectional study. The pretesting of the tools was conducted for one month before starting the data collection. After pre-testing, appropriate adjustments were made to the data collection instruments prior to their utilisation in the main investigation.

3.10 Study variables

3.10.1 Dependent variables

For the cross-sectional study design, HRQoL and DRPs were the dependent variables, while survival outcomes (Cancer-specific survival, metastasis-free survival, cancer-specific survival after metastasis, tumour response and mortality) were the dependent variables for the retrospective cohort study.

3.10.2 Independent variables

Disease-related factors (disease progression or recurrence, advanced stage of the disease at the time of diagnosis, co-morbidities and histological type of cancer), patient-related factors (age, gender, compliance), and drug-related factors (number of drugs prescribed, types of treatment regimens and treatment duration) significantly affected the dependent variables in both study designs.

3.11 Data quality control procedure

The data collection instruments were assessed by two oncology pharmacists and one oncology physician about the contents' adequacy. A pretest was also conducted for each type of cancer to assess the feasibility of the data collection instruments. The final data collection instrument was designed after incorporating all the required modifications. The principal investigator continuously checked the data collection instrument's completeness throughout the one-year and six months data collection period. Data quality was also ensured at the data entry and analysis level by rigorous examination for errors.

3.12 Reliability of the instruments

The study employed various established tools, including RECIST criteria, Naranjo's causality assessment scale, Schumock and Thornton ADRs Preventability Assessment Scale, Modified Hartwig and Siegel ADRs Severity Assessment Scale and EORTC Quality of Life Questionnaire, to ensure the reproducibility of the instruments. Additionally, the reliability of the data collection instrument was evaluated through the administration of the Cronbach alpha test ($\alpha > 0.7$) (Davda et al., 2021; Salas et al., 2020).

3.13 Validity of the instruments

To ensure the validity of the data collection instruments, the study employed several measures, including pre-testing the data collection tools, recruiting representative samples of the target population, and seeking expert opinions. For each study design, a representative sample size was computed based on the standard sample size calculation formula in proportion to the total target population for each type of gastrointestinal cancer. The Delphi method was employed to collect the expert opinion of the data collection tools (Nasa et al., 2021). The predesigned data collection tools were sent to one medical oncologist, two oncology pharmacists and one epidemiologist to collect their expert opinions on the data collection instruments. Two rounds of feedback were obtained from the experts about the data collection instruments. After analysing the expert opinion and pretest study, all necessary adjustments were implemented to the final data collection instruments.

3.14 Data management

3.14.1 Data management for the cross-sectional study

Data were collected anonymously by allocating a unique identification number for each study participant. The accuracy of the data was checked regularly during the day of the data collection. The raw data (filled questionnaires) were stored under lock and key in a cabinet, accessible only to the investigators, research assistants, and data analysts. The electronic data were also stored under password protection of a personal computer. A backup copy was also preserved in a flash disk and external hard disk with secure access only to the principal investigator. The data will be archived for a minimum of 5 years after the final publication of the study (The University of North Carolina, 2012). Then five years later, all the raw data will be destroyed according to the principles of good clinical practice (Switula, 2000).

3.14.2 Data management for the retrospective cohort study

For this study design, data were collected anonymously by allocating unique research identification numbers for each medical record of the selected patients. During the data collection, the research assistants reviewed the patients' medical records in a private room of the study setting to maintain confidentiality. The accuracy of the filled questionnaires was checked daily during data collection. The hard copies of the data were kept in a secure cabinet with a lock and key. It was accessed only by investigators, research assistants, and data analysts. The electronic copy of the data was stored in a password-encrypted personal computer. To avoid the loss of data, a backup copy was also archived in a flash disk and external hard disk under a lock and key cabinet. As per the research law, the data will be stored for a minimum of five years after publication. Five years later, the raw data will be discarded as per the regulation of good clinical practice.

3.15 Data analysis

Data entry, clean up and analysis were carried out with Statistical Package for the Social Sciences (SPSS) version 26.0 statistical software. Descriptive, bivariable and multivariable statistical analyses were conducted in the study.

3.15.1 Descriptive statistics

Descriptive statistics such as mean, range, median and standard deviations were used to present the values of continuous variables like age and median survival time. Frequencies and percentages were used to present categorical variables such as sociodemographic and clinical characteristics of the study participants. The normality of the distribution for continuous variables was evaluated through the use of the Shapiro-Wilk test (Mishra et al., 2019). A p-value of >0.05 in this test was considered a normal distribution. The mean values were reported for normally distributed continuous variables. A p-value of ≤0.05 in the Shapiro-Wilk test was considered a skewed distribution. The median values were reported for skewed continuous variables.

3.15.2 Bivariable analyses

This analysis was conducted to assess the association between the independent variables (sociodemographics, clinical characteristics and treatment regimens) with the outcome variables, such as DRPs, HRQoL and survival. A bivariable binary logistic regression analysis was used

to assess the determinants of DRPs and HRQoL. A crude odds ratio (COR) was used to determine the strength of association in the bivariable binary logistic regression analysis. A bivariable Cox regression analysis was conducted to identify the determinants of survival among gastrointestinal cancers. A crude hazard ratio (CHR) was used to report the strength of association in the bivariable Cox regression analysis. Statistical significance was assumed when the p-value was ≤0.05.

In the retrospective cohort study, the median and mean survival time was estimated using the Kaplan-Meier analysis. The statistical difference in median and mean survival time across different clinical parameters and treatment regimens was assessed using the log-rank test. A p-value of ≤0.05 in the log-rank test was considered a statistically significant difference in the survival time across different parameters.

3.15.3 Multivariable analyses

These analyses were conducted to assess the potential determinants of the outcome variables after adjusting the confounding factors affecting the outcome variables. In the cross-sectional study, multivariable binary logistic regression analysis was employed to identify the determinants of DRPs and HRQoL. An adjusted odds ratio (AOR) was used to report the strength of the association. Potential determinants of survival were examined with multivariable Cox regression analysis. An adjusted hazard ratio (AHR) was used to report the strength of association in these analyses and statistical significance was assumed when the p-value was ≤0.05.

3.16 Ethical considerations

3.16.1 Study approvals

Approval for the study was granted by the Ethics and Research Committee of the Kenyatta National Hospital/University of Nairobi (Approval No: KNH-ERC/A/337) (Appendix VII). A research permit was obtained from the National Commission for Science, Technology and Innovation (NACOSTI) (License No: NACOSTI/P/22/18113) to legally conduct this study in Kenya (Appendix IX). After approval, the application letter was submitted to the Medical Research Department of KNH to seek permission and register the study. After registering (study Number: 123/2021) the study (Appendix VIII), an application letter was presented to the Cancer Treatment Centre of Kenyatta National Hospital to get authorization to collect data from the

patients and their medical records for the cross-sectional study. Official permission was also obtained from the European Organization for Research and Treatment of Cancer to use the validated HRQoL questionnaire for the respective cancer types.

3.16.2 Informed consent

For the cross-sectional study, written consent was obtained from the patients to interview and assess their medical records. The research assistants performed the consent process by offering a comprehensive explanation of the study. The participants were given the opportunity to ask questions for any clarification and those who agreed were requested to sign the form. The research assistants proceeded to collect the data soon after consenting. To ensure adherence to provisions in the form, a suitable place was identified in the clinical area where the researcher handled one participant at a time away from the others. For the retrospective cohort study design, informed written consent was waived by the Ethics Committee and Cancer Treatment Centre of Kenyatta National Hospital.

3.16.3 Confidentiality

In order to maintain the anonymity of the patients, their personal information, including names and addresses, was not documented during data collection in both study designs. The interview phase of the data collection was conducted in the private doctor's room to ensure the privacy and confidentiality of patients during data collection. The review of patient records was conducted in the locked private rooms of the Health Information Department of KNH.

3.16.4 Benefits of the study

The study participants were not incentivised to participate in the research. However, their voluntary participation will help to improve the HRQoL and survival outcomes in gastrointestinal cancer patients. The key findings of the study will be shared with the hospital's Oncology Department with the hope of improving cancer care. The survival outcome findings of the study were shared with the scientific community through publication in peer-reviewed journals (Degu et al., 2023b, 2023a, 2023c).

3.16.5 Risks of the study

For the cross-sectional study design, the study participants had minimal risk and discomfort during the interview phase since it was conducted for a maximum of twenty minutes in the

private doctor's rooms of the hospital. It was also conducted voluntarily after an adequate understanding of the study objectives. Informed written consent was also obtained and later removed from the main data collection tool to conceal patient identification. The retrospective cohort study and the review of medical records of the cross-sectional study did not cause any discomfort to the study participants since we only used their medical records.

CHAPTER FOUR: THE PREVALENCE AND TYPES OF DRUG-RELATED PROBLEMS AMONG PATIENTS WITH ESOPHAGEAL, GASTRIC AND COLORECTAL CANCER AT KENYATTA NATIONAL HOSPITAL

Abstract

Background

More than 15% of hospitalisations are due to drug-related problems. The risk of adverse drug reactions during cancer therapy is high since most anti-cancer therapies are toxic and have a limited therapeutic index. Although a substantial number of drug-related problems are preventable, there is a dearth of large-scale research on drug-related problems in Kenyan gastrointestinal cancer patients.

Objective

To assess the prevalence and determinants of drug-related problems among patients with gastrointestinal cancer.

Methods

A cross-sectional study was carried out to evaluate drug-related problems among 160 esophageal, 103 gastric and 96 colorectal cancer patients. The study included all adult patients with gastric, esophageal and colorectal cancer with complete documentation of diagnosis, stage and treatment. After training research assistants, investigator-administered questionnaires and data abstraction tools were used to collect the data. Patient-specific details such as socio-demographic and clinical characteristics were recorded after assessing medical records and interviewing patients. Drug-related problems were identified using the standard cancer treatment guidelines for each gastrointestinal cancer. The entry of data and analysis were performed using SPSS version 26.0 software.

Results

The study showed that drug-related problems were prevalent among esophageal (83, 51.9%), gastric (61, 59.2%) and colorectal (60, 62.5%) cancer patients. The need for additional drug therapy and adverse drug reactions were the most common types of drug-related problems. The majority of identified adverse drug reactions exhibited mild severity levels and were preventable.

Co-morbidity and advanced-stage disease were the significant determinants of drug-related problems among gastrointestinal cancer patients**.**

Conclusions

Drug-related problems were prevalent among patients with gastrointestinal cancer. Most of the identified adverse drug reactions had mild severity levels and were preventable. Co-morbidity and advanced stages of disease were the statistically significant determinants of drug-related problems. Thus, close monitoring is required in patients with multiple co-morbidities and advanced stages to curb this high burden of drug-related problems.

4.1 Introduction

Drug-related problem is an undesired event that arises during drug therapy that may compromise the intended treatment outcomes (Pharmaceutical Care Network Europe Association, 2020; Ruths et al., 2007). A systematic review study exhibited that the incidence of drug-related problems was 70.04% (Ni et al., 2021). More than 15% of hospitalizations are attributed to DRPs, with the highest admission in elderly and polypharmacy-treated patients (Ayalew et al., 2019). Nevertheless, a remarkable proportion of drug-related problems are potentially avoidable (Demessie & Berha, 2022; Kemal et al., 2022; Lim et al., 2022; Zhang et al., 2021). Previous research has shown that adverse drug reactions contribute to most DRP-related hospital admissions (Chan et al., 2014). Among hospitalized patients, the average mortality rate due to DRPs is 2.7% (Ayalew et al., 2019). Chemotherapy-related neutropenia is responsible for more than 50% of hospitalization in cancer patients (Vandyk et al., 2012). Older cancer patients have a substantial risk of drug-related adverse effects (Lund et al., 2018). Moreover, elderly patients with cancer are more at risk of experiencing harmful drug-drug interactions due to the frequent use of several medications (Ramasubbu et al., 2021). Without optimal intervention, DRPs are linked to considerably longer hospital stays and higher healthcare costs (Cipolle et al., 2012; Ko et al., 2014). Furthermore, studies have shown a higher treatment cost and hospitalization due to drug-related problems (Freitas et al., 2017; Mathew et al., 2019; Pattanaik et al., 2009).

Drug-drug interactions are more likely to occur in cancer patients due to the complexity of their treatment regimens. As their disease progresses, they are more likely to experience complications such as organ failure or metabolic changes (Bulsink et al., 2013).

The pharmacological treatment of cancer is complex and associated with the risk of toxicities (Cehajic et al., 2015). Similarly, complications associated with anticancer medications are common and offer a considerable challenge to healthcare providers (Iftikhar et al., 2015). A study in elderly patients with solid cancer revealed that the majority of patients suffer from anticancer drug toxicities (Versteeg et al., 2014). Since most antineoplastic regimens are cytotoxic, DRPs are tremendous in cancer therapy (Jaehde et al., 2008; Zhang et al., 2021). A previous study in Ethiopia reported a 74.7% prevalence of DRPs in cancer patients (Sisay et al., 2015), while a 93.8% prevalence of DRPs was reported in Kenya among patients with cervical cancer (Degu et al., 2017). A comprehensive investigation of DRPs may assist healthcare providers in reducing DRPs in cancer patients (Koh et al., 2005). Nevertheless, extensive investigations on DRPs in patients with gastrointestinal cancer in Kenya are insufficient.

4.2 General objective

The main objective of the study was to determine the prevalence, types and determinants of drug-related problems among gastrointestinal cancer patients.

4.3 Specific objectives

1. To estimate the prevalence of DRPs among patients with esophageal, gastric and colorectal cancer.
2. To identify the types of DRPs among patients with esophageal, gastric and colorectal cancer.
3. To identify the determinants of DRPs among patients with esophageal, gastric and colorectal cancer.

4.4 Results

4.4.1 Sociodemographic characteristics of gastrointestinal cancer patients

Most patients with colorectal cancer were under the age of 60, whereas the majority of those with esophageal and stomach cancers were 60 years and above. This categorization was used to compare the occurrence of the disease between the young and old patients. The mean age of esophageal, gastric and colorectal cancer patients was 60.5± 12.7 years, 59.8±1.3 years and 53±1.5 years, respectively. The age ranged from 24-95 years in esophageal cancer, 26-88 years in gastric cancer and 18-88 years in colorectal cancer patients. Most gastrointestinal cancer

patients were males and had a primary level of education. Alcohol consumption and cigarette smoking were significant in 24.4 %(39) esophageal and 21.4 %(22) of gastric cancer patients **(Table 4.1)**.

Table 4.1: Socio-demographic characteristics of gastrointestinal cancer patients

	Type of cancer		
	Esophageal cancer (n=160)	**Gastric cancer** (n=103)	**Colorectal cancer** (n=96)
Variable	Frequency (%)	Frequency (%)	Frequency (%)
Age (in years)			
< 60 years	71(44.4)	47(45.6)	66(68.8)
≥60 years	89(55.6)	56(54.4)	30(31.2)
Gender			
Male	97(60.6)	64(62.1)	62(64.6)
Female	63(39.4)	39(37.9)	34(35.4)
Marital status			
Single	25(15.6)	4(3.9)	13(13.5)
Married	122(76.3)	93(90.3)	74(77.1)
Divorced	2(1.3)	3(2.9)	3(3.1)
Widowed	11(6.8)	3(2.9)	6(6.3)
Educational status			
Primary	72(45.0)	47(45.6)	40(41.7)
Secondary	49(30.6)	39(37.9)	37(38.5)
Tertiary	22 (13.8)	8(7.8)	12(12.5)
Informal	17(10.6)	9(8.7)	7(7.3)
Occupational status			
Self-employed	99(61.9)	67(65.0)	58(60.4)
Unemployed/Retired	42(26.3)	18(17.5)	21(21.9)
Other (driver, contractor, artisan)	8(5.0)	11(10.7)	10(10.4)
Housewife	8(5.0)	6(5.8)	3(3.1)
Government employee	3(1.8)	1(1.0)	4(4.2)
History of substance use			
None	109(68.1)	71(68.9)	89(92.8)
Alcohol alone	5(3.1)	9(8.7)	3(3.1)
Cigarette smoking alone	7(4.4)	1(1.0)	1(1.0)
Both alcohol and cigarette smoking	39(24.4)	22(21.4)	3(3.1)
Family history of cancer	8(5.0)	4(3.9)	5(5.2)

4.4.2 Clinical characteristics of gastrointestinal cancer patients

Adenocarcinoma was the most common histological type of gastric (101, 98.1%) and colorectal (95, 99%) cancer, while squamous cell carcinoma was found in 145 (90.6%) esophageal cancer

patients. In the three gastrointestinal malignancies, most patients presented at later stages (stages III and IV) and had at least one concurrent condition. Hypertension and anaemia were prevalent co-morbidities in esophageal and gastric cancer patients, while hypertension and diabetes mellitus were prevalent in colorectal cancer patients. The study showed lung and liver as the most common distant organ metastasis sites **(Table 4.2)**.

Table 4.2: Clinical characteristics of gastrointestinal cancer patients

	Esophageal cancer (n=160)	Gastric cancer (n=103)	Colorectal cancer (n=96)
Variable	Frequency (%)	Frequency (%)	Frequency (%)
Histological type of cancer			
Adenocarcinoma	15(9.4)	101(98.1)	95(99)
Squamous cell carcinoma	145(90.6)	2(1.9)	1(1.0)
Stage of cancer at diagnosis			
Stage I	11(6.9)	1(1.0)	3(3.1)
Stage II	55(34.4)	21(20.4)	11(11.5)
Stage III	53(33.1)	46(44.7)	32(33.3)
Stage IV	41(25.6)	35(33.9)	50(52.1)
Comorbidity			
Present	89(55.6)	65(63.1)	41(42.7)
Absent	71(44.4)	38(36.9)	55(57.3)
Number of comorbidities			
One	72(45.0)	23(22.3)	20(20.8)
Two	13(8.1)	25(24.3)	13(13.5)
≥Three	4(2.5)	17(16.5)	8(8.3)
Most prevalent comorbidities			
Hypertension	22(13.8)	19(18.4)	19(19.8)
Anaemia	19(11.9)	28(27.2)	5(5.2)
Acute kidney injury	16(10.0)	7(6.8)	5(5.2)
Pneumonia	13(8.1)	3(2.9)	3(3.1)
Retroviral disease	9(5.6)	5(4.9)	5 (5.2)
Thromboembolism	8(5)	3(2.9)	5(5.2)
Peptic ulcer disease	7(4.4)	13(12.6)	5(5.2)
Diabetes mellitus	4(2.5)	14(13.6)	8(8.3)
Sepsis	0(0.0)	0(0.0)	7(7.3)
Distant metastasis at diagnosis	**n=41**	**n=35**	**n=50**
Lung	25(60.9)	8(22.9)	12(24)
Liver	10(24.4)	13(37.1)	18(36)
Liver and lung	3(7.3)	7(20.0)	11(22)
Bone	3(7.3)	2(5.7)	0(0)
Ovary	0(0.0)	4(11.4)	1(2)
Pancreas	0(0.0)	1(2.9)	0(0)
Liver, lung and bone	0(0.0)	0(0.0)	4(8)
Brain and liver	0(0.0)	0(0.0)	1(2)
Thyroid	0(0.0)	0(0.0)	1(2)
Uterus	0(0.0)	0(0.0)	1(1)
Spleen	0(0.0)	0(0.0)	1(1)

4.4.3 Treatment regimen of gastrointestinal cancer patients

Esophageal cancer patients were most frequently treated with surgery (49, 30.6%) and the combination of chemotherapy and radiotherapy (32, 20.0%). Chemotherapy (36, 35.0%) and surgery (23, 22.3%) were the most prominent gastric cancer therapies. Twenty-six percent (25, 26.0%) of patients with colorectal cancer had a combination treatment strategy consisting of surgery and chemotherapy **(Table 4.3)**.

Table 4.3: Treatment regimen of gastrointestinal cancer patients

	Type of cancer		
	Esophageal cancer	**Gastric cancer**	**Colorectal cancer**
	n=160	n=103	n=96
Treatment regimen	**Frequency (%)**	**Frequency (%)**	**Frequency (%)**
Surgery	49(30.6)	23 (22.3)	12(12.5)
Chemotherapy and radiotherapy	32(20.0)	6(5.8)	16(16.7)
Chemotherapy	6(3.8)	36(35.0)	21(21.9)
Radiotherapy	17(10.6)	1(1.0)	1(1.0)
Surgery and chemotherapy	4(2.5)	13(12.6)	25(26.0)
Symptomatic management	30(18.8)	20(19.4)	6(6.3)
Radiotherapy, chemotherapy and surgery	11(6.9)	4(3.9)	15(15.6)
Radiotherapy and surgery	11(6.9)	0(0.0)	0(0.0)

Cisplatin and 5-fluorouracil-based regimen (30, 18.8%) followed by carboplatin and paclitaxel (8,5%) were the most frequently used chemotherapeutic agents among esophageal cancer patients. In gastric cancer patients, the FLOT (fluorouracil, leucovorin, oxaliplatin and docetaxel) regimen accounted for 28 (27.2%) study participants. Further, the FOLFOX-based regimen (folinic acid, 5-fluorouracil and oxaliplatin) was used in 8 (7.8%) gastric cancer patients. However, FOLFIRI (folinic acid, 5-fluorouracil and irinotecan) (1.0%), DCF (Docetaxel, cisplatin and 5-fluorouracil) (1.0%) and DOF (Docetaxel, Oxaliplatin and 5-Fluorouracil) (1%) were the least commonly used chemotherapy regimens among gastric cancer patients. More than half (57, 59.4%) of colorectal cancer patients were treated with FOLFOX-based regimens **(Table 4.4)**.

Table 4.4: Chemotherapy regimens used in the management of gastrointestinal cancers

Chemotherapy regimens	Frequency (%)
Esophageal cancer chemotherapy regimens (n=160)	
Cisplatin and 5-fluorouracil	30(18.8)
Carboplatin and paclitaxel	8(5.0)
FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin)	4(2.5)
Cisplatin and paclitaxel	4(2.5)
Capecitabine	2(1.3)
Cisplatin	2(1.3)
Cisplatin and capecitabine	1(0.6)
DCX (docetaxel, cisplatin and capecitabine)	1(0.6)
Gastric cancer chemotherapy regimens (n=103)	
FLOT (fluorouracil, leucovorin, oxaliplatin and docetaxel)	28(27.2)
FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin)	8(7.8)
CAPOX (capecitabine and oxaliplatin)	7(6.8)
Capecitabine	4(3.9)
CF (Cisplatin and 5-fluorouracil)	4(3.9)
EOX (Epirubicin, oxaliplatin and capecitabine)	2(1.9)
Cisplatin and Capecitabine	2(1.9)
FOLFIRI (folinic acid , 5-fluorouracil and irinotecan)	1(1.0)
DCF (Docetaxel, cisplatin and 5-fluorouracil)	1(1.0)
DOF (Docetaxel, Oxaliplatin and 5-Fluorouracil)	1(1.0)
Docetaxel	1(1.0)
Colorectal cancer chemotherapy regimens (n=96)	
FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin)	57(59.4)
CAPOX (capecitabine and oxaliplatin)	8(8.3)
FOLFIRI (folinic acid , 5-fluorouracil and irinotecan	7(7.3)
Capecitabine	5(5.2)

4.4.4 Drug-related problems among gastrointestinal cancer patients

DRPs were found in 83 (51.9%), 61 (59.2%), and 60 (62.5%) of patients with esophageal, gastric, and colorectal cancer, respectively. Additionally, 115, 78, and 89 DRPs were found in

esophageal, gastric and colorectal cancer patients, respectively. Patients with esophageal, gastric and colorectal cancers had 0.72±0.1, 0.8±0.1 and 0.9±0.1 mean number of DRPs, respectively.

The study indicated the highest prevalence of DRPs in male, co-morbid and advanced-stage (III and IV) patients. Older patients (60 years and above) with esophageal (30% vs 21.9%) and gastric (30.1% vs 29.1%) cancer had higher drug-related problems, while colorectal cancer patients older than 60 years and above had a lower prevalence (19.8% vs 42.7%) of DRPs **(Table 4.5)**.

Table 4.5: Prevalence of drug-related problems among patients with gastrointestinal cancer

	Type of cancer		
Variables	**Esophageal cancer**	**Gastric cancer**	**Colorectal cancer**
	n=160	n=103	n=96
	DRPs Frequency (%)	DRPs Frequency (%)	DRPs Frequency (%)
Age			
<60 years	35(21.9)	30(29.1)	41(42.7)
≥ 60 years	48(30.0)	31(30.1)	19(19.8)
Gender			
Male	54(33.8)	33(32.0)	36(37.5)
Female	29(18.1)	28(27.1)	24(25.0)
Comorbidity			
Present	49(30.6)	42(40.8)	31(32.3)
Absent	34(21.3)	19(18.4)	29(30.2)
Stage of cancer			
Stage I	5(3.1)	1(1.0)	2(2.1)
Stage II	27(16.9)	10(9.7)	6(6.3)
Stage III	28(17.5)	26(16.3)	18(18.8)
Stage IV	23(14.4)	24(15.0)	34(35.4)

DRPs: Drug-related problems

The study found that esophageal cancer patients treated with symptomatic management (22, 13.8%), surgery (21, 13.1%) and chemotherapy-radiotherapy combination (16, 10%) experienced significant drug-related problems. Gastric cancer patients treated with chemotherapy (23, 22.3%) and colorectal cancer patients treated with chemotherapy (14, 14.6%) and a combination of chemotherapy and surgery (15, 15.6%) had the highest DRPs **(Table 4.6)**.

Table 4.6: Prevalence of drug-related problems among different treatment modalities

	Type of cancer		
	Esophageal cancer	**Gastric cancer**	**Colorectal cancer**
	n=160	n=103	n=96
Treatment regimen	Frequency (%)	Frequency (%)	Frequency (%)
Surgery	21(13.1)	7(6.8)	7(7.3)
Symptomatic management	22 (13.8)	15(14.6)	5(5.2)
Chemotherapy and radiotherapy	16(10.0)	4(3.9)	12(12.5)
Radiotherapy	7(4.4)	1(1.0)	0(0.0)
Chemotherapy	5(3.1)	23(22.3)	14(14.6)
Radiotherapy, chemotherapy &surgery	9(5.6)	3(2.9)	7(7.3)
Radiotherapy and surgery	2(1.3)	0(0.0)	0(0.0)
Surgery and chemotherapy	1(0.6)	8(7.8)	15(15.6)

In esopahgeal cancer patients, cisplatin and 5-fluorouracil-based regimens treated patients (14, 8.8%) had the highest DRPs. However, DRPs were least common among cisplatin and capecitabine and DCX regimen-treated esophageal cancer patients. In gastric cancer patients, FLOT (18, 17.5%) and CAPOX (6, 5.8%) regimens had a significant proportion of DRPs. Nonetheless, DRPs were the least prevalent in the other chemotherapeutics regimens of gastric cancer. Colorectal cancer patients receiving the FOLFOX regimen had a disproportionately high percentage of DRPs (36, 37.5%) compared to the other regimens **(Table 4.7)**.

Table 4.7: Drug-related problems among chemotherapy-treated patients with gastrointestinal cancer

Chemotherapy regimens	Frequency of DRPs (%)
Esophageal cancer chemotherapy regimens (n=160)	
Cisplatin and 5-fluorouracil	14(8.8)
Carboplatin and paclitaxel	4(2.5)
Cisplatin and paclitaxel	4(2.5)
FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin)	3(1.9)
Capecitabine	2(1.3)
Cisplatin	2(1.3)
Cisplatin and capecitabine	1(0.6)
DCX (docetaxel, cisplatin and capecitabine)	1(0.6)
Gastric cancer chemotherapy regimens (n=103)	
FLOT (fluorouracil, leucovorin, oxaliplatin and docetaxel)	18(17.5)
CAPOX (capecitabine and oxaliplatin)	6(5.8)
FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin)	4(3.9)
CF (Cisplatin and 5-fluorouracil)	3(2.9)
Cisplatin and Capecitabine	2(1.9)
EOX (Epirubicin, oxaliplatin and capecitabine)	1(1.0)
Capecitabine	1(1.0)
DCF (Docetaxel, cisplatin and 5-fluorouracil)	1(1.0)
DOF (Docetaxel, Oxaliplatin and 5-Fluorouracil)	1(1.0)
Docetaxel	1(1.0)
Colorectal cancer chemotherapy regimens (n=96)	
FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin)	36(37.5)
CAPOX (capecitabine and oxaliplatin)	5(5.2)
FOLFIRI (folinic acid , 5-fluorouracil and irinotecan	4(4.2)
Capecitabine	3(3.1)

DRPs: Drug-related problems

The most common DRPs identified in esophageal cancer patients were the need for additional drug therapy (39, 33.9%), drug-drug interaction (26, 22.6%), ADRs (22, 19.1%) and unnecessary drug therapy (13, 11.3%). The leading DRPs among gastric cancer patients were ADRs (40, 51.3%), need for additional drug therapy (16, 20.5%) and drug-drug interactions (13, 16.7%). ADRs (41, 46.1%), need for additional drug therapy (15, 16.9%) and dosing problems were the predominant DRPs among colorectal cancer patients (11, 12.3%). In all three gastrointestinal

cancers, the need for new drug therapy and combination therapies were the most common reasons for the need for additional drug therapy in our setting (**Table 4.8)**.

Table 4.8: Types of drug-related problems among gastrointestinal cancer patients

	Type of cancer		
	Esophageal cancer (n=115)	**Gastric cancer** (n=78)	**Colorectal cancer** (n=89)
Types of drug-related problems	**Frequency (%)**	**Frequency (%)**	**Frequency (%)**
Need for additional drug therapy	39(33.9)	16(20.5)	15(16.9)
Conditions require new drug therapy	20 (51.3)	8(50)	9(60)
Combination therapy required	13(33.3)	6(37.5)	4(26.7)
Preventive therapy needed	6(15.4)	2(12.5)	2(13.3)
Drug-drug interaction	26(22.6)	13(16.7)	10(11.2)
Adverse drug reaction	22(19.1)	40(51.3)	41(46.1)
Unnecessary drug therapy	13(11.3)	1(1.3)	6(6.7)
Ineffective drug therapy	6(5.2)	1(1.3)	6(6.7)
Dosage too low	5(4.3)	6(7.7)	10(11.2)
Dosage too high	4(3.5)	1(1.3)	1(1.1)

The severity levels of the 26 drug-drug interactions identified in esophageal cancer patients were 38.7% minor, 26.9% moderate, 19.2% severe and 15.4% significant. Most drug-drug interactions in gastric cancer patients were significant (69.0%), while the smallest proportion (15.0%) had a minor drug-drug interaction. An equal percentage (7.7%) of moderate and serious drug-drug interactions was exhibited among gastric cancer patients. In colorectal cancer patients, 30.0% minor and 20.0% moderate and an equal percentage (10.0%) of serious and significant drug-drug interactions were identified **(Figure 4.1)**. The detail list of the interacting drugs is described in Appendix X**.**

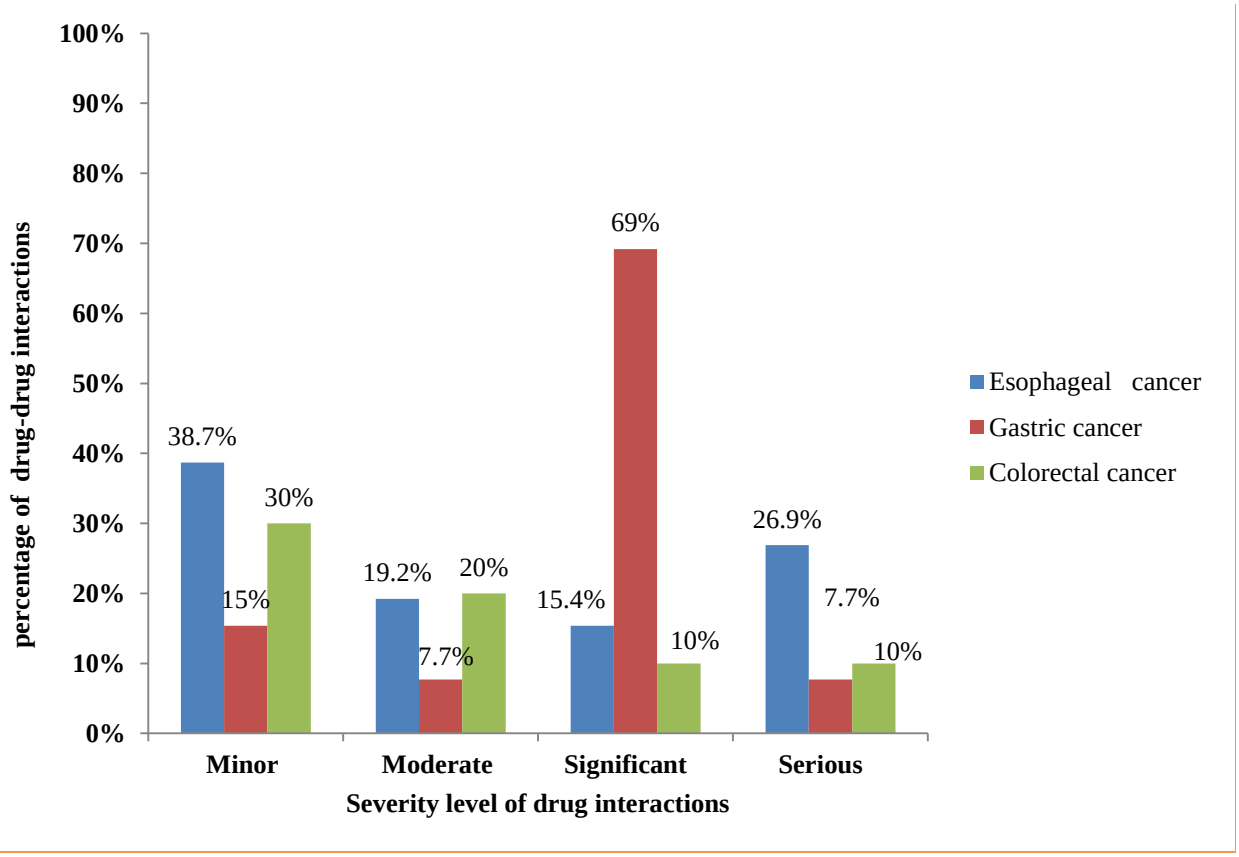


Figure 4.1: Severity level of drug-drug interactions among gastrointestinal cancer patients

4.4.4.1 Adverse drug reactions among gastrointestinal cancer patients

Male and co-morbid patients had a higher prevalence of ADRs. Furthermore, patients with stage III and IV disease had a higher prevalence of ADRs than stage I and II disease. ADRs were more common in older (≥ 60 years) esophageal (14, 63.6%) cancer patients. A higher prevalence of ADRs (29, 70.7%) was observed among colorectal cancer patients below 60 years **(Table 4.9)**.

Table 4.9: Sociodemographic and clinical characteristics among patients experiencing adverse drug reactions

	Type of cancer		
Variables	**Esophageal cancer**	**Gastric cancer**	**Colorectal cancer**
	n=22	n=40	n=41
	ADR Frequency (%)	ADR Frequency (%)	ADR Frequency (%)
Age			
<60 years	8(36.4)	21(52.5)	29(70.7)
≥ 60 years	14(63.6)	19(47.5)	12(29.3)
Gender			
Male	17(77.3)	21(52.5)	23(56.1)
Female	5(22.7)	19(47.5)	18(43.9)
Comorbidity			
Present	15(68.2)	21(52.5)	23(56.1)
Absent	7(31.8)	19(47.5)	18(43.9)
Stage of cancer			
Stage I	0 (0.0)	0(0.0)	0(0.0)
Stage II	6(27.3)	6(15.0)	3(7.3)
Stage III	6(27.3)	14(35.0)	16(39.0)
Stage IV	10(45.5)	20(50.0)	22(53.7)

ADR: Adverse drug reactions

Esophageal and gastric cancer patients treated with a combination of chemotherapy and radiotherapy (13, 59.0%) and chemotherapy alone (24, 60.0%) had the highest percentage of ADRs, respectively. Furthermore, chemotherapy-treated colorectal cancer patients (15, 37.0%) had the highest proportion of ADRs **(Figure 4.2)**.

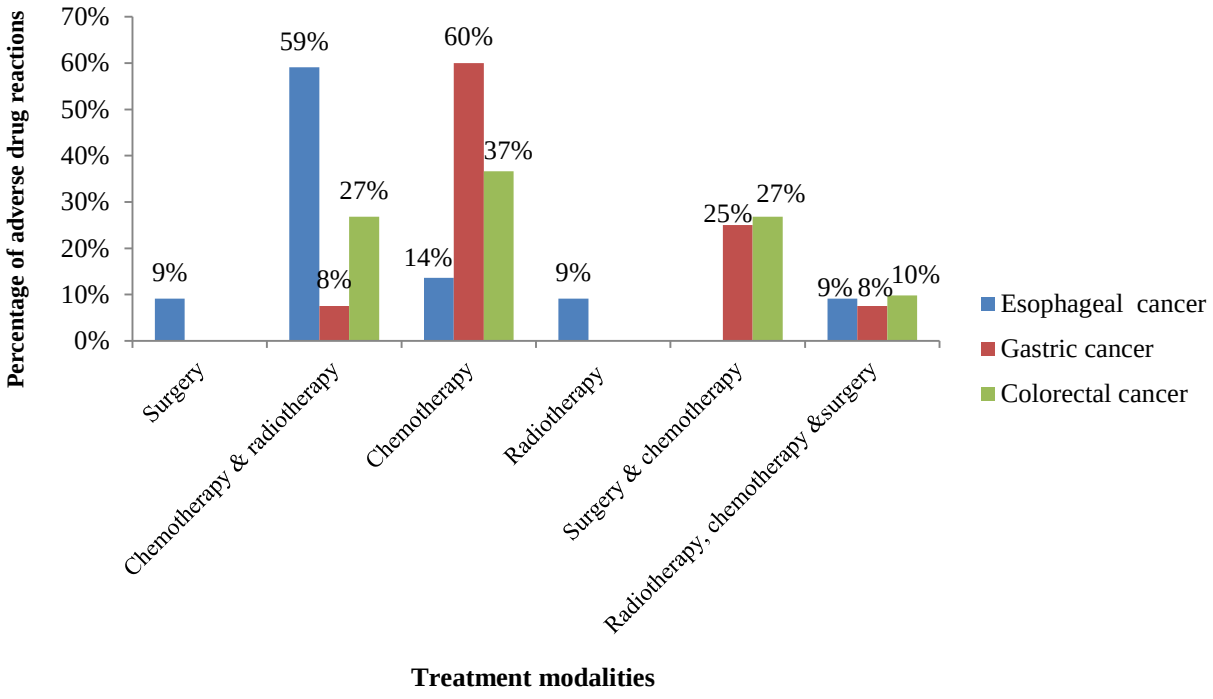


Figure 4.2: Prevalence of adverse drug reactions among different treatment modalities

The present study reported a higher percentage of ADRs in cisplatin and 5-fluorouracil (6, 27.3%) and cisplatin and paclitaxel (4, 18.2%) based regimens of esophageal cancer patients. FLOT (22, 55 %) and CAPOX (7, 17.5%) regimens accounted for most ADRs among gastric cancer patients. FOLFOX (23, 56.1%) and FOLFIRI (6, 14.6%) regimens of colorectal cancer patients had a sizeable percentage of ADRs. Cisplatin and capecitabine, DCX, and DCF regimens had the smallest proportion of ADRs **(Table 4.10)**.

Table 4.10: Frequency of adverse drug reactions induced by chemotherapy regimens among gastrointestinal cancer patients

Chemotherapy regimen	Adverse drug reactions
Chemotherapy regimens for esophageal cancer (n=22)	**Frequency (%)**
Cisplatin and 5-fluorouracil	6(27.3)
Cisplatin and paclitaxel	4(18.2)
FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin)	2(9.1)
Cisplatin	2(9.1)
Capecitabine	2(9.1)
Cisplatin and capecitabine	1(4.5)
DCX (docetaxel, cisplatin and capecitabine)	1(4.5)
Chemotherapy regimens for gastric cancer (n=40)	
FLOT (fluorouracil, leucovorin, oxaliplatin and docetaxel)	22(55.0)
CAPOX (capecitabine and oxaliplatin)	7(17.5)
FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin)	3(7.5)
Cisplatin+ 5-fluorouracil	3(7.5)
Cisplatin+Capecitabine	3(7.5)
Docetaxel	1(2.5)
DCF (Docetaxel, cisplatin and 5-fluorouracil)	1(2.5)
Chemotherapy regimens for colorectal cancer (n=41)	
FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin)	23(56.1)
FOLFIRI (folinic acid , 5-fluorouracil and irinotecan	6(14.6)
CAPOX (capecitabine and oxaliplatin)	4(9.8)
Capecitabine	1(2.4)

In esophageal and gastric cancer patients, nausea/vomiting and anaemia were the leading ADRs. Neutropenia (13, 31.7%), anaemia (8, 19.5%), diarrhoea (6, 14.6%) and peripheral neuropathy (5, 12.2%) were the most often reported ADRs in patients with colorectal cancer. **(Table 4.11)**.

The details of the chemotherapy regimens responsible for the occurrence of the specific ADR types are described in **Appendix XI**.

Table 4.11: Types of adverse drug reactions identified among gastrointestinal cancer patients

	Type of cancer		
	Esophageal cancer	**Gastric cancer**	**Colorectal cancer**
	(n=22)	(n=40)	(n=41)
Types of adverse drug reactions	**Frequency (%)**	**Frequency (%)**	**Frequency (%)**
Nausea and vomiting	9(40.9)	10(25)	4(9.8)
Anaemia	3(13.6)	9(22.5)	8(19.5)
Neutropenia	2(9.1)	8(20.0)	13(31.7)
Diarrhoea	2(9.1)	3(7.5)	6(14.6)
Peripheral neuropathy	1(4.5)	4(10.0)	5(12.2)
Excessive bleeding	1(4.5)	0(0.0)	0(0.0)
Hypokalemia	1(4.5)	0(0.0)	0(0.0)
Leukopenia	1(4.5)	3(7.5)	0(0.0)
Renal toxicity	1(4.5)	2(5.0)	0(0.0)
Anisocytosis	1(4.5)	0(0.0)	0(0.0)
Oedema of the lower limb	0(0.0)	1(2.5)	0(0.0)
Oral mucositis	0(0.0)	0(0.0)	3(7.3)
Hyperpigmentation of palm	0(0.0)	0(0.0)	1(2.4)
Hypersensitivity reactions	0(0.0)	0(0.0)	1(2.4)

4.4.4.2 Causality, severity and preventability of adverse drug reactions

Most of the identified ADRs had possible causality scores in esophageal (18, 81.8%), gastric (29, 72.5%) and colorectal (36, 87.8%) cancer patients. Nonetheless, neither definite nor doubtful causality scores were present for any of the detected ADRs among the studied gastrointestinal cancer patients. Most of the observed ADRs had mild severity levels and were definitely preventable for each type of gastrointestinal cancer. Nevertheless, only a small proportion of ADRs exhibited serious severity levels **(Table 4.12)**.

Table 4.12: **Causality, severity and preventability of adverse drug reactions among gastrointestinal cancer patients**

	Type of cancer		
	Esophageal cancer (n=22)	**Gastric cancer (n=40)**	**Colorectal cancer (n=41)**
Causality of ADRs	Frequency (%)	Frequency (%)	Frequency (%)
Probable (score 5-8)	4(18.2)	11(27.5)	5(12.2)
Possible (score 1-4)	18(81.8)	29(72.5)	36(87.8)
Severity of ADRs			
Mild	10(45.5)	29(72.5)	25(61)
Moderate	9(40.9)	6(15.0)	15(36.6)
Severe	3(13.6)	5(12.5)	1(2.4)
Preventability ADRs			
Definitely preventable	14(63.6)	26(65.0)	30(73.2)
Probably preventable	7(31.8)	10(25.0)	9(22.0)
Non-preventable	1(4.6)	4(10.0)	2(4.8)

ADRs: Adverse drug reactions

4.4.4.3 Determinants of DRPs among gastrointestinal cancer patients

Compared to those without comorbid illnesses, esophageal, gastric and colorectal cancer patients with co-morbidities were 2.4 (AOR=2.4, 95% CI=1.6, 2.9, p=0.03), 2.0 (AOR=2.0, 95% CI=1.8-5.3, p=0.02) and 4.4 (AOR=4.4, 95% CI=1.6-12.8, p=0.01) times more likely to have DRPs, respectively. The study findings indicated that patients diagnosed with advanced stages (III and IV) of esophageal cancer were 2.8 times (AOR=2.8, 95% CI=1.4-3.6, p=0.03) more likely to experience DRPs compared to those in early stages. Similarly, advanced-stage gastric (AOR=2.2, 95% CI=1.4-3.7, p=0.03) and colorectal (AOR=2.1, 95% CI=1.2-5.3, p=0.03) cancer patients had a higher likelihood of experiencing DRPs. Patients diagnosed with esophageal cancer with adenocarcinoma had significantly higher odds of experiencing DRPs than those with squamous cell carcinoma (AOR=3.8, 95% CI=1.2-15.1, p=0.04).

Gastric cancer who received surgical intervention exhibited a reduced likelihood of experiencing DRPs (AOR=0.1, 95% CI=0.2-0.4, p=0.001) compared to those who were subjected to a

combination of treatment modalities. The impact of treatment regimens on DRPs in patients with esophageal and colorectal cancer was not statistically significant. Age, gender and education levels were not significant determinants of DRPs among all patients **(Table 4.13)**.

Table 4.13: **Determinants of drug-related problems among patients with gastrointestinal cancer**

Variable	Type of cancer											
	Esophageal cancer				Gastric cancer				Colorectal cancer			
	Bivariable Analysis		Multivariable Analysis		Bivariable Analysis		Multivariable Analysis		Bivariable Analysis		Multivariable Analysis	
	COR (95%CI)	P-value	AOR (95%CI)	P-value	COR (95%CI)	P-value	AOR (95%CI)	P-value	COR (95%CI)	P-value	AOR (95%CI)	P-value
Age (in years)												
<60 years	1		1		1		1		1		1	
≥60 years	1.2 (0.6-2.2)	0.6	0.8 (0.4-1.5)	0.4	1.7 (0.8-3.7)	0.2	2.3(0.9-6.2)	0.08	0.9(0.4-2.3)	0.9	1.4(0.5-4.2)	0.6
Gender												
Female	1		1		1		1		1		1	
Male	1.5 (0.8-2.8)	0.2	1.3(0.6-2.7)	0.5	0.4(0.2-1.9)	0.5	0.3(0.1-1.9)	0.4	0.6(0.2-1.4)	0.2	0.5(0.2-1.4)	0.2
Education level												
Formal education	1		1		1		1		1		1	
Informal education	0.3(0.2-12.9)	0.06	0.3 (0.1-0.9)	0.4	0.7(0.2-2.9)	0.6	0.4(0.1-2.2)	0.3	1.3(0.3-6)	0.8	2.2(0.4-13.6)	0.4
Co-morbidity												
Absent	1		1		1		1		1		1	
Present	2.3(1.7-3.5)	**0.04***	2.4 (1.6-2.9)	**0.03***	1.8(1.8-4.1)	**0.01***	2.0(1.8-5.3)	**0.02***	2.8(1.1-6.7)	**0.02***	4.4(1.6-12.8)	**0.01***
Histological type												
Squamous cell carcinoma	1		1		1		1		1		1	
Adenocarcinoma	4.2 (1.1-15.4)	**0.03***	3.8 (1.2-15.1)	**0.04***	0.1(0.3-1.3)	0.9	0.1(0.4-1.3)	0.8	0.4(0.5-1.6)	0.6	0.5(0.4-1.9)	0.7
Stage of the disease												
Early stage (I and II)	1		1		1		1		1		1	
Advanced stage (III and IV)	1.8 (1.7-2.4)	**0.04***	2.8(1.4-3.6)	**0.03***	1.6(1.2-2.4)	**0.03***	2.2(1.4-3.7)	**0.03***	2.8(0.2-2.4)	**0.02***	2.1(1.2-5.3)	**0.03***
Treatment regimen												
Combination therapy	1		1		1		1		1		1	
Surgery	0.6 (0.3-1.2)	0.1	0.6 (0.3-1.3)	0.2	0.2(0.1-0.6)	**0.003***	0.1(0.2-0.4)	**0.001***	0.7 (0.2-2.2)	0.5	0.4(0.1-2.4)	0.3
Chemotherapy	3.8 (0.4-33.8)	0.2	2.9 (0.3-28.4)	0.4	0.8 (0.3-1.9)	0.6	1.0(0.3-2.8)	0.9	1.1 (0.4-3.2)	0.8	1.1 (0.4-3.4)	0.9
Radiotherapy	0.5 (0.2-1.5)	0.2	0.5 (0.2-1.5)	0.2	0.3(0.1-1.8)	0.7	0.4(0.1-1.9)	0.9	0.6 (0.2-1.8)	0.9	0.7 (0.2-1.9)	0.9

CI: Confidence interval, AOR: Adjusted odds ratio, COR: crude odds ratio, * statistically significant, p-value ≤0.05

4.4.4.4 Determinants of need for additional drug therapy and drug-drug interactions among gastrointestinal cancer patients

Advanced-stage (III and IV) colorectal cancer patients were 5.8 times (AOR: 5.8, 95% CI: 1.1-12.3, p=0.04) more likely to need additional drug therapy as compared to early-stage patients. Nonetheless, none of the other parameters were the significant determinants of the need for additional drug therapy among colorectal cancer patients. In esophageal and gastric cancer patients, none of the variables was the significant determinant of the need for additional drug therapy.

Gastric cancer patients who had comorbidities were 6.8 times (AOR: 6.8, 95% CI: 1.2-4.5, p: 0.01) more likely to experience drug-drug interactions as compared to non-comorbid patients. However, none of the variables was the significant determinant of drug-drug interaction among esophageal and gastric cancer patients **(Table 4.14 and Table 4.15).**

Table 4.14: Determinants of need for additional drug therapy among patients with gastrointestinal cancer

Variable	Type of cancer											
	Esophageal cancer				Gastric cancer				Colorectal cancer			
	Bivariable Analysis		Multivariable Analysis		Bivariable Analysis		Multivariate Analysis		Bivariable Analysis		Multivariable Analysis	
	COR (95%CI)	P-value	AOR (95%CI)	P-value	COR (95%CI)	P-value	AOR (95%CI)	P-value	COR (95%CI)	P-value	AOR (95%CI)	P-value
Age (in years)												
<60 years	1		1		1		1		1		1	
≥60 years	0.9(0.5-1.9)	0.9	1.1(0.4-2.2)	0.9	1.2(0.4-1.4)	0.3	2.1(0.5-7.3)	0.3	2.1(0.2-2.6)	0.2	2.7(0.7-11.2)	0.2
Gender												
Female	1		1		1		1		1		1	
Male	0.2(0.2-1.8)	0.5	1.0(0.5-2.2)	0.9	1.2(0.3-1.5)	0.5	0.7(0.2-2.5)	0.6	0.6(0.2-1.8)	0.4	0.9(0.3-3.3)	0.9
Co-morbidity												
Absent	1		1		1		1		1		1	
Present	0.7 (0.3-1.4)	0.3	0.7(0.3-1.4)	0.3	1.2(0.3-1.4)	0.4	1.2(0.9-1.9)	0.9	0.2(0.1-1.2)	0.6	0.1(0.2-1.8)	0.4
Histological type												
Squamous cell carcinoma	1		1		1		1		1		1	
Adenocarcinoma	1.6 (0.5-5.1)	0.4	1.7(0.5-5.8)	0.4	1.3(0.2-1.6)	0.6	1.2(0.2-2.4)	0.1	0.3(0.2-1.6)	0.5	0.2(0.2-1.8)	0.3
Stage of the disease												
Early stage (I & II)	1		1		1		1		1		1	
Advanced stage (III & IV)	0.9 (0.5-2.1)	0.9	1.0(0.5-2.2)	0.9	1.2(0.3-1.6)	0.7	1.4(0.3-6.5)	0.6	4.2(1.5-8.7)	**0.01***	5.8(1.1-12.3)	**0.04***
Treatment regimen												
Combination therapy	1		1		1		1		1		1	
Surgery	0.5(0.2-1.2)	0.1	0.5(0.2-1.2)	0.1	0.4(0.2-1.3)	0.4	0.1(0.2-2.4)	0.1	0.4(0.2-2.6)	0.2	0.5(0.3-1.9)	0.4
Chemotherapy	1.3(0.2-7.3)	0.7	1(0.2-6.6)	0.9	1.3(0.2-2.3)	0.9	0.1(0.3-1.9)	0.2	0.4(0.4-1.6)	0.1	0.2(0.4-1.7)	0.2
Radiotherapy	0.7(0.2-2.6)	0.6	0.8(0.2-2.8)	0.7	0.8(0.2-1.3)	0.6	0.9(0.2-1.7)	1.0	0.6(0.2-2.2)	0.4	0.1(0.2-1.8)	0.2

Table 4.15: Determinants of drug-drug interactions among patients with gastrointestinal cancer

Variable	Type of cancer											
	Esophageal cancer				Gastric cancer				Colorectal cancer			
	Bivariable Analysis		Multivariable Analysis		Bivariable Analysis		Multivariable Analysis		Bivariable Analysis		Multivariable Analysis	
	COR (95%CI)	P-value	AOR (95%CI)	P-value	COR (95%CI)	P-value	AOR (95%CI)	P-value	COR (95%CI)	P-value	AOR (95%CI)	P-value
Age (in years)												
<60 years	1		1		1		1		1		1	
≥60 years	0.7(0.2-1.6)	0.2	0.8(0.2-2.1)	0.6	0.2(0.1-1.7)	0.2	0.3(0.1-1.4)	0.1	0.4(0.2-2.9)	0.2	0.5(0.1-1.9)	0.3
Gender												
Female	1		1		1		1		1		1	
Male	1.2(0.4-1.7)		1.7(0.6-4.8)		0.2(0.2-2.4)	0.4	0.4(0.1-1.6)	0.2	0.2(0.4-2.6)	0.1	0.4(0.1-2.1)	0.3
Co-morbiditv												
Absent	1		1		1		1		1		1	
Present	2.1(0.9-3.6)	0.1	2.2(0.8-6.5	0.1	5.4(1.4-2.8)	**0.03***	6.8(1.2-4.5)	**0.01***	0.4(0.3-2.4)	0.4	0.6(0.1-2.8)	0.5
Histological type												
Squamous cell carcinoma	1		1		1		1		1		1	
Adenocarcinoma	0.4(0.3-1.7)	0.3	0.5(0.1-2.8)	0.4	0.2(0.3-1.7)	0.4	0.4(0.2-1.9)	0.2	0.3(0.2-2.3)	0.2	0.5(0.1-2.8)	0.3
Stage of the disease												
Early stage (I and II)	1		1		1		1		1		1	
Advanced stage (III and IV)	0.4(0.2-1.9)	0.3	0.8(0.3-2.1)	0.6	0.4(0.2-2.4)	0.4	0.6(0.1-3.3)	0.6	2.3(0.4-2.8)		3.3(0.6-12.3)	0.8
Treatment regimen												
Combination therapy	1		1		1		1		1		1	
Surgery	1.3(0.2-3.2)	0.4	1.9(0.7-5.2)	0.2	1.2(0.4-2.8)	0.2	1.5(0.5-1.6)	0.4	0.9(0.7-1.9)	0.2	1.1(0.6-2.1)	0.3
Chemotherapy	1.1(0.3-2.2)	0.2	1.2(0.6-2.4)	0.1	1.1(0.2-3.4)	0.1	1.2(0.2-2.4)	0.2	0.8(0.4-2.8)	0.2	1.3(0.3-2.5)	0.5
Radiotherapy	0.2(0.4-3.2)	0.3	0.6(0.1-2.9)	0.5	0.2(0.1-3.4)	0.4	0.4(0.1-2.6)	0.2	1.2(0.6-2.7)	0.7	1.5(0.4-3.1)	0.9

4.4.4.5 Determinants of ADRs among gastrointestinal cancer patients

Among the patients with esophageal (AOR=5.9, 95% CI=1.8-13.2, p=0.04), gastric (AOR=1.7, 95% CI=1.6-4.9, p=0.03) and colorectal (AOR=1.8, 95% CI=1.3-2.5, p=0.03) cancer, chemotherapy-treated patients had a higher odds of developing adverse drug reactions. However, age, gender, co-morbidity, histology types and cancer stage were not statistically significant determinants of ADRs **(Table 4.16)**.

Table 4.16: Determinants of adverse drug reactions among gastrointestinal cancer patients

Variable	Type of cancer											
	Esophageal cancer				Gastric cancer				Colorectal cancer			
	Bivariable Analysis		Multivariable Analysis		Bivariable Analysis		Multivariable Analysis		Bivariable Analysis		Multivariable Analysis	
	COR (95%CI)	P-value	AOR (95%CI)	P-value	COR (95%CI)	P-value	AOR (95%CI)	P-value	COR (95%CI)	P-value	AOR (95%CI)	P-value
Age (in years)												
<60 years	1		1		1		1		1		1	
≥60 years	0.9(0.3-2.4)	0.8	1.1(0.3-3.4)	0.9	1.5(0.7-3.6)	0.3	2.2 (0.8-6.3)	0.1	2 (0.7-5.6)	0.2	2.9(0.9-9.8)	0.1
Gender												
Female	1		1		1		1		1		1	
Male	1.6(0.5-4.8)	0.4	2(0.6-6.8)		0.6(0.3-1.4)	0.2	0.4(0.1-1.1)	0.1	0.5(0.2-1.3)	0.2	0.5(0.2-1.3)	
Co-morbidity												
Absent	1		1		1		1		1		1	
Present	1.5(0.5-4.4)	0.4	1.9(0.6-6.2)	0.3	0.5(0.2-1.1)	0.08	0.4(0.1-1.3)	0.1	1.5(0.6-3.7)	0.4	2.7(0.9-7.7)	0.1
Histological type												
Squamous cell carcinoma	1		1		1		1		1		1	
Adenocarcinoma	2.3 (0.6-9.3)	0.2	2(0.4-10.1)	0.4	1(0.1-1.8)	0.9	0.9(0.2-1.9)	0.9	0.7(0.2-1.7)	0.8	0.8(0.2-1.9)	0.8
Stage of the disease												
Early stage (I and II)	1		1		1		1		1		1	
Advanced stage (III and IV)	0.4(0.1-1.3)	0.1	0.4(0.1-1.6)	0.2	0.5(0.1-1.5)	0.2	1.7(0.4-7.4)	0.5	0.4(0.1-1.7)	0.2	1.9 (0.3-13.7)	0.5
Treatment regimen												
Combination therapy	1		1		1		1		1		1	
Surgery	0.3 (0.1-1.4)	0.1	0.3(0.1-1.5)	0.2	0.3(0.2-1.3)	0.9	0.1(0.3-1.3)	0.9	0.7(0.1-1.3)	0.9	0.6(0.2-1.4)	0.9
Chemotherapy	7(1.3-12.9)	**0.03***	5.9 (1.8-13.2)	**0.04***	2.1 (1.8-5.2)	**0.03***	1.7 (1.6-4.9)	**0.03***	1.7(1.2-2.4)	**0.03***	1.8 (1.3-2.5)	**0.03***
Radiotherapy	0.4(0.1-3.6)	0.4	0.3 (0.1-2.7)	0.3	0.4(0.3-2.3)	0.9	0.3 (0.2-1.6)	0.9	0.9(0.2-2.9)	0.9	0.8(0.2-3.9)	0.9

4.5 Discussion

The present study sought to characterize the DRPs among adult patients with gastrointestinal cancers attending the largest tertiary referral hospital in East and Central Africa. The findings showed that the prevalence of DRPs was high among esophageal, gastric and colorectal cancer patients. These findings corroborate the findings among Indian (Paul et al., 2023) and Chinese studies (Zhang et al., 2021). The reasons for the high rates of prevalence could be due to the intricacy of cancer therapies, the use of various medications and the presence of comorbidities in cancer patients. Across the African continent, various researchers on cancer patients have found conflicting prevalence in Ethiopia (Sisay et al., 2015), Kenya (Degu et al., 2017) and Nigeria (Mustapha et al., 2018). The explanations of the variations could be attributed to differences in methodology, sample size, clinical characteristics of the patients and level of cancer care.

A high prevalence of DRPs was also reported in other types of cancer (Degu & Kebede, 2021; Kefale et al., 2022). Colorectal cancer patients had a considerably greater prevalence of DRPs compared to the findings of the study in Ethiopia (Kefale et al., 2022). Nonetheless, a Turkish study found that following the third cycle of chemotherapy, a similar prevalence of DRPs was exhibited among colorectal cancer patients (Tezcan et al., 2018). This considerable problem of DRPs in our setting may be associated with the frequent use of cytotoxic chemotherapeutic regimens in managing this condition.

The need for additional drug therapy and ADRs were the two most common DRPs identified among gastrointestinal cancer patients. In light of the high prevalence of DRPs, there is a pressing need to maximize clinical pharmacists' involvement in managing gastrointestinal cancer patients. An Ethiopian study also revealed that drug-drug interactions, ADRs and the need for additional drug therapy were the prominent DRPs in colorectal cancer patients (Kefale et al., 2022). The significant rate of ADRs in patients with colorectal cancer is likely related to the substantial use of chemotherapy-based regimens. Obviously, chemotherapy use is associated with several ADRs due to its cytotoxicity.

The present study revealed the highest DRPs were detected among males, patients with co-morbidity and advanced-stage cancer. Due to frequent unhealthy lifestyles, including smoking

cigarettes and drinking alcohol, males are more likely to get gastrointestinal malignancies than women (Islami et al., 2018).

The predominant patients had an advanced stage of disease at diagnosis. Consequently, the risk of metabolizing organ failure will be higher in patients with advanced stages of cancer since the liver is the principal organ affected by distant metastasis of gastrointestinal cancers (Chen et al., 2012). In addition, co-morbidity patients are mostly on multiple medications that can escalate the risk of drug interaction and ADRs. Hence, such causes may result in more risk of getting DRPs.

Drug-related problems were higher among geriatric esophageal and gastric cancer patients than those below 60 years. This might be due to the age-related reduction of drug metabolism that comes with aging (Kinirons & O'Mahony, 2004; Mangoni & Jackson, 2003). Moreover, the mean age of esophageal and gastric cancer patients was higher (≥ 60 years) than colorectal cancer patients. This can predispose those patients to have a higher risk of experiencing DRPs. In contrast, DRPs were lower in 60 years and older patients with colorectal cancer. This might be related to a higher percentage of locally advanced and metastatic disease below 60 years aged colorectal cancer patients. In addition, a review report found that younger colorectal cancer patients exhibited aggressive tumour characteristics that might have considerable disease progression at diagnosis (Done & Fang, 2021). This may harm the metabolising and excretory organs and aggravate treatment-related toxicities. Colorectal cancer patients younger than 60 were shown to have a greater prevalence of co-morbid diseases, which can increase the risk of having DRPs in this age group.

Cisplatin and 5-fluorouracil-based regimens treated esophageal cancer patients, FLOT-based regimens treated gastric cancer patients and FOLFOX regimens treated colorectal cancer patients had a disproportionately high percentage of DRPs. Similarly, an Ethiopian study reported that the FOLFOX regimen accounted for 38.4% of DRPs in colorectal cancer patients (Kefale et al., 2022). Studies conducted in Singapore and India found a predominance of chemotherapy-related DRPs in patients with cancer (Reji et al., 2018; Yeoh et al., 2015).

Cancer patients are often administered a wide variety of medicines, such as cytotoxic anticancer agents, palliative care medications, and medications to address comorbid conditions, thereby predisposing them to an increased risk of drug-drug interactions (Riechelmann & Krzyzanowska,

2019; van Leeuwen et al., 2013). A quarter of the identified drug-drug interactions were serious in esophageal cancer patients, which requires alternative pharmacological treatment modalities. Most gastric cancer patients had significant drug-drug interactions. A similar rate of significant and serious drug-drug interactions was identified in colorectal cancer patients. In contrast, in Ethiopian colorectal cancer patients, 58% significant and 4% severe drug-drug interactions were identified (Kefale et al., 2022). A study on Chinese cancer patients stated a predominance of severe drug-drug interactions (Wang et al., 2019). Further, cancer patients receiving chemotherapy had severe and mild drug-drug interactions (Turossi-Amorim et al., 2022).

The prevalence of ADRs was higher in males and co-morbid patients. Patients with advanced-stage disease had higher ADR prevalence than early-stage patients. This may be because as the disease progresses, the body's ability to metabolise and excrete medications decreases, causing them to build up and increase the likelihood of ADRs.

ADRs are more prevalent in cancer patients taking chemotherapy (Monestime et al., 2021; Ramasubbu et al., 2020; Saini et al., 2015; Workalemahu et al., 2020). Patients with esophageal and gastric cancer who had chemotherapy with radiation and chemotherapy alone had the greatest rates of ADRs, respectively. Moreover, chemotherapy-treated colorectal cancer patients had the highest percentage of ADRs. Interestingly, a higher prevalence of ADRs in cancer patients receiving chemotherapy has been reported in similar studies (Krishnarajan et al., 2021; Varghese et al., 2021). This high prevalence of ADRs might be related to the substantial capacity of these treatment approaches for inducing harm in actively proliferating normal cells in the body.

There was a higher percentage of ADRs among esophageal cancer patients treated with cisplatin and 5-fluorouracil, as well as cisplatin and paclitaxel-based regimens. In other cancer patients, the cisplatin and 5-fluorouracil combination regimen accounted for most ADRs (Rao, 2015). FLOT and CAPOX regimens accounted for the most ADRs among gastric cancer patients. A similar study reported that the FLOT regimen accounted for the majority of neutropenia in metastatic gastric cancer patients (Al-Batran et al., 2008) and 37.1% in resectable gastric cancer patients (Farrokhi et al., 2022). FOLFOX and FOLFIRI regimens used in colorectal cancer patients had a sizeable percentage of ADRs in our setting, which agrees with the previous study

where FOLFOX and FOLFIRI accounted for the highest proportion of ADRs (Negarandeh et al., 2020).

The most prevalent ADRs among patients with esophageal cancer were nausea and vomiting, followed by anaemia. Nausea/ vomiting, anaemia and neutropenia were the most common ADRs seen in gastric cancer patients. This is consistent with the findings of Ethiopian cancer patients, which found that nausea and vomiting, neutropenia and anaemia were the most frequent ADRs observed (Belachew et al., 2016). Moreover, a study on Indian cancer patients also stated that nausea and vomiting were found to be the most common ADRs (Chopra et al., 2016).

Neutropenia, anaemia, diarrhoea and peripheral neuropathy were the most frequent ADRs in patients with colorectal cancer. A Nepal investigation revealed that nausea, vomiting and neuropathies as the most common ADRs in patients with cancer (Tamang et al., 2022). In addition, a study conducted in Iran found that the most often detected ADRs in cancer patients were nausea and vomiting and neutropenia (Lavan et al., 2019). The revelations of these studies suggest that implementing effective preventive measures is required to lessen the burden of the above ADRs in our setting.

Most of the observed ADRs had possible causality scores and mild severity levels. Correspondingly, an Indian investigation indicated that the majority of ADRs in patients with cancer had a possible causality score and a mild severity level (Wahlang et al., 2017).

Another study also demonstrated that the predominant proportion of adverse drug reactions were possible causality scores and mild severity in patients with cancer (Chopra et al., 2016). In contrast, earlier research found that 50% of ADRs were probable causality scores and moderate severity levels (Tamang et al., 2022). An Ethiopian investigation found that the utmost ADRs in cancer patients were severe adverse drug reactions (Belachew et al., 2016).

In our setting, the majority of the observed ADRs were preventable, which concurred with previous studies (Lavan et al., 2019; Sharma et al., 2018; Singh et al., 2017; Singh & Singh, 2018). In contrast, other studies reported that most ADRs in patients with cancer were non-preventable (Ramasubbu et al., 2020; Thakur et al., 2022).

Among gastrointestinal cancer patients, advanced stages of disease and co-morbidity were the significant determinants of DRPs. A comparable study in Ethiopia found that patients with colorectal cancer who were older, had co-morbidities and used more than five drugs had higher odds of having DRPs (Kefale et al., 2022). A cervical cancer study also showed that cancer stage and co-morbidity were significant determinants of DRPs (Kefale et al., 2022). In other studies, co-morbidity was significantly associated with the occurrence of DRPs (Degu & Kebede, 2021; Sisay et al., 2015).

Advanced-stage (III and IV) disease was the significant determinants of need for additional drug therapy among colorectal cancer patients. Nonetheless, none of the variables was the significant determinant of the need for additional drug therapy among esophageal and gastric cancer patients.

In gastric cancer patients, comorbidity was the significant determinant of drug-drug interactions. However, none of the variables was the significant determinant of drug-drug interaction among esophageal and gastric cancer patients. This could probably be linked to the use of multiple medications in co-morbid gastric cancer patients that can increase the chance of potential drug-drug interactions. In other studies older age (>61 years) and the use of more than seven drugs were a significant determinants of potential drug-drug interactions in cancer patients (Ismail et al., 2020; Tavakoli-Ardakani et al., 2013).

Among gastrointestinal cancer patients chemotherapy was the significant determinants of adverse drug reactions suggesting the need for preventive measures to reduce the burden of ADRs among those patients. Other study reported polypharmacy and drug-drug interactions were the significant factors affecting the occurrence of ADRs in older cancer patients (Mohamed et al., 2023).

Strengths and limitations of the study

The study comprehensively assessed DRPs using predesigned data collection tools by comparing them with the standard treatment protocols of each gastrointestinal cancer. However, the study did not address the impact of the identified DRPs on treatment outcomes and healthcare costs. In addition, the study did not make clinical pharmacist interventions for the identified DRPs. The causality of the ADRs may not be accurately determined in this study design.

4.6 Conclusions

DRPs were highly prevalent among patients with gastrointestinal cancer. Most of the identified ADRs had mild severity levels and were preventable. Co-morbidity and advanced stages of disease were the statistically significant determinants of DRPs.

4.7 Recommendations for policy and practice

DRPs were highly prevalent in gastrointestinal cancer patients due to comorbidities and advanced-stage disease. Therefore, close monitoring is required in patients with multiple illnesses and advanced stages to reduce this high burden of DRPs. The study showed that drug-drug interactions were more frequent among patients with gastrointestinal cancer. Therefore, medication interaction checker software should be used extensively at the prescription and dispensing stages to minimize the significant morbidity of this undesired occurrence. Since most ADRs are preventable, preventive measures such as detailed assessment of medical history, dose optimization, supportive care, patient education and pharmacovigilance should be implemented during chemotherapy treatment to minimize the frequency and severity of ADRs among patients with gastrointestinal cancer.

4.8 Recommendations for further research

Further studies should be done to help design DRPs-preventive strategies such as medication reconciliation, risk factor identifications, clinical pharmacist-led interventions and patient education in gastrointestinal cancer patients. Future prospective cohort studies involving a large number of cancer patients should be conducted to assess the impact of DRPs on the economic burden from the patient, hospital and healthcare provider perspectives.

CHAPTER FIVE: HEALTH-RELATED QUALITY OF LIFE AMONG PATIENTS WITH ESOPHAGEAL, GASTRIC AND COLORECTAL CANCER AT KENYATTA NATIONAL HOSPITAL

Abstract

Background

Despite the advancement of modern treatment approaches, advanced stages of gastrointestinal cancer patients progress rapidly and can jeopardise the patient's health-related quality of life. In addition, a significant decline in quality of life is observed as cancer progresses, with a sharp decline in the advanced stages. There is insufficient data about gastrointestinal cancer patients' health-related quality of life.

Objective

To assess health-related quality of life in esophageal, gastric and colorectal cancer patients.

Methods

A cross-sectional study was employed among 160 esophageal, 103 gastric, and 96 colorectal cancer patients. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaires were used to assess the health-related quality of life. Data were collected using a researcher-administered questionnaire after training the research assistants. The data entry and analysis were carried out using SPSS 26.0 statistical software. A bivariable and multivariable binary logistic regression analysis was employed to investigate determinants of health-related quality of life at a 0.05 level of significance.

Results

The present study showed that most esophageal (118, 73.7%), gastric (75, 72.8%) and colorectal (75%, 72) cancer patients had a poor overall health-related quality of life in our setting. However, most gastrointestinal cancer patients did not have significant problems in the symptoms domain of health-related quality of life. Co-morbid esophageal cancer patients were 3.9 times (AOR=3.9, 95% CI= 2.4-5.8, p=0.02) more likely to have poor HRQoL compared to patients without co-morbidities. In gastric cancer patients, co-morbid patients had 2.3 times

(AOR=2.3, 95% CI= 2.2-4.6, p=0.01) more likely to have a poor HRQoL than patients without co-morbid conditions. Likewise, co-morbid colorectal cancer patients had higher odds of worse HRQoL (AOR=2.5, 95% CI= 1.3-4.5, p=0.03). Furthermore, advanced-stage (stages III and IV) esophageal (AOR=2.8, 95% CI= 1.3-3.7, p=0.03), gastric (AOR=1.8, 95% CI= 1.5-5.3, p=0.04) and colorectal (AOR=10.3, 95% CI= 1.8-13.4, p=0.03) cancer patients had a higher odds of having a poor HRQoL as compared to patients with early-stage disease (stages I and II).

Conclusions

Most patients had a poor health-related quality of life. However, most gastrointestinal cancer patients did not have significant problems in the symptoms domain of health-related quality of life. Advanced-stage and co-morbidities were significant determinants of poor health-related quality of life. Therefore, early diagnosis and optimal treatment modalities are also indisputably important to mitigate health-related quality of life.

5.1 Introduction

Health-related quality of life is defined as the extent to which a person's life functions and their perceived well-being in physical, mental, and social health domains (Karimi & Brazier, 2016). From diagnosis to treatment, cancer survivors face mental, physical, and economic challenges and confusion regarding their social roles (Kim & Yoon, 2021). Furthermore, cancer patients requiring palliative care have markedly diminished HRQoL (Selman et al., 2011).

EORTC QLQ-30, EORTC QLQ–OES18, EORTC QLQ–STO22 and EORTC QLQ–CR29 are standard tools to assess the HRQoL among gastrointestinal cancer patients (Blazeby et al., 2003, 2004; Fayers et al., 2001; Whistance et al., 2009). The EORTC QLQ-30 is the core quality of life questionnaire for cancer patients. It entails items that can assess physical scales (physical, role, emotional, cognitive and social functioning), global health status and symptoms scales (Fayers et al., 2001). The EORTC QLQ–OES18 (symptom domains), EORTC QLQ–STO22 (symptom domains) and EORTC QLQ–CR29 (symptom and functional domains) questionnaires are supplementary modules to be considered in conjunction with EORTC QLQ-30 to assess cancer-specific HRQoL in esophageal, gastric and colorectal cancer patients, respectively (Blazeby et al., 2003, 2004; Fayers et al., 2001; Whistance et al., 2009).

A recent systematic review reported that a substantial proportion of cancer patients had a suboptimal overall HRQoL in Sub-Saharan Africa (Qan et al., 2022). In developing countries, HRQoL is generally low among cancer patients (Abegaz et al., 2018; Nayak et al., 2017).

Advanced-stage cancer patients have low physical and emotional well-being (Jacob et al., 2019). In addition, a significant reduction in HRQoL is observed as cancer progresses, with a sharp decline in the advanced stages (Tran et al., 2020; Zhang et al., 2022). Despite using multiple modern treatment approaches, patients with advanced stages of gastrointestinal cancer deteriorate rapidly and can jeopardise the patient's HRQoL (Wang et al., 2021).

Although several studies reported poor overall HRQoL of patients with gastrointestinal cancer (Flyum et al., 2021; Liu et al., 2018; Thong et al., 2023; van Amelsfoort et al., 2021), there is a paucity of comprehensive data in the Sub-Saharan African countries, including Kenya. Thus, the present investigation evaluated the HRQoL of patients with gastrointestinal cancer at Kenyatta National Hospital.

5.2 General objective

To evaluate the HRQoL of patients with esophageal, gastric and colorectal cancer.

5.3 Specific objectives

1. To determine the HRQoL among patients with esophageal, gastric and colorectal cancer.
2. To examine the determinants of the HRQoL among patients with esophageal, gastric and colorectal cancer.

5.4 Results

5.4.1 HRQoL among gastrointestinal cancer patients

Most esophageal cancer patients (73.7%, 118) had a poor overall HRQoL. One-fourth (42, 26.3%) of the esophageal cancer patients had a good HRQoL in the study setting. The mean HRQoL physical and cognitive functioning score was 62.0±1.7 and 78.0±1.9, respectively. Nonetheless, the enrolled esophageal cancer patients had poor HRQoL in the role (46.5±2.5), emotional (52.6±2.6), and social domains (28.3±2.1) of HRQoL **(Table 5.1)**. Most esophageal cancer patients had poor HRQoL in physical (103, 64.4%) and cognitive domains (129, 80.6%). More than half of the patients had poor HRQoL in the social (134, 83.8%), emotional (92,

57.5%) and role (89, 55.6%) domains of HRQoL **(Figure 5.1)**. The mean score of all symptoms scales of EORTC QLQ-C30 except financial difficulties was <60, which suggested a good HRQoL in symptom scales. The majority of the EORTC QLQ-OES18 symptoms scales also had a mean score of less than 60, which corroborated the findings of the EORTC QLQ-C30 symptoms scale. Nevertheless, the dysphagia and financial difficulties mean scores were 72.2±1.7 and 79.4±2.1, respectively, suggesting a poor HRQoL in the symptom scales of dysphagia and financial difficulties **(Table 5.1)**.

Table 5.1: Health-related quality of life among esophageal cancer patients (n=160)

Questionnaire	Quality of life scale/item	Mean± SEM
EORTC QLQ-C30	Global health status	47.0±1.5
	Functional scales	
	Cognitive functioning	78.0±1.9
	Physical functioning	62.0±1.7
	Emotional functioning	52.6±2.6
	Role functioning	46.5±2.5
	Social functioning	28.3±2.1
	Symptom scales/items	
	Financial difficulties	79.4±2.1
	Appetite loss	51.3±2.7
	Fatigue	50.9±2.0
	Pain	49.1±2.4
	Nausea and vomiting	33.2±2.4
	Constipation	20.3±2.3
	Diarrhoea	20.0±2.3
	Insomnia	18.1±2.0
	Dyspnoea	14.0±1.8
EORTC QLQ- OES18	**Symptom scales/items**	
	Dysphagia	72.2±1.7
	Trouble with taste	55.8±2.6
	Reflux	47.3±2.2
	Trouble swallowing saliva	31.7±2.7
	Eating	33.1±1.8
	Dry mouth	29.2±2.6
	Trouble with coughing	24.6±2.5
	Pain	23.9±1.7
	Choked when swallowing	23.5±2.3
	Trouble talking	19.8±2.0

EORTC QLQ 30: European Organisation for Research and Treatment of Cancer quality of life questionnaire, EORTC QLQ-OES18: European Organisation for Research and Treatment of Cancer quality of life questionnaire for oesophageal Cancer, SEM: Standard error of the mean.

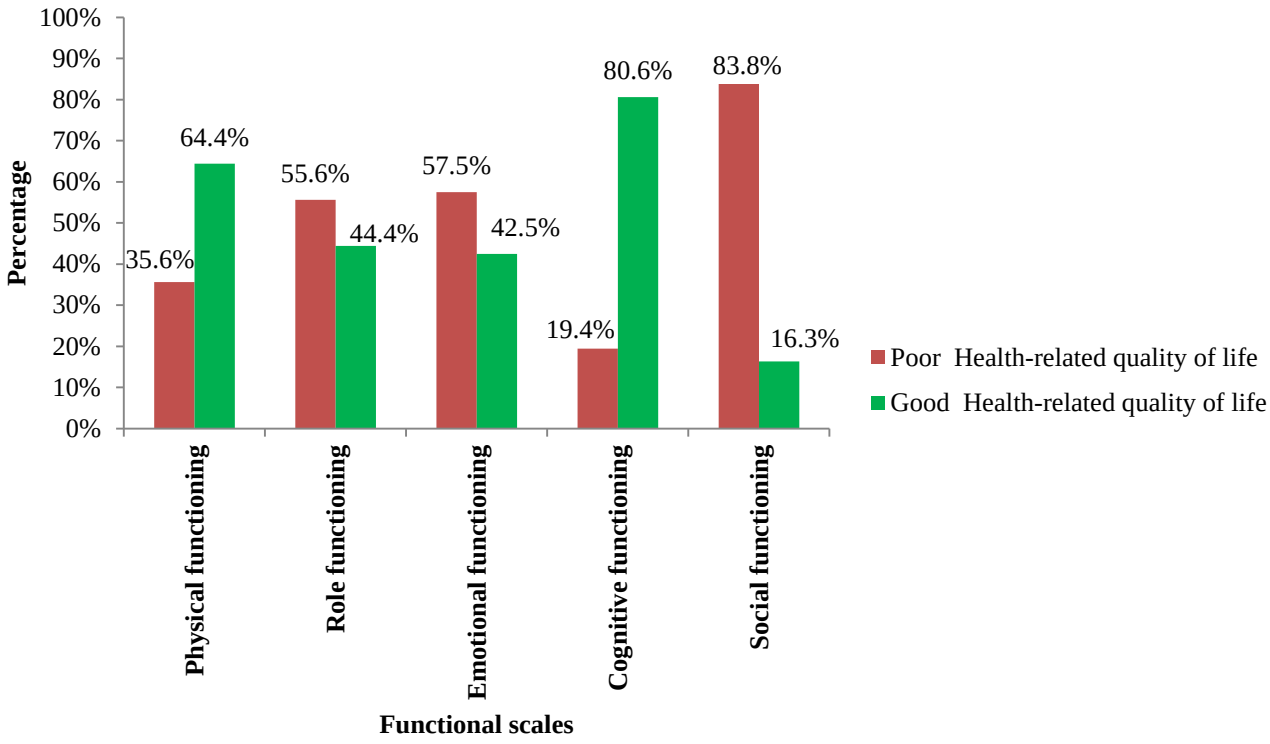


Figure 5.1: Health-related quality of life in the functional domains among esophageal cancer patients (n=160)

The study depicted that 75 (72.8%) of gastric cancer patients had a poor overall HRQoL, while 28 (27.2%) had a good HRQoL. The mean scores for emotional and cognitive functioning were 62.5±3.5 and 85.4±1.9 among gastric cancer patients, respectively. The mean score of the physical (57.2±2.1), role (37.1±3.0) and social (36.6±2.9) functioning were below the recommended mean score **(Table 5.2)**. Furthermore, more than two third of the patients had a poor HRQoL in the role (74, 71.8%) and social (78, 75.7%) functioning domains of HRQoL. However, more than 50.0% of gastric cancer patients had good HRQoL in the physical (58, 56.3%), emotional (59, 57.3%) and cognitive (95, 92.2%) domains of HRQoL **(Figure 5.2)**.

In almost all of the symptom scales of EORTC QLQ-C30 and EORTC QLQ- STO22, the mean score was above the recommended level (<60) of mean score among gastric cancer patients. However, taste problems (67.3±3.3) and financial difficulties (81.2±2.7) were the major issues in the symptom scales of the HRQoL domain among patients with gastric cancer **(Table 5.2)**.

Table 5.2: Health-related quality of life among gastric cancer patients (n=103)

Questionnaire	Quality of life scale/item	Mean± SEM
EORTC QLQ-C30	Global health status	50.7±1.6
	Functional scales	
	Cognitive functioning	85.4±1.9
	Emotional functioning	62.5±3.5
	Physical functioning	57.2±2.1
	Role functioning	37.1±3.0
	Social functioning	36.6. ±2.9
	Symptom scales / items	
	Financial difficulties	81.2±2.7
	Fatigue	53.4±2.2
	Pain	52.1±2.9
	Appetite loss	50.8±3.2
	Nausea and vomiting	29.9±2.9
	Dyspnoea	18.4±3.1
	Diarrhoea	16.5±2.3
	Constipation	16.2±2.4
	Insomnia	14.9±2.4
EORTC QLQ- STO22	**Symptom scales/items**	
	Taste	67.3±3.3
	Anxiety	56.2±3.1
	Reflux	55.9±2.6
	Pain	50.4±2.5
	Eating	47.7±2.8
	Body image	34.0±3.5
	Dysphagia	22.1±2.2
	Dry mouth	21.7±3.1
	Hair loss	6.8±1.9

EORTC QLQ 30: European Organisation for Research and Treatment of Cancer quality of life questionnaire, EORTC QLQ-STO22: European Organisation for Research and Treatment of Cancer quality of life questionnaire for gastric Cancer, SEM: Standard error of the mean.

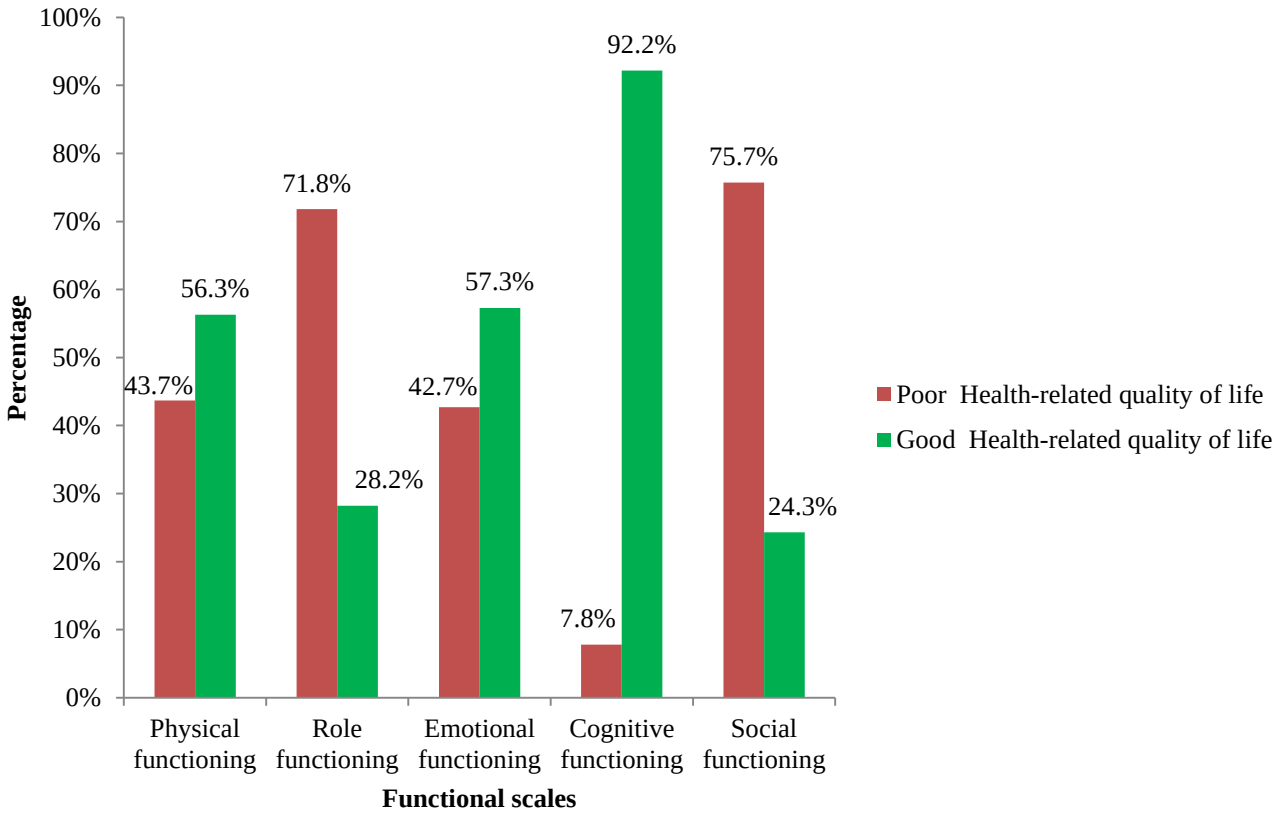


Figure 5.2: Health-related quality of life in the functional domains among gastric cancer patients (n=103)

Most colorectal cancer patients (72, 75%) had a poor overall HRQoL, while 24(25%) had a good overall HRQoL. As per the EORTC QLQ-C30 scale, colorectal cancer patients had good physical (65.9±2.0) and cognitive (83.0±2.0) functioning HRQoL. However, colorectal cancer patients had poor role (58.5±3.0), emotional (52.9±3.4) and social (44.1±2.8) functioning. According to the EORTC QLQ-CR29 scale, colorectal cancer patients had good body image (66.8±2.9) and sexual interest in both men (78.1±6.3) and women (92.3±2.4) though they had poor mean anxiety (41.0±3.5) and weight score (58.0±3.6). In the EORTC QLQ-C30 and EORTC QLQ-CR29 symptom scales, most of the symptoms had a mean score of less than 60, indicating the absence of significant symptoms-related problems **(Table 5.3)**.

Table 5.3: Health-related quality of life among colorectal cancer patients (n=96)

Questionnaire	Quality of life scale/item	Mean± SEM
EORTC QLQ-C30	Global health status	48.9±1.9
	Functional scales	
	Cognitive functioning	83.0±2.0
	Physical functioning	65.9±2.0
	Role functioning	58.5±3.0
	Emotional functioning	52.9±3.4
	Social functioning	44.1±2.8
	Symptom scales/items	
	Financial difficulties	70.1±2.9
	Fatigue	47.9±2.7
	Appetite loss	42.4±3.6
	Pain	31.8±2.7
	Insomnia	25.7±3.1
	Nausea and vomiting	22.4±2.3
	Dyspnoea	16.3±2.7
	Diarrhoea	16.0±2.5
	Constipation	13.5±2.3
EORTC QLQ-CR29	**Functional scales**	
	Sexual interest (women)	92.3±2.4
	Sexual interest (men)	78.1±6.3
	Body image	66.8±2.9
	Weight	58.0±3.6
	Anxiety	41.0±3.5
	Symptom scales/items	
	Taste	40.0±3.1
	Bloating	39.2±3.2
	Flatulence	34.0±2.8
	Abdominal pain	31.9±2.7
	Sore skin	30.6±2.9
	Urinary frequency	30.2±2.3
	Stool frequency	24.1±1.9
	Buttock pain	21.9±2.9
	Dry mouth	20.1±2.8
	Blood and mucus in stool	18.2±2.4
	Faecal incontinence	16.0±2.5
	Embarrassment	15.3±2.6
	Dysuria	13.5±1.9
	Hair loss	12.8±2.1
	Stoma care problems	5.6±1.7
	Urinary incontinence	4.5±1.2
	Impotence	3.8±1.4
	Dyspareunia	1.0±0.6

EORTC QLQ 30: European Organisation for Research and Treatment of Cancer quality of life questionnaire, EORTC QLQ-CR29: European Organisation for Research and Treatment of Cancer quality of life questionnaire for Colorectal Cancer, SEM: Standard error of the mean.

More than half of colorectal cancer patients had good HRQoL in the physical (66, 68.8%), role (54, 56.3%) and cognitive (82, 85.4%) functional domains. However, 64 (66.7%) and 53(55.2%) colorectal cancer patients had poor HRQoL in the social and emotional functioning domains of HRQoL, respectively **(Figure 5.3)**.

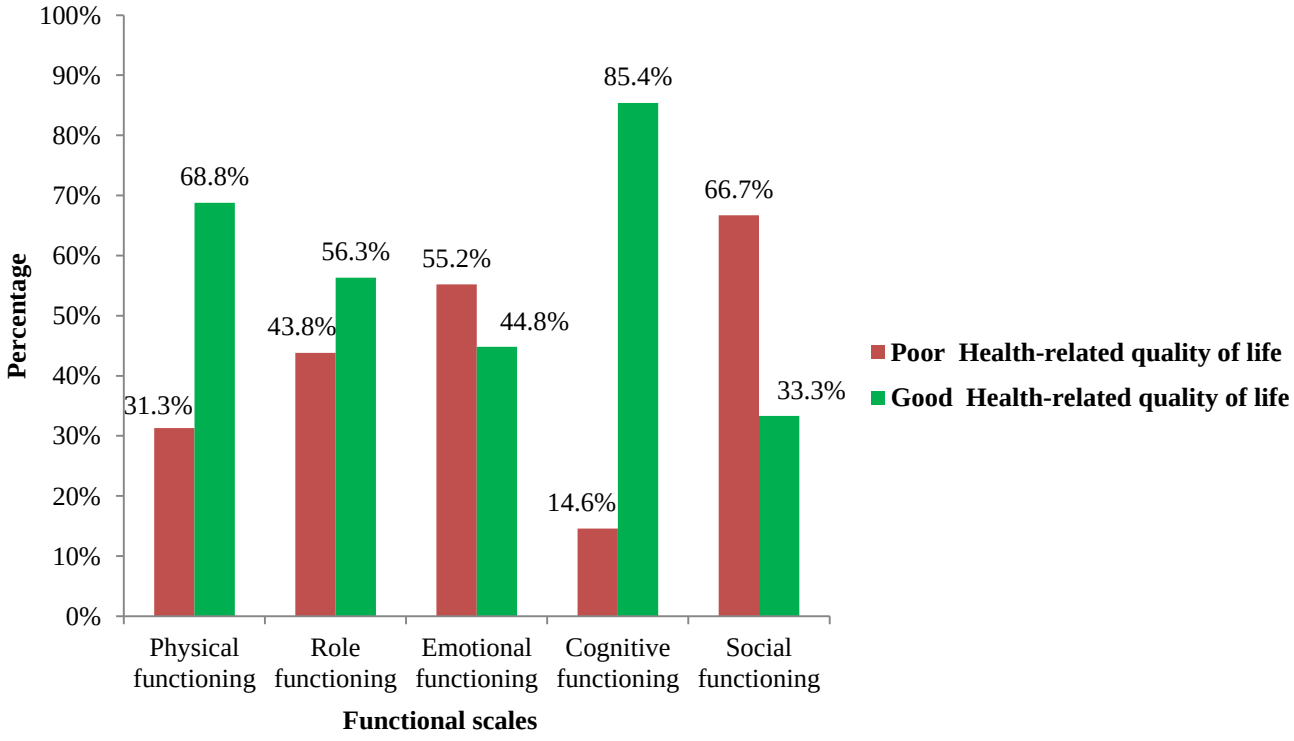


Figure 5.3: Health-related quality of life in the functional domains among colorectal cancer patients (n=96)

5.4.2 HRQoL among patients with different sociodemographic and clinical characteristics

The predominant percentage of esophageal and gastric cancer patients with poor HRQoL were males, above 60 years of age and co-morbid patients. In contrast, most colorectal cancer patients below 60 years of age without any co-existing co-morbid conditions had a poor overall HRQoL. Male patients and those with advanced gastrointestinal cancers (stage III and IV) typically had a poorer overall HRQoL **(Table 5.4)**.

Table 5.4: Health-related quality of life among patients with different sociodemographic and clinical characteristics

Variables	Esophageal cancer (n=160)		Gastric cancer (n=103)		Colorectal cancer (n=96)	
	Good HRQoL (%)	Poor HRQoL (%)	Good HRQoL (%)	Poor HRQoL (%)	Good HRQoL (%)	Poor HRQoL (%)
Age						
<60 years	18(11.3)	53(33.1)	14(13.6)	33(32.0)	15(15.6)	51(53.1)
≥ 60 years	24(15)	65(40.6)	14(13.6)	42(40.8)	9(9.4)	21(21.8)
Gender						
Male	24(15.0)	73(45.6)	17(16.5)	47(45.6)	14(14.6)	48(50.0)
Female	18(11.3)	45(28.1)	11(10.7)	28(27.2)	10(10.4)	24(25.0)
Comorbidity						
Present	22(13.8)	67(41.8)	21(20.4)	44(42.7)	13(13.5)	28(29.2)
Absent	20(12.5)	51(31.9)	7(6.8)	31(30.1)	11(11.5)	44(45.8)
Stage of cancer						
Stage I	3(1.9)	8(5.0)	0(0.0)	1(0.9)	0(0.0)	3(3.1)
Stage II	12(7.5)	43(26.9)	7(6.8)	14(13.6)	3(3.1)	8(8.3)
Stage III	15(9.4)	38(23.7)	14(13.6)	32(31.1)	11(11.5)	21(21.8)
Stage IV	12(7.5)	29(18.1)	7(6.8)	28(27.2)	10(10.4)	40(41.8)

HRQoL: Health-related quality of life

5.4.3 HRQoL of patients on different treatment modalities

A substantial proportion of esophageal cancer patients who underwent esophagectomy (36, 22.5%) had poor overall HRQoL. In addition, 24 (15%) of them who had combined chemotherapy and radiotherapy also had poor overall HRQoL. In gastric cancer patients, use of chemotherapy (18, 17.5%) and gastrectomy (28, 27.2%) led to significantly deranged HRQoL. Similarly, chemotherapy (18, 18.8%) and a combination of surgery and chemotherapy (21, 21.9%) treated colorectal cancer patients had a significantly reduced HRQoL. However, radiotherapy (1, 1%) treated gastric and colorectal cancer patients had minimally deranged HRQoL **(Table 5.5)**.

Table 5.5: Health-related quality of life among different treatment modalities

	Good HRQoL Frequency (%)	Poor HRQoL Frequency (%)
Esophageal cancer treatment regimens (n=160)		
Esophagectomy	13(8.1)	36(22.5)
Chemotherapy and radiotherapy	8(5.0)	24(15.0)
Chemotherapy	2(1.3)	4(2.5)
Radiotherapy	1(0.6)	16(10.0)
Esophagectomy and chemotherapy	1(0.6)	2(1.3)
Symptomatic management	10(6.3)	20(12.5)
Radiotherapy, chemotherapy and esophagectomy	2(1.3)	9(5.6)
Radiotherapy and esophagectomy	5(3.1)	7(4.3)
Gastric cancer treatment regimens (n=103)		
Gastrectomy	5(4.9)	18(17.5)
Chemotherapy and radiotherapy	2(1.9)	4(3.9)
Chemotherapy	8(7.8)	28(27.2)
Radiotherapy	0(0.0)	1(1.0)
gastrectomy and chemotherapy	3(2.9)	10(9.7)
Symptomatic management	9(8.7)	11(10.7)
Radiotherapy, chemotherapy and gastrectomy	1(1.0)	3(2.9)
Colorectal cancer treatment regimens (n=96)		
Surgery	5(5.2)	7(7.3)
Chemotherapy and radiotherapy	7(7.3)	9(9.4)
Chemotherapy	3(3.1)	18(18.8)
Radiotherapy	0(0.0)	1(1.0)
Surgery and chemotherapy	4(4.2)	21(21.9)
Symptomatic management	1(1.0)	5(5.2)
Radiotherapy, chemotherapy and surgery	4(4.2)	11(11.5)

HRQoL: Health-related quality of life

5.4.4 HRQoL among gastrointestinal cancer patients on different chemotherapeutic modalities

A significant proportion (22, 13.8%) of esophageal cancer patients treated with cisplatin and 5-fluorouracil combination therapy had poor HRQoL. Furthermore, 23 (22.3%) patients with gastric cancer treated with FLOT-based regimens had poor HRQoL. Nearly half of the colorectal cancer patients (45, 46.9%) on FOLFOX regimens had poor HRQoL **(Table 5.6)**.

Table 5.6: Health-related quality of life among gastrointestinal cancer patients on different chemotherapeutic regimens

Chemotherapy regimens	Good HRQoL Frequency (%)	Poor HRQoL Frequency (%)
Esophageal cancer chemotherapy regimens (n=160)		
Cisplatin and 5-fluorouracil	8(5.0)	22(13.8)
Carboplatin and paclitaxel	2(1.3)	6(3.8)
Cisplatin and paclitaxel	0(0.0)	4(2.5)
FOLFOX (Folinic acid, 5-fluorouracil and oxaliplatin)	2(1.3)	2(1.3)
Capecitabine	0(0.0)	3(1.9)
Cisplatin	1(0.6)	1(0.6)
Cisplatin and capecitabine	0(0.0)	1(0.6)
DCX (Docetaxel, cisplatin and capecitabine)	1(0.6)	0(0.0)
Gastric cancer chemotherapy regimens (n=103)		
FLOT (Fluorouracil, leucovorin, oxaliplatin and docetaxel)	5(4.9)	23(22.3)
CAPOX (Capecitabine and oxaliplatin)	2(1.9)	5(4.9)
FOLFOX (Folinic acid, 5-fluorouracil and oxaliplatin)	1(1.0)	7(6.8)
CF (Cisplatin and 5-fluorouracil)	1(1.0)	3(2.9)
Cisplatin &Capecitabine	1(1.0)	1(1.0)
EOX (Epirubicin, oxaliplatin and capecitabine)	0(0.0)	2(1.9)
Capecitabine	2(1.9)	2(1.9)
DCF (Docetaxel, cisplatin, and 5-fluorouracil)	1(1.0)	0(0.0)
DOF (Docetaxel, oxaliplatin and 5-Fluorouracil)	0(0.0)	1(1.0)
Docetaxel	0(0.0)	1(1.0)
Colorectal cancer chemotherapy regimens (n=96)		
FOLFOX (Folinic acid, 5-fluorouracil and oxaliplatin)	12(12.5)	45(46.9)
CAPOX (Capecitabine and oxaliplatin)	3(3.1)	5(5.2)
FOLFIRI (Folinic acid , 5-fluorouracil and irinotecan	1(1.0)	6(6.3)
Capecitabine	2(2.1)	3(3.1)

HRQoL: Health-related quality of life

5.4.5 Determinants of HRQoL among gastrointestinal cancer patients

Co-morbidity esophageal cancer patients were 3.9 times (AOR=3.9, 95% CI= 2.4-5.8, p=0.02) more likely to have poor HRQoL compared to those without co-morbidities. In gastric cancer patients, co-morbid patients had 2.3 times (AOR=2.3, 95% CI= 2.2-4.6, p=0.01) more likely to have a poor HRQoL than patients without co-morbid conditions. Likewise, co-morbid colorectal cancer patients had higher odds of worse HRQoL (AOR=2.5, 95% CI= 1.3-4.5, p=0.03). Furthermore, advanced-stage (stages III and IV) esophageal (AOR=2.8, 95% CI= 1.3-3.7, p=0.03), gastric (AOR=1.8, 95% CI= 1.5-5.3, p=0.04) and colorectal (AOR=10.3, 95% CI= 1.8-13.4, p=0.03) cancer patients had a higher odds of having a poor HRQoL as compared to patients with early-stage disease (stages I and II). The age, gender, education level, histological type and treatment regimens were not statistically significant determinants of poor HRQoL **(Table 5.7)**.

Table 5.7: Determinants of health-related quality of life among gastrointestinal cancer patients

	Esophageal cancer				Gastric cancer				Colorectal cancer			
Variable	Bivariable Analysis COR (95%CI)	P-value	Multivariable Analysis AOR(95%CI)	P-value	Bivariable Analysis COR (95%CI)	P-value	Multivariable Analysis AOR(95%CI)	P-value	Bivariable Analysis COR (95%CI)	P-value	Multivariable Analysis AOR(95%CI)	P-value
Age (in years)												
<60 years	1		1		1		1		1		1	
≥60 years	1.1(0.5-2.2)	0.8	1.2(0.5-2.6)	0.7	1.3(0.5-3)	0.6	1.7(0.6-4.6)	0.3	1.5 (0.6-3.8)	0.4	0.9(0.3-3.1)	0.9
Gender												
Male	1		1		1		1		1		1	
Female	0.8 (0.4-1.7)	0.6	1.1 (0.5-2.4)	0.8	1.1(0.4-2.6)	0.8	1.1(0.4-3)	0.8	1.4(0.6-3.7)	0.5	1.5(0.5-4.2)	0.4
Education level												
Formal education	1		1		1		1		1		1	
Informal education	1.6 (0.6-4.6)	0.4	1.8(0.6-5.9)	0.3	0.3(0.1-1)	0.06	0.2(0.1-2.2)	0.1	1.2(0.2-6.7)	0.8	1.5(0.2-10.8)	0.7
Co-morbidity												
Absent			1		1		1		1		1	
Present	2.8 (1.4-2.7)	**0.03***	3.9(2.4-5.8)	**0.02***	2.5 (1.2-4.2)	**0.04***	2.3(2.2-4.6)	**0.01***	1.5(1.2-2.4)	**0.02***	2.5(1.3-4.5)	**0.03***
Histological type												
Squamous cell carcinoma	1		1		1		1		1		1	
Adenocarcinoma	0.4 (0.1-1.9)	0.2	0.4(0.1-1.8)	0.2	0.6(0.2-1.4)	0.4	0.5(0.3-1.2)	0.2	0.6(0.2-1.4)	0.7	0.7(0.3-1.6)	0.8
Stage of the disease												
Early stage (I &II)	1		1		1		1		1		1	
Advanced stage (III &IV)	1.7 (1.4-2.5)	**0.04***	2.8(1.3-3.7)	**0.03***	2.8(1.4-4.1)	**0.02***	1.8(1.5-5.3)	**0.04***	2.3(1.3-4.9)	**0.03***	10.3(1.8-13.4)	**0.03***
Treatment regimen												
Combination therapy	1		1				1		1		1	
Surgery	0.8 (0..4-1.9)	0.7	0.9(0.4-2.1)	0.8	1.9	0.6	2.4(0.7-8.6)	0.2	0.4 (0.1-1.3)	0.1	0.1 (0.1-0.9)	0.4
Chemotherapy	1.2 (0.2-6.9)	0.8	1.5 (0.2-9.6)	0.7	1.8	0.7	1.5(0.5-4.5)	0.5	1.9 (0.5-7.6)	0.3	2.2 (0.5-8.9)	0.3
Radiotherapy	0.1 (0.2-1.2)	0.1	0.1 (0.2-1.2)	0.06	1.2	0.2	1.2 (0.3-1.4)	1.0	1.7 (0.6-2.3)	0.2	0.1 (0.3-2.2)	1.0

CI: Confidence interval, AOR: Adjusted odds ratio, COR: crude odds ratio, * statistically significant, p-value ≤0.05

5.5 Discussions

Although several studies indicated a generally diminished HRQoL in gastrointestinal cancer patients (Flyum et al., 2021; Liu et al., 2018; Thong et al., 2023; van Amelsfoort et al., 2021), there is a notable scarcity of research focusing on HRQoL in gastrointestinal cancer patients in sub-Saharan Africa, including Kenya. Therefore, this study purposed to investigate HRQoL among esophageal, gastric and colorectal cancer patients.

The study revealed that esophageal cancer patients had poor overall HRQoL which suggests the need to ensure effective treatment and improve long-term outcomes to enhance quality of life. This finding is in agreement with other studies which reported a significantly impaired HRQoL among esophageal cancer patients (Dalhammar et al., 2022; Dan Wang et al., 2019; Liu et al., 2018; Scarpa et al., 2011; Schandl et al., 2016). Various studies reported that older, co-morbid and advanced-stage cancer patients had poor HRQoL (Backemar et al., 2020; Jacob et al., 2019; Quinten et al., 2015; Ximenes et al., 2020, 2021). Hence, this high burden of poor HRQoL revealed in our study could be linked to the predominance of co-morbid and advanced-stage esophageal cancer patients in our setting. In sub-Saharan Africa, cancer care is suboptimal due to the shortage of diagnostic facilities and the high cost of treatment (Omotoso et al., 2023). Therefore, this lack of access to optimal healthcare services and treatments can also worsen the low HRQoL.

The mean HRQoL score of physical and cognitive functioning was higher in esophageal cancer patients, suggesting good HRQoL in these domains. In contrast, studies in Sweden revealed that esophageal cancer patients had poor HRQoL in their physical functioning (Dalhammar et al., 2022; Sunde et al., 2021). However, esophageal cancer patients had suboptimal HRQoL in the role, emotional, global health and social domains of HRQoL that might be related to psychological distress due to the diagnosis of cancer and its treatment-related adverse drug reactions and future uncertainties.

The majority of esophageal cancer patients had good HRQoL in the symptom scales, with the exception of challenges related to financial difficulties. In contrast, several studies showed poor HRQoL in the symptom scales among esophageal cancer patients (Dalhammar et al., 2022; Sunde et al., 2021; Wang et al., 2022). These variations could be the possibility of having better symptomatic management care in our setting as a national referral facility.

The majority of gastric cancer patients exhibited poor overall HRQoL. This is in agreement with other studies (van Amelsfoort et al., 2021; Zhang et al., 2022; Zhang et al., 2018). The mean emotional and cognitive functioning scores were higher among gastric cancer patients. However, the mean score of the physical, role, global health and social functioning was low (<60), suggesting a poor HRQoL in those functional scales of HRQoL in gastric cancer patients. Similarly, previous studies reported gastric cancer patients had a worse functioning score in most domains (Dalhammar et al., 2022; Wang et al., 2022). Therefore, optimal management and early initiation treatment modalities are essential to improve this domain of HRQoL. In the symptom domains, most gastric cancer patients had a good quality of life except for the problem with taste symptoms.

Colorectal cancer patients generally exhibited a suboptimal score (<60) on the global, role, emotional and social functioning even though physical and cognitive functioning were satisfactory. This finding is contrasted with the German study which reported a high median score in all the physical domains and global scales (Ratjen et al., 2018). Moreover, previous studies reported that most colorectal cancer patients had good HRQoL in the global score (Jansen et al., 2010; Siddiqui et al., 2023). These disparities in HRQoL between our setting and other studies are likely attributable to differences in the quality of care, stage of disease and co-morbidity. The higher prevalence of co-morbidities (Cummings et al., 2018) and the advanced stages of diseases (Marventano et al., 2013) at diagnosis may be linked to the poor HRQoL in the above domains due to the refractory nature of the diseases and the complexity of regimens used to treat those conditions.

In the symptom scale, colorectal cancer patients had a mean score of less than 60 in most of the symptom items, indicating the absence of major symptoms-related problems. Vietnamese and Chinese studies reported substantial problems with pain and anxiety symptoms among colorectal cancer patients (Huang et al., 2018; Tran et al., 2020). In addition, most colorectal cancer survivors had long-term depression, distress and bowel problems (Jansen et al., 2010). The absence of major symptoms-related problems in colorectal cancer patients might be related to the availability of effective symptom management and social support in the study setting. Furthermore, studies have documented that a significant number of cancer survivors face financial difficulties (Altice et al., 2017; Gordon et al., 2017; Yabroff et al., 2020), suggesting

that a subsidized cost of cancer care may be vital in improving HRQoL in colorectal cancer patients.

In our setting, co-morbidities and advanced stage of disease were the significant determinants of poor HRQoL. This is probably due to the necessity of more extensive and aggressive treatment regimens which can derange HRQoL. A Chinese study revealed that the level of education and nutritional support significantly affected the HRQoL in esophageal cancer patients (Dan Wang et al., 2019). A study showed that patients with early-stage disease had a better HRQoL than advanced-stage esophageal cancer patients (Wen et al., 2015). An Ethiopian review reported the metastatic stage and low income level as determinants of poor HRQoL in cancer patients (Ayalew et al., 2022). Hence, it is crucial to implement vigilant monitoring and promptly initiate the most effective treatment approaches for patients with comorbidities and advanced-stage gastrointestinal cancer.

Strengths and limitations of the study

The study comprehensively investigated HRQoL by using standard general and cancer-specific HRQoL assessment tools among the selected gastrointestinal cancers. This was the first study that investigated the determinants of HRQoL in esophageal, gastric and colorectal cancer patients in Kenya. Hence, it can be used as baseline data for further studies. Nonetheless, the study was conducted in a single healthcare facility and did not address the long-term impacts of various treatment approaches on HRQoL. Moreover, the tools used to assess HRQoL require the patients to recall events that happened in the past. Thus, the responses were dependent on the individuals' memories, and recall bias was possible. Because of the cross-sectional nature of the study, the HRQOL assessment took place only at a specific point in the patient's life, with no subsequent observations or follow-up.

5.6 Conclusions

Most esophageal (73.7%), gastric (72.8%) and colorectal (75%) cancer patients had poor overall HRQoL in our setting. However, most gastrointestinal cancer patients did not have significant problems in the symptoms domain of HRQoL. Co-morbidity and advanced stage of disease were the significant determinants of poor HRQoL.

5.7 Recommendations for policy and practice

Most of the patients had advanced-stage disease; hence, regular exercise, proper nutrition, psychosocial support, adequate symptoms and pain management should be given to improve the HRQoL of gastrointestinal cancer survivors. Gastrointestinal cancer patients had a poor overall HRQoL due to chemotherapy, comorbidities and advanced cancer. Therefore, intensification of routine monitoring of the disease and the treatments should be actively implemented to improve the HRQoL. Early diagnosis and access to optimal treatment modalities are also indisputably important to mitigate HRQoL. In our context, the majority of patients had financial difficulties in the symptom domains of HRQoL. As a result, healthcare institutions should provide subsidised cancer care nationwide to improve HRQoL significantly. In addition, the maximal involvement of cancer patients in health insurance schemes is vital to overcome the financial burden related to the cost of cancer care.

5.8 Recommendations for further research

The study was limited to a single hospital setting and did not address the long-term impacts of various treatment approaches on HRQoL. Hence, a large prospective cohort study should be conducted to assess the long-term impacts of various treatment modalities on the HRQoL of gastrointestinal cancer patients.

CHAPTER SIX: SURVIVAL OUTCOMES AMONG ESOPHAGEAL CANCER PATIENTS AT KENYATTA NATIONAL HOSPITAL

Abstract

Background

Despite significant advances in therapy, contemporary esophageal cancer therapeutic interventions offer minimal survival benefits. In addition, patients with esophageal cancer in developing countries have a dismal survival rate despite the availability of modern therapies. There is a lack of such data among Kenyan patients.

Objective

To evaluate the determinants of survival outcomess among esophageal cancer patients.

Methods

A retrospective one-arm cohort study was employed among 299 randomly sampled adult patients with esophageal cancer. A data abstraction tool was used to collect the patients' clinical characteristics and survival outcome parameters. Treatment response, mortality, survival times and distance metastasis were measured during the follow-up period. Data entry and statistical analysis were performed with SPSS version 26.0 software. The Kaplan-Meier and Cox regression analyses were used to assess the median survival time and determinants of mortality, respectively.

Results

Patients with esophageal cancer had significant mortality (43.1%), disease progression (20.1%), and non-response (13%), with a 25% five-year survival. During the follow-up period, 11.1% of patients demonstrated signs of distant metastases. The determinants of survival in the advanced stage (III &IV) disease were radiotherapy (AHR: 3.3, 95% CI: 1.4-7.8, p=0.007), chemotherapy (AHR:3.9, 95% CI: 1.2-6.1, p=0.020) and chemoradiation (AHR:5.6, 95% CI:1.6-10.2, p=0.006). Esophagectomy (AHR: 1.9, 95% CI: 1.2-3.6, p=0.049) was the only therapy with a significant determinant of survival of patients with early-stage (I and II) disease.

Conclusions

Esophageal cancer patients had high mortality (43.1%) and low (25%) five-year survival. Thus, there is an urgent need for early identification and optimal management to enhance survival in patients with esophageal cancer.

6.1 Introduction

Esophageal cancer is the seventh most common type of cancer globally, with Asian countries experiencing the highest incidence rate (Huang et al., 2021). Furthermore, it is still a major cause of death and morbidity across the globe (Kamangar et al., 2020; Uhlenhopp et al., 2020). The mortality and incidence of cancer of the esophagus are rising in Africa, with a larger preponderance in men owing to frequent cigarette smoking and drinking of alcohol (Asombang et al., 2019). Esophageal cancer is rising at a worrisome rate in regions of Sub-Saharan Africa with unequal geographic distributions (Kachala, 2010).

This cancer has two main histological types: squamous cell carcinoma and adenocarcinoma, with squamous cell carcinoma predominating globally (Jain & Dhingra, 2017; Melhado et al., 2010). Consuming processed meat, drinking alcohol, smoking cigarettes, and drinking hot tea are significantly associated with the risk of developing esophageal cancer (Asombang et al., 2019; Castro et al., 2018).

At diagnosis, the majority of patients are identified at a late stage, already having either local or distant metastases. In addition, numerous treatments do not provide satisfactory improvements in survival rates in contrast to other cancer patients (Yang et al., 2020). In spite of the advancements in the treatment of cancer of the esophagus, the prognosis for the disease remains very dismal (Asombang et al., 2019; Huang & Yu, 2018). Complications that arise after surgery are the leading cause of mortality in patients diagnosed with esophageal cancer (Xu et al., 2020). Nonetheless, a prior review in Africa showed that esophagectomy and chemoradiation treatment resulted in a marginally better survival rate (Asombang et al., 2019). The overall survival rate at five years is quite poor, with the lowest possibilities of cure (Fan et al., 2020; He et al., 2020; Wong & Malthaner, 2000). Although various therapeutic options are available, the prognosis remains dismal. As a result, obtaining the targeted therapeutic aim remains difficult (He et al., 2021). Hence, the study purposed to investigate the survival outcomes among esophageal cancer patients at KNH.

6.2 General objective

To assess the survival outcomes among esophageal cancer patients.

6.3 Specific objectives

1. To determine the median and mean survival time and year of survival among patients with esophageal cancer.
2. To assess the response to treatment and new metastasis among patients with esophageal cancer.
3. To identify the determinants of survival among patients with esophageal cancer.

6.4 Results

6.4.1 Sociodemographic characteristics of esophageal cancer patients

The study reported that the median age of the patients was 58.0±12.7 years (range 18-93 years), with six months median follow-up time. Most patients were males (178, 59.5%) and had a primary level of education (177, 59.2%), while the least proportion had no formal education. Most patients (145, 48.5%) were occupationally self-employed. The majority of the patients (298, 99.7%) did not have any family history of cancer **(Table 6.1).**

Table 6.1: Socio-demographic characteristics of esophageal cancer patients (n=299)

Variable	Frequency (%)
Age (in years)	
< 60 years	155(51.8)
≥60 years	144(48.2)
Gender	
Male	178(59.5)
Female	121(40.5)
Marital status	
Single	22(7.4)
Married	250(83.6)
Divorced	7(2.3)
Widowed	20(6.7)
Educational status	
Primary	177(59.2)
Secondary	103(34.4)
Tertiary	12(4.0)
Informal	7(2.3)
Occupational status	
Housewife	18(6.0)
Government employee	18(6.0)
Unemployed/Retired	43(14.4)
Self-employed	145(48.5)
Family history of cancer	
No	298(99.7)
Yes	1(0.3)

6.4.2 Clinical characteristics of esophageal cancer patients

The most prevalent histological form of esophageal cancer was squamous cell carcinoma (281, 94%). Most patients were diagnosed with stages II and III of the disease, accounting for 247 cases (82.7%), while 38 cases (12.7%) were diagnosed with stage IV at the time of diagnosis. The most prevalent sites of metastases were the lung and liver. However, only a few patients experienced multiorgan metastases. Comorbid diseases were present in 124 (41.5%) patients. Hypertension, pneumonia, anaemia, and retroviral disease were the most common co-morbidities **(Table 6.2)**.

Table 6.2: Clinical characteristics of esophageal cancer patients (n=299)

Variable	Frequency (%)
Histological type of cancer	
Adenocarcinoma	18(6)
Squamous cell carcinoma	281(94)
Stage of cancer	
Stage I	14(4.7)
Stage II	141(47.2)
Stage III	106(35.5)
Stage IV	38(12.7)
Comorbidity	
Present	124(41.5)
Absent	175(58.5)
Number of comorbidities	
One	70(23.4)
Two	36(12.0)
≥Three	18(6.0)
Type of comorbidity	
Hypertension	31(10.4)
Pneumonia	22(7.4)
Anaemia	21(7.0)
Retroviral disease	21(7.0)
Acute kidney injury	17(5.7)
Diabetes mellitus	13(4.3)
Sepsis	8(2.7)
Upper gastrointestinal bleeding	8(2.7)
Benign prostatic hyperplasia	7(2.3)
Deep vein thrombosis	6(2)
Chronic kidney disease	5(1.7)
Tuberculosis	5(1.7)
Pulmonary embolism	5(1.7)
Gastric outlet obstruction	4(1.3)
Upper airway obstruction	4(1.3)
Obstructive jaundice	3(1.0)
Chronic heart failure	3(1.0)
Hepatitis	2(0.7)
Esophageal candidiasis	2(0.7)
Cor pulmonale	2(0.7)
Epilepsy	2(0.7)
Gastroesophageal reflux disease	1(0.3)
Arthritis	1(0.3)
stroke	1(0.3)
Hypothyroidism	1(0.3)
Atelectasis	1(0.3)
Distance metastasis at diagnosis	38(12.7)
lung	23(7.7)
Liver	9(3.0)
Brain	2(0.7)
Pancreas	1(0.3)
Bone	1(0.3)
Liver, spleen and lung	1(0.3)
Liver and lung	1(0.3)

6.4.3 Haematological profile of esophageal cancer patients

Most patients had normal haematological parameters in the last follow-up period, although 49 (16.4%) patients had significantly deranged haemoglobin levels. Furthermore, most patients also had normal renal and liver function tests. Nonetheless, 17(5.7%) patients had deranged renal function tests **(Table 6.3)**.

Table 6.3: Haematological parameters of esophageal cancer patients in the last follow-up period (n=299)

Laboratory parameters	Frequency (%)
Total white blood cells	
Normal	296(99.0)
Low	3(1.0)
Neutrophils	
Normal	295(98.7)
Low	4(1.3)
Haemoglobin	
Normal	250(83.6)
Low	49(16.4)
Platelets	
Normal	293(98.0)
Low	6(2.0)
Serum creatinine	
Normal	282(94.3)
Increased	17(5.7)
Liver function test	
Normal	296(99.0)
Significantly deranged	3(1.0)

6.4.4 Treatment regimens of esophageal cancer patients

The predominant treatment modalities employed in our setting were esophagectomy (192, 64.2%), radiotherapy (107, 35.8%), and chemotherapy (69, 23.1%). Symptomatic treatment was used in 18(6%) participants. Among the cohort of patients who underwent chemotherapy, 26 patients (8.7%) were given carboplatin and paclitaxel regimens **(Table 6.4)**.

Table 6.4: Treatment regimens of esophageal cancer patients (n=299)

Treatment regimen	Frequency (%)
Esophagectomy	192(64.2)
Radiotherapy	107(35.8)
Chemotherapy	69(23.1)
Radiotherapy with weekly cisplatin	34(11.4)
Symptomatic management	18(6.0)
Chemotherapy regimens	
Carboplatin+paclitaxel	26(8.7)
Cisplatin+paclitaxel	16(5.4)
Cisplatin+5- fluorouracil	15(5.0)
Folinic acid, fluorouracil and oxaliplatin	3(1.0)
Docetaxel+cisplatin+5- fluorouracil	3(1.0)
Cisplatin+ capecitabine	3(1.0)
Etoposide+cisplatin	1(0.3)
Oxaliplatin+capecitabine	1(0.3)
5- Fluorouracil	1(0.3)

6.4.5 Survival outcomes of esophageal cancer patients

During the follow-up, 29 (11.1%) esophageal cancer patients showed evidence of new distant metastases. The most frequent sites of metastasis were the liver, lungs and brain **(Table 6.5)**.

Table 6.5: Distant metastasis in the last follow-up period among esophageal cancer patients

	Frequency (%)
Distant metastasis in the last follow-up period (n=261)	
No	232(88.9)
Yes	29(11.1)
Sites of metastasis in the last follow-up period (n=261)	
Lung	16(6.1)
Liver	6(2.3)
Brain	3(1.1)
Thyroid	1(0.4)
Pancreas	1(0.4)
Peritoneal cavity	1(0.4)
Lung and liver	1(0.4)

A total of 129 patients, accounting for 43.1% of the study, experienced mortality during the study period. The remaining 170 patients had censored observations. In the last follow-up period,

60 patients (20.1%) exhibited disease progression, while 39 patients (13.0%) demonstrated non-responsive to treatment. Forty-three (14.4%) patients exhibited a partial response, while 23 (7.7%) had a complete response **(Figure 6.1)**.

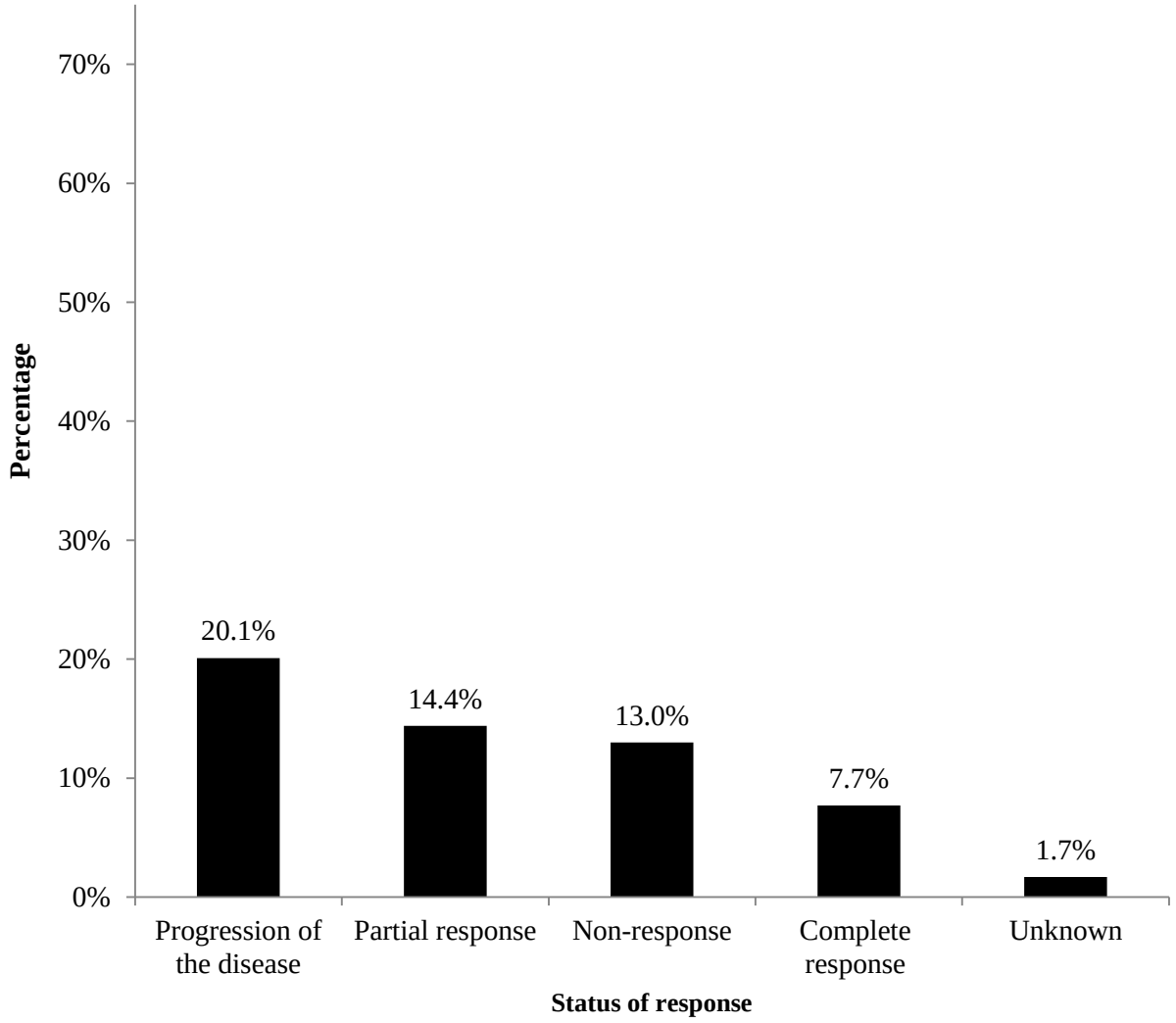


Figure 6.1: Responses to treatment during the last follow-up period (n=299)

The study revealed that the survival of patients at one-year and five-year intervals was 86.0% and 25.0%, respectively. Notwithstanding this fact, the survival declined from one year (86.0%) to five years (25.0%) **(Figure 6.2)**.

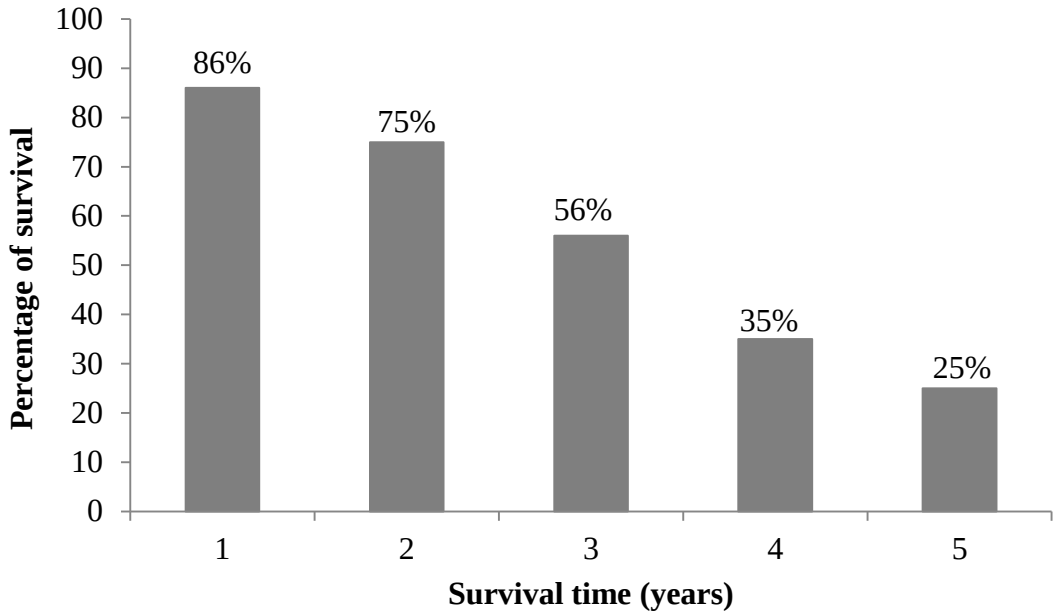


Figure 6.2: Percentage of survival among the study participants (n=299)

The median cancer-specific survival was 43±2.3 months from the time of diagnosis until the final follow-up or mortality. The median metastasis-free survival from diagnosis to the appearance of the first metastasis was 45.8±4.2 months. Despite this, the median cancer-specific survival after metastasis was 23±2.7 months.

There was no significant variation in median survival time across age categories, genders, cancer stages and histological classifications. Patients with comorbidities (24±2.6 months) and distant metastases at diagnosis (11.9±1.3 months) had a lower median survival time than their counterparts. Chemoradiation, radiotherapy and esophagectomy-treated patients exhibited no changes in median survival time compared to their comparator groups. Patients who underwent chemoradiation exhibited a longer median survival time than patients treated with other methods (84.1±1.7 months) **(Table 6.6, Figure 6.3, Figure 6.4, Figure 6.5, Figure 6.6)**.

Table 6.6: Median and mean survival time among esophageal cancer patients (n=299)

Variables	Median survival time (months)± standard error (95% CI)	Mean survival time (months)± standard error (95% CI)	Log-rank test (p-value)
Age (years)			0.8
< 60 years	38±1.1(22.2-41)	87.3±10.1(67.5-107.1)	
≥ 60 years	24±6.4(0.2.-25.4)	41.7±6.4(29.9-54.4)	
Gender			0.1
Male	67.1±4.6(36-79.1)	55.1±4.6(46-64.1)	
Female	84±1.4(51.3-99.2)	71.7±10.4(51.3-92.2)	
Comorbidity			**<0.001***
Present	24±2.6(8.8-64.9)	55.9±3.6(48.8-62.9)	
Absent	66.2±10.6(6.7-77.4)	57.6±10.6(36.7-78.4)	
Stage of cancer			0.4
Early-stage (I and II)	84±4.8 (4.5-89.7)	72.6±11.8 (49.5-95.7)	
Advanced stage (III and IV)	62.8±6(44-71.5)	67.8±7(54-81.5)	
Histological type of cancer			0.9
Adenocarcinoma	57.1±8.2.2(33.7-6.9)	53.1±8.2(37.1-69.1)	
Squamous cell carcinoma	84±2.2(55.7-89.7)	75.8±9.2(57.7-93.7)	
Distant metastasis at diagnosis			**<0.001***
Yes	11.9±1.3(8.4-13.6)	18.9±3.5(11.9-25.9)	
No	84.3±5.2(66.7-89.9)	80.3±9.4(61.7-98.9)	
Distant metastasis in the follow-up period			0.4
Yes	54±4.2(43.1-65.4)	64.2±5.7(53.1-75.4)	
No	84±5.5(55.3-85.7)	86.9±15.2(57.3-116.7)	
Treatment regimen			
Chemotherapy			**0.01***
No	59.1±5.2(39.1-65.1)	57.1±4.1(49.1-65.1)	
Yes	84±10.1(48.6-87.9)	68.3±10.1(48.6-87.9)	
Esophagectomy			0.4
No	72.3±2.5(34.5-78.5)	63.9±12.5(39.5-88.5)	
Yes	83.3±5.9(38.6-85.9)	70.3±5.9(58.6-81.9)	
Radiotherapy			0.1
No	72.4±8.2(35.9-74.9)	75.4±9.9(55.9-94.9)	
Yes	82.4±6.9(52.9-88.1)	69.5±5.9(57.9-81.1)	
Chemoradiation			0.2
No	62.67±5.6(25-69.6)	63.6±5.6(52.6-74.6)	
Yes	84.1±1.7(52.2-89.9)	94.1±13.7(67.2-120.9)	
Symptomatic management			**0.01***
No	62±9.4(21.2-87.2)	79.5±9.3(61.3-97.6)	
Yes	24±11.1(15.4-28.5)	37.4±10.7(16.4-58.5)	

*Statistically significant p-value ≤0.05, CI: Confidence interval

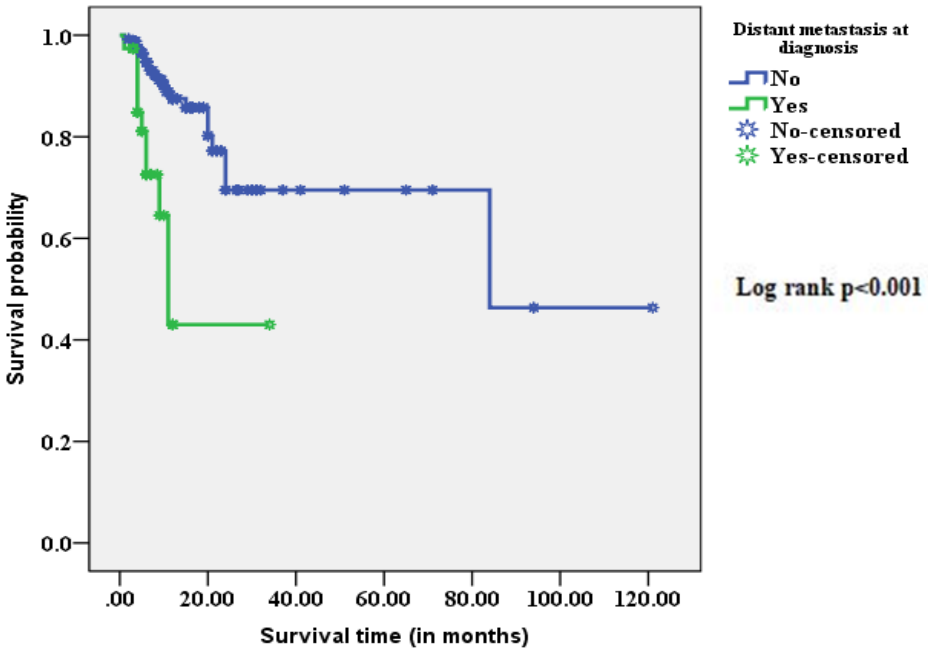


Figure 6.3: Kaplan-Meier survival curve among distant metastasis esophageal cancer patients

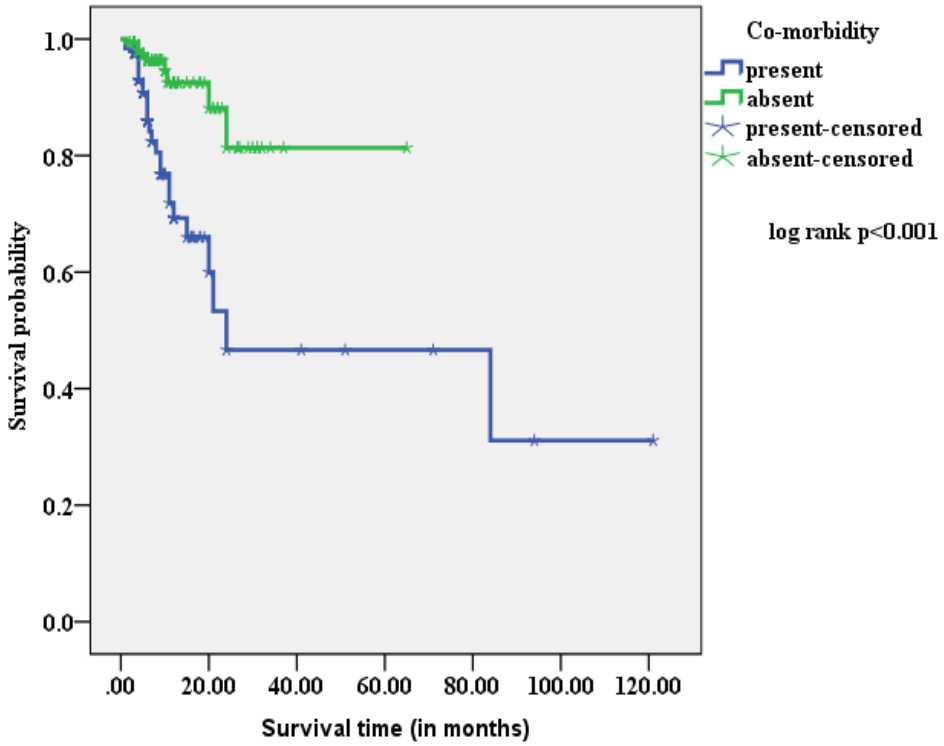


Figure 6.4: Kaplan-Meier survival curve among comorbid esophageal cancer patients

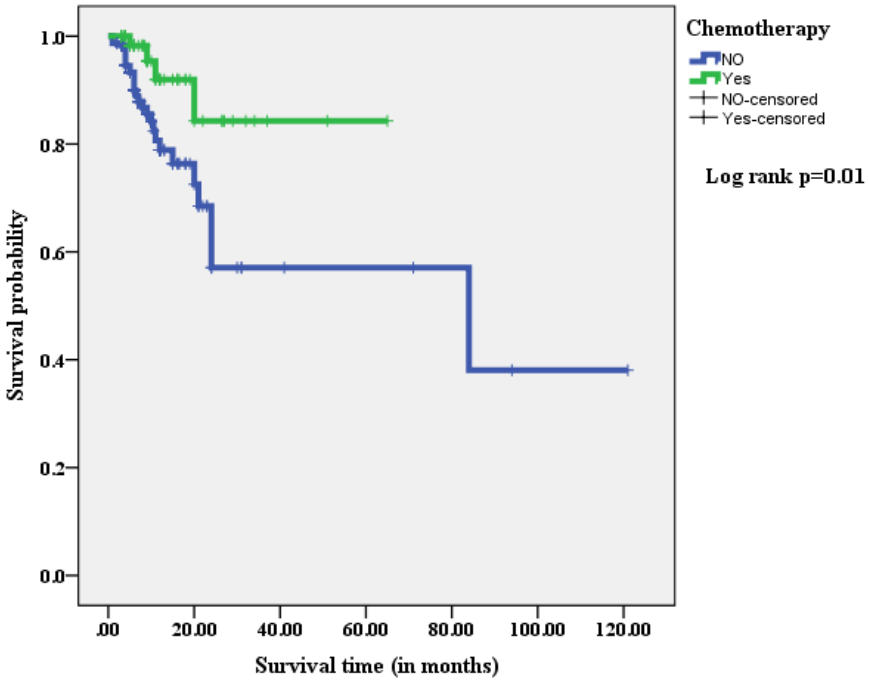


Figure 6.5: Kaplan-Meier survival curve among chemotherapy treated esophageal cancer patients

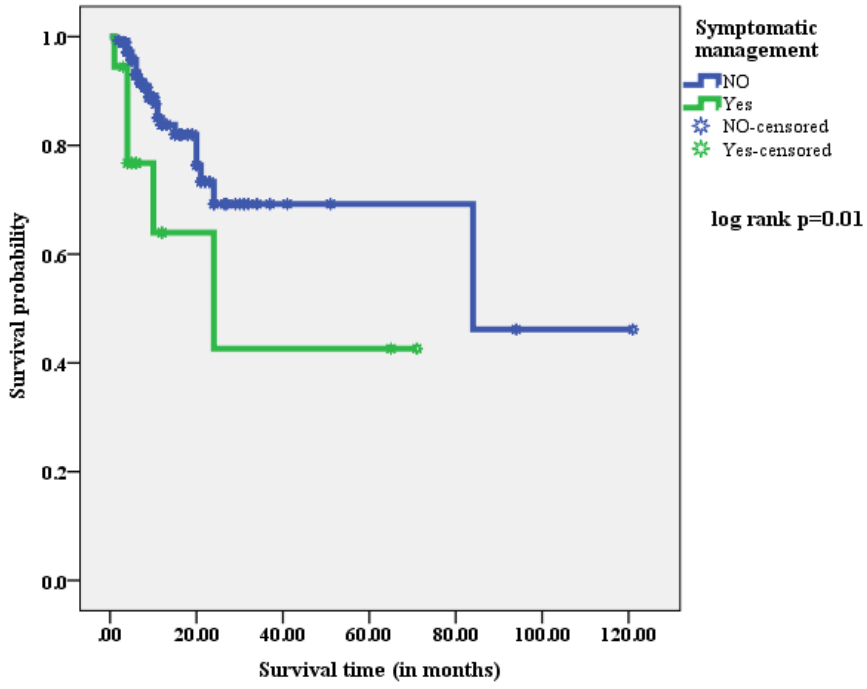


Figure 6.6: Kaplan-Meier survival curve among symptomatically treated esophageal cancer patients

6.4.6 Determinants of survival outcomes among esophageal cancer patients

Patients in advanced stages (stage III &IV) of the cancer with concomitant comorbidities had a 7.5-fold greater death risk than patients who did not have comorbidities (AHR: 7.5, 95% CI: 2.2-12, p=0.001). Moreover, individuals who were not subjected to radiotherapy (AHR: 3.3, 95% CI:1.4-7.8, p=0.007), chemotherapy (AHR:3.9, 95% CI: 1.2-6.1, p=0.020), and chemoradiation (AHR:5.6, 95% CI:1.6-10.2, p=0.006) exhibited a greater likelihood of mortality in comparison to patients who underwent the corresponding therapeutic interventions. In the early stage disease (stages I and II), patients who did not undergo esophagectomy had a higher risk of death (AHR: 1.9, 95% CI: 1.2-3.6, p=0.049) than those treated with esophagectomy. Despite this, the other treatments did not significantly influence the survival of patients diagnosed with early-stage diseases. The survival outcomes of patients with early-stage and advanced-stage cancer were not significantly influenced by histological type of cancer, age and gender **(Table 6.7)**.

Table 6.7: Determinants of mortality among early and advanced-stage esophageal cancer patients

	Early stage (I&II) disease				Advanced stage (III&IV) disease			
Variables	**Bivariable analysis**		**Multivariable analysis**		**Bivariable analysis**		**Multivariable analysis**	
	CHR (95% CI)	**P-value**	**AHR (95% CI)**	**P-value**	**CHR (95% CI)**	**P-value**	**AHR (95% CI)**	**P-value**
Adenocarcinoma	1		1		1		1	
Squamous cell carcinoma	2.1(1.2-3.4)	0.577	2.3(1.2-3.3)	0.982	0.8(0.2-3.4)	0.731	1.2(0.3-5.9)	0.799
Male	1		1		1		1	
Female	3.1(1.1-9.1)	**0.034***	2.9(0.9-9.1)	0.059	0.9(0.4-2.4)	0.897	0.9(0.3-2.5)	0.886
Comorbidity absent	1		1		1		1	
Comorbidity present	1.6(0.9-2.7)	0.083	1.7(0.6-5.1)	0.351	2.7(1.5-4.6)	**0.001***	7.5(2.2-12)	**0.001***
Age <60 years	1		1		1		1	
Age ≥60 years	0.6(0.4-1.1)	0.623	2.3(0.7-7.1)	0.163	0.9(0.5-1.3)	0.485	0.9(0.4-2.6)	0.976
Radiotherapy								
Yes	1		1		1		1	
No	1.3(0.7-2.1)	0.396	1.4(0.7-2.6)	0.311	1.5(0.8-2.5)	0.175	3.3(1.4-7.8)	**0.007***
Esophagectomy								
Yes	1		1		1		1	
No	1.3(0.8-2.2)	0.262	1.9(1.2-3.6)	**0.049***	1.0(0.6-1.6)	0.906	2.8(0.8-3.9)	0.435
Chemotherapy								
Yes	1		1		1		1	
No	1.5(0.8-2.7)	0.248	1.4(0.7-2.7)	0.342	2.6(0.9-7.1)	**0.04***	3.9(1.2-6.1)	**0.020***
Chemoradiation								
Yes	1		1		1		1	
No	1.1(0.5-2.3)	0.838	2.1(0.8-5.0)	0.133	2.3(0.8-6.4)	0.104	5.6(1.6-10.2)	**0.006***

*Statistically significant p-value ≤0.05, CHR: Crude hazard ratio, AHR: Adjusted hazard ratio

6.5 Discussion

The purpose of the study was to examine the survival outcomes of patients diagnosed with esophageal cancer. The five-year survival of esophageal cancer patients was lower compared to findings from Iran, China and South Korea (Delpisheh et al., 2014; Hou et al., 2019; Suzuki et al., 2021). This variation is most likely related to differences in tumour grade, quality of care, comorbidities and age, which may significantly influence the survival of patients.

The median survival time was longer than the study from Ethiopia (4 months). Moreover, the three-year survival in the Ethiopian study (2.4%) was lower than in our setting (Hassen et al., 2021). Despite this, patients from Western countries had a longer median survival time than those from Africa (Chen et al., 2017; Jung et al., 2020; Nassri et al., 2018; Ye et al., 2022). These inconsistencies indicated that cancer treatment in African countries is suboptimal.

The mortality of esophageal cancer in our setting was higher than United States, South Korea, and Japan (Chang et al., 2022; Enofe et al., 2018; Suzuki et al., 2021). This finding may be attributable to the availability of better medical treatment in those countries. Over 80% of esophageal cancer fatalities were reported in developing countries (Van Loon et al., 2018). Likewise, the mortality from esophageal cancer is relatively high in Africa (Asombang et al., 2019). In Sub-Saharan Africa, cancer treatment is the least-priority healthcare service due to the massive burden of infectious diseases and economic constraints. This may lead to high cancer mortality (Jamison et al., 2006).

The study showed that 20.1% of patients exhibited disease progression, while 13.0% and 7.7% of patients demonstrated non-response and complete response to treatment, respectively. In contrast, a study in China (48.9%) and Germany (41.1%) revealed that most esophageal cancer patients had a complete response after treatment (Soror et al., 2018; Zhao et al., 2020). This difference might be attributed to delayed diagnosis that significantly impacted the intended treatment response since a significant proportion of the patients were diagnosed at an advanced stage. A previous study reported patients in the metastatic stage had poor prognoses (Zhang et al., 2021). Therefore, the high metastasis at diagnosis and follow-up could be responsible for the higher prevalence of disease progression in our setting. Co-morbidities in cancer patients may considerably affect survival (Dolan et al., 2013; He et al., 2015; Ichikawa et al., 2016). This higher prevalence of co-morbidities (41.5%) in our setting is linked to higher mortality, disease progression and non-response.

There was no significant difference in survival time observed between patients who underwent esophagectomy, radiotherapy and chemoradiation and those who did not receive any of these treatments. Conversely, a study in Ethiopia found that chemotherapy, radiotherapy and surgery were the significant determinants of survival in esophageal cancer patients (Hassen et al., 2021). Furthermore, a study revealed a fairly low overall survival, although surgically treated patients had an increased survival (Chen et al., 2013). The results of our study indicated that patients who underwent chemoradiation exhibited the highest median survival time compared to those who received other therapeutic modalities. These findings may suggest prioritising chemoradiation treatment strategies in patients with esophageal cancer.

A high Charlson comorbidity score and age may have a detrimental impact on the survival of patients with esophageal cancer (Enofe et al., 2018). Likewise, our findings showed that advanced-stage patients with comorbidities had a higher risk of mortality. The increased mortality might have been attributable to complications arising from multiple co-morbidities that the patients had, like hypertension, sepsis, acute kidney injury and retroviral disease. The findings suggest that patients with co-morbidities that might potentially endanger their lives should be monitored closely.

Despite significant advances in therapy, contemporary esophageal cancer therapeutic interventions offer minimal survival benefits (Yang et al., 2020). Esophagectomy and chemoradiation were shown to be the most effective treatment regimens for improving survival in patients diagnosed with esophageal cancer in Africa (Asombang et al., 2019). In advanced-stage patients, chemoradiation, chemotherapy, radiotherapy and esophagectomy treatment modalities were the determinants of survival in our setting. Another study also reported that chemotherapy-treated patients had improved survival (Kim et al., 2016). Therefore, at advanced stages, these treatment modalities are generally recommended to enhance the survival of these patients.

Nevertheless, esophagectomy was the only determinant of survival in patients with early-stage esophageal cancer. This agrees with another study that reported the significant benefit of surgery in improving survival in recurrent esophageal cancer (Sugawara et al., 2023). Another study reported that chemotherapy, radiotherapy, and esophagectomy were the primary determinants of survival in esophageal cancer patients (Hassen et al., 2021). Furthermore, locally advanced

patients treated with chemoradiation and esophagectomy had long-term overall survival (Sio et al., 2016). This may be due to their direct effect on cancer cells and their ability to prevent cancer from spreading to distant organs.

Strengths and limitations of the study

The study comprehensively examined the survival outcomes of patients with esophageal cancer in a large sample size with long-term follow-up. This was the first study that evaluated the determinants that impacted survival in esophageal cancer patients in Kenya. Hence, it can be used as baseline data for further studies. The incompleteness of medical records was the main limitation of the retrospective cohort study due to the retrospective nature of the study. In this case, the data's accuracy depended on the correctness of the documentation in the study setting.

6.6 Conclusions

Esophageal cancer patients exhibited significant mortality, disease progression, and non-response to treatment. Survival in advanced-stage patients was significantly influenced by treatment modalities such as chemotherapy, chemoradiation, radiotherapy and esophagectomy. The sole factor influencing the survival of patients in the early stages was esophagectomy.

6.7 Recommendations for policy and practice

Due to the significant rate of disease progression and non-response to treatment, early initiation of optimal treatment is highly recommended to mitigate survival outcomes. The late presentation at diagnosis leading to a high mortality among patients with esophageal cancer suggests that widespread screening and awareness programs should be instituted to avert the disaster.

6.8 Recommendations for further research

A prospective cohort study in a multi-centre setting should be conducted to assess the long-term impacts of various treatment modalities on the long-term survival outcomes of esophageal cancer patients.

CHAPTER SEVEN: SURVIVAL OUTCOMES AMONG PATIENTS WITH GASTRIC CANCER AT KENYATTA NATIONAL HOSPITAL

Abstract

Background

The survival outcome of gastrointestinal cancer patients worldwide exhibits significant variability, despite the potential for prolonged survival with early detection. Furthermore, certain regions have a higher prevalence of gastric cancer amongst the younger population. Nevertheless, only a handful of studies were available in East African countries to evaluate survival outcomes in gastric cancer patients.

Objective

To evaluate the survival outcomes of adult patients diagnosed with gastric cancer at Kenyatta National Hospital.

Methods

A retrospective one-arm cohort study was employed among 247 randomly sampled gastric cancer patients. The study included adult patients diagnosed with gastric cancer in the last five years (2016-2020) who had complete documentation of the disease stage and treatment regimens. The data collection process utilised a data abstraction tool that consisted of socio-demographic, clinical parameters and the duration between the initial diagnosis and the final follow-up period or mortality. Survival outcomes were presented as mortality, new distant metastasis, treatment response, median survival time and years of survival. Data entry and analysis were carried out using SPSS statistical software version 26.0. The study utilised the Kaplan-Meier method to calculate the median survival time, while the Cox regression analysis was employed to identify the factors contributing to mortality.

Results

The study revealed that 64 (33.3%) patients had new distant metastases during the follow-up period, and 104 (42.1%) experienced disease progression. In addition, the mortality (33.6%) was high and poor five-year survival (32.7%) in patients diagnosed with gastric cancer. Comorbidity (AHR: 3.3, 95% CI: 1.3-8.7, p=0.014), advanced-stage diseases (AHR: 2.4, 95% CI: 1.1-5.2, p=0.03), chemotherapy (AHR: 5.2, 95% CI: 1.5-17.8, p=0.008) and gastrectomy (AHR: 1.7, 95% CI: 1.1-2.6, p=0.016) were significant determinants of survival.

Conclusions

Most patients had new metastases, disease progression and a poor five-year survival rate. Chemotherapy, gastrectomy, comorbidity and advanced-stage diseases were significant determinants of survival.

7.1 Introduction

The rising incidence of cancer has prompted more research on cancer treatment and prevention (Gavhane et al., 2011). Cancers of the colon, stomach, esophagus, and liver are the most predominant gastrointestinal tract (GIT) cancers globally (Somi et al., 2019). In addition, GIT malignancies are responsible for 35% of all global cancer-related fatalities (Arnold et al., 2020).

Even though the prevalence of some GIT cancers has decreased, these cancers continue to cause significant challenges to human beings (Arnold et al., 2020). Gastric cancer has declined considerably over the last 50 years due to reduced meat consumption, *Helicobacter pylori* infection and smoking (Rawla & Barsouk, 2019). Despite the progress made in cancer therapy, the prognosis for advanced gastric cancer remains suboptimal, necessitating further enhancements to improve survival rates (Leiting & Grotz, 2019). Gastric cancer is an age-related malignancy frequently diagnosed in the geriatric population. Thus, attaining the required treatment outcomes is challenging owing to age-related reduction in organ function (Joharatnam-Hogan et al., 2020).

Despite gastric cancers being reduced in industrialized countries in the past five decades, outcomes after treatment are suboptimal due to late diagnosis at an advanced stage. Even

though several attempts have been implemented to improve treatment, advanced stages of GIT cancer patients still have a suboptimal prognosis (Lordick et al., 2014). In addition, the overall survival rate of gastric cancer patients remains poor despite some degree of improvement (Hu et al., 2021; Li et al., 2022). Due to insufficient treatment and diagnostic facilities, the prognosis for cancer patients in sub-Saharan Africa is poor (Olaleye & Ekrikpo, 2017). However, existing research in East Africa is few and inadequate. Thus, this study purposed to assess survival outcomes among patients with gastric cancer at KNH.

7.2 General objective

To assess the determinants of survival outcomes among gastric cancer patients.

7.3 Specific objectives

1. To determine median and mean survival time and year of survival among patients with gastric cancer.
2. To assess the response to treatment and new distant metastasis among patients with gastric cancer.
3. To identify the determinants of survival outcomes among patients with gastric cancer.

7.4 Results

7.4.1 Sociodemographic characteristics of gastric cancer patients

The median age of the patients was 60.0±0.9 years, with an interquartile range of 51-69 years. Most (161, 65.2%) patients were males and had a primary level of education (172, 69.6%). The majority were married (187, 75.7%) and had no family history of cancer (241, 97.6%). The median duration of follow-up was five months (range: 1-62 months) **(Table 7.1)**.

Table 7.1: Socio-demographic characteristics of gastric cancer patients (n=247)

Variable	Frequency (%)
Age (in years)	
< 60 years	122(49.4)
≥60 years	125(50.6)
Gender	
Male	161(65.2)
Female	86(34.8)
Marital status	
Single	55(22.3)
Married	187(75.7)
Widowed	5(2.0)
Educational status	
Primary	172(69.6)
Secondary	39(15.8)
Tertiary	15(6.1)
Informal	21(8.5)
Occupational status	
Housewife	20(8.1)
Government employee	34(13.8)
Unemployed/Retired	42(17.0)
Self-employed	75(30.4)
Other	76(30.8)
Family history of cancer	
No	241(97.6)
Yes	6(2.4)

Other: Student, Contractor, Driver, Teacher, Artisan, house help

7.4.2 Clinical characteristics of the study participants

The majority of patients (244, 98.8%) had adenocarcinoma and stages II and III at diagnosis. At the time of diagnosis, 55 (22.3%) patients exhibited signs of distant organ metastasis, with the liver being the most prevalent site (34, 13.8%). Multiorgan metastases were observed in 11 (4.4%) patients. Nearly three-fifths (147, 59.5%) of the participants experienced concurrent co-morbidities, with the majority having one co-morbid disease. The most prevalent co-morbidities were anaemia (58, 23.5%) and hypertension (31, 12.6%) **(Table 7.2)**.

Table 7.2: Clinical characteristics of gastric cancer patients (n=247)

Variable	Frequency (%)
Histological type of cancer	
Adenocarcinoma	244 (98.8)
Squamous cell carcinoma	3(1.2)
Stage of cancer	
Stage I	6 (2.4)
Stage II	93(37.7)
Stage III	93(37.7)
Stage IV	55(22.3)
Co-morbidity	
Present	147(59.5)
Absent	100(40.5)
Number of co-morbidities	
One	97(39.3)
Two	30 (12.1)
≥Three	20(8.1)
Type of co-morbidity	
Anaemia	58(23.5)
Hypertension	31(12.6)
Peptic ulcer disease	25(10.1)
Ascites	17(6.9)
Acute kidney injury	16 (6.5)
Diabetes mellitus	15(6.1)
Upper gastrointestinal bleeding	10(4.0)
Gastric outlet obstruction	10(4.0)
Chronic kidney disease	6(2.4)
Deep vein thrombosis	6(2.4)
Obstructive jaundice	4(1.6)
Benign prostatic hyperplasia	4(1.6)
Heart failure	4(1.6)
Asthma	3(1.2)
Hypovolemic shock	2(0.8)
Pulmonary embolism	3(1.2)
Pneumonia	2(0.8)
Retroviral disease	2(0.8)
Adenoid cystic carcinoma	2(0.8)
Alcoholic liver disease	1(0.4)
Hydronephrosis	1(0.4)
Pancytopenia	1(0.4)
Acute pancreatitis	1(0.4)
Chronic pancreatitis	1(0.4)
Gastroesophageal reflux disease	1(0.4)
Distance metastasis at diagnosis	55(22.3)
Liver	34(13.8)
lung	8 (3.2)
Liver and pancreas	3 (1.2)
Liver and lung	3 (1.2)
Liver and brain	2 (0.8)
Liver and spleen	1(0.4)
Liver, pancreas and adrenal gland	1(0.4)
Liver and bone	1(0.4)
Peritoneal cavity	1(0.4)
Bone	1(0.4)

7.4.3 Haematological profiles of the participants

Most patients had normal serum creatinine, liver function test, and haematological profile during the last follow-up. However, 81(32.8%) and 14(5.7%) had low haemoglobin and neutrophil levels, respectively. In addition, 16(6.5%) and 17 (6.9%) had increased serum creatinine and deranged liver function tests, respectively **(Table 7.3)**.

Table 7.3: Haematological parameters of gastric cancer patients in the last follow-up period (n=247)

Haematological profile	Frequency (%)
Total white blood cells	
Normal	240(97.2)
Low	7(2.8)
Neutrophils	
Normal	233(94.3)
Low	14(5.7)
Haemoglobin	
Normal	166(67.2)
Low	81(32.8)
Platelets	
Normal	239(96.8)
Low	8(3.2)
Serum creatinine	
Normal	231(93.5)
Increased	16(6.5)
Liver function test	
Normal	230(93.1)
Significantly deranged	17(6.9)

7.4.4 Treatment regimens of the study participants

Chemotherapy was the preferred treatment modality for the majority of patients diagnosed with gastric cancer, accounting for 150 cases (60.7%). Among these, the combination regimen of folinic acid, fluorouracil, and oxaliplatin was the most frequently used chemotherapy regimen (39, 15.8%). Gastrectomy and radiotherapy were used on 114 (46.2%) and 27 (10.9%) patients, respectively **(Table 7.4**).

Table 7.4: Treatment regimens of gastric cancer patients (n=247)

Treatment regimen	Frequency (%)
Chemotherapy	150(60.7)
Folinic acid+fluorouracil+oxaliplatin	39(15.8)
Symptomatic management	37(15.0)
Cisplatin+ fluorouracil	28(11.3)
Radiotherapy	27(10.9)
Fluorouracil +docetaxel+oxaliplatin+lecovorin	15(6.1)
Epiroubiccin+oxaliplatin+capecitabine	12(4.9)
Epirubicin+cisplatin+capecitabine	9(3.6)
Cisplatin+capecitabine	7(2.8)
Epirubicin+cisplatin+ fluorouracil	6(2.4)
Cisplatin+docetaxel	5(2.0)
Cispaltin+paclitaxel	5(2.0)
Irinotecan+ fluorouracil +folinic acid	2(0.8)
Capecitabine	4(1.6)
Docetaxcel+cisplatin+ fluorouracil	4(1.6)
Oxaliplatin+capecitabine	3(1.2)
Docetaxel+ fluorouracil	3(1.2)
Etoposide+cisplatin	3(1.2)
Capecitabine+docetaxel	2(0.8)
Fluorouracil +folinic acid	2(0.8)
Capecitabine+ fluorouracil	1(0.4)
Gastrectomy	114(46.2)

7.4.5 Survival outcomes of gastric cancer patients

During the follow-up period, 64 (33.3%) patients developed new distant organ metastases. The most prevalent dissemination sites were metastases to the liver (29, 15.1%) and lung (11, 5.7%). Multiorgan metastases were present in 4 (2%) patients **(Table 7.5)**.

Table 7.5: Distant metastasis in the last follow-up period among gastric cancer patients (n=192)

Sites of metastasis	Frequency (%)
Liver	29(15.1)
Lung	11(5.7)
Peritoneal cavity	5(2.6)
Spleen	4(2.1)
Lung and liver	3(1.6)
Pancreas	2(0.5)
Colon	2(1.0)
Liver and pancreas	2(1.0)
Ovary	1(0.5)
Bone	1(0.5)
Bone and liver	1(0.5)
Lung and ovary	1(0.5)
Liver and kidney	1(0.5)
Lung, liver and gall bladder	1(0.5)

One hundred and four (42.1%) patients experienced disease progression over the course of the follow-up period. Moreover, the mortality was 83 (33.6%), although 4(1.6%) had unknown treatment outcomes. Thirty-six (14.6%) and 19(7.7%) patients had complete and partial responses, respectively **(Figure 7.1)**.

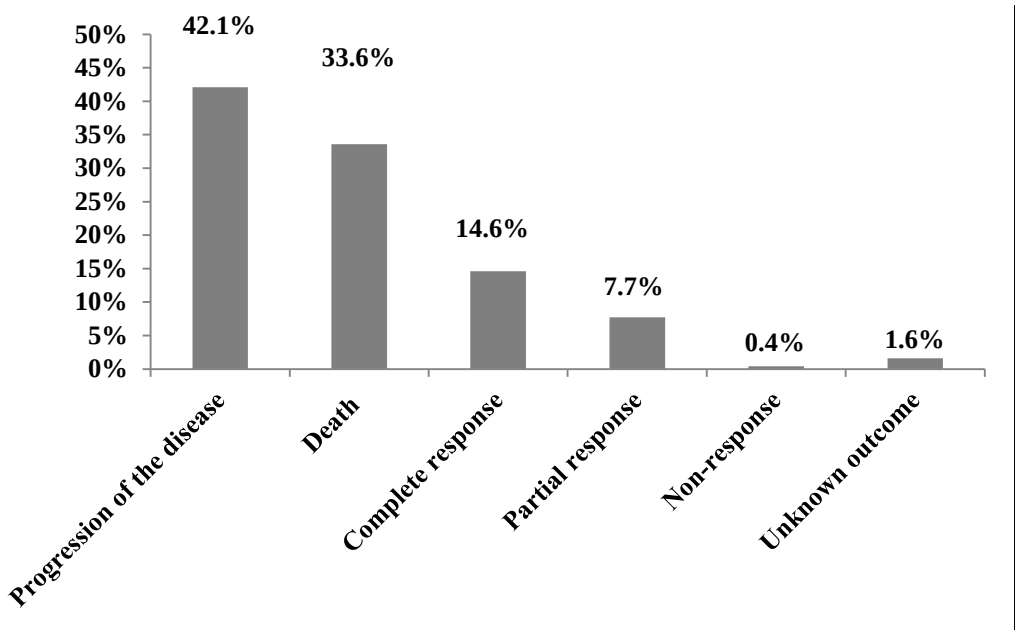


Figure 7.1: The treatment response of patients during the last follow-up period (n=247)

The five-year survival for patients with gastric cancer was 32.7%. Most patients survived the first year of therapy, but survival decreased from one year to five years after diagnosis **(Figure 7.2)**.

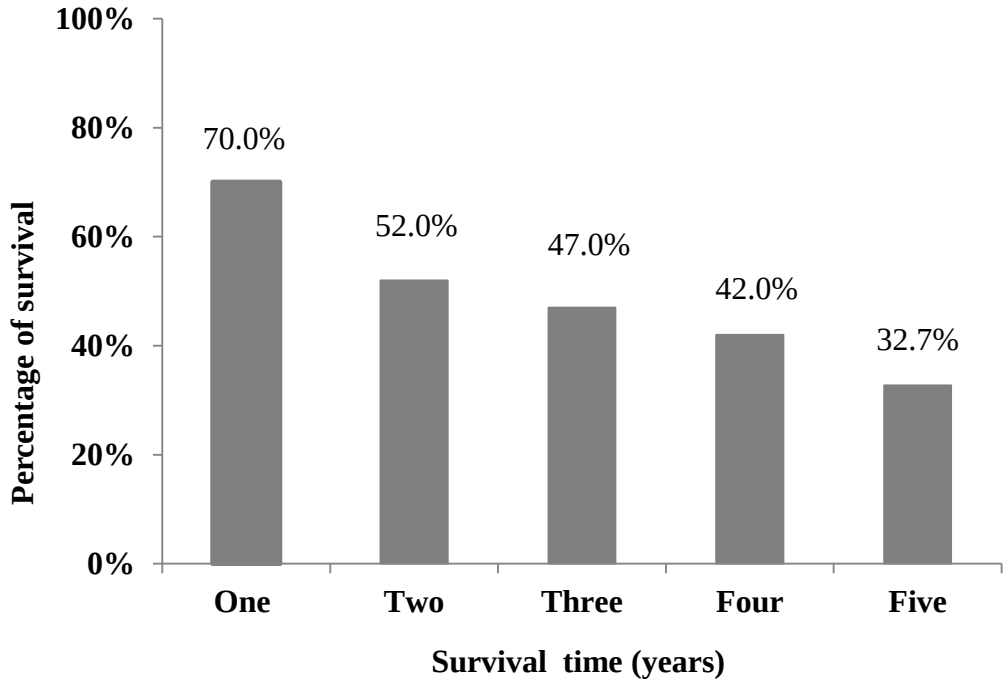


Figure 7.2: Percentage of survival among gastric cancer patients (n=247)

The median cancer-specific survival and median metastasis-free survival times were 49 ± 3.1 months and 56.6±2.2 months, respectively. In addition, the median cancer-specific survival after metastasis was 11 ±2.6 months.

There were no significant variations in the median survival time across gender, age groups and histological type of cancer compared to their respective counterparts. The median survival time of patients with co-morbidity (43.0±8.3 months), advanced stage (30.2±4.9 months) and metastases at diagnosis (12±1.2 months) was significantly lower than that of their respective comparison groups. Patients who underwent radiotherapy (54.1±6.3 months), gastrectomy (48±18.6 months) and chemotherapy (48±5.8 months) had a longer median survival time. However, compared to patients who did not get radiotherapy, the median survival time did not change substantially in radiotherapy-treated gastric cancer patients **(Table 7.6, Figure 7.3-Figure 7.7)**.

Table 7.6: Median and mean survival time among gastric cancer patients (n=247)

Variables	Median survival time (months)± standard error (95% CI)	Mean survival time (months)± standard error (95% CI)	Log-rank test (p-value)
Age (years)			0.7
< 60 years	47.2±3.2(33.5-53.2)	46.4±3.5(39.5-53.2)	
≥ 60 years	43.1±7.7(27.8-52.3)	46.1±2.6(40.9-51.3)	
Gender			0.9
Male	48±3.4(13.9-50.6)	46.4±3.4(39.7-53.2)	
Female	43±12.7 (18.1-67.8)	47.9±2.9 (42.2-53.6)	
Co-morbidity			**0.03***
Present	43.0±8.3(26.7-59.2)	44.4±3.1(38.3-50.6)	
Absent	56.2±2.9 (4.2-57.6)	53.9±1.9 (50.2-57.6)	
Stage of cancer			**0.05***
Early-stage (I and II)	43.1±2.2 (36.7-59.4)	53.1±3.2 (46.7-59.4)	
Advanced stage (III and IV)	30.2±4.9 (24.9-56.5)	40.7±2.9 (34.9-46.5)	
Histological type of cancer			0.8
Adenocarcinoma	43.2±7.3 (28.5-55.7)	49.1±2.4 (44.4-53.7)	
Squamous cell carcinoma	24.8±2.8 (11.1-31.6)	17.3±2.2 (13.1-21.6)	
Distant metastasis at diagnosis			**< 0.001***
Yes	12±1.2(9.7-14.3)	13.3±1.6(10.1-16.4)	
No	48±7.7 (32-63.2)	54.6±2.2 (50.4-58.8)	
Distant metastasis in the follow-up period			**0.04***
Yes	33.9±9.7(8.6-39.2)	43.9±2.7(38.6-49.2)	
No	43.3±3.8(6.3-44.8)	53.5±3.7(46.3-60.8)	
Treatment regimen			
Chemotherapy			**< 0.001***
No	31±2.0(14.7-35.6)	18.7±2.0(14.7-22.6)	
Yes	48±5.8 (36.5-59.5)	56.9±2.0 (52.9-62.9)	
Gastrectomy			**0.041***
No	43±7.4(28.4-57.6)	45.3±3.5(38.5-52.1)	
Yes	48±18.6(11.4-84.6)	49.1±2.9(43.4-54.9)	
Radiotherapy			0.3
No	42.2±8.3 (26.6-59.2)	45.2±2.5(40.2-49.9)	
Yes	54.1±6.3(41.7-72.2)	52.1±5.3(41.7-62.5)	
Symptomatic therapy			**< 0.001***
No	48.±7.8(32.5-63.5)	55.1±2.1(51.0-59.1)	
Yes	9.2±4.1(1.2-17.2)	6.7±0.9(4.9-8.5)	

*Statistically significant p-value ≤0.05

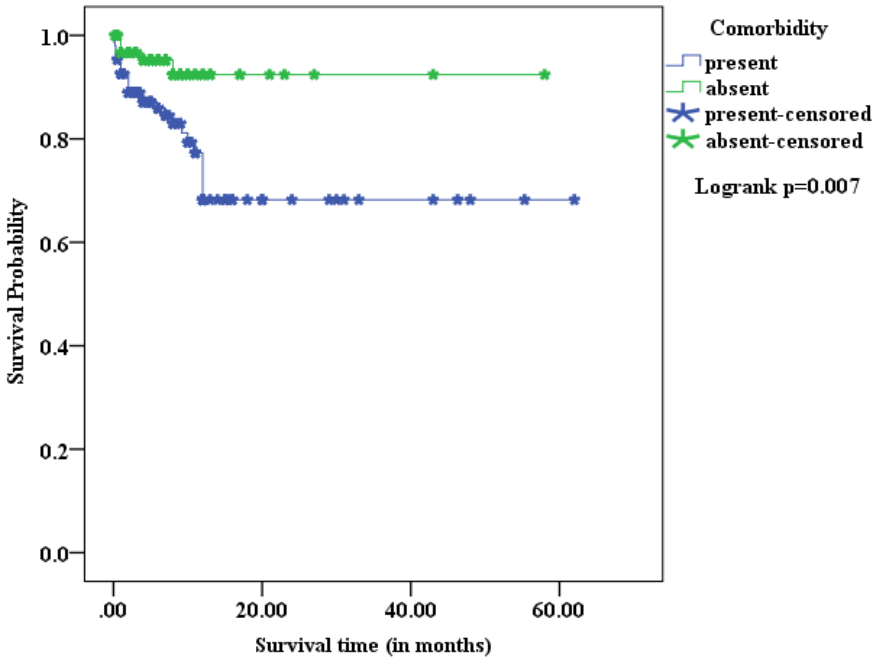


Figure 7.3: Kaplan-Meier curve of overall survival time variation of gastric cancer patients based on co-morbidities

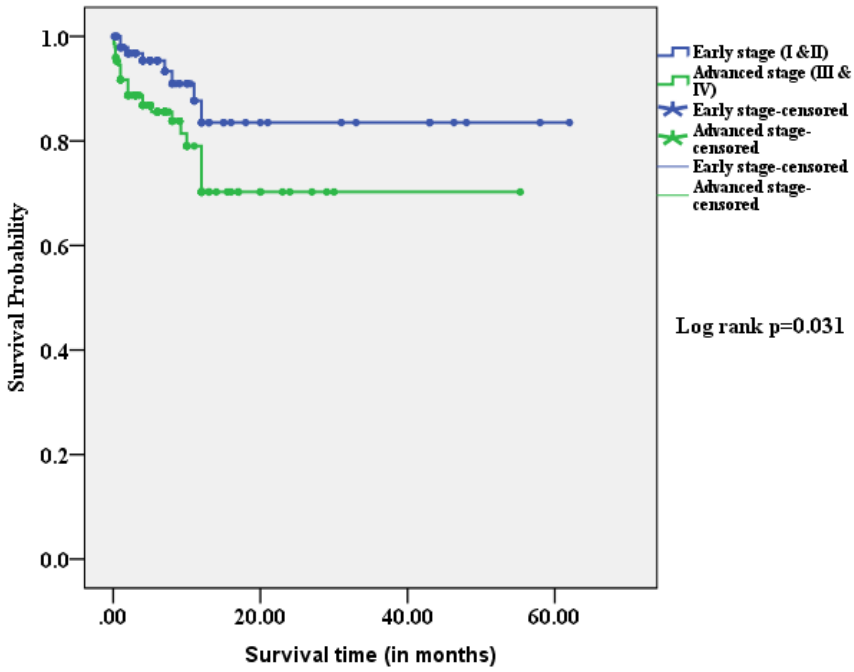


Figure 7.4: Kaplan-Meier curve of overall survival time variation of gastric cancer patients based on the stage of the disease

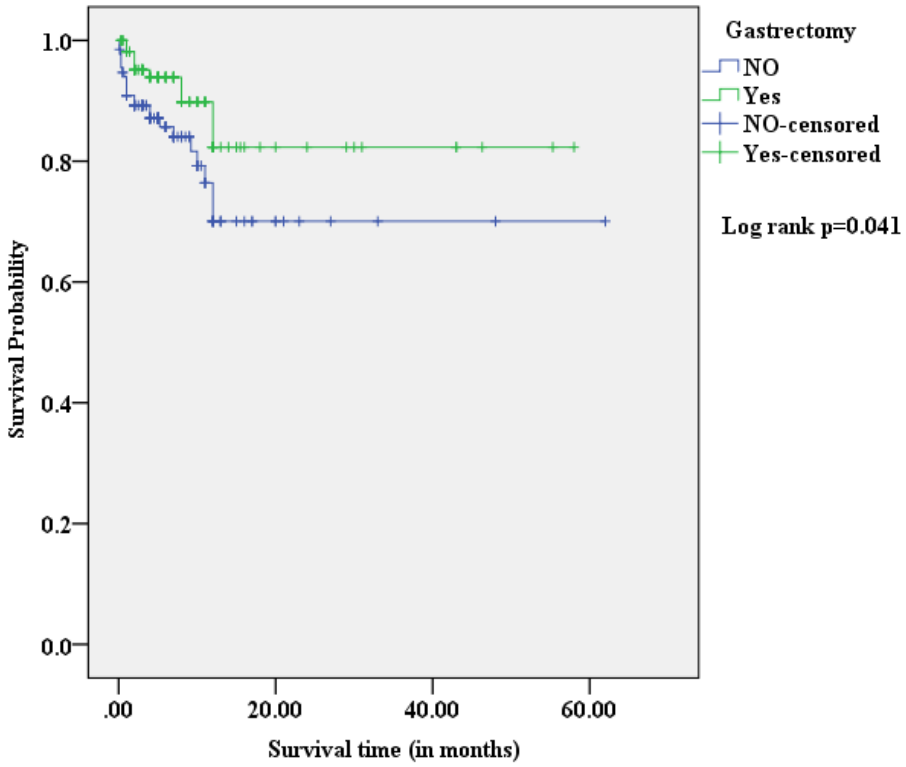


Figure 7.5: Kaplan-Meier curve of overall survival time variation of gastric cancer patients based on gastrectomy treatment

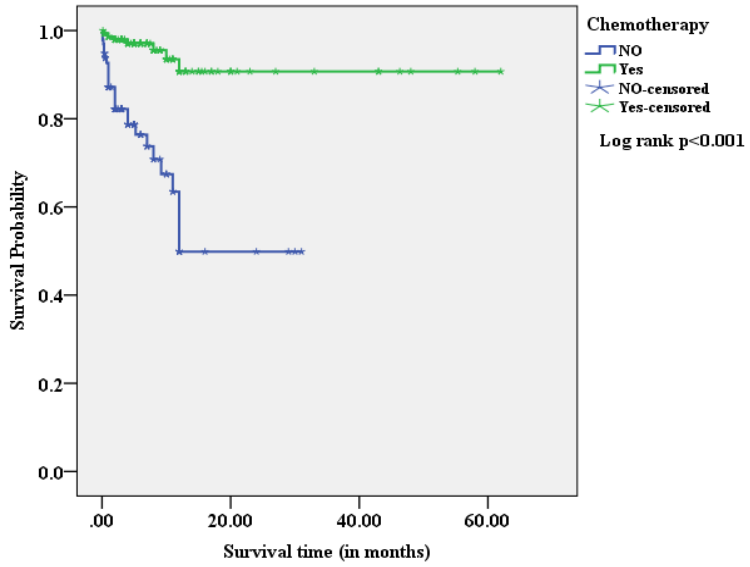


Figure 7.6: Kaplan-Meier curve of overall survival time variation of gastric cancer patients based on chemotherapy treatment

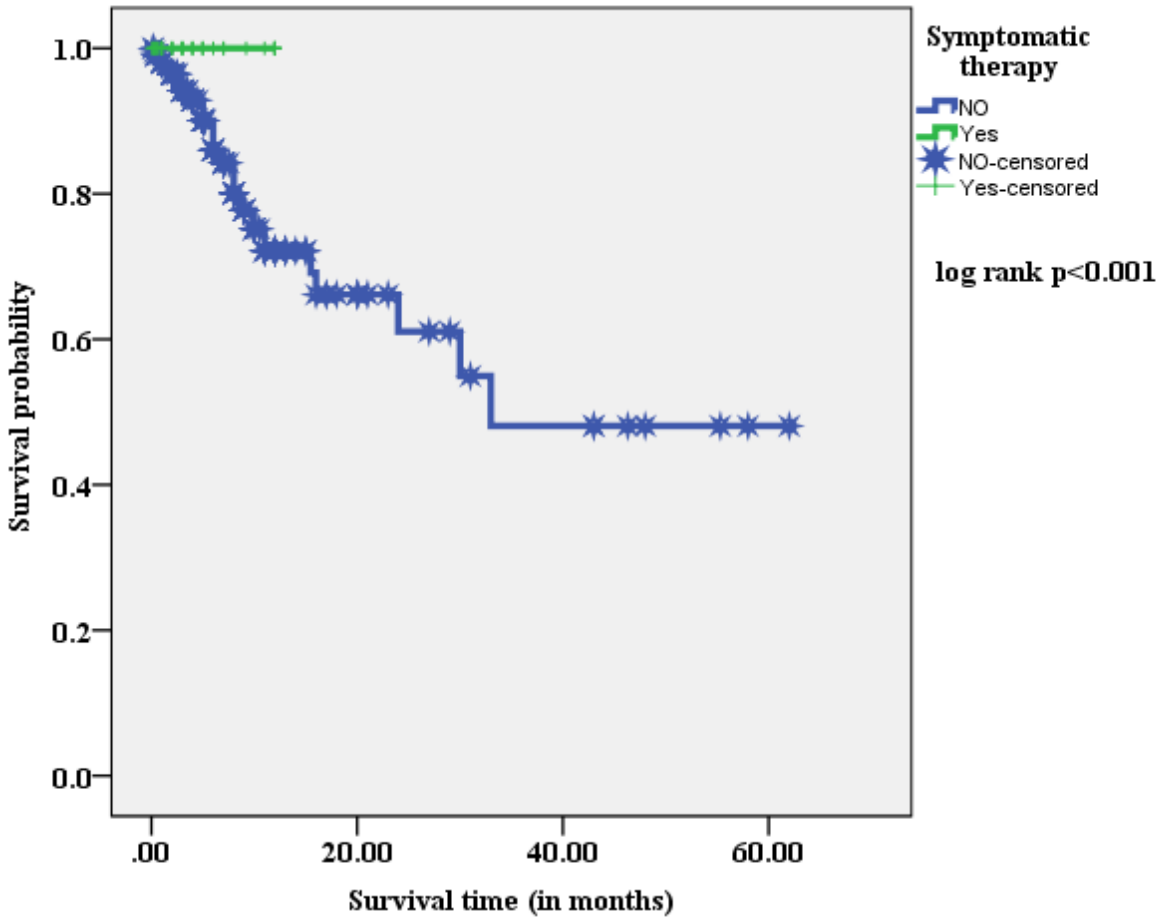


Figure 7.7: Kaplan-Meier curve of overall survival time variation of gastric cancer patients based on symptomatic therapy

7.4.6 Determinants of survival outcomes among gastric cancer patients

Co-morbidity increased the risk of death for patients by 3.3 times compared to those without co-morbidity (AHR: 3.3, 95% CI: 1.3-8.7, p=0.014). Patients who were diagnosed with advanced-stage diseases (AHR: 2.4, 95% CI: 1.1-5.2, p=0.03) and distant metastases (AHR: 7.7, 95% CI: 3.1-19.1, p <0.001) had a significantly higher risk of mortality compared to their counterparts. Patients who did not undergo chemotherapy (AHR: 5.2, 95% CI: 1.5-17.8, p=0.008) and gastrectomy (AHR: 1.7, 95% CI: 1.1-2.6, p=0.016) exhibited a significantly higher risk of mortality compared to those who received the respective treatment modalities. The study found that survival was not significantly influenced by age, gender, histological type of cancer, radiotherapy and distant metastasis during the follow-up period **(Table 7.7)**.

Table 7.7: Determinants of mortality among the gastric cancer patients (n=247)

Variable	Bivariable analysis		Multivariable analysis	
	CHR (95% CI)	**P-value**	**AHR (95% CI)**	**P-value**
Age (years)				
< 60 years	1		1	
≥ 60 years	0.8(0.4-1.6)	0.537	0.9 (0.4-1.9)	0.741
Gender				
Male	1		1	
Female	0.9(0.5-1.9)	0.919	2.1(0.9-4.8)	0.067
Co-morbidity				
Absent	1		1	
Present	3.4(1.3-8.8)	**0.012***	3.3 (1.3-8.7)	**0.014***
Stage of cancer				
Early-stage (I and II)	1		1	
Advanced stage (III and IV)	2.3(1.1-5.2)	**0.038***	2.4(1.1-5.2)	**0.03***
Histological type of cancer				
Adenocarcinoma	1		1	
Squamous cell carcinoma	1.2(0.2-9.1)	0.840	0.2(0.1-1.5)	0.103
Distant metastasis at diagnosis				
No	1		1	
Yes	6.4(3.2-12.8)	**<0.001***	7.7(3.1-19.1)	**<0.001***
Distant metastasis in the follow-up period				
No	1		1	
Yes	0.5(0.2-1.2)	0.130	0.6(0.2-1.8)	0.326
Treatment regimen				
Chemotherapy				
Yes	1		1	
No	7.5(3.2-17.3)	**<0.001***	5.2(1.5-17.8)	**0.008***
Gastrectomy				
Yes	1		1	
No	2.1(1.1-4.5)	**0.04***	1.7(1.1-2.6)	**0.016***
Radiotherapy				
Yes	1		1	
No	1.5(0.5-4.9)	0.507	0.8(0.2-3.2)	0.754
Symptomatic therapy				
Yes	1		1	
No	0.08(0.1-0.2)	**<0.001***	0.3(0.1-0.9)	**0.034***

*Statistically significant p-value ≤0.05, CHR: Crude hazard ratio, AHR: Adjusted hazard ratio

In the subgroup analyses, chemotherapy (p<0.001) and gastrectomy (p=0.012) were significant survival determinants in patients below 60 years of age. Similarly, chemotherapy (p=0.001) and gastrectomy (p=0.028) treatment modalities were significant determinants of survival in older (≥ 60) years gastric cancer patients. The stage of disease, co-morbidity and radiotherapy treatment were not significantly associated with survival in both age groups. Chemotherapy (p <0.001) and gastrectomy (p=0.001) were significant determinants of mortality in male patients. Conversely, chemotherapy was the sole determinant of survival in female gastric cancer patients (p=0.001) **(Table 7.8)**.

Table 7.8: Subgroup analysis of the determinants of mortality based on age and gender among gastric cancer patients

Variables	Categories	Bivariable analysis		Multivariable analysis	
		CHR (95% CI)	P-value	AHR (95% CI)	P-value
< 60 years	Comorbidity				
	Absent	1		1	
	Present	3.5(1-11.9)	0.051	1.3 (0.3-5.2)	0.678
	Early-stage (I &II)	1		1	
	Advanced stage (III & IV)	0.3(0.1-1.0)	0.06	0.7 (0.2-2.2)	0.519
	Chemotherapy				
	Yes	1		1	
	No	4.5 (1.5-15.9)	**0.007***	11.7(3.1-12.0)	**<0.001***
	Gastrectomy				
	Yes	1		1	
	No	2.5(0.9-6.5)	0.066	3.7 (1.3-10.4)	**0.012***
	Radiotherapy				
	Yes	1		1	
	No	0.9(0.2-2.5)	0.386	1.1 (0.2-3.3)	0.744
≥ 60 years	Co-morbidity				
	Absent	1		1	
	Present	3.2(0.7-14.5)	0.123	1.5 (0.3-7.5)	0.624
	Early-stage (I &II)	1		1	
	Advanced stage (III & IV)	0.6(0.2-1.8)	0.371	0.5(0.1-1.5)	0.200
	Chemotherapy				
	Yes	1		1	
	No	10.5(3.0-20.2)	**<0.001***	10.1 (2.6-20.2)	**0.001***
	Gastrectomy				
	Yes	1		1	
	No	1.8(0.6-5.9)	0.305	4.1(1.2-14.2)	**0.028***
	Radiotherapy				
	Yes	1		1	
	No	0.8(0.2-2.7)	0.664	1.2(0.4-4.5)	0.788
Male	Co-morbidity				
	Absent	1		1	
	Present	2.1(0.7-6.3)	0.178	0.6(0.2-2.2)	0.446
	Early-stage (I &II)	1		1	
	Advanced stage (III & IV)	0.4(0.1-1.1)		0.4(0.2-1.2)	0.113
	Chemotherapy				
	Yes	1		1	
	No	7.2(2.4-21.5)	**<0.001***	13.6(3.8-30.2)	**<0.001***
	Gastrectomy				
	Yes	1		1	
	No	2.7 (1.2-7.5)	**0.05***	5.4(1.9-15.5)	**0.001***
	Radiotherapy				
	Yes	1		1	
	No	1.3(0.6-2.8)	0.441	1.5(0.7-3.2)	
Female	Comorbidity				
	Absent	1		1	
	Present	8.3(1.1-10.2)	**0.042***	2.3(0.6-3.4)	0.127
	Early-stage (I &II)	1		1	
	Advanced stage (III & IV)	0.5(0.1-1.9)		1.0(0.2-4.5)	0.963
	Chemotherapy				
	Yes	1		1	
	No	8.4(2.3-23.3)	**0.001***	10.3(2.5-10.0)	**0.001***
	Gastrectomy				
	Yes	1		1	
	No	1.4(0.4-4.4)	0.569	2.9(0.8-10.3)	0.105
	Radiotherapy				
	Yes	1		1	
	No	1.0(0.4-2.9)	0.939	1.3(0.4-4.5)	0.665

*Statistically significant p-value ≤0.05, CHR: Crude hazard ratio, AHR: Adjusted hazard ratio.

The advanced stage of gastric cancer (stage III and IV) was found to be significantly influenced by chemotherapy (p<0.002), gastrectomy (p=0.002), radiotherapy (p=0.01), and co-morbidity (p=0.04) in terms of survival. During the early stages (I and II) of the disease, gastrectomy (p=0.02) was identified as the only significant factor affecting survival **(Table 7.9)**.

Table 7.9: Subgroup analysis of the determinants of mortality based on the stages of the disease among gastric cancer patients (n=247)

Variables	Categories	Bivariable analysis		Multivariable analysis	
		CHR (95% CI)	P-value	AHR (95% CI)	P-value
Early stage (I&II)					
	Chemotherapy				
	Yes	1		1	
	No	2.5(0.6-10.3)	0.200	3.4(0.7-15.4)	0.114
	Gastrectomy				
	Yes	1		1	
	No	1.9(0.5-8.3)	0.352	2.5(0.5-13.2)	**0.02***
	Radiotherapy				
	Yes	1		1	
	No	0.4(0.1-2.1)	0.296	0.6(0.1-3.4)	0.535
	Co-morbidity				
	Absent	1		1	
	Present	1.1(0.3-4.6)	0.912	0.7(0.1-3.3)	0.640
Advanced stage (III&IV)					
	Chemotherapy				
	Yes	1		1	
	No	13.8(4.1-20.2)	**<0.001***	16.6(4.5-20.2)	**<0.002***
	Gastrectomy				
	Yes	1		1	
	No	1.9(0.8-4.6)	0.140	4.2(1.7-10.4)	**0.002***
	Radiotherapy				
	Yes	1		1	
	No	3.5(0.5-26.6)	**0.002***	3.2 (0.4-24.2)	**0.01***
	Co-morbidity				
	Absent	1		1	
	Present	6.2(1.5-20.2)	**0.013***	2.7(1.3-7.9)	**0.04***

*Statistically significant p-value ≤0.05, CHR: Crude hazard ratio, AHR: Adjusted hazard ratio.

7.5 Discussion

This study aimed to investigate the survival outcomes in gastric cancer patients. Our study revealed that 32.7% five-year survival with a notable decrease in survival from the initial year of diagnosis to the fifth year. Similarly, earlier research revealed that the five-year survival for gastric cancer patients was low in China (42.9%) and Turkey (15.5%), with a decline from the first to the fifth year (Basaran et al., 2015; Li et al., 2022). Moreover, studies from Cameroon (4.6%) and Saudi Arabia (19.6%) also showed low five-year survival (Alshahrani et al., 2020; Bang et al., 2020). A previous review report revealed a relatively low survival in Africa (12.7%) (Lambert et al., 2012) compared to Korea (47.6%), Japan (72.1%), Europe (18.6%) and Thailand (17.2%) (Tuo et al., 2022). This low survival in the study setting is possibly related to the high metastases at diagnosis (22.3%) and during the follow-up period (33.3%) when treatment options are limited or less effective.

As compared to the studies from Cameroon (5.9±7.5 months), Tunisia (26.5 months), and Nigeria (13.6 months), the median cancer-specific survival time of patients with gastric cancer was higher (49 ± 3.1 months) in our setting (Ahmed et al., 2011; Arfaoui et al., 2006; Bang et al., 2020). In contrast, research conducted in Turkey revealed a longer overall median survival time (51 months) (Yaprak et al., 2019). This fairly shorter survival time in the study setting is likely attributable to delayed treatment commencement and late diagnosis because most gastric cancer patients had metastatic disease.

In the study setting, 42.1% of patients experienced disease progression in the follow-up period while 14.6% and 7.7% of patients had complete and partial responses, respectively. Contrastingly, an Italian study reported that 34% had a partial response and 5% of gastric cancer patients had progressive disease (Achilli et al., 2017). Another study in Norway showed that gastric cancer patients had a lower complete response (2.4%) and disease progression (10%) as compared to gastric cancer patients in our setting (Sandø et al., 2023).

The mortality of gastric cancer patients was 33.6% which was considerably lower than the Cameroon study (70.8%) (Bang et al., 2020) and higher than the anticipated mortality (3.8%) for the African population (Asombang et al., 2014). An early diagnosis increases the chance of survival and reduces mortality in gastric cancer patients (Adham et al., 2017). This high mortality and disease progression in our setting may be attributable to delayed diagnosis and treatment.

The research revealed no significant variations in median survival time across gender, age groups and cancer histology. In contrast, an earlier study demonstrated that female and younger patients exhibited lower and higher survival, respectively (Li et al., 2017). Nevertheless, patients with co-morbidities and metastatic disease had significantly lower median survival times.

Chemotherapy and gastrectomy-treated patients had considerably longer median survival times than those treated with other modalities. This is in agreement with another study which showed that gastrectomy and chemotherapy treatment modalities exhibited a more prolonged median survival in gastric cancer patients (Hu et al., 2021). A Saudi Arabia study also revealed a longer median survival time in chemotherapy-treated patients and a shorter median survival time in surgically treated gastric cancer patients compared to findings from our setting (Alshahrani et al., 2020). These differences in survival time across studies are likely attributable to differences in age, sample size, quality of care, cancer stage and co-morbidity. Nevertheless, the median survival time of radiotherapy-treated patients was not significantly different from that of non-radiotherapy-treated patients.

Co-morbidities have a detrimental effect on the prognosis of patients with gastric cancer (Iwai et al., 2021; Morishima et al., 2019). Patients with co-morbidities had a greater mortality risk than those without co-morbidities. Patients with advanced-stage diseases had a higher risk of mortality than early-stage diseases. There is a reported higher mortality hazard in the metastatic stage of the disease (Talebi et al., 2020; Yang et al., 2011). Statistically, patients with gastric cancer who did not receive chemotherapy and gastrectomy had a higher risk of dying than those with the respective treatments. This is likely attributable to late-stage presentation, which may have a poor prognosis despite the introduction of treatment modalities due to the progression of the disease. The finding in the present study is consistent with other studies where gastrectomy and chemotherapy were linked with lower mortality in gastric cancer patients (He et al., 2017; Nakao et al., 2021; Peng et al., 2020).

In the subgroup analysis, chemotherapy, gastrectomy, radiotherapy and comorbidity were determinants of survival in patients with advanced gastric cancer (stages III and IV). Other studies reported that surgery and chemotherapy were the determinants of survival in advanced

gastric cancer patients (Biondi et al., 2019; Sougioultzis et al., 2011). Gastrectomy was the only determinant of survival in patients diagnosed with early-stage (stages I & II) gastric cancer which agrees with another study that reported gastrectomy was the significant determinant of survival in early-stage gastric cancer (Butte et al., 2008).

Although a study in Korea reported higher mortality in geriatric patients, age was not a significant determinant of survival in our setting (Lee et al., 2019). Gender was not a significant determinant of survival in our setting despite other studies reporting that women have better overall and cancer-specific survival than men (Li et al., 2020; Luan et al., 2022). A multicenter study in Iran showed age, size of the tumour, grade of the tumour and types of treatment were significant predictors of survival (Talebi et al., 2020). Hence, tailored treatment approaches should be considered to minimise mortality in metastatic and co-morbid gastric cancer patients.

Strengths and limitations of the study

The study comprehensively examined the survival outcomes of patients with gastric cancer in a large sample size with long-term follow-up. This was the first study that evaluated the determinants that impacted survival in gastric cancer patients in Kenya. Hence, it can be used as baseline data for further studies. The incompleteness of medical records was the main limitation of the retrospective cohort study due to the retrospective nature of the study. In this case, the data's accuracy depended on the correctness of the documentation in the study setting.

7.6 Conclusions

A considerable proportion of patients with gastric cancer had disease progression (42.1%) and low (32.7%) five-year survival. In the early stages of the disease, gastrectomy was the sole significant determinant of survival. Survival in advanced-stage patients was significantly influenced by chemotherapy, gastrectomy, radiotherapy and co-morbidity.

7.7 Recommendations for policy and practice

Most patients had an advanced stage at diagnosis. Hence, it is imperative to implement nationwide educational programmes pertaining to the timely detection and effective management of gastric cancer to improve survival. There was a high prevalence of poor survival outcomes; hence early initiation of optimal treatment is indispensable to improving survival outcomes. The results of the regression analysis suggested that gastrectomy during the early stages of gastric

cancer, while radiotherapy, chemotherapy and gastrectomy during the advanced stages, were viable treatment modalities that may enhance the survival of patients with this condition. Due to the aggressive character, lower median survival time and frequent detection at an advanced stage, early screening and vigorous treatment are strongly recommended to improve the survival of patients with gastric squamous cell carcinoma.

7.8 Recommendations for further research

Multi-centre cohort studies with large samples should be conducted to reliably assess the factors that influence the survival outcomes of patients with gastric cancer. A prospective cohort study should be conducted to investigate the long-term impacts of various treatment modalities on the long-term survival outcomes of patients with gastric cancer.

CHAPTER EIGHT: SURVIVAL OUTCOMES AMONG COLORECTAL CANCER PATIENTS AT KENYATTA NATIONAL HOSPITAL

Abstract

Background

Although a growing burden of colorectal cancer in Africa, survival of colorectal cancer remains low. Notwithstanding, there is a scarcity of data on colorectal cancer patients' survival outcomes in Kenya.

Objective

To assess the survival outcomes of patients diagnosed with colorectal cancer who received treatment at Kenyatta National Hospital.

Methods

A one-arm retrospective cohort study was conducted on 232 randomly selected medical records of adult patients diagnosed with colorectal cancer. A predesigned data abstraction tool was used to collect data from the medical records of the patients. All the required data, including sociodemographic information, clinical characteristics and outcome measurement parameters, were collected by reviewing the documented medical records of the patients retrospectively from diagnosis to the last hospital visit. The statistical software used for data entry and analysis was SPSS version 26.0. Kaplan Meier analyses were used to determine median survival time. The findings of the study were presented using percentage, mean, median, standard deviation, frequency tables and figures.

Results

During the follow-up period, almost one-third (34.1%) of patients showed disease progression, with 18 (7.8%) exhibited no response to treatment and 41 (23.6%) had new distant metastases. The observed survival significantly declined from 87.9% during the initial year to 45.4% by the fifth year, and the mortality was 22.8%. In early-stage patients, age, gender, histology types, co-morbidity and treatment regimens were not determinants of survival. However, the risk of dying was higher among older (≥ 60 years) (AHR=2.7, 95% CI= 1.5-4.8, p=0.001) and co-morbid

(AHR=2.7, 95% CI= 1.1-6.3, p=0.03) advanced-stage colorectal patients. Advanced-stage patients who received surgery (AHR=1.5, 95% CI= 1.1-1.9,p=0.01) and radiotherapy (AHR=4.7, 95% CI= 1.7-5.5, p=0.04) had a decreased probability of dying.

Conclusions

In the follow-up period, colorectal cancer patients had a high mortality, disease progression and distant metastasis. Older age, co-morbidity, surgery and radiotherapy were significant factors influencing survival in the advanced stage of the disease. Nonetheless, none of the variables had a significant association in impacting survival among early-stage patients. These dismal survival rates illustrate the need for early detection and treatment of colorectal cancer in our setting.

8.1 Introduction

There were around 19.3 million new cases and 10 million cancer-related mortality globally in the year 2020 (Sung et al., 2021). Breast, lung, colorectal, prostate and gastric cancer were the most common solid cancers diagnosed worldwide (Sung et al., 2021). Colorectal cancer is the third most frequently diagnosed cancer of the GIT and the second major cause of cancer mortality (Keum & Giovannucci, 2019; Sharma et al., 2022; Sung et al., 2021). In 2020, colorectal cancer accounted for 0.94 million deaths and 1.9 million new cases globally. Moreover, the global incidence of colorectal cancer cases is expected to reach 3.2 million by 2040 (Xi & Xu, 2021). This dramatic rise in incidences of colorectal cancer across many countries will hugely impact global health care (Guren, 2019). The mortality and incidence rates continue to rise steadily in many underdeveloped countries (Arnold et al., 2017).

Studies in Africa have shown a rise in the burden of colorectal cancer owing to the rising incidence of preventable risk factors such as smoking, alcohol use and sedentary lifestyles (Awedew et al., 2022). Although colorectal cancer is predominantly detected in the elderly, there is an increasing incidence of diagnosis among individuals under the age of 50 (Keum & Giovannucci, 2019). Furthermore, young people with cancer have considerable psychological and reproductive problems and a heightened risk of mortality and morbidity (Guren, 2019).

A systematic review showed that Iranian colorectal cancer patients had better five-year survival rates (Maajani et al., 2019). Conversely, most patients with colorectal cancer in undeveloped countries are diagnosed late, with a worse 5-year relative survival (Lim et al., 2020; Magaji et

al., 2017; Veettil et al., 2017). Furthermore, survivors of colorectal cancer are still minimal in Sub-Saharan countries, with the lowest prognosis with late diagnosis (Gullickson et al., 2021). An earlier study in Ghana found that overall five-year survival was low (16%) (Agyemang-Yeboah et al., 2018). However, data are scarce regarding the survival of patients with colorectal cancer in our setting. Hence, the purpose of this study was to assess the survival outcomes among colorectal cancer patients at KNH.

8.2 General objective

To assess the survival outcomes among colorectal cancer patients.

8.3 Specific objectives

1. To determine median and mean survival time, new distant metastasis, mortality and year of survival among patients with colorectal cancer.
2. To assess treatment response among patients with colorectal cancer.
3. To identify the determinants of survival outcomes among patients with colorectal cancer

8.4 Results

8.4.1 Sociodemographic characteristics of the study participants

The median age of the study participants was 55.0±13.3 years, with a range of 18-95 years. A majority of the participants (139, 59.9%) were under the age of 60. The study's median follow-up duration was 20.4 months, with a range of 1 to 60 months. The patients were predominantly males (126, 54.3%) and self-employed (88, 37.9%). Most of the study participants were married (175, 75.4%) and had a primary and secondary level of education. In addition, almost all patients did not have a family history of cancer (231, 99.6%) **(Table 8.1)**.

Table 8.1: Sociodemographic characteristics participants (n=232)

Variable	Frequency (%)
Age (in years)	
< 60 years	139(59.9)
≥60 years	93(40.1)
Gender	
Male	126(54.3)
Female	106(45.7)
Marital status	
Single	34(14.7)
Married	175(75.4)
Divorced	17(7.3)
Widowed	6(2.6)
Educational status	
Primary	100(43.1)
Secondary	101(43.5)
Tertiary	30(13.0)
Informal	1(0.4)
Occupational status	
Self-employed	88(37.9)
Unemployed/Retired	43(18.5)
Government employee	23(9.9)
Housewife	15(6.5)
Other	63(27.2)
Family history of cancer	
No	231(99.6)
Yes	1(0.4)

8.4.2 Clinical characteristics of the study participants

Adenocarcinoma was the most frequent histological form of colorectal cancer (231, 99.6%). The majority of patients (194, 83.6%) had advanced disease at diagnosis (stages III and IV). In spite of this, 38 patients (16.4%) were diagnosed while the disease was still in its early stages (I and II). A quarter of the study participants (58, 25%) demonstrated metastases in various organs, with the liver (26, 11.2%) and lung (17, 7.3%) being the most frequent sites of dissemination. Nonetheless, multiorgan metastases were seen in 15 (6.5%) patients. The majority of participants (156, 67.2%) did not have any preexisting diseases. The most common comorbidities were hypertension (12, 20.3%), intestinal obstruction (18, 7.8%) and anaemia (16, 6.9%) **(Table 8.2)**.

Table 8.2: Clinical characteristics of colorectal cancer patients (n=232)

Variable	Frequency (%)
Histological type of cancer	
Adenocarcinoma	231(99.6)
Squamous cell carcinoma	1(0.4)
Stage of cancer	
Stage I	7(3.0)
Stage II	31(13.4)
Stage III	136(58.6)
Stage IV	58(25.0)
Comorbidity	
Present	76(32.8)
Absent	156(67.2)
Number of comorbidities	
One	47(20.3)
Two	22(9.5)
≥Three	7(3.0)
Type of comorbidity	
Hypertension	28(12.1)
Intestinal obstruction	18(7.8)
Anaemia	16(6.9)
Retroviral disease	8(3.4)
Acute kidney injury	7(3.0)
Hydronephrosis	4(1.7)
Benign prostatic hyperplasia	3(1.3)
Upper gastrointestinal bleeding	3(1.3)
Chronic kidney disease	3(1.3)
Stroke	3(1.3)
Diabetes mellitus	3(1.3)
Ascites	2(0.9)
Congestive heart failure	2(0.9)
Obstructive jaundice	2(0.9)
Chronic liver disease	2(0.9)
Peptic ulcer disease	2(0.9)
Pneumonia	2(0.9)
Asthma	2(0.9)
Hemophilia	1(0.4)
Renal calculi	1(0.4)
Deep vein thrombosis	1(04)
Pulmonary embolism	1(0.4)
Arthritis	1(0.4)
Acute liver failure	1(0.4)
Septic shock	1(0.4)
Distance metastasis at diagnosis	58(25)
Liver	26(11.2)
Lung	17(7.3)
Liver & lung	6(2.6)
Bone	3(1.3)
Liver, bone & lung	3(1.3)
Liver & brain	2(0.9)
Liver &bone	1(0.4)

8.4.3 Haematological profiles of the participants

The majority of patients had normal haematological parameters in the last follow-up period. In addition, most of them (230, 99.1%) had normal liver and renal function tests. Nonetheless, 38 (13.8%) patients had low haemoglobin levels in the last follow-up period **(Table 8.3)**.

Table 8.3: Haematological parameters of colorectal cancer patients in the last follow-up period (n=232)

Laboratory parameters	Frequency (%)
Total white blood cells	
Normal	230 (99.1)
Low	2(0.9)
Neutrophils	
Normal	229(98.7)
Low	3(1.3)
Haemoglobin	
Normal	200(86.2)
Low	32(13.8)
Platelets	
Normal	230(99.1)
Low	2(0.9)
Serum creatinine	
Normal	226(97.4)
Increased	6(2.6)
Liver function test	
Normal	230(99.1)
Significantly deranged	2(0.1)

8.4.4 Treatment regimens of colorectal cancer patients

The most common forms of treatment for colorectal cancer patients were chemotherapy (198, 85.5%) and surgery (152, 65.5%). Among the chemotherapeutic regimen, FOLFOX regimens (186, 80.2%) were the most frequently used treatment modalities **(Table 8.4)**.

Table 8.4: Treatment regimens of colorectal cancer patients (n=232)

Treatment regimen	Frequency (%)
Chemotherapy	198(85.3)
Surgery	152(65.5)
Radiotherapy	54(23.3)
Symptomatic management	12(5.2)
Chemotherapy regimens	
Folinic acid, fluorouracil & oxaliplatin	186(80.2)
Oxaliplatin & capecitabine	7(3.0)
Cisplatin+5-fluorouracil	2(0.9)
Capecitabine	2(0.9)
Folinic acid, 5-fluorouracil & irinotecan	1(0.4)

8.4.5 Survival outcomes of the study participants

The study showed that 41 (23.6%) patients had new distant organ metastasis. Most metastases occurred in the lung (15, 8.6%) and liver (9, 5.2%). Multiorgan metastasis was involved in five (2.9 %) patients.

The mortality was 22.8% and 179(77.2%) patients had censored observations in the last follow-up period. Seventy-nine (34.1%) patients had disease progression, 18(7.8%) had no response to the treatment and 2(0.9%) had stable disease. Thirty-seven (15.9%) and 20 (8.6%) participants had complete and partial responses, while 23 (9.9%) had unknown outcomes **(Figure 8.1)**.

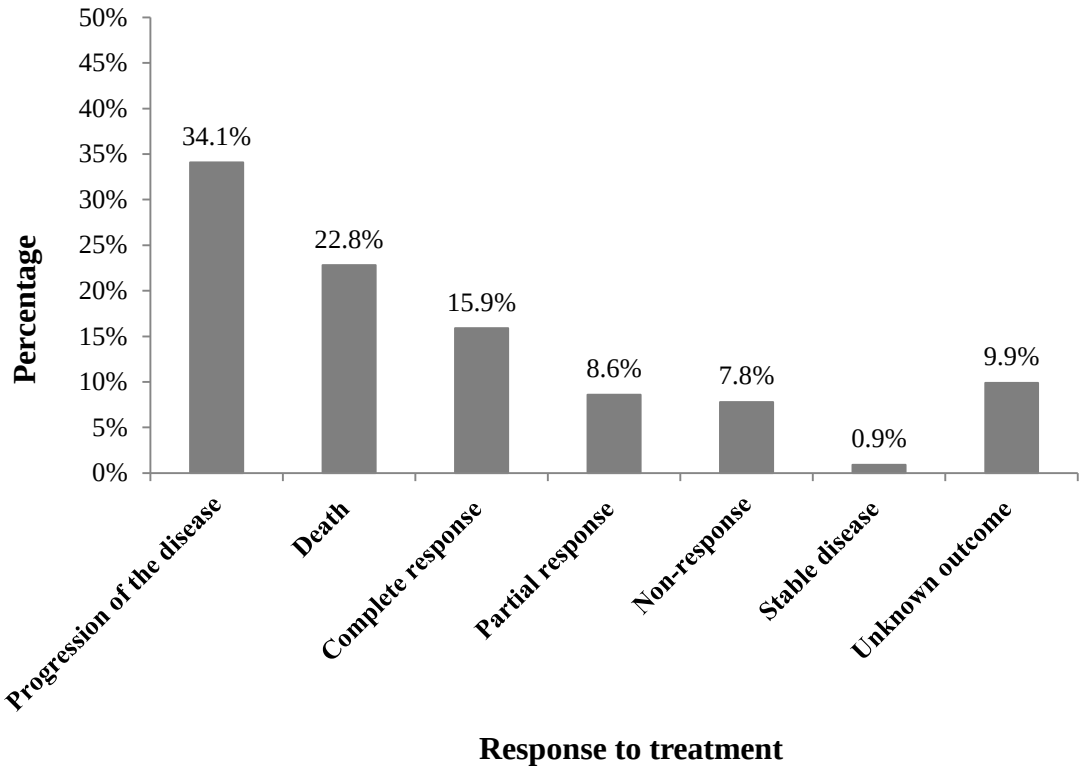


Figure 8.1: Treatment response of patients during the last follow-up period (n=232)

As shown in **Figure 8.2**, the percentage of patients who survived over the first year dropped from 87.9% to 45.4% over the course of five years. The study also revealed that the median cancer-specific survival was 57.2±2.1 months, while the median survival time from the date of cancer diagnosis to the first radiological metastasis (median metastasis-free survival) was 53±1.6 months. The median survival time from the date of first radiologic metastasis until death or last follow-up (median survival after metastasis) was 42.8±2.2 months.

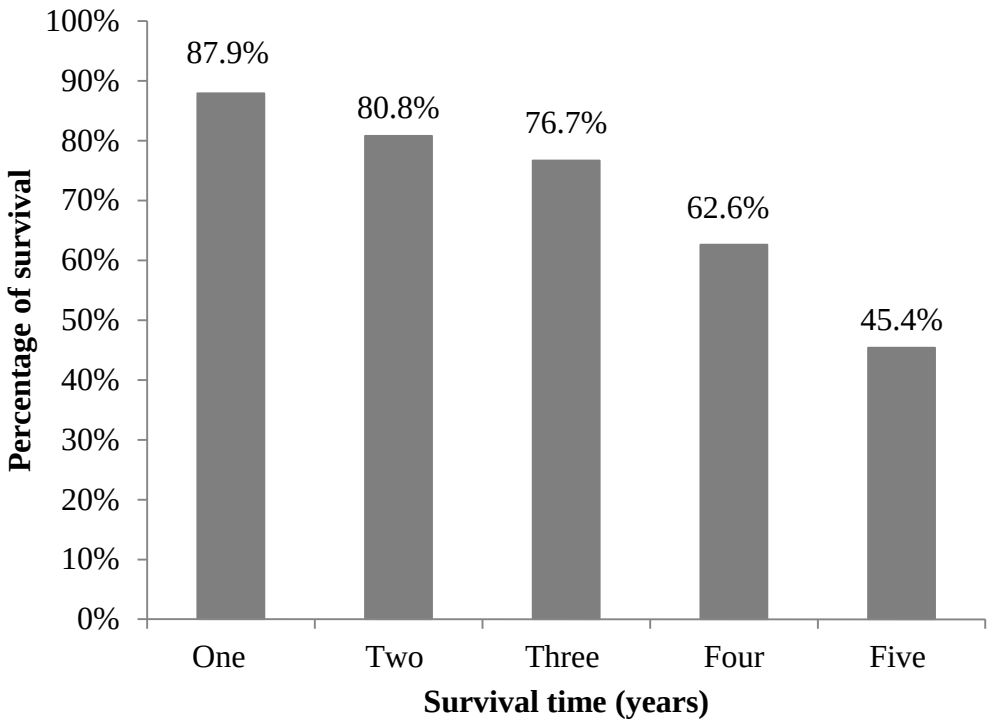


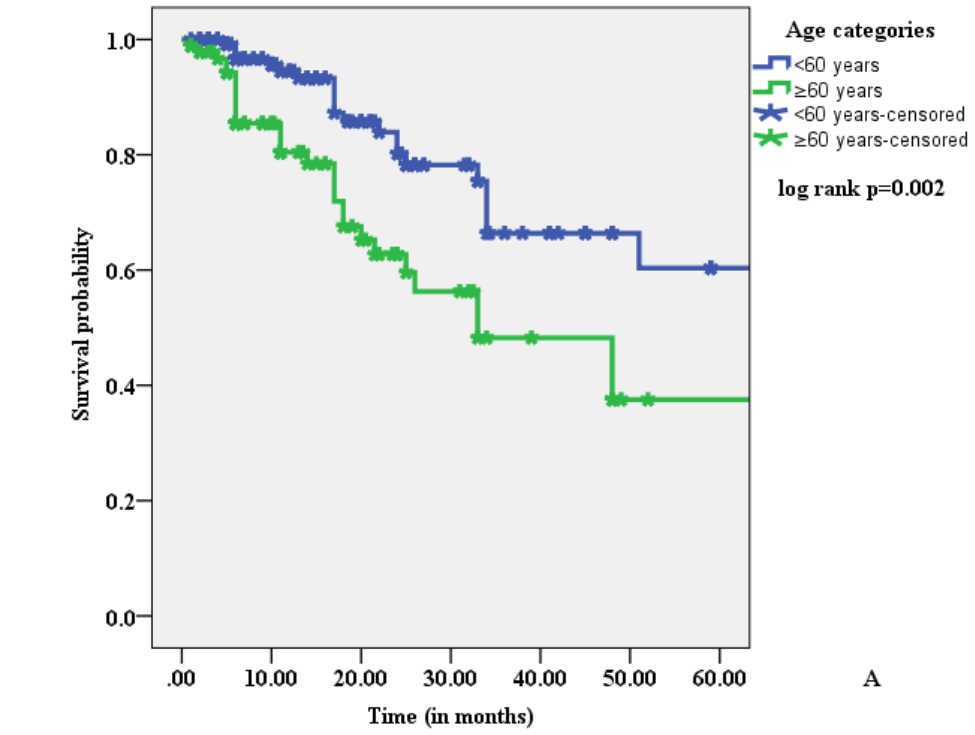
Figure 8.2: Percentage of survival among colorectal cancer patients (n=232)

The study revealed that patients aged 60 and above (33.0±9.6 months) had a lower median survival time than those below 60 years (48.0±17.3 months). Those with co-morbid conditions had shorter median survival (34.0 ±6.9 months) than those without co-morbid diseases (48.0±15.5 months). Patients with distant metastases had a shorter median survival time compared to those without metastasis. The median survival time was lower for patients with stage IV disease (25.8±5.7 months) as compared to stage I (51.0±2.3 months), II (48.0±4.7 months), and III (32.8±5.7 months) disease. The median survival time of patients who had surgery and radiotherapy was longer than patients who did not get these treatment modalities. Nevertheless, a significant difference in median survival time was not observed between genders and chemotherapy-treated colorectal cancer patients **(Table 8.5, Figure 8.3 and Figure 8.4)**.

Table 8.5: Median and mean survival time among colorectal cancer patients (n=232)

Variables	Median survival time (months)± SE (95% CI)	Mean survival time (months)± SE (95% CI)	Log-rank test (p-value)
Age (years)			**0.002***
< 60 years	48.0±17.3(43.9-112.0)	119.2±21.5(50-120)	
≥ 60 years	33.0±9.6(14.1-51.9)	61.3±11.5(38.6-83.9)	
Gender			0.5
Male	48.0±10.9(56.4-99.5)	89.3±18.4(53-125)	
Female	48.1±15.5 (47.6-108.4)	88.1±12.6(63-112)	
Co-morbidity			**0.002***
Present	34.0±6.9(20.4-47.6)	49.7±4.7(40.5-58.9)	
Absent	48.0±15.5 (47.6-108.4)	177.6±23.1(120-180)	
Stage of cancer			**0.002***
Stage I	51.0±2.3(23.2-62.5)	168.2± 32.4(104.7-231.6)	
Stage II	48.0±4.7(70.7-131.6)	86.9± 11.1(65.2-108.6)	
Stage III	32.8±5.7(21.7-43.9)	51± 2.3(30-52)	
Stage IV	25.8±5.7(21.7-43.9)	32.8± 5.7(21.6-43.9)	
Distant metastasis at diagnosis			**0.003***
Yes	48.0±19.4(39.9-116.0)	34.9±6(23.2-46.8)	
No	26.0±4.0 (18.2-33.8)	79.2±17.9(58.1-88.2)	
Distant metastasis in the follow-up period			**<0.001***
Yes	34.0±6.7(20.9-47.1)	49.4±4.7(40.1-58.6)	
No	48.0±15.5(47.6-108.3)	69±7.6(34.2-70.6)	
Treatment regimen			
Chemotherapy			0.8
No	51.0±16.1(47.6-108.4)	61±2.7(30.2-64.9)	
Yes	48.0±15.4 (46.4-109.6)	69±5.6(32.4-74.3)	
Surgery			**0.01***
No	33.0±11.7(10.1-55.9)	40±2.4(34.2-56.2)	
Yes	48.0±15.5(47.6-108.4)	72±(52.3-76.8)	
Radiotherapy			**<0.001***
No	34.0±7.5(19.3-48.7)	52±2.9(28.2-56.7)	
Yes	48.0±15.6(47.6-108.5)	69±3.9(48.2-75.3)	

*Statistically significant p-value ≤0.05, CI: Confidence interval, SE: standard error



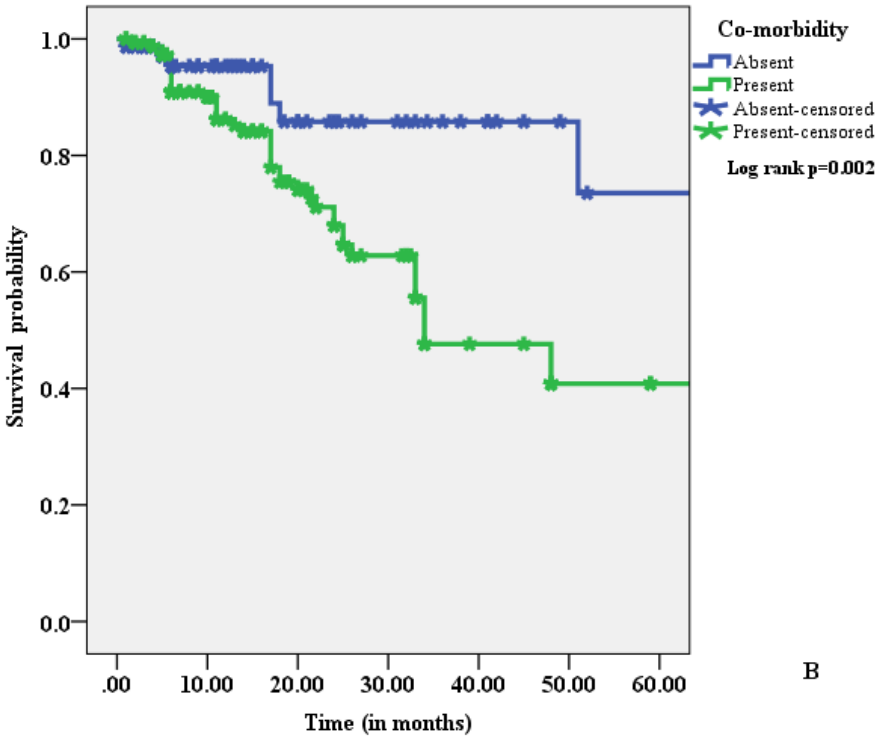
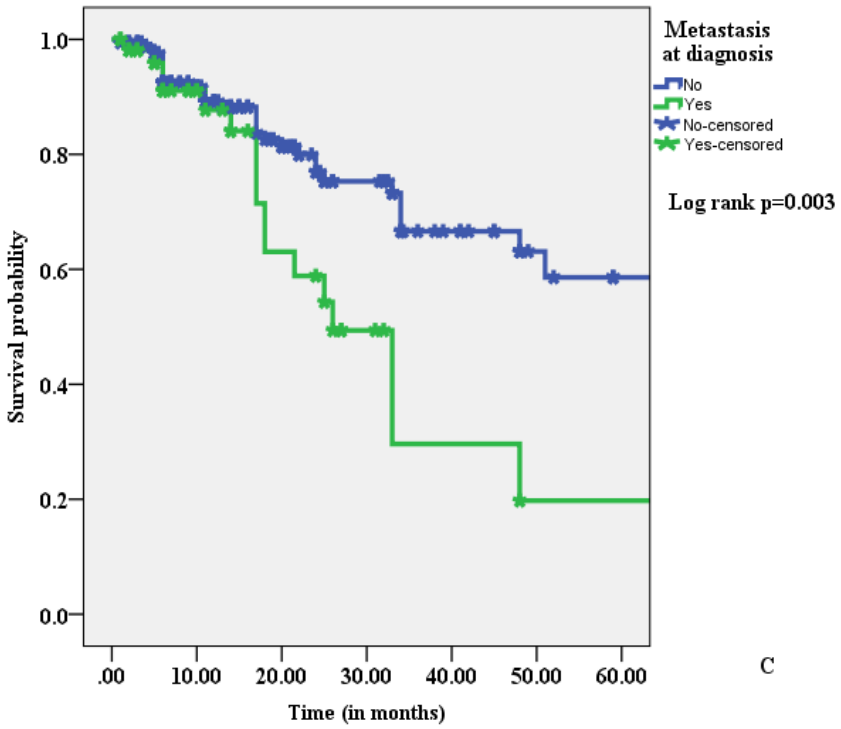
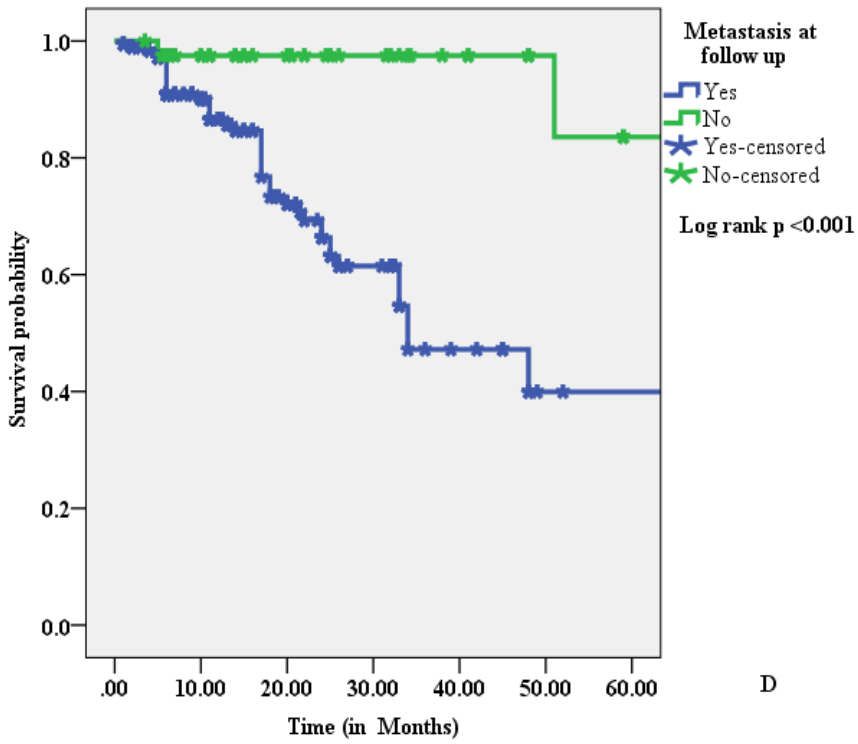


Figure 8.3: Kaplan-Meier survival curve of colorectal cancer patients based on age categories and co-morbidity


Metastasis at diagnosis
No
Yes
No-censored
Yes-censored
Log rank p=0.003
Survival probability
1.0
0.8
0.6
0.4
0.2
0.0
.00
10.00
20.00
30.00
40.00
50.00
60.00
Time (in months)

C


Metastasis at follow up
Yes
No
Yes-censored
No-censored
Log rank p <0.001
Survival probability
1.0
0.8
0.6
0.4
0.2
0.0
.00
10.00
20.00
30.00
40.00
50.00
60.00
Time (in Months)

D

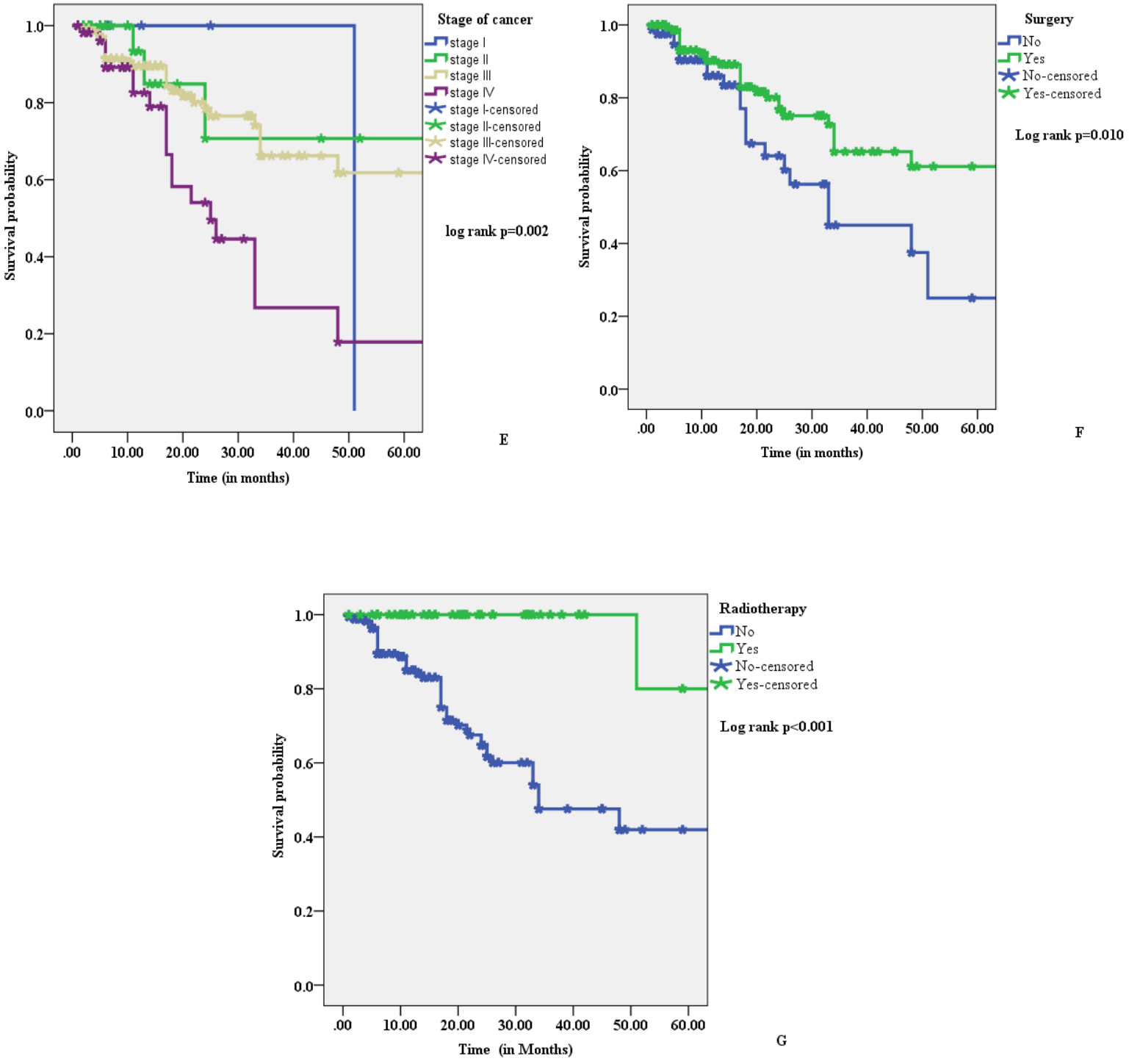


Figure 8.4: Kaplan-Meier survival curve of colorectal cancer patients based on metastasis, stage and treatment regimen.

8.4.6 Determinants of survival among colorectal cancer patients

The present study depicted that co-morbid patients had 2.4 times increased mortality risk than those without co-morbidity (AHR=2.4, 95% CI= 1.2-3.5, p=0.04). Patients with distance metastasis at diagnosis and follow-up period had 1.6 (AHR=1.6, 95% CI= 1.1-2.3, p=0.04) and 6.9 (AHR=2.4, 95% CI= 1.6-12.3, p=0.01) times more hazards of dying than patients without metastasis, respectively. Patients who did not undergo surgical intervention had 2.2 times more hazards of dying than those who underwent surgery (AHR=2.2, 95% CI= 1.8-3.6, p=0.04). Furthermore, patients with radiotherapy had a lower risk of death than those without radiotherapy treatment (AHR=13.5, 95% CI= 1.7-20.2, p=0.002). Gender, age, histological type, cancer stage, chemotherapy and symptomatic management were not significant determinants of survival in colorectal cancer patients **(Table 8.6)**.

Table 8.6: Determinants of mortality among colorectal cancer patients (n=232)

Variable	Bivariable analysis		Multivariable analysis	
	CHR (95% CI)	P-value	AHR (95% CI)	P-value
Age (years)				
< 60 years	1		1	
≥ 60 years	0.4(0.3-0.7)	**0.03***	0.7(0.4-1.4)	0.3
Gender				
Male	1		1	
Female	1.1(0.8-1.5)	0.5	1.1(0.6-1.9)	0.9
Co-morbidity				
Absent	1		1	
Present	3.4(1.5-7.5)	**0.003***	2.4(1.2-3.5)	**0.04***
Stage of cancer				
Early-stage (I &II)	1		1	
Advanced stage (III & IV)	0.5(0.2-1.5)	0.2	0.6(0.2-2.3)	0.5
Histological type of cancer				
Adenocarcinoma	1		1	
Squamous cell carcinoma	4.5(0.2-12.3)	0.8	2.1(0.9-3.6)	0.9
Distant metastasis at diagnosis				
No	1		1	
Yes	2.3 (1.3-4.1)	**0.004***	1.6(1.1-2.3)	**0.04***
Distant metastasis in the follow-up period				
No	1		1	
Yes	3.2(1.6-6.4)	**0.001***	6.9(1.6-12.3)	**0.01***
Treatment regimen				
Chemotherapy				
Yes	1		1	
No	0.9 (0.6-1.6)	0.8	2.2(0.3-13.8)	0.4
Surgery				
Yes	1		1	
No	1.4 (1.1-1.9)	**0.01***	2.2(1.8-3.6)	**0.04***
Radiotherapy				
Yes	1		1	
No	4.4(1.6-11.9)	**0.003***	13.5(1.7-20.2)	**0.002***
Symptomatic therapy				
Yes	1		1	
No	0.9(0.4-1.8)	0.8	0.6(0.1-5.7)	0.6

*Statistically significant p-value ≤0.05, CHR: Crude hazard ratio, AHR: Adjusted hazard ratio

In the sub-group analysis, age, gender, histology types, co-morbidity and treatment regimens were not determinants of survival among early-stage patients. However, the mortality hazard was higher among older (≥ 60 years) (AHR=2.7, 95% CI= 1.5-4.8, p=0.001) and co-morbid (AHR=2.7, 95% CI= 1.1-6.3, p=0.03) advanced-stage colorectal patients.

Patients with advanced stage who did not receive surgery (AHR=1.5, 95% CI= 1.1-1.9, p=0.01) and radiotherapy (AHR=4.7, 95% CI= 1.7-5.5, p=0.04) had a higher risk of dying **(Table 8.7)**.

Table 8.7: Determinants of mortality among early and advanced-stage colorectal cancer patients

Variables	Categories	Bivariable analysis		Multivariable analysis	
		CHR (95% CI)	P-value	AHR (95% CI)	P-value
Early stage (I &II)	**Age (years)**				
	< 60 years	1		1	
	≥ 60 years	0.1(0.1-2.2)	0.4	0.4(0.2-2.7)	0.5
	Gender				
	Male	1		1	
	Female	0.6(0.2-1.9)	0.3	0.7(0.1-1.8)	0.2
	Co-morbidity				
	Absent	1		1	
	Present	1.8(0.2-3.5)	0.4	1.2(0.2-2.5)	0.3
	Histology type				
	Adenocarcinoma	1		1	
	Squamous cell carcinoma	2.1 (0.1-2.8)	0.7	1.8 (0.2-2.9)	0.8
	Treatment regimen				
	Chemotherapy				
	Yes	1		1	
	No	0.9(0.3-2.9)	0.9	0.6(0.1-9.7)	0.7
	Surgery				
	Yes	1		1	
	No	1.3(0.4-4.2)	0.6	1.8(0.4-7.2)	0..4
	Radiotherapy				
	Yes	1		1	
	No	1.1(0.3-3.6)	0.9	1.1(0.3-5.4)	0.7
	Symptomatic therapy				
	Yes	1		1	
	No	0.7(0.3-1.7)	0.6	0.9(0.2-1.9)	0.2
Advanced stage (III&IV)	**Age (years)**				
	< 60 years	1		1	
	≥ 60 years	2.8(1.6-4.9)	**0.001***	2.7(1.5-4.8)	**0.001***
	Gender				
	Male	1		1	
	Female	1.2(0.9-1.5)	0.4	1.1(0.8-1.5)	
	Co-morbidity				
	Absent	1		1	
	Present	2.8(1.2-6.5)	**0.02***	2.7(1.1-6.3)	**0.03***
	Histology type				
	Adenocarcinoma	1		1	
	Squamous cell carcinoma	4.5 (0.1-5.5)	0.8	2.5 (0.2-3.5)	0.6
	Treatment regimen				
	Chemotherapy				
	Yes	1		1	
	No	1.2(0.6-2.1)	0.6	4.5(0.6-12.6)	0.1
	Surgery				
	Yes	1		1	
	No	1.4(1.1-1.9)	**0.02***	1.5(1.1-1.9)	**0.01***
	Radiotherapy				
	Yes	1		1	
	No	5.8(1.5-22.2)	**0.01***	4.7(1.7-5.5)	**0.04***
	Symptomatic therapy				
	Yes	1		1	
	No	0.9(0.4-1.8)	0.8	2.1(0.6-7.1)	0.2

*Statistically significant p-value ≤0.05, CHR: Crude hazard ratio, AHR: Adjusted hazard ratio

8.5 Discussion

This study aimed to investigate survival outcomes among colorectal cancer patients at the largest teaching and referral hospital in East and Central Africa. Developing countries experienced a higher burden of colorectal cancer and low five-year survival (Gullickson et al., 2021) than developed countries such as Korea, the United States, Canada and Europe (Jiang et al., 2021). Despite advances in managing colorectal cancer, patients in sub-Saharan African countries still have poor survival (Gullickson et al., 2021). The study revealed a reduction in colorectal cancer patients' survival from one year to five years after diagnosis. In contrast, the findings in the Caucasian population showed relatively higher five-year survival (Rawla et al., 2019). Studies from Ghana and Indonesia also showed low overall survival for those patients (Agyemang-Yeboah et al., 2018; Dharmaji et al., 2021). In contrast, a study from nine European countries reported a higher (89.2%) fiver-year cancer-specific survival compared to our setting (45.4%) (Cardoso et al., 2022). Moreover, a systematic review revealed a higher (57.3%) five-year survival than the findings in our study setting (Nikbakht et al., 2020). In Africa, the limited availability of screening facilities, poor knowledge about the disease and the importance of early screening were the most common barriers to implementing early detection of colorectal cancer (Schliemann et al., 2021). Therefore, this variation might be related to the inadequacy of early screening programs, late diagnosis, high cost of treatment and limited access to cancer treatment services in the study setting.

The median cancer-specific survival time in our setting (57.2±2.1 months) was higher than the studies from Ghana (15 months), Ethiopia (34.8 months) and Cameroon (43 months) (Agyemang-Yeboah et al., 2018; Atinafu et al., 2022; Engbang et al., 2021). The observed variations could be ascribed to disparities in screening programs, stage of disease at diagnosis and quality of medical care.

The finding showed that colorectal cancer patients had a high mortality in our setting, as observed in Ethiopia, Djibouti, Rwanda, Nigeria and South Africa (Atinafu et al., 2022; Awedew et al., 2022; Motsuku et al., 2021). These variations could be linked to the difference in the study population, duration of follow-up in the studies, and clinical characteristics of the patients. Studies reported that colorectal cancer patients with a late diagnosis had the worst survival (Padilla-Ruiz et al., 2022; Pita-Fernández et al., 2016). This high mortality in the study setting

might be linked to late diagnosis and delayed initiation of optimal treatment due to scarce cancer treatment centres. Despite the growing incidence and death related to cancer in Africa, cancer research and healthcare services have been given minimal attention (Hamdi et al., 2021). This insufficient health coverage may impede poor patients' ability to obtain optimal diagnostic and therapeutic interventions, which can remarkably affect the anticipated treatment outcomes.

In the last follow-up period, about a third of the patients had disease progression. Furthermore, 7.8% had no response and 15.9% had a complete response to the treatment modalities. Similarly, a previous study also showed that 15.3% of colorectal cancer patients had a complete response to the treatment (Bulut et al., 2021). Thus, it is essential to develop effective patient-specific interventional methods to mitigate high rates of disease progression and non-response to treatment.

The findings of a study conducted in African nations revealed that a diagnosis at a younger age (<50 years) and in the advanced stages of the disease was linked to unfavourable survival outcomes (Gullickson et al., 2021). The lower survival and a higher percentage of disease progression in our setting may be related to the above factors, such as the advanced stage and younger age at diagnosis.

During the course of follow-up, 23.6% of patients developed new distant organ metastases. A similar investigation reported the incidence of distant organ metastasis at 17.31% (Liu et al., 2022). Another investigation demonstrated that approximately half of the patients exhibited distant metastasis following surgical excision of the primary tumours (Filip et al., 2020). Patients with metastases are less likely to attain long-term remission than those with localised cancer (Ganesh & Massagué, 2021). Therefore, optimal management of colorectal cancer patients at the early stages is indispensable to halt the progression of the disease since metastatic tumours do not respond to the current therapies.

Colorectal cancer patients with distant organ metastasis and co-morbidities had a greater hazard of dying. Furthermore, patients treated with radiotherapy and surgery had a lower mortality hazard than those who were not. This is in agreement with another study where surgically treated patients had better survival and stage IV patients had a higher risk of mortality (Teka et al., 2021). Although chemotherapy was not a significant determinant of survival in our findings,

other studies reported that chemotherapy-treated colorectal cancer patients had a lower risk of mortality (Azzam et al., 2020; Mahmoudi et al., 2022). A study in Ethiopia stated that age (≥60 years), comorbidity and stage of the tumour were determinants of survival in patients with colorectal cancer (Atinafu et al., 2022). Another study also reported age and co-morbidity as a predictor of survival (Van Eeghen et al., 2015). Although studies reported that women and younger patients had better survival than men and older colorectal cancer patients (Maajani et al., 2019; Schmuck et al., 2020; Yang et al., 2017), these attributes were not significant in our setting.

Strengths and limitations of the study

The study comprehensively examined the survival outcomes of patients with colorectal cancer in a large sample size with long-term follow-up. This was the first study that evaluated the determinants that impacted survival in colorectal cancer patients in Kenya. Hence, it can be used as baseline data for further studies. The incompleteness of medical records was the main limitation of the retrospective cohort study due to the retrospective nature of the study. In this case, the data's accuracy depended on the correctness of the documentation in the study setting.

8.6 Conclusions

There was a high mortality (22.8%), disease progression (34.1%), non-response to the treatment (7.8%) and new distant metastases (23.6%) in the study setting. Older age, co-morbidity, surgery and radiotherapy were significant determinants of survival in the advanced stage of the disease. However, none of them had a significant association with survival among early-stage patients.

8.7 Recommendations for policy and practice

Due to the high mortality and disease progression, improving the healthcare system is crucial for providing colorectal cancer patients with access to screening, early detection and effective therapies. In addition, early initiation of optimal therapy with adequate monitoring is indispensable to improve survival outcomes.

8.8 Recommendations for further research

Multi-centre prospective cohort studies should be employed to determine the long-term survival outcomes of colorectal cancer patients.

CHAPTER NINE: SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

9.1 Introduction

This study evaluated DRPs, HRQoL and survival outcomes among patients with gastrointestinal cancers at KNH. This chapter summarises the main findings of this study. It also incorporates the general conclusions, recommendations, limitations, and dissemination plan. The new contribution to the body of knowledge is also highlighted in this chapter.

9.2 Summary

The study investigated the prevalence and types of DRPs among patients diagnosed with gastrointestinal cancer **(Chapter 4)**. More than 50% of patients with gastrointestinal cancer had DRPs. The highest prevalence of DRPs was observed among males, those with co-morbidities and those in advanced stages of gastrointestinal cancers (III and IV). Patients with comorbidities take more drugs, and therefore, the likelihood of drug interactions is high. The drugs are metabolized and eliminated mainly by the liver and kidneys. A patient with cancer is generally weak and these organs tend to get overwhelmed.

Need for additional drug therapy, drug-drug interaction and ADRs were the most frequent categories of DRPs. This high prevalence of the need for additional drug therapy could probably be linked to the resource constraints of the patients to initiate optimal therapy. The high prevalence of drug-drug interactions was due to the many drugs used concurrently during therapy. Drugs used to manage cancer are inherently toxic and exhibit many side effects.

In esopahgeal cancer patients, cisplatin & 5-fluorouracil-based regimens treated patients had the highest DRPs. In gastric cancer patients, FLOT and CAPOX regimens had a substantial proportion of DRPs. Colorectal cancer patients receiving the FOLFOX regimen had a disproportionately high percentage of DRPs compared to the other regimens.

The most commonly observed ADRs among patients with esophageal and gastric cancer were nausea/vomiting and anaemia. The most frequently identified ADRs in patients with colorectal cancer were neutropenia, anaemia and diarrhoea. The majority of the identified ADRs in gastrointestinal cancer patients were possible causality scores, mild severity level and potentially preventable.

The HRQoL was also assessed using the standard EORTC QLQ-C30, EORTC QLQ- OES18, EORTC QLQ- STO22 and EORTC QLQ-CR29 HRQoL questionnaires (Chapter 5). The study revealed that most patients had a poor overall HRQoL. This could probably be linked to the predominance of advanced disease at diagnosis and the high prevalence of co-morbidity, which can complicate the treatment regimens. Drug-related problems were prevalent, and ADRs were among the leading categories of DRPs identified, which can probably contribute to the low HRQoL. Over half of the patients had poor HRQoL in social and role domains of HRQoL. Most esophageal cancer patients had poor HRQoL in physical and cognitive domains compared to gastric and colorectal cancer patients. In almost all symptom domains of HRQoL, the mean score was above the recommended level of the mean score. This suggests that most gastrointestinal cancer patients did not have major problems in the symptoms domain of HRQoL.

The study also investigated the survival outcomes in patients with esophageal, gastric and colorectal cancers **(Chapters 6-8)**. Most gastrointestinal cancer patients had a high mortality, low five-year survival and disease progression during the follow-up period. This might be related to the predominance of co-morbid, older and advanced-stage disease patients, which can negatively affect survival despite optimal therapy. In addition, the majority of our patients had financial difficulties covering the cost of diagnosis and treatment of their conditions. Consequently, most patients may not get optimal and timely initiation of therapy.

Advanced-stage (stages III & IV) and co-morbidities were significant determinants of DRPs and poor HRQoL among patients with gastrointestinal cancer. In advanced-stage esophageal cancer, chemoradiation, chemotherapy and radiotherapy treatment modalities were the significant determinants of survival. Chemotherapy, gastrectomy, radiotherapy and co-morbidity were the survival determinants in advanced gastric cancer. Older age, co-morbidity, surgery and radiotherapy were significant determinants of survival in advanced colorectal cancer. Surgery was the sole factor in determining survival in patients with early-stage esophageal and gastric cancer. Nevertheless, none of the variables had a significant association in impacting survival among early-stage colorectal patients.

9.3 General conclusions

DRPs, including the need for additional drug therapy and ADRs, were prevalent among patients with gastrointestinal cancer due to comorbidities and advanced cancer, which require multiple

combination therapies. Nausea/vomiting, neutropenia and anaemia were the most frequent ADRs due to the emetogenic and myelosuppressive effects of cancer chemotherapy. Nonetheless, most identified ADRs had mild severity levels and were preventable. Gastrointestinal cancer patients had a poor overall HRQoL due to surgery, chemotherapy, comorbidities and advanced cancer. The study revealed high mortality and low five-year survival, probably due to disease progression, non-response to therapy and metastases. However, esophagectomy and gastrectomy were determinants of survival in the early stages of esophageal and gastric cancers. Nonetheless, none of the variables had a significant impact on the survival of early-stage colorectal patients. Radiotherapy was the significant determinant of survival for patients with advanced-stage esophageal, gastric and colorectal cancer. Moreover, patients with advanced-stage gastric and colorectal cancer had a higher mortality risk due to multiple co-morbidities.

9.4 Recommendations for policy and practice

DRPs were prevalent among gastrointestinal cancer patients due to comorbidities and advanced-stage disease. Therefore, close monitoring is required in patients with multiple illnesses and advanced stages to reduce this high burden of DRPs. The study showed that drug-drug interactions were more frequent among patients with gastrointestinal cancer. Therefore, medication interaction checker software should be used extensively at the prescription and dispensing stages to minimize the significant morbidity of this undesired occurrence. Since most ADRs are preventable, preventive measures such as detailed assessment of medical history, dose optimization, supportive care, patient education and pharmacovigilance should be implemented during chemotherapy treatment to minimize the frequency and severity of ADRs among patients with gastrointestinal cancer.

Since most patients have advanced-stage disease, regular exercise, proper nutrition, psychosocial support, adequate symptoms and pain management should be given to improve the HRQoL of gastrointestinal cancer survivors. Early diagnosis and access to optimal treatment modalities are also indisputably important to mitigate HRQoL.

Due to the high mortality, disease progression and non-response to treatment, early initiation of optimal treatment is highly recommended to mitigate survival outcomes. The late presentation at diagnosis leading to a high mortality among patients with gastrointestinal cancer suggests that widespread screening and awareness programs should be instituted to avert the disaster.

9.5 Recommendations for further research

Further studies should be done to design DRPs-preventive strategies such as medication reconciliation, risk factor identifications, clinical pharmacist-led interventions and patient education in gastrointestinal cancer patients. Future prospective cohort studies involving a large number of cancer patients should be conducted to assess the impact of DRPs on the economic burden from the patient, hospital and healthcare provider perspectives.

A prospective cohort study in a multi-centre setting should be conducted to assess the long-term impacts of various treatment modalities on HRQoL and the long-term survival outcomes of gastrointestinal patients. In addition, a multi-centre prospective cohort study is recommended to reliably assess the determinants of DRPs, HRQoL and survival outcomes in patients with gastrointestinal cancer in Kenya.

9.6 Strengths, weaknesses and limitations of the study

The study comprehensively assessed DRPs using predesigned data collection tools by comparing them with the standard treatment protocols of each gastrointestinal cancer. The study also comprehensively examined the survival outcomes of patients with gastrointestinal cancer in a large sample size with long-term follow-up. Standard general and cancer-specific HRQoL assessment tools were used to investigate the HRQoL of the selected gastrointestinal cancers. This was the first study that evaluated the determinants that impacted survival in esophageal, gastric and colorectal cancer patients in Kenya. Hence, it can be used as baseline data for further studies.

Despite the study's several strengths, it has some limitations, as described below.

The tools used to assess HRQoL require the patients to recall events that happened in the past. Thus, the responses were dependent on the individuals' memories, and recall bias was possible. Patients with significant problems in remembering past events were excluded from the study to alleviate this problem. The incompleteness of medical records was the main limitation of the retrospective cohort study due to the retrospective nature of the study. In this case, the data's accuracy depended on the correctness of the documentation in the study setting. To mitigate this problem, we have included only completed records of patients in the study as per the eligibility criteria.

9.7 Knowledge generated from the study

From the study, we found that the prevalence of DRPs was high, and most patients had a poor overall HRQoL due to co-morbidity and advanced stages of the disease. The five-year survival of patients was low, probably due to disease progression, non-response to therapy and metastases. However, the surgical treatment approach was the significant determinant of survival in the early stages of esophageal and gastric cancers. Radiotherapy was the significant determinant of survival for patients with advanced-stage gastrointestinal cancer patients. Moreover, patients with advanced-stage gastric and colorectal cancer had a higher mortality risk due to multiple co-morbidities.

9.8 Dissemination plan

The findings of the current study will be given to the Medical Research Office and the Oncology Department of KNH for further action on the key findings. A copy of the results will be given to the Cabinet Secretary of Health of Kenya, NACOSTI and the Ethics and Review Committee of KNH/UoN. It will also be disseminated by presenting at local and international cancer conferences. Five articles were published in reputable international cancer journals (Appendix XII).

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APPENDICES

Appendix I: Participant information and consent form

Title of the study: Evaluation of drug-related problems, health-related quality of life and survival outcomes among patients with gastrointestinal cancers at Kenyatta National Hospital.

Principal investigator and institutional affiliation

Amsalu Degu (PhD student in Clinical Pharmacy)

Department of Pharmacology, Clinical Pharmacy and Pharmacy Practice, Faculty of Health Sciences, University of Nairobi

Co-investigators and institutional affiliation

1. Peter Karimi (PhD)

   Department of Pharmacology, Clinical Pharmacy and Pharmacy Practice, Faculty of Health Sciences, University of Nairobi
2. Sylvia Opanga (PhD)

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3. David Nyamu (PhD)

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Introduction

I am Amsalu Degu, studying PhD in Clinical Pharmacy at the University of Nairobi, Department of Pharmacology, Clinical Pharmacy and Pharmacy Practice, Faculty of Health Sciences. I am doing my Ph.D. research on gastrointestinal cancers, which are among the leading type of cancer in Kenya. I will give you information and invite you to be part of this research.

Purpose of the research

The prevalence of DRPs, health-related quality of life, and survival outcomes are unknown in the study setting among patients with gastrointestinal cancers. Hence, the findings of the present study will serve as baseline data for further investigations.

Participant selection

You are invited to take part in this research because we feel that your input will be extremely valuable as the information will be used to identify gaps in treatment outcomes.

Voluntary participation or withdrawal from the study

Your participation in this research is voluntary. It is your choice whether to participate or not. If you choose not to participate, you are not going to lose any service that you are getting from the hospital. Even after joining the study, you still have the right to withdraw from the study at any time you want.

Risks and benefits

Participating in this study may be associated with no or minimal risk and discomfort during the interview since it will take at most ten minutes. You will not be provided any incentive to take part in the research. However, your participation is likely to help cancer treatment care at Kenyatta National Hospital.

Confidentiality

The information that we collect from this research project will be kept private. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is, and we will lock that information up with a lock and key. I will be very grateful if you are willing to participate in this study, and hence we can do something positive towards cancer treatment outcomes. Finally, it is my great pleasure to forward my deepest gratitude in advance for your kind cooperation and for giving permission to access your medical records.

Who to contact

If you have any questions, you free to ask any questions at any time about the study and regarding your right as a research volunteer. If you wish to ask questions later, you may contact the principal investigator using the following address: Amsalu Degu, University of Nairobi, School of Pharmacy. Email: amsaludegu@yahoo.com, Tel: +254745063687.

This proposal has been reviewed and approved by the Kenyatta National Hospital (KNH)/University of Nairobi (UON) Ethics Review Committee, a committee whose task is to ensure that research participants are protected from harm. Hence, you can get further information

regarding your rights as a study participant from the Secretary of KNH/UON ethics and research committee using the following address.

uonknh_erc@uonbi.ac.ke, P.O Box 20723-00202 Nairobi, Tel. 2726300 Ext. 44102.

Statement of consent

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with the principal investigator. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw at anytime. I freely agree to participate in this research study. I understand that all efforts will be made to keep information regarding my personal identity confidential. By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

Participant printed name: _____

Participant signature / Thumb stamp _____Date _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and willingly given his/her consent.

_____ _____ _____

Name of Researcher/person taking the consent Signature Date

Appendix II: Data collection format for the cross-sectional study design

I. Socio-demographic characteristics of the patients

Patient Study Number: ☐ Age in years: ☐

Gender: Male ☐ Female ☐

Marital status: ☐ Single ☐ Married ☐ Divorced ☐ Widowed

Educational Status: Primary ☐ Secondary ☐ Tertiary ☐ Informal ☐

Occupational status:

Housewife ☐ Government Employee ☐ Unemployed/Retired ☐ Self-employed ☐

Others (Specify) _____

II. History of substance use

- ☐ Alcohol
- ☐ Smoking cigarette
- ☐ Chewing khat
- ☐ None

Family history of cancer Yes_____ No_____

III. Clinical characteristics of the patients

1. Histological type of cancer_____Stage of cancer_____
2. Co-morbidity: Present ☐ Absent ☐ If present, (specify) _____
3. Treatment regimens of the patient
   A. Radiotherapy
   B. Chemotherapy
   C. Surgery
   D. Combination therapy (specify)_____
   E. Types of chemotherapy regimen given (if given)

      _____

      _____

IV: Drug-related problems identification tool

1. Is there any drug-related problem present? Yes___No____if yes specify the number_____
2. Is there any need for additional drug therapy? Yes___ No___
3. Is there any ineffective drug therapy? Yes___ No___
4. Is there any unnecessary drug therapy in the treatment regimen? Yes___ No___
5. Dose of the drug in the treatment regimen: Appropriate____ Dosage too low_____ Dosage too high____
6. Is there any drug interaction? Yes _____ No_____

   If yes for question 6, specify the drug interaction

   ▭ Serious ▭ Significant ▭ Moderate ▭ Minor

7. Is there any adverse drug reaction? Yes _____ No_____

   If yes, specify the adverse drug reaction _____

V: Naranjo Adverse Drug Reaction Probability (causality assessment) Scale

Question	**Yes**	**No**	**Do Not Know**
1. Are there previous conclusive reports on this reaction?	+1	0	0
2. Did the adverse reaction appear after the suspected drug was administered?	+2	-1	0
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0
4. Did the adverse reaction reappear when the drug was readministered?	+2	-1	0
5. Are there alternative causes that could on their own have caused the reaction?	-1	+2	0
6. Did the reaction reappear when a placebo was given?	-1	+1	0
7. Was the drug detected in blood or other fluids in	+1	0	0

concentrations known to be toxic?			
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0
10. Was the adverse reaction confirmed by any objective evidence?	+1	0	0
Total Score:			
Interpretation of scores Total score ≥9: Definite Total score 5-8:Probable Total score 1-4: Possible Total score ≤0: Doubtful			

Based on the total score, ADR is:

Definite (score ≥9) ☐ Possible (score 1-4) ☐

Probable (score 5-8) ☐ Doubtful (score ≤0) ☐

VI: Severity of ADR based on modified Hartwig and Siegel scale

Severity scale	Severity Level	Description of the above-identified reaction(s)	Yes	No
Mild	Level 1	The ADR requires no change in treatment with the suspected drug.		
	Level 2	The ADR requires that the suspected drug be withheld, discontinued or otherwise changed		
Moderate	Level 3	The ADR requires that the suspected drug be withheld, discontinued, or otherwise changed, and/ or an antidote or another treatment is required. There is no increase in length of stay.		
	Level 4 (a)	Any level 3 ADR that increases the length of stay by at least one day.		
	Level 4 (b)	The ADR is the reason for admission		
Severe	Level 5	Any level 4 ADR that requires intensive medical care.		
	Level 6	The ADR causes permanent harm to the patient.		
	Level 7(a)	The ADR directly leads to the death of the patient.		
	Level 7(b)	The ADR indirectly leads to the death of the patient		

VII: Preventability of ADR based on modified Schumock and Thornton scale (Tick √ in the most appropriate preventability scale bases on the ADR listed)

S.No	Schmuck and Thornton Criteria	Yes	No
	A. Definitely preventable ADRs		
1.	Was there a history of allergy or a previous reaction to the drug?		
2.	Was the drug involved inappropriate for the patient's clinical condition?		
3.	Was the dose, route, or frequency of administration inappropriate for the patient's age, weight, or disease state?		
4.	Was toxic serum drug concentration or lab monitoring test documented?		
5.	Was there a known treatment for ADEs?		
	B. Probably preventable ADRs		
6.	Was therapeutic drug monitoring or other necessary lab tests not performed?		
7.	Was the drug interaction involved in ADRs?		

8.	Was poor compliance involved in ADRs?		
9.	Were preventative measures not prescribed or administered to the patient?		
C. Non-preventable ADRs			
10.	If all the above criteria are not fulfilled.		

Answering "yes" to one or more of the questions in section "A" implies that an ADR is DEFINITELY preventable and If answers are all negative to section "A," then proceed to Section "B." Answering "yes" to one or more of the questions in section "B" implies that an ADR is PROBABLY preventable, and if the answers are all negative to section "B," then proceed to Section "C." In Section "C" the ADR is NOT preventable.

On the basis of Schmuck and Thornton criteria, ADRs are:

Definitely preventable ADRs ☐ Probably preventable ADRs ☐

Non-preventable ADRs ☐

Appendix III: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 Version 3.0

	Not at all	**A little**	**Quite A bit**	**Very much**
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4
During the past week:	**Not at all**	**A little**	**Quite A bit**	**Very much**
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions, please circle the number between 1 and 7 that best applies to you

	Very poor						Excellent
29. How would you rate your overall health during the past week?	1	2	3	4	5	6	7
30. How would you rate your overall quality of life during the past week?	1	2	3	4	5	6	7

Appendix IV: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Colorectal Cancer Module 29 (EORTC QLQ – CR29)

During the past week:	Not at All	A Little	Quite a Bit	Very Much
31. Did you urinate frequently during the day?	1	2	3	4
32. Did you urinate frequently during the night?	1	2	3	4
33. Have you had any unintentional release (leakage) of urine?	1	2	3	4
34. Did you have pain when you urinated?	1	2	3	4
35. Did you have abdominal pain?	1	2	3	4
36. Did you have pain in your buttocks/anal area/rectum?	1	2	3	4
37. Did you have a bloated feeling in your abdomen?	1	2	3	4
38. Have you had blood in your stools?	1	2	3	4
39. Have you had mucus in your stools?	1	2	3	4
40. Did you have a dry mouth?	1	2	3	4
41. Have you lost hair as a result of your treatment?	1	2	3	4
42. Have you had problems with your sense of taste?	1	2	3	4

During the past week:	Not at All	A Little	Quite a Bit	Very Much
43. Were you worried about your health in the future?	1	2	3	4
44. Have you worried about your weight?	1	2	3	4
45. Have you felt physically less attractive as a result of your disease or treatment?	1	2	3	4
46. Have you been feeling less feminine/masculine as a result of your disease or treatment?	1	2	3	4
47. Have you been dissatisfied with your body?	1	2	3	4
48. Do you have a stoma bag (colostomy/ileostomy)? (please circle the correct answer)	Yes		No	

During the past week:	Not at All	A Little	Quite a Bit	Very Much
Answer these questions ONLY IF YOU HAVE A STOMA BAG, if not please continue below:				
49. Have you had unintentional release of gas/flatulence from your stoma bag?	1	2	3	4
50. Have you had leakage of stools from your stoma bag?	1	2	3	4
51. Have you had sore skin around your stoma?	1	2	3	4
52. Did frequent bag changes occur during the day?	1	2	3	4
53. Did frequent bag changes occur during the night?	1	2	3	4
54. Did you feel embarrassed because of your stoma?	1	2	3	4
55. Did you have problems caring for your stoma?	1	2	3	4

Answer these questions ONLY IF YOU DO NOT HAVE A STOMA BAG:				
49. Have you had unintentional release of gas/flatulence from your back passage?	1	2	3	4
50. Have you had leakage of stools from your back passage?	1	2	3	4
51. Have you had sore skin around your anal area?	1	2	3	4
52. Did frequent bowel movements occur during the day?	1	2	3	4
53. Did frequent bowel movements occur during the night?	1	2	3	4
54. Did you feel embarrassed because of your bowel movement?	1	2	3	4

During the past 4 weeks:	Not at All	A Little	Quite a Bit	Very Much
For men only:				
56. To what extent were you interested in sex?	1	2	3	4
57. Did you have difficulty getting or maintaining an erection?	1	2	3	4

For women only:				
58. To what extent were you interested in sex?	1	2	3	4
59. Did you have pain or discomfort during intercourse?	1	2	3	4

Appendix V: European Organization for Research and Treatment of Cancer Quality of Life questionnaire esophageal Cancer Module 18 (EORTC QLQ – OES18)

During the past week:		Not at all	A little	Quite a bit	Very much
31.	Could you eat solid food?	1	2	3	4
32.	Could you eat liquidised or soft food?	1	2	3	4
33.	Could you drink liquids?	1	2	3	4
34.	Have you had trouble with swallowing your saliva?	1	2	3	4
35.	Have you choked when swallowing?	1	2	3	4
36.	Have you had trouble enjoying your meals?	1	2	3	4
37.	Have you felt full up too quickly?	1	2	3	4
38.	Have you had trouble with eating?	1	2	3	4
39.	Have you had trouble with eating in front of other people?	1	2	3	4
40.	Have you had a dry mouth?	1	2	3	4
41.	Did food and drink taste different from usual?	1	2	3	4
42	Have you had trouble with coughing?	1	2	3	4
43.	Have you had trouble with talking?	1	2	3	4
44.	Have you had acid indigestion or heartburn?	1	2	3	4
45.	Have you had trouble with acid or bile coming into your mouth?	1	2	3	4
46.	Have you had pain when you eat?	1	2	3	4
47.	Have you had pain in your chest?	1	2	3	4
48.	Have you had pain in your stomach?	1	2	3	4

Appendix VI: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Gastric Cancer Module 22 (EORTC QLQ – STO22)

During the past week:	Not at All	A Little	Quite a Bit	Very Much
31. Have you had problems eating solid foods?	1	2	3	4
32. Have you had problems eating liquidised or soft foods?	1	2	3	4
33. Have you had problems drinking liquids?	1	2	3	4
34. Have you had discomfort when eating?	1	2	3	4
35. Have you had pain in your stomach area?	1	2	3	4
36. Have you had discomfort in your stomach area?	1	2	3	4
37. Did you have a bloated feeling in your abdomen?	1	2	3	4
38. Have you had trouble with acid or bile coming into your mouth?	1	2	3	4
39. Have you had acid indigestion or heartburn?	1	2	3	4
40. Have you had trouble with belching?	1	2	3	4
41. Have you felt full up too quickly after beginning to eat?	1	2	3	4
42. Have you had trouble enjoying your meals?	1	2	3	4
43. Has it taken you a long time to complete your meals?	1	2	3	4
44. Have you had a dry mouth?	1	2	3	4
45. Did food and drink taste different from usual?	1	2	3	4
46. Have you had trouble with eating in front of other people?	1	2	3	4
47. Have you been thinking about your illness?	1	2	3	4
48. Have you worried about your weight being too low?	1	2	3	4
49. Have you felt physically less attractive as a result of your disease or treatment?	1	2	3	4
50. Have you worried about your health in the future?	1	2	3	4
51. Have you lost any hair?	1	2	3	4
52. Answer this question only if you lost any hair: If so, were you upset by the loss of your hair?	1	2	3	4

Appendix VII: Data abstraction form for the retrospective cohort study design

I. Socio-demographic characteristics of the patients

Patient Study Number:_____ Age in years:_____

Gender: Female ☐ Male ☐

Marital status: ☐ Single ☐ Married ☐ Divorced ☐ Widowed

Educational Status: Primary ☐ Secondary ☐ Tertiary ☐ Informal ☐

Occupational status:

Housewife ☐ Government Employee ☐ Unemployed/Retired ☐ Self-employed ☐

Others (Specify _____

II. Clinical characteristics of the patients

1. Family history of cancer Yes_____ No_____
2. Histological type of cancer_____Stage of cancer_____
3. Co-morbidity: Present ☐ Absent ☐ If present, (specify) _____
4. Is there any distant metastasis at the time of diagnosis? Yes_____ No_____ if yes, specify the site_____
5. Relevant laboratory parameters in the last follow-up period
   A. Total WBC count: Normal____ significantly low_____
   B. Neutrophils: Normal____ significantly low_____
   C. Haemoglobin: Normal____ significantly low_____
   D. Platelet count: Normal____ significantly low_____
   E. Serum creatinine level: Normal____ significantly increased_____
   F. Liver function test: Normal____ significantly increased_____
6. Treatment regimens of the patient
   a. Radiotherapy
   b. Chemotherapy (specify the regimen)_____
   c. Surgery (total or partial gastrectomy)_____
   d. Combination therapy (specify)_____

III. Treatment outcome measuring parameters

1. Is there any distant metastasis of cancer during the follow-up period? Yes___ No____ If yes specify the site of metastasis_____
2. What is the status of the patient after the treatment in the last follow-up period?
    A. Dead
    B. Censured (Survived or Unknown)
3. What is the total number of months from the date of primary cancer diagnosis until the occurrence of death_____or last follow-up _____
4. Total number of months from the date of primary cancer diagnosis until the occurrence of first radiologic metastasis_____
5. What is the total number of months from the date of first radiologic metastasis until the occurrence of death_____or last follow-up _____
6. What is the cancer response status during the last follow-up period?
    A. Complete response
    B. Partial response
    C. Non-response
    D. Progression of the disease
    E. Unknown

Appendix VII: UoN/KNH ethics approval letter

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

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Website: http://www.erc.uonbi.ac.ke
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Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/337

27th September, 2021

Dr. Amsalu Degu Defersha
Reg. No.U80/58139/2021
PhD Candidate
Dept. of Pharmaceutics and Pharmacy Practice
School of Pharmacy
College of Health Sciences
University of Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 27 SEP 2021 KNH/UoN-ERC P. O. Box 20723 - 00202 NAIROBI

Dear Dr. Defersha

RESEARCH PROPOSAL: EVALUATION OF DRUG RELATED PROBLEMS, HEALTH-RELATED QUALITY OF LIFE, AND SURVIVAL OUTCOMES AMONG PATIENTS WITH GASTROINTESTINAL CANCERS AT KENYATTA NATIONAL HOSPITAL (P195/03/2021)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 27th September 2021 – 26th September 2022.

This approval is subject to compliance with the following requirements:

i. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
ii. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
iii. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from KNH- UoNERC for each batch of shipment.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (Attach a comprehensive progress report to support the renewal).
vii. Submission of an executive summary report within 90 days upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M.L CHINDIA
SECRETARY, KNH- UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chair, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Pharmacy, UoN
The Chair, Dept.of Pharmaceutics and Pharmacy Practice,UoN
Supervisors: Dr. Peter Karimi, Dept. of Pharmaceutics and Pharmacy Practice, UoN
Dr. Sylvia A. Opanga, Dept. of Pharmaceutics and Pharmacy Practice, UoN
Dr. David G. Nyamu, Dept. of Pharmaceutics and Pharmacy Practice, UoN

Appendix VIII: Study registration certificate

KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   Amsalu Degu Defersha
2. Email address: amsaludegu@yahoo.com Tel No. 0745063687
3. Contact person (if different from PI).....
4. Email address: ..... Tel No. .....
5. Study Title
   Evaluation of drug related Problems, health related Quality of life and survival outcomes among patients with gastrointestinal cancers at Kenyatta National Hospital
6. Department where the study will be conducted CTC
   (Please attach copy of Abstract)
7. Endorsed by KNH Head of Department where study will be conducted.
   Name Dr A. Noorani Signature ..... Date 13/10/2021
8. KNH UoN Ethics Research Committee approved study number KNH-ERC/A/337
   (Please attach copy of ERC approval) P195/03/2021
9. I Amsalu Degu Defersha commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Medical Research.
   Signature ..... Date 13-10-2021
10. Study Registration number (Dept/Number/Year) CTC/123/2021
    (To be completed by Medical Research Department)
11. Research and Program Stamp KENYATTA NATIONAL HOSPITAL 18 OCT 2021

All studies conducted at Kenyatta National Hospital must be registered with the Department of Medical Research and investigators must commit to share results with the hospital.

Version 2: Augus 2014

Appendix IX: National Commission for Science, Technology & Innovation (NACOSTI) research permit

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY & INNOVATION

Ref No: 632909

Date of Issue: 22/June/2022

RESEARCH LICENSE

This is to Certify that Dr.. Amsalu Degu Defersha of University of Nairobi, has been licensed to conduct research in Nairobi on the topic: Evaluation of drug-related problems, health-related problems, and survival outcomes among patients with gastrointestinal cancers at Kenyatta National Hospital for the period ending : 22/June/2023.

License No: NACOSTI/P/22/18113

632909

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY & INNOVATION

Verification QR Code

Appendix X: Interacting drugs and their severity level among gastrointestinal cancer patients

		Severity level			
Interacting drugs in esophageal cancer (n=26)	**Frequency (%)**	**Minor**	**Moderate**	**Significant**	**Serious**
Atenolol+Nifedipine	1(3.8)	0(0)	1(3.8)	0(0)	0(0)
Carvedilol + Spironolactone	1(3.8)	0(0)	0(0)	1(3.8)	0(0)
Cefazolin + Heparin	1(3.8)	0(0)	0(0)	1(3.8)	0(0)
Ceftriaxone + Heparin	2(7.7)	0(0)	0(0)	0(0)	2(7.7)
Cefuroxime + Heparin	1(3.8)	0(0)	0(0)	0(0)	1(3.8)
Clarithromycin + Fluconazole	1(3.8)	0(0)	0(0)	0(0)	1(3.8)
Metronidazole+dexamethasone	1(3.8)	1(3.8)	0(0)	0(0)	0(0)
Fluconazole + Cotrimoxazole	1(3.8)	0(0)	0(0)	1(3.8)	0(0)
Fluconazole+ Efavirenz	1(3.8)	0(0)	1(3.8)	0(0)	0(0)
Metronidazole + Atorvastatin	1(3.8)	0(0)	0(0)	1(3.8)	0(0)
Atenolol+ Diclofenac	1(3.8)	0(0)	1(3.8)	0(0)	0(0)
Norepinephrine+ Furosemide	1(3.8)	1(3.8)	0(0)	0(0)	0(0)
Omeprazole+Digoxin	1(3.8)	0(0)	0(0)	0(0)	1(3.8)
Ondansetron + Metformin	1(3.8)	0(0)	0(0)	1(3.8)	0(0)
Paclitaxel + lopinavir	1(3.8)	0(0)	0(0)	0(0)	1(3.8)
Paracetamol+Enoxaparin	1(3.8)	1(3.8)	0(0)	0(0)	0(0)
Paracetamol + Enoxaparin	1(3.8)	1(3.8)	0(0)	0(0)	0(0)
Paracetamol +Heparin	2(7.7)	2(7.7)	0(0)	0(0)	0(0)
Phenytoin+Tramadol	1(3.8)	1(3.8	0(0)	0(0)	0(0)
Rifampin+Omeprazole	1(3.8)	1(3.8	0(0)	0(0)	0(0)
Tramadol+ Carbamazepine	1(3.8)	1(3.8	0(0)	0(0)	0(0)
Paracetamol+ Metoclopramide	3(11.5)	2(7.7)	0(0)	0(0)	0(0)
Interacting drugs in gastric cancer (n=13)					
Amitriptyline + Haloperidol	1(7.7)	0(0)	0(0)	1(7.7)	0(0)
Amlodipine + Metformin	1(7.7)	0(0)	0(0)	1(7.7)	0(0)
Atenolol + Nifedipine	1(7.7)	0(0)	0(0)	1(7.7)	0(0)
Azithromycin + Heparin	1(7.7)	0(0)	0(0)	0(0)	1(7.7)
Enoxaparin + Losartan	1(7.7)	0(0)	0(0)	1(7.7)	0(0)
Metoclopramide + Paracetamol	1(7.7)	1	0(0)	0(0)	0(0)
Metronidazole + Digoxin	1(7.7)	0(0)	0(0)	1(7.7)	0(0)
Nifedipine + Amitriptyline	1(7.7)	0(0)	0(0)	1(7.7)	0(0)
Omeprazole + Ferrous Sulfate	3(23.1)	0(0)	0(0)	3(23.1)	0(0)
Paracetamol+metronidazole	1(7.7)	1	0(0)	0(0)	0(0)
Torsemide + Metformin	1(7.7)	0(0)	0(0)	1(7.7)	0(0)
Interacting drugs in colorectal cancer (n=10)					
Ciprofloxacin + Ondansetron	1(10)	0(0)	0(0)	0(0)	1(10)
Fentanyl + Morphine	2(20)	0(0)	0(0)	0(0)	2(20)
Metoclopramide + Nitrofurantoin	1(10)	1(10)	0(0)	0(0)	0(0)
Metronidazole + Diclofenac	1(10)	1(10)	0(0)	0(0)	0(0)
Metronidazole + Meloxicam	1(10)	1(10)	0(0)	0(0)	0(0)
Omeprazole + Cefuroxime	1(10)	0(0)	0(0)	0(0)	0(0)
Omeprazole + Iron Sucrose	1(10)	0(0)	0(0)	1(10)	0(0)
Phenytoin + Losartan	1(10)	0(0)	0(0)	0(0)	1(10)
Pregabalin + Tramadol	1(10)	0(0)	0(0)	1(10)	0(0)

Appendix XI: Chemotherapeutic regimens and their adverse drug reactions among gastrointestinal cancer patients

	Types of adverse drug reactions									
Chemotherapy regimens for esophageal cancer (n=22)	**Anemia**	**Anisocytosis**	**Excessive bleeding**	**Hypokalemia**	**Leukopenia**	**Neutropenia**	**Nausea/vomiting**	**Renal toxicity**		**Diarrhoea**	**Peripheral neuropathy**
Cisplatin and 5-fluorouracil	2(9.1)	0(0)	1(4.5)	0(0)	1(4.5)	1(4.5)	5(22.7)	1(4.5)		2(9.1)	0(0)
Cisplatin and paclitaxel	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	3(13.6)	0(0)		0(0)	0(0)
FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin)	0(0)	0(0)	0(0)	0(0)	0(0)	1(4.5)	0(0)	0(0)		0(0)	1(4.5)
Cisplatin	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(4.5)	0(0)		0(0)	0(0)
Capecitabine	0(0)	0(0)	0(0)	1(4.5)	0(0)	0(0)	0(0)	0(0)		0(0)	0(0)
Cisplatin and capecitabine	0(0)	1(4.5)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)		0(0)	0(0)
DCX (docetaxel, cisplatin and capecitabine)	1(4.5)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)		0(0)	0(0)
	Types of adverse drug reactions										
Chemotherapy regimens for gastric cancer (n=40)	**Anemia**	**Edema of lower limb**	**Hypersensitivity reaction**	**Leukopenia**	**Neutropenia**	**Peripheral neuropathy**		**Renal toxicity**	**Nausea/Vomiting**	**Diarrhea**	
FLOT (fluorouracil, leucovorin, oxaliplatin and docetaxel)	2(5)	0(0)	0(0)	3(7.5)	4(10)	0(0)		1(2.5)	5(12.5)	3(7.5)	
CAPOX (capecitabine and oxaliplatin)	2(5)	0(0)	0(0)	0(0)	0(0)	4(10)		0(0)	0(0)	0(0)	
FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin)	1(2.5)	0(0)	0(0)	0(0)	1(2.5)	0(0)		0(0)	0(0)	0(0)	
Cisplatin+ 5-fluorouracil	3(7.5)	0(0)	0(0)	0(0)	2(5)	0(0)		1(2.5)	0(0)	0(0)	
Cisplatin+Capecitabine	0(0)	0(0)	0(0)	0(0)	1(2.5)	0(0)		0(0)	1(2.5)	0(0)	
Docetaxel	0(0)	1(2.5)	0(0)	0(0)	0(0)	0(0)		0(0)	0(0)	0(0)	
DCF (Docetaxel, cisplatin and 5-fluorouracil)	1(2.5)	0(0)	0(0)	0(0)	0(0)	0(0)		0(0)	4(10)	1(2.5)	
	Types of adverse drug reactions										
Chemotherapy regimens for colorectal cancer (n=41)	**Anemia**	**Diarrhea**	**Neutropenia**	**Oral mucositis**	**Peripheral neuropathy**	**Nausea/Vomiting**		**Hyperpigmentation of palm**		**Hypersensitivity reaction**	
FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin)	4(9.8)	3(7.3)	9(21.9)	3(7.3)	3(7.3)	4(9.8)		0(0)		0(0)	
FOLFIRI (folinic acid , 5-fluorouracil and irinotecan	2(4.9)	3(7.3)	2(4.9)	0(0)	1(2.4)	0(0)		0(0)		1(2.4)	
CAPOX (capecitabine and oxaliplatin)	1(2.4)	0(0)	2(4.9)	0(0)	1(2.4)	0(0)		1(2.4)		0(0)	
Capecitabine	1(2.4)	0(0)	0(0)	0(0)	0(0)	0(0)		0(0)		0(0)	

Appendix XII: Copies of the published articles

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Cancer Medicine Open Access WILEY

RESEARCH ARTICLE

Predictors of survival outcomes among patients with gastric cancer in a leading tertiary, teaching and referral hospital in Kenya

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Abstract

Introduction: The incidence of gastrointestinal malignancies in Kenya is increasing, although there is a paucity of data on survival outcomes among gastric cancer patients. Hence, this study aimed to assess survival outcomes among adult gastric cancer patients at Kenyatta National Hospital.

Methods: A retrospective cohort study design was used to assess the survival outcomes among 247 gastric cancer patients. All medical records of adult (≥18 years) gastric cancer patients with complete medical records of diagnosis, stage of cancer, and treatment regimen in the study setting in the last 5 years (2016–2020) were included. A simple random sampling technique was employed to select the study participants. Data were collected using a data abstraction tool composed of socio-demographic and clinical characteristics. Survival outcomes were reported as the percentage of mortality, mean survival estimate, and mean cancer-specific survival. The data were entered and analyzed using version 20.0 SPSS statistical software. The mean survival estimates and predictors of mortality were computed using the Kaplan–Meier and Cox regression analysis.

Results: The study showed that 33.3% (64) had new distant metastasis, and 42.1% (104) had disease progression. Besides, the mortality rate was high (33.6%), and 14.6% and 7.7% of patients had complete and partial responses, respectively. The five-year survival was 32.7% among gastric cancer patients. Comorbidity ($p = 0.014$), advanced-stage diseases ($p = 0.03$), chemotherapy ($p = 0.008$), and gastrectomy ($p = 0.016$) were significant determinants of mortality.

Conclusions: A significant proportion of patients had distant metastasis, disease progression, and a low five-year survival rate. Hence, early cancer-screening programs are indispensable to circumvent disease progression and improve survival outcomes.

KEYWORDS

gastric cancer, mortality, predictors, survival outcomes

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ORIGINAL ARTICLE

Cancer Reports | WILEY

Survival outcomes among colorectal cancer patients at Kenyatta National Hospital: A retrospective cohort study

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Abstract

Background: Colorectal cancer is a growing burden in Africa. However, survival for patients with colorectal cancer remains low in sub-Saharan African countries, with the poorest survival, particularly at a late stage at diagnosis. Despite this, there is a paucity of sufficient data about the survival outcomes of colorectal cancer patients in Kenya.

Aims: This study aimed to determine the survival outcomes among colorectal cancer patients at Kenyatta National Hospital.

Methods and Results: A retrospective cohort study was employed among 232 eligible medical records of colorectal cancer patients. Simple random sampling was used to select the medical records of the patients. The included medical records of the study participants were followed up retrospectively from the date of primary cancer diagnosis until the last visit to the hospital. All relevant data, such as sociodemographics, clinical characteristics, and outcome-measuring parameters, were recorded in the predesigned data abstraction tool by reviewing the documented clinical records of the patients. The data were entered and analyzed using International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS) version 26 software. Mean, median, standard deviation, frequency tables, and figures were used to present the data. Kaplan Meier analyses were employed to determine survival outcomes. The mean age of the study participants was 54.1 ± 13.3 years, and the majority were males (126, 54.3%). Almost a third (34.1%) of patients had evidence of disease progression despite treatment in the follow-up period, with 7.8% showing no response to therapy and 23.6% experiencing new distant metastasis. The survival rate dwindled from the first year (87.9%) to the fifth year (45.4%), and the mortality rate was 22.8%

Conclusion: There was a high mortality rate, disease progression, and distant metastasis in the last follow-up period suggesting the need to strengthen the healthcare system by ensuring access to prevention, early diagnosis, and optimal treatment of colorectal cancer.

KEYWORDS
colorectal cancer, Kenyatta national hospital, mortality, survival outcomes

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ORIGINAL ARTICLE

Chronic Diseases and Translational Medicine

Determinants of survival outcomes among esophageal cancer patients at a national referral hospital in Kenya

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Edited by Yi Cui

Abstract

Introduction: The overall 5-year survival rate for esophageal cancer patients in low- and middle-income countries was reported to be low, despite the availability of advanced treatments. Thus, this study aimed to assess determinants of survival outcomes among esophageal cancer patients in Kenya.

Methods: A retrospective cohort study was employed among 299 adult esophageal cancer patients. The data were collected using a data abstraction tool consisting of patients' clinical characteristics and survival outcome measuring parameters. Statistical Package for the Social Sciences (SPSS) statistical software (version 20.0, IBM. USA) was used to analyze the data. The Kaplan–Meier and Cox regression analyses were used to determine the survival outcome and determinants of mortality, respectively.

Results: The mortality rate was 43.1%, and 11.1% of patients demonstrated distant metastases in the follow-up period. Despite treatment, 20.1% had progressed disease, and 13.0% did not respond to treatment. Radiotherapy (AHR: 3.3, 95% CI: 1.4–7.8, $p = 0.007$), chemotherapy (AHR: 3.9, 95% CI: 1.2–6.1, $p = 0.020$), and chemoradiation (AHR: 5.6, 95%CI: 1.6–10.2, $p = 0.006$) were the significant determinants of survival in advanced stage (III and and IV) patients.

Conclusions: There was a high mortality rate, disease progression, and nonresponse of esophageal cancer patients. Hence, it is essential to improve the survival of patients through early detection and timely initiation of the available treatment options.

KEYWORDS

determinants, esophageal cancer, mortality, survival outcomes

Key points

There was a high mortality rate, disease progression, and nonresponse of esophageal cancer patients. Radiotherapy, chemotherapy, and chemoradiation were the significant determinants of survival in the advanced stage (III and and IV). Esophagectomy was the only treatment modality with a statistically significant effect on the survival outcomes of early-stage patients (I and II). Therefore, this study gave direction about the essence of early detection and timely initiation of the available treatment options to improve survival.

Original Article

JOURNAL OF ONCOLOGY PHARMACY PRACTICE

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Drug-related problems among esophageal, gastric and colorectal cancer patients at the National and referral hospital in Kenya

Amsalu Degu[1,2], Peter N Karimi[2], Sylvia A Opanga[2] and David G Nyamu[2]

Abstract

Introduction: Cancer therapy has remarkable potential for drug-related problems due to the high cytotoxicity and narrow therapeutic index of most anti-neoplastic regimens. However, there is a lack of comprehensive studies on drug-related problems in patients with gastrointestinal cancer in Kenya. Therefore, the present study aimed to investigate the prevalence, types and predictors of drug-related problems among gastrointestinal cancer patients at Kenyatta National Hospital.

Methods: A cross-sectional study was used to assess the prevalence of drug-related problems among a random sample of 160 esophageal, 103 gastric, and 96 colorectal cancer patients. Data were collected using a researcher-administered questionnaire and data abstraction tool after training the data collectors. Patient-specific details such as socio-demographic features, histological cancer types, cancer stage, comorbidity types, and treatment regimen were recorded after the review of medical records and patient interviews. The potential of drug-related problems was determined as per the standard guidelines. The data were entered and analysed using version 26.0 SPSS statistical software.

Results: Most esophageal (51.9%), gastric (59.2%), and colorectal (62.5%) cancer patients had a high prevalence of drug-related problems. The need for additional drug therapy and adverse drug reactions were the predominant categories of drug-related problems. Most adverse drug reactions identified had possible categories of causality score, mild severity levels, and definitely preventable types of adverse drug reactions among all gastrointestinal cancer patients. Comorbidity and advanced-stage disease were significant predictors of drug-related problems.

Conclusions: Drug-related problems were prevalent among gastrointestinal cancer patients in our setting. Comorbidity and advanced stages of disease were significant predictors of drug-related problems.

Keywords

Drug-related problems, Gastrointestinal cancers, Predictors, Kenyatta National Hospital

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ORIGINAL ARTICLE

Cancer Reports | WILEY

Health-related quality of life among patients with esophageal, gastric, and colorectal cancer at Kenyatta National Hospital

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Abstract

Background: Despite the advancement of modern treatment approaches, several studies indicated a diminished health-related quality of life (HRQoL) in patients with gastrointestinal cancer. However, there is insufficient data about the HRQoL of gastrointestinal cancer patients in Kenya.

Aims: The study aimed to investigate HRQoL and its determinants in gastrointestinal cancer patients at Kenyatta National Hospital.

Methods: A cross-sectional study was employed among 160 esophageal, 103 gastric, and 96 colorectal cancer patients. The patient list, identified by unique hospital identification numbers, was obtained from records. Eligibility was assessed based on predetermined criteria, and the hospital identification numbers were reshuffled. Study participants were then randomly selected daily during the data collection period. Data were collected using a researcher-administered European Organization for Research and Treatment of Cancer quality of life questionnaire. The data entry and analysis were carried out using Statistical Package for the Social Sciences 26.0 statistical software. A bivariate and multivariate binary logistic regression analysis was employed to investigate determinants of HRQoL at a 0.05 level of significance.

Results: Most esophageal ($N = 118$, 73.7%), gastric ($N = 75$, 72.8%), and colorectal ($N = 72$, 75%) cancer patients had poor overall HRQoL. In the social ($p = .04$) and cognitive ($p = .02$) domain of HRQoL, esophageal cancer patients had a significantly lower mean score as compared to gastric cancer patients. Colorectal cancer patients had the highest mean score in physical functioning ($p = .01$) as compared with gastric cancer patients. Nonetheless, gastric cancer patients had the highest mean score in emotional functioning domains of quality of life as compared to esophageal ($p = .04$) and colorectal ($p < .001$) cancer patients The study revealed a low mean HRQoL score in the majority of the symptom domains of quality of life. A statistically significant difference in all domains of HRQoL was not observed in various treatment modalities of gastrointestinal cancer. Advanced-stage (stages III and IV) and co-morbidities were significant determinants of poor HRQoL.

Appendix XIII: Turnitin plagiarism report

Dr. Peter N. Karimi

16/3/2024

Evaluation of drug-related problems, health-related quality of life and survival outcomes among patients with gastrointestinal cancers at Kenyatta National Hospital

Endorsed
Dr. E.M. Guantai - Chairman
21 March 2024

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