THE INCIDENCE AND EARLY OUTCOMES OF CERVICAL ESOPHAGOGASTRIC ANASTOMOTIC LEAKS FOLLOWING ONCOLOGIC ESOPHAGECTOMY AT KENYATTA NATIONAL HOSPITAL.

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2022

DECLARATION

I declare that this dissertation is my original work and has not been presented for the award of any degree at any other institution or university. Wherever I have used another person's work, I have accordingly acknowledged and referenced.

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DEDICATION

To all the little boys and girls in the village, who dare to dream.

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ACRONYMS AND ABBREVIATIONS

EC - Esophageal Cancer

AL – Anastomotic Leakage

CEGAL – Cervical Esophago-Gastric Anastomotic Leak

KNH – Kenyatta National Hospital

UoN - University of Nairobi

ECCG - Esophagectomy Complications Consensus Group

TNM - Tumor Node and Metastasis

DEFINITION OF OPERATIONAL TERMS

Early Outcomes: occurring within 30 days of surgery

Oncologic esophagectomy : a surgical procedure in which part or the entire esophagus is removed and replaced with a neoesophagus in patients with esophageal cancer.

Anastomotic Leak: a full-thickness gastrointestinal defect involving esophagus, anastomosis, staple line, or conduit irrespective of presentation or method of identification.

Hospital mortality: death occurring during the hospital stay, after esophagectomy.

Length of hospital stay: time spent in hospital between the day of surgery and day of discharge.

Time to oral feeding: duration between day of surgery and day of successful initiation of oral feeds.

Neoadjuvant treatment: induction therapy (chemotherapy, radiotherapy, and hormone therapy), given to shrink a tumor before the main treatment, usually surgery.

Independent variable: a variable whose variation does not depend on that of another, and whose changes are assumed to have a direct effect on the dependent variable.

Dependent variable: represents outcome being tested/ measured resulting from altering inputs (independent variables).

ABSTRACT

Background: Oncologic Esophagectomy is a cornerstone in the management of resectable esophageal cancer, with postoperative anastomotic leaks a common complication. Few studies have looked specifically at the mortality and morbidity associated with cervical esophagogastric anastomotic leaks as a complication of oncologic esophagectomy.

Study Objective: To describe the incidence and early outcomes of cervical esophago-gastric anastomotic leak among patients undergoing oncologic esophagectomy at Kenyatta National Hospital.

Methodology: A 7 year retrospective cohort study of 205 patients who underwent oncologic esophagectomy, with a cervical esophago-gastric anastomosis at KNH between January 2014 and December 2021was performed. Data was collected via consecutive sampling of all patients who underwent oncologic esophagectomy;of particular interest was whether they developed an anastomotic leak and its associated complications such as mortality, length of hospital stay, time to oral intake and need for surgical intervention.

Results : Out of 205 patients who underwent esophagectomy, 41 developed CEGAL giving an incidence of 20% with only 12%(n=5) requiring surgical intervention. The overall mortality rate was 5.85%(n=12). There was an association between presence of CEGAL and length of hospital stay ($p<0.0001$) and delayed resumption of oral feeding ($p<0.0001$). However there was no association between CEGAL and increased risk of mortality ($p=0.118$).

Conclusion: The presence of CEGAL increases length of hospital stay and the duration to resumption of oral feeds, with no significant effect on hospital mortality.

CHAPTER ONE

1.0 BACKGROUND

1.1 Introduction

Esophageal carcinoma (EC) is a malignant condition affecting the esophagus. It is currently one of the leading causes of cancer related deaths in Kenya [1]. EC is the sixth leading cancer death in the world, with an estimated 544,076 deaths and up to 604,100 new cases [2]. Data from GLOBOCAN estimates that in the year 2020, esophageal carcinoma accounted for 3.1% of all the new cancer cases and 5.5% of all the cancer related deaths [2]. The prevalence and mortality rates of EC are higher in developing countries as compared to developed countries. Regions with the highest rates of EC are found in central and southern Asia, eastern and southern Africa.[3].

Kenya belongs to this so-called endemic zone with the current incidence of 17.6 per 100,000 against the global incidence of 5.5 per 100,000 [5]. Regions having the largest number of EC cases in Kenya are in Western and Central Kenya. 11% of newly diagnosed cancers in Kenya are EC, and is the second most prevalent cancer in the country, accounting for the highest rate of cancer deaths. 70–80% of all EC cases in our country are often diagnosed in the late stages[5].

Despite recent advances in the treatment and diagnosis of EC, it has continued to have a poor prognosis with a five year survival rate of between15% to 20% [6].

The management of esophageal cancer is dependent on the TNM stage at diagnosis, with esophageal resection forming the cornerstone of treatment.[8] For early lesions endoscopic techniques such as endoscopic mucosal resection and endoscopic mucosal dissection, have been used with good outcomes.[8] Surgery alone is indicated for nodal negative early lesions e.g. T1N0M0.[9]. Generally, esophagectomy remains the key treatment option for all patients with non-metastatic nodal positive esophageal cancer. For these patients, the current recommendation is neoadjuvant concurrent chemoradiotherapy followed by esophagectomy 4-8 weeks later [10].

An esophagectomy is a surgical procedure in which part or the entire esophagus is removed and replaced with a neoesophagus that can be developed from a gastric, jejunal or colonic conduit. Generally, there are different kinds of esophagectomy procedures depending on the number of incisions required and where they are made. A lot of factors often influence this decision, including the tumor's location, and the preference of the surgeon[11].

Depending on the specific type of esophagectomy done, the conduit anastomosis can either be in the neck or the chest.

Esophagectomies are often associated with a number of complications. These include anastomotic leak, conduit necrosis, chylothorax, recurrent laryngeal nerve (RLN), gastrointestinal and intrathoracic hemorrhage, and stricture formation. Of these, anastomotic leak is believed by most authors to be the most severe complication. The aim of this study was to show the incidence and early outcomes of cervical esophago-gastric anastomotic leak post esophagectomy in our setting.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Introduction

Esophageal carcinoma (EC) is a neoplastic condition affecting the esophagus. It is currently one of the leading causes of cancer related deaths in Kenya. The disease usually begins in the mucosal layer of the esophagus and may arise at any section along the length of the esophagus before eventually spreading to the outward layers. Histological subtypes are mainly squamous cell carcinoma and adenocarcinoma. Other rare subtypes include spindle cell carcinoma and small cell carcinoma.

In Kenya, squamous cell carcinoma is currently the most common subtype of esophageal carcinoma, accounting for more than 90% of all the cases of esophageal carcinoma in the country [1]. Adenocarcinoma makes up a significant portion of all the new distal esophageal carcinoma cases in the country and is mainly linked to obesity and Barrett's esophagus.

2.2 Burden of Esophageal Carcinoma

EC is currently one of the leading causes of cancer related deaths in Kenya [1]. It is the sixth leading cancer death in the world, with an estimated 544,076 deaths and up to 604,100 new cases [2]. Data from GLOBOCAN estimates that in the year 2020, esophageal carcinoma accounted for 3.1% of all the new cancer cases and 5.5% of all the cancer related deaths [2]. The prevalence and mortality rates of esophageal cancer are higher in developing countries as compared to developed countries. Regions with the highest rates of EC are found in central and southern Asia, eastern and southern Africa.[3].

Kenya belongs to this so-called endemic zone with the current incidence of 17.6 per 100,000 against the global incidence of 5.5 per 100,000 [5]. Regions having the largest number of EC cases in Kenya are in Western and Central Kenya. 11% of newly diagnosed cancers in Kenya are EC, and is the second most prevalent cancer in the country, accounting

for the highest rate of cancer deaths. Despite recent advances in the treatment and diagnosis of EC, it has continued to have a poor prognosis with the five year survival rate at between 15% to 20% [5].

2.3 Presentation and Diagnosis of EC

The most common presentation of EC is progressive dysphagia and weight loss. It's a symptom of locally advanced illness with an esophageal lumen of less than 13 mm in diameter. Nevertheless, esophageal cancer is often asymptomatic in the early stages. In the USA 6 - 10% of patients with EC are asymptomatic at the time of diagnosis. These are cases detected incidentally or during screening in patients with pre malignant lesions[5].Time from presentation to diagnosis usually varies and is primarily characterized by significant delays in the diagnosis of the EC patients [6].

In Kenya, 70-80% of patients present in the late stages of the disease [6]. As a result, a significant majority of EC patients at Kenyatta National Hospital (KNH) are diagnosed at advanced stages of the disease thereby significantly limiting their therapeutic options. In Kenya endoscopy and histopathology are the most common diagnostic tools for EC [6]. Once a diagnosis is made staging is done via use of a computer tomography scan of the chest and abdomen.

2.4 Management of EC

2.4.1 Overview

The management of esophageal cancer is dependent on the Tumor Node and Metastasis (TNM) stage at diagnosis. with esophageal resection forming the cornerstone of treatment.[7] For early lesions endoscopic techniques such as mucosal resection and mucosal dissection have been used with good outcomes.[7] Esophagectomy alone is indicated for nodal negative early lesions e.g. T1N0M0.[8]. Generally, esophagectomy remains the key treatment option for all patients with non-metastatic nodal positive

esophageal cancer. For these patients,the current recommendation is neoadjuvant concurrent chemoradiotherapy followed by esophagectomy 4-8 weeks later [9].

2.4.2 Esophagectomy

An esophagectomy is a surgical procedure in which part or the entire esophagus is removed and replaced with neoesophagus that can be developed from a gastric, jejunal or colonic conduit. Generally, there are different types of esophagectomy procedures depending on the number of incisions required and where they are made. A lot of factors often influence this decision, including the tumor's location and the preference of the surgeon[10].
Depending on the specific type of esophagectomy done, the conduit anastomosis can either be in the neck or the chest. In our setting a tri incisional esophagectomy with a gastric conduit and a cervical anastomosis is prefered.

2.4.3 Complications of Esophagectomy

Esophagectomies are often associated with a number of complications. Common complications can broadly be classified as major and minor as well as medical or surgical. Major surgical complications include anastomotic leak, conduit necrosis, thoracic duct leak, recurrent laryngeal nerve (RLN), gastrointestinal and intrathoracic hemorrhage, tracheobronchial tree injury, tumor rupture, and late onset stricture formation. On the other hand, minor surgical complications include wound infection, effusion, pneumothorax, intra-abdominal collection, and feeding tube issues. Of these anastomotic leakage is believed by most authors to be the most severe complication.

2.5 Cervical Esophagogastric Anastomotic Leakage(CEGAL)

Esophagectomy is a cornerstone in the management of locally advanced esophageal cancer. Esophagogastric AL is one of the most severe complications of esophageal resection and leads to significant morbidity and mortality. Moreover, anastomotic leakage following esophagectomy might affect long-term quality of life and is linked to poor oncologic

outcomes [10]. Anastomotic leakage can manifest in a variety of ways, ranging from a minor leak with moderate symptoms to a big defect with widespread contamination and fulminant sepsis [10]. Although the incidence rates and risk factors for anastomotic leakage are widely documented, few researchers have looked specifically at cervical anastomotic leaks and their outcomes.

2.6 Definition and Classification of Anastomotic leakage

A definite understanding of what constitutes an AL after esophagectomy has long been a matter of debate. Several attempts have been made to establish a commonly accepted definition but none has achieved wide acceptance. Larburu et al, defined AL as "as the disruption of the anastomosis that leads to extravasation of the intraluminal content."[11] The Esophagectomy Complications Consensus Group (ECCG) defines AL as 'a full-thickness gastrointestinal defect involving esophagus, anastomosis, staple line, or conduit irrespective of presentation or method of identification' and grades it into three severity types (Table 1) [12]

Table 1: ECCG Grading of Anastomotic Leakage

Leak classification	Type	Description/Criteria
Anastomotic Leak	I	Local defect requiring no change in therapy
	II	Localized defect requiring non-surgical intervention
	III	Localized defect requiring surgical intervention
Conduit necrosis	I	Focal, Identified Endoscopically

	II	Focal,Identified endoscopically and not associated with free anastomotic or conduit leak
	III	Extensive necrosis

Based on a systematic review of 97 studies, a standard definition was proposed by Bruce[13] and later integrated by Lerut[14] and Price[15] as shown in Table 2.

Table 2: Main Classification/definition systems of Anastomotic Leakage

Study	Classification	Grade	Definition/Criteria
Bruce 2001 [13]	Radiological	-	● No clinical signs ● Detected only on routine Imaging
	Clinical minor	-	● Luminal contents through the drain or wound site ● Fever > 38 degrees celsius Or leukocytosis >10,000/L ● Leak may also be detected on imaging studies
	Clinical major	-	● As clinical minor with severe disruption of anastomosis
Lerut 2002 [14]	Radiological	-	● No clinical signs
	Clinical Minor	-	● Local Inflammation cervical wound ● X ray contained leak ● Fever, ↑ WBC, ↑ CRP
	Clinical major	-	● Severe disruption on endoscopy ● Sepsis

	Conduit necrosis	-	• Endoscopic confirmation
Price 2013 [15]	Radiological	I	• No clinical signs or symptoms • Purely radiological diagnosis
	Clinical minor	II	• Minor Clinical signs • Radiologically contained intrathoracic leak • Fever, leukocytosis
	Clinical major	III	• Significant anastomotic disruption requiring surgical revision • Minor anastomotic disruption with systemic sepsis
	Conduit necrosis	IV	• Conduit necrosis necessitating esophageal diversion

In recent times, the ECCG definition/classification system has been increasingly adopted for reporting on AL after esophagectomy.

2.7 Incidence of Cervical anastomotic leakage

The incidence of cervical esophago-gastric anastomotic leak (CEGAL) widely varies in published reports. Most authors give a range of between 5-25% [9].

Tabatabai, in a 1 year prospective study done in Iran, published a CEGAL incidence of 21.3%[9] whereas Aminian from a 5 year retrospective study in Iran published a CEGAL incidence of 13.2%[16]. A 10 year retrospective study in Canada reported an incidence of 8.3%.[17] In Spain, in a 2013 publication from a 8 year retrospective study reported an incidence of 23.3%[11] In the USA,a 10 year retrospective review of 892 patients reported an incidence of 14.2%[12].

Locally, Ogendo in 2005 published results from a 5 year retrospective study of between 1998-2004 at Kenyatta National Hospital, reporting an incidence of 17.7%[7]. The research

involved analyzing the data of 201 of patients with carcinoma of the esophagus who had undergone oesophagectomy. The researchers concluded that Post oesophagectomy leakage is one of the major complications related to esophagectomy at Kenyatta National Hospital (KNH). In Ethiopia, Allemu reported an incidence of 15.8% from a 5 year retrospective study[18]

2.8 Risk factors and Presentation of CEGAL

There are a number of risk factors contributing to cervical esophago-gastric anastomotic leak post esophagectomy. A retrospective study conducted by Cooke, et al., 2019 based on an analysis of a database of 1,133 patients sought to determine the potential risk factors associated with CEGAL. The findings of the study revealed that the main risk factors for the cervical esophago-gastric anastomotic leak include the existence of preoperative comorbidities, postoperative arrhythmia, active smoking history of the patient as well as the esophagogastric surgeries[10]. Tabatabai et al., 2019 in a prospective study on 61 patients identified weight loss, respiratory complication and intraoperative blood loss volume as key risk factors[9], whereas Aminian et al., 2011 identified preoperative hypertension and higher creatinine levels as independent and significant risk factors for CEGAL[16]

The presentation of CEGAL varies from asymptomatic to fulminant sepsis[10,20,21,22] .

The most common presentation of CEGAL is cervical wound drainage with fever[10,21] . Other presentations include tachycardia, neck pain and pleural effusion [10,21]. The time to presentation ranges from 3-10 days post operatively.[10]

2.9 Diagnosis and management of CEGAL

A number of strategies are currently being used in the diagnosis of cervical esophago-gastric anastomotic leak. They include clinical, incidental finding on routine radiological investigation or via endoscopic investigation[22]

Clinical diagnosis is based on symptoms and signs as mentioned in the section on presentation above. Routine gastrograffin swallow or methylene blue dye test done on day 7 post operative can pick up an asymptomatic CEGAL.[22]

Once CEGAL has been diagnosed, management varies from conservative to operative.[22] Conservative measures include avoidance of oral intake, antibiotics and local wound dressing.[19,22] The surgical options available include, chest tube insertion, anastomotic take down and esophagostomy fashioning.[19,22]

2.10 Outcomes Following Development of CEGAL

The morbidity and mortality associated specifically with CEGAL has not been widely studied. The outcome parameters that have been studied include, mortality rate, length of hospital stay, duration of ICU stay, time to oral feeding and need for surgical intervention.[9,11,16,21,23,24,] as shown in table 3 below. Late complications include stricture formation with need for serial endoscopic dilatation.[9,11,16,21,23,24]

Table 3 : Outcomes of Cervical Esophagogastric Anastomotic Leaks

Author/Year	**Study**	**Findings**
Tabatabai 2009[9]	Incidence and Risk factors of AL n= 61	• Mortality - No association • Need for surgery - 69.2% • Stricture formation - 41.7%
Schuchert 2010 [23]	Impact of AL on Outcomes n= 235	• Mortality - 3.3% • Hospital stay - 18 days • Stricture formation - 57%
Aminian 2011 [16]	Predictors and Outcomes of Cervical AL n= 418	• Mortality - No Association • Hospital stay - 21.5 days • ICU stay - No Association
Larburu 2013[11]	Cervical AL after esophagectomy n= 77	• Mortality - 5.5% • Hospital stay - 28.5 days • Stricture formation -

		33.3%
Van Rossum 2017 [24]	Management and Outcome of CEGAL n= 286	• Mortality - No Association • Hospital stay - (11-98) days • ICU stay - (1-65) days • Time to Oral intake - (7-122) days
Verstegen 2019 [21]	Meta Analysis : Management of AL post esophagectomy n= 273	• Mortality - 8% • Hospital stay - 22 days • ICU stay - No association • Need for surgery - 17%

The study evaluated the following outcome parameters: length of hospital stay, time to oral intake, need for surgical intervention and post-operative mortality.

2.11 Statement of the problem

Cervical esophago-gastric anastomotic leak (CEGAL) is a common complication of oncologic esophagectomy anastomosis with significant morbidity and mortality.

The incidence of this problem, and associated complications is not known in Kenya due to lack of adequate data on the subject since no study has looked into cervical anastomosis and associated outcomes e.g. time to oral intake and need for surgical intervention after leak. This hinders adequate patient education, management and planning including sensitization of surgeons and departments dealing with this problem.

2.12 Study Justification

Esophagectomy is a common surgery, with CEGAL a frequent and severe complication. Understanding the magnitude of this problem would help inform the cardiothoracic department, the hospital and other relevant stakeholders on the need to mitigate its negative impact on patient care. Currently, no known studies have been done on this subject at KNH.

2.13 Study Question

1. What is the incidence of cervical esophago-gastric anastomotic leak(CEGAL)?
2. What are the early outcomes of cervical esophago-gastric anastomotic leak?

2.14 Objectives

2.14.1 Broad Objective

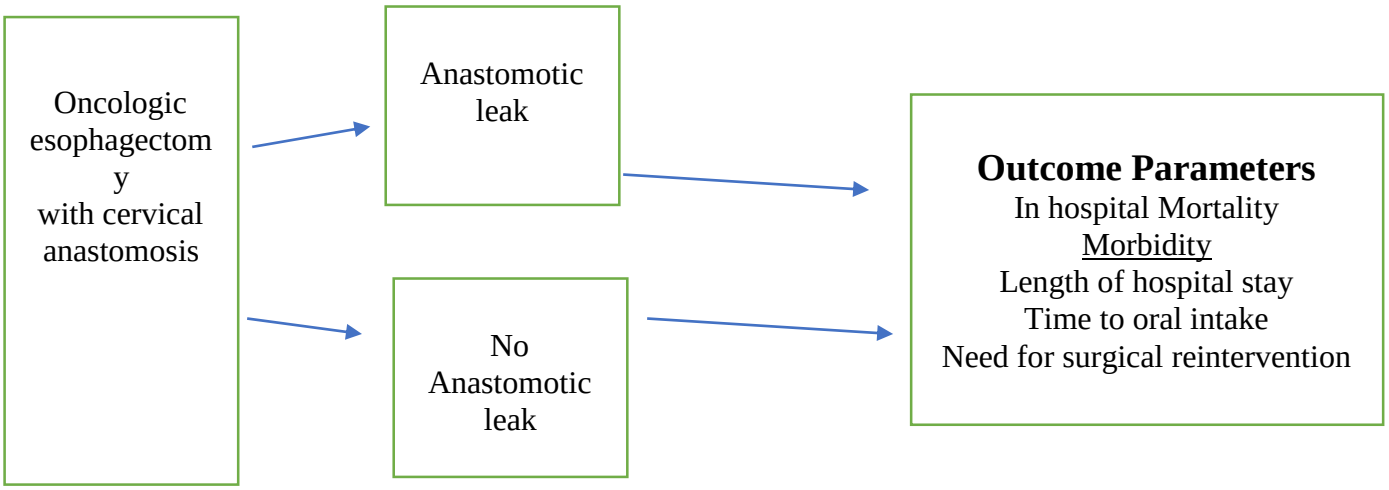
To describe the incidence and early outcomes of cervical esophago-gastric anastomotic leak among patients undergoing oncologic esophagectomy at Kenyatta National Hospital.

2.14.2 Specific Objectives

1. To establish the incidence of CEGAL among patients undergoing oncologic esophagectomy at Kenyatta National Hospital.
2. To determine the length of hospital stay, time to oral intake and the need for surgical intervention associated with CEGAL.
3. To determine the in hospital mortality associated with CEGAL.

2.15 Conceptual Framework

Figure 1: Conceptual framework showing interaction between various study variables.



CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Design

This was a retrospective cohort study. The cohort were all patients that underwent oncologic esophagectomy with a cervical esophago-gastric anastomosis during the study period. They were further classified on whether they developed a cervical esophago-gastric anastomotic leak or not. Complications arising from the leak, for those who leaked were assessed.

3.2 Study Period

The data for this study was collected from files spanning seven years between 1st January 2014 and 31st December 2021. As a look at the raw data showed 377 esophagectomies had been done in that period. Those provided adequate numbers and current data.

3.3 Study Site

The study was carried out at the Kenyatta National Hospital (KNH), Health Records and Information Department where patients for the study were enrolled from its registries. KNH is a national referral hospital where complex surgical cardiothoracic cases are referred and managed.

3.4 Study Population

All patients 18 years of age and above who had a confirmed diagnosis of esophageal cancer, and underwent esophagectomy with a cervical esophago-gastric anastomosis at Kenyatta National Hospital.

3.5 Sample Size Determination

To calculate the sample size for the estimate of the incidence of anastomotic leak for the 95% confidence interval the following formula was used (Cochran, 1977):

$$N = \frac{Z^2 \text{x (P) (1-P)}}{d^2}$$

Z value for p = 0.05 or 95% confidence intervals = 1.96

P = Estimated prevalence / incidence of CEGAL (Estimated incidence is 15.8% [19])

d = Desired level of precision (0.05)

Hence a sample size of 205 persons was deemed adequate.

3.6 Sampling procedure

The patients who were admitted with a diagnosis of esophageal cancer and underwent esophagectomy with a cervical esophago-gastric anastomosis from 1st January 2014 to 31st December 2021 were recruited as a cohort in this study through a consecutive sampling approach, whereby every patient meeting the inclusion criteria was added to the study until the sample size was met.

3.6.1 Inclusion Criteria

All the patients above the age of 18 years with a confirmed diagnosis of esophageal cancer who underwent esophagectomy with a cervical esophago-gastric anastomosis at KNH.

3.6.2 Exclusion Criteria

Patients with incomplete data.

3.7 Study Procedures

3.7.1 Data Collection

Data sources for this study were the files and theater logbooks for patients who underwent oncologic esophagectomies with a cervical esophago-gastric anastomosis at Kenyatta National Hospital during the period 2014-2021.

Data was collected by the principal investigator at the KNH health information department for a period of two and a half months. The data collection sheets were filled and securely stored.

Due to the Coronavirus pandemic, the personnel collecting data was masked and gloved at all times; with observance of strict hand hygiene and adherence to the KNH-University of Nairobi (UoN) ethics and research committee guidelines on conduct of research during the Covid-19 pandemic.

3.7.2 Study Variables

Using the data collection sheet (Appendix 1), the following variables were derived from the patients' records.

Independent variables

The occurrence of cervical anastomotic leak as an independent variable.

Dependent variables

Dependent variables were the post CEGAL complications such as mortality, length of hospital stay, time to oral intake, need for surgical reintervention

3.8 Data analysis

The data was collected via an online data collection tool. Data cleaning was subsequently done to ensure consistency and accuracy of the data.Analysis was done using Stata 14.0 (StataCorp, College Station, Texas).

Descriptive statistics such as mean, median and interquartile range were used to describe characteristics of the study participants.

For hypothesis testing, Chi-square test and wilcoxon signed-rank test were.

P values of less than 0.05 were considered statistically significant.

Results were presented in bar plots and pie charts, box plots and frequency tables.

3.8.1 Quality assurance

The researcher was well trained and well versed in his responsibilities, data collection and documentation. Weekly proficiency checks were done to ensure that the data obtained was consistently accurate and without errors.

The reproducibility of analytical results was guaranteed by ensuring proper documentation, data availability and clear analytical procedures.

The researcher remained honestly dedicated to meeting the objectives of the study and avoided influence from external parties or conflict of interest.

3.9 Dissemination of results and publication policy

The results of the study will be available to the UoN surgery and research library. The recommendations will also be shared with the KNH cardiothoracic department to possibly modify our approach to the management of such patients and contribute to policy making. The findings will also be presented to peer-reviewed journals for publication under due protocol and affiliation to KNH and UoN cardiothoracic surgical department.

3.10 Ethical Considerations

The institutional consent and approval were sought from the KNH-UoN Ethics and Research Committee.

The authorization to conduct the study was also obtained from KNH administration.

The participants remained anonymous and unique identification numbers were used thereby observing confidentiality and privacy throughout the duration of the study.

The data collected was used for research purposes only and the hard copies were stored in a lockable vault while the soft copies of data were password protected.

RESULTS

A total of 205 patients that met the inclusion criteria were included in the analysis.

Demographic characteristics of patients

The results of the demographic characteristics of the patients indicated that 112 (54.6%) of the patients were male, while 93 (45.4%) of them were female. The mean age of the patients was 56 years, where the youngest was 28 years and the oldest 85 years while the median was 57 (IQR 49.0 – 63.0) years old.

Table 4: Patient Characteristics

Gender	**Frequency (n=205)**	**Percentage**
Male	112	54.6
Female	93	45.4
Age		
< 30	2	0.97
31-40	21	10.24
41-50	36	17.56
51-60	80	39.02
61-70	44	21.46
> 70	21	10.24

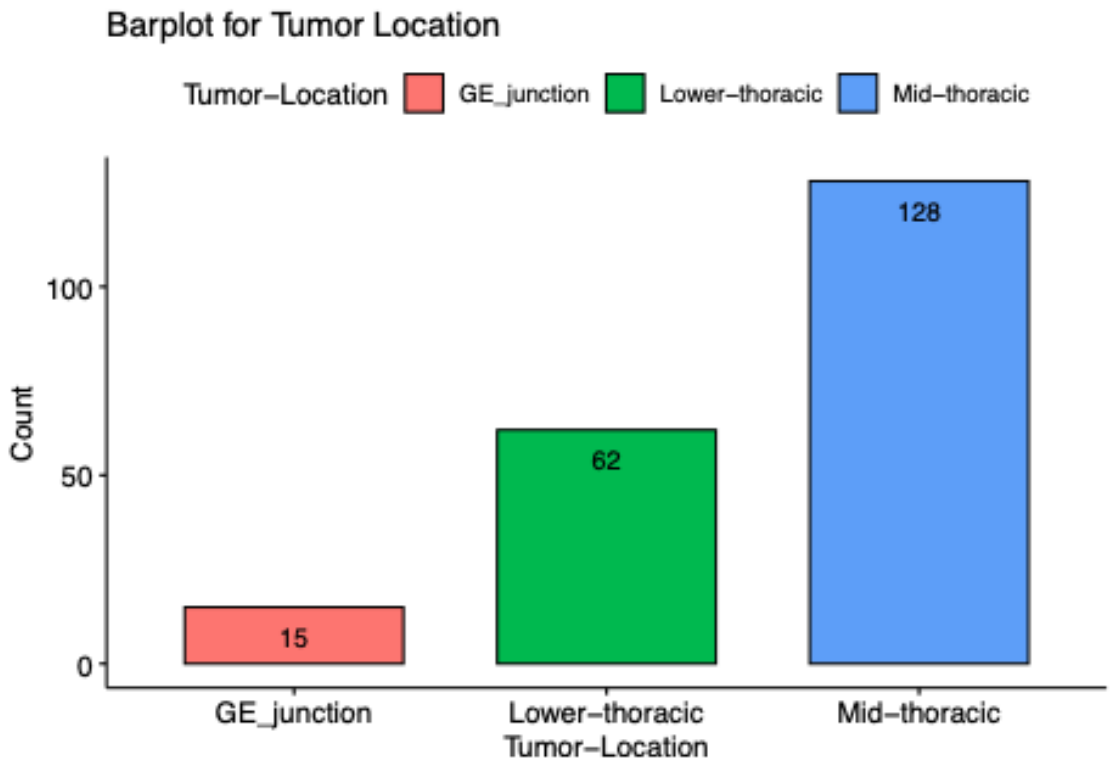
A density distribution revealed that the spread of the age data was a normal distribution as shown in the chart below.

Figure 2 : Density of plot of patient age

Tumor Characteristics

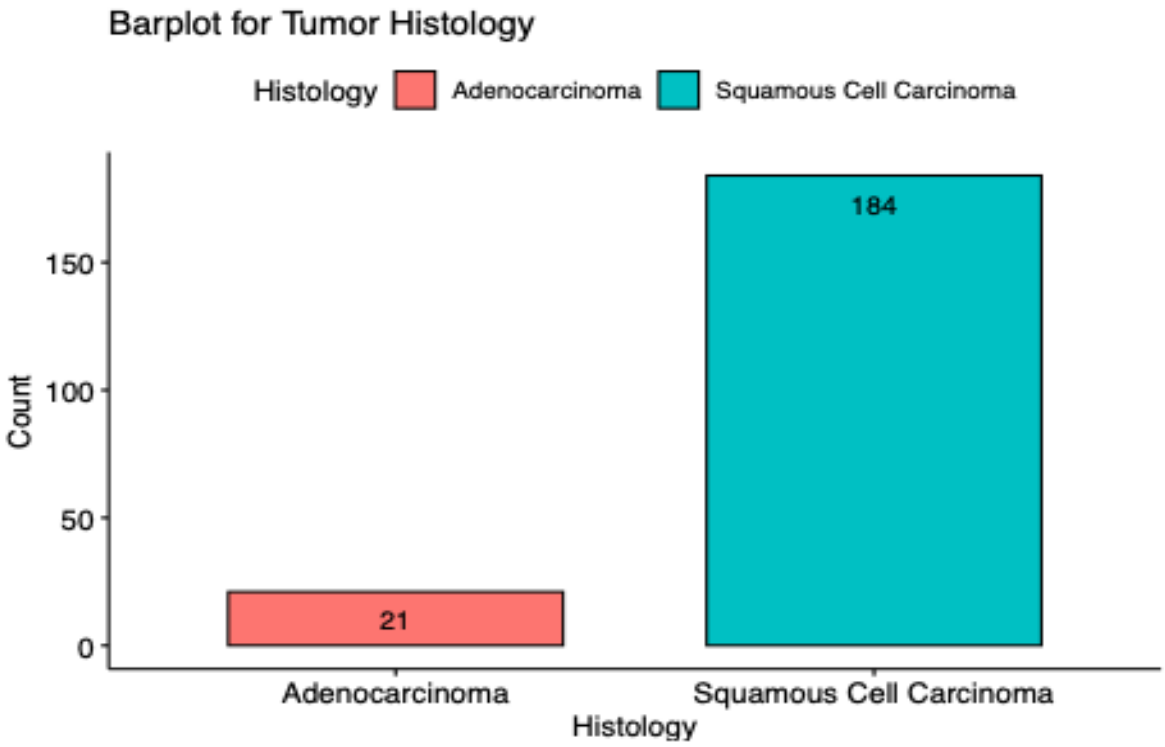
Most patients at the time of diagnosis had a mid-thoracic tumor (62.4%) whereas 30.2 % had lower thoracic tumor and 7.4% had a gastro-esophageal junction tumor, as demonstrated in the Bar Plot below.

Figure 3 : A Bar Plot showing the gross tumor characteristics



Histologically 89.8% (n=128)of the tumors were squamous cell carcinoma, whereas 10.2 % (n=62)were adenocarcinoma.

Figure 4: A Bar Plot showing the tumor histologic types.

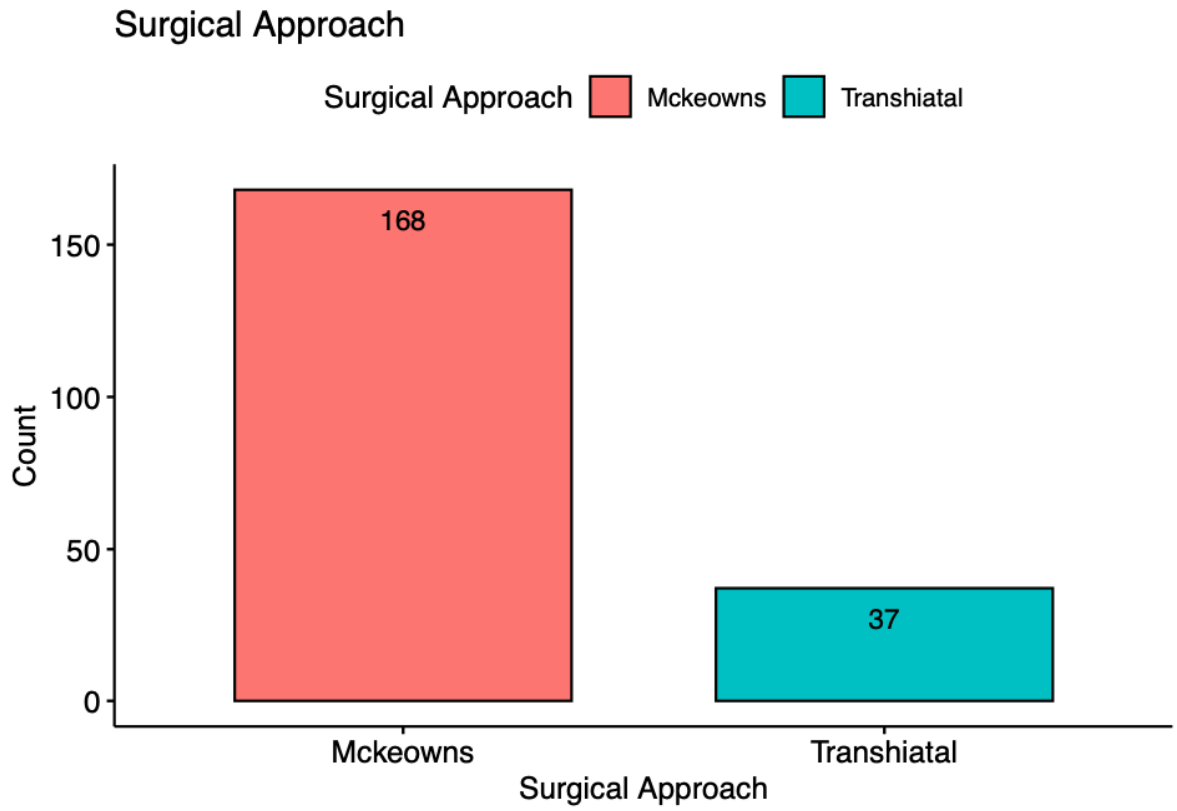


Surgical Approach

82% of esophagectomies were done via Mckeowns technique with 18% being Transhiatal esophagectomies.

For these patients only 20% had undergone neo adjuvant chemoradiotherapy

Figure 5: A Bar Plot showing the Type of Esophagectomies done

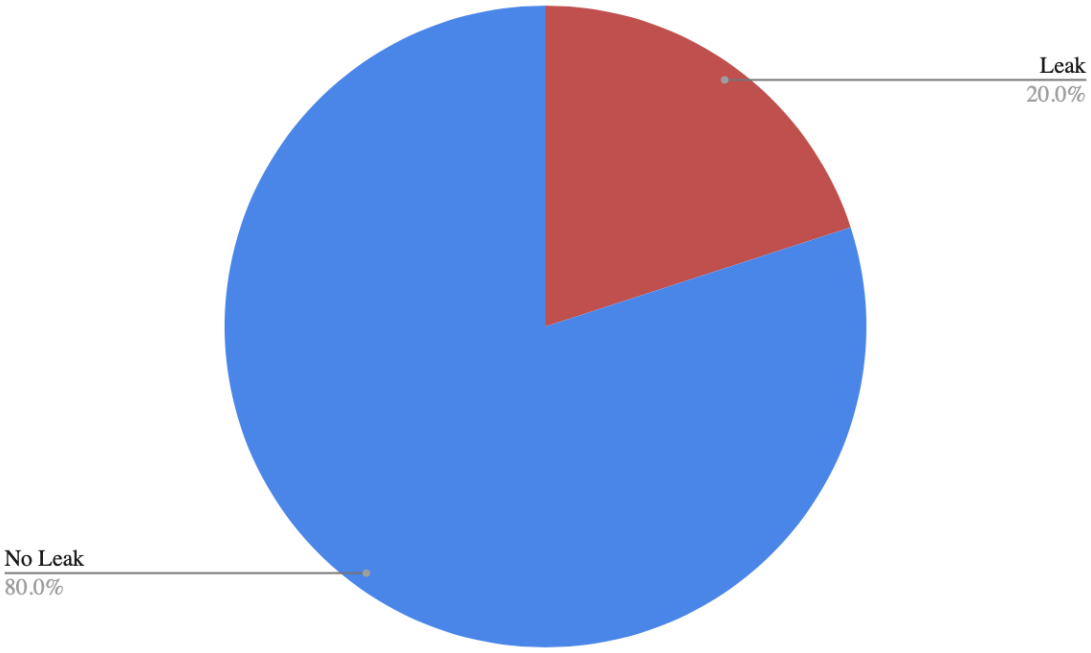


Cervical Esophagogastric Anastomotic Leaks

Incidence

From the surgeries undertaken, 41 patients developed CEGAL. This reveals a CEGAL incidence of 20%.

Figure 6 : A Pie Chart showing the incidence of CEGAL



Time to detection of leaks

The time to detection of the CEGAL ranged from 7 - 49 days with a mean of 11.99 days, a median of 8 days and IQR of 1 day (7-9) as shown in the table below.

Table 5 : Table showing days to detection of CEGAL

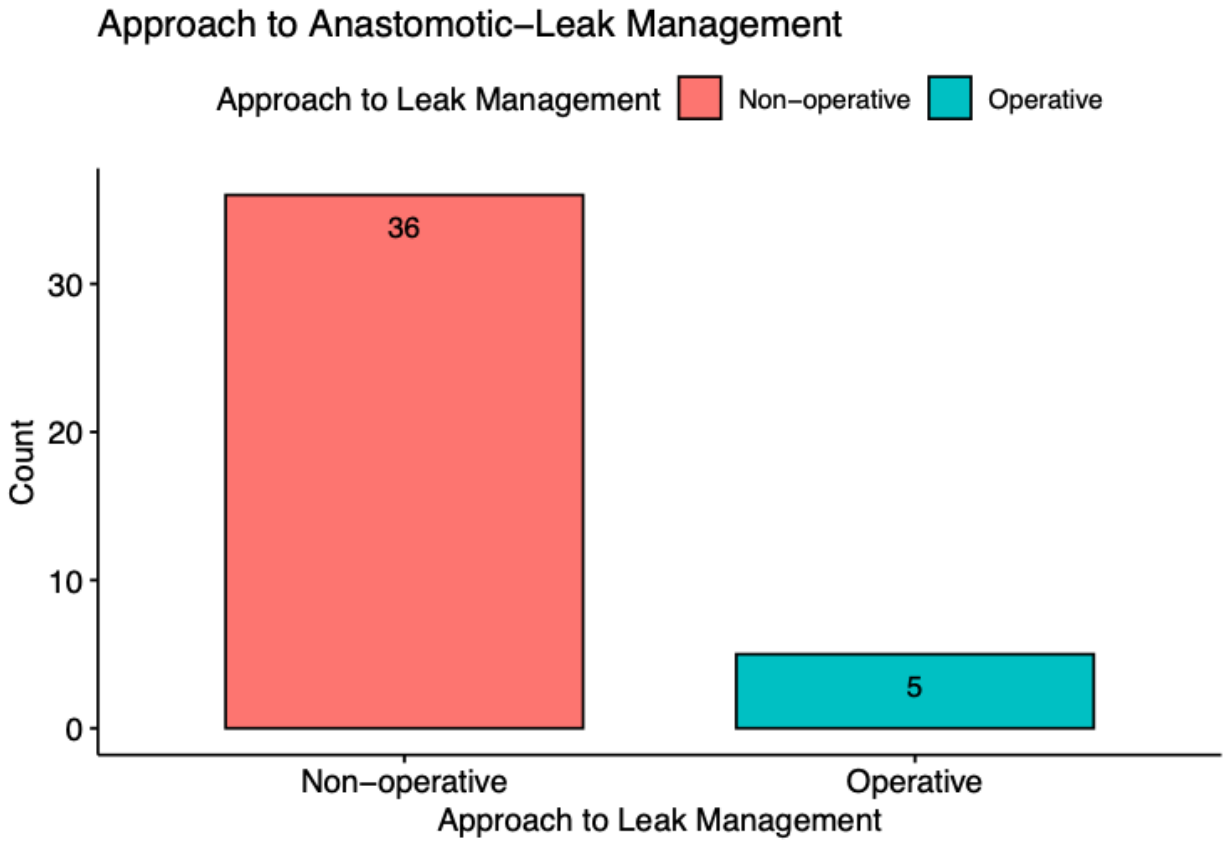
Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
7.00	8.00	8.00	11.99	9.00	49.00

Approach to Leak Management

Of the 41 patients that developed CEGAL, only 5 of them required some form of surgical intervention. This ranged from chest tube insertion to thoracotomy. This puts the need for surgery post CEGAL at 12%.

Three of the patients required chest tubes and 2 had thoracotomy done.

Figure 7: A Bar Plot showing the Approach to Leak Management

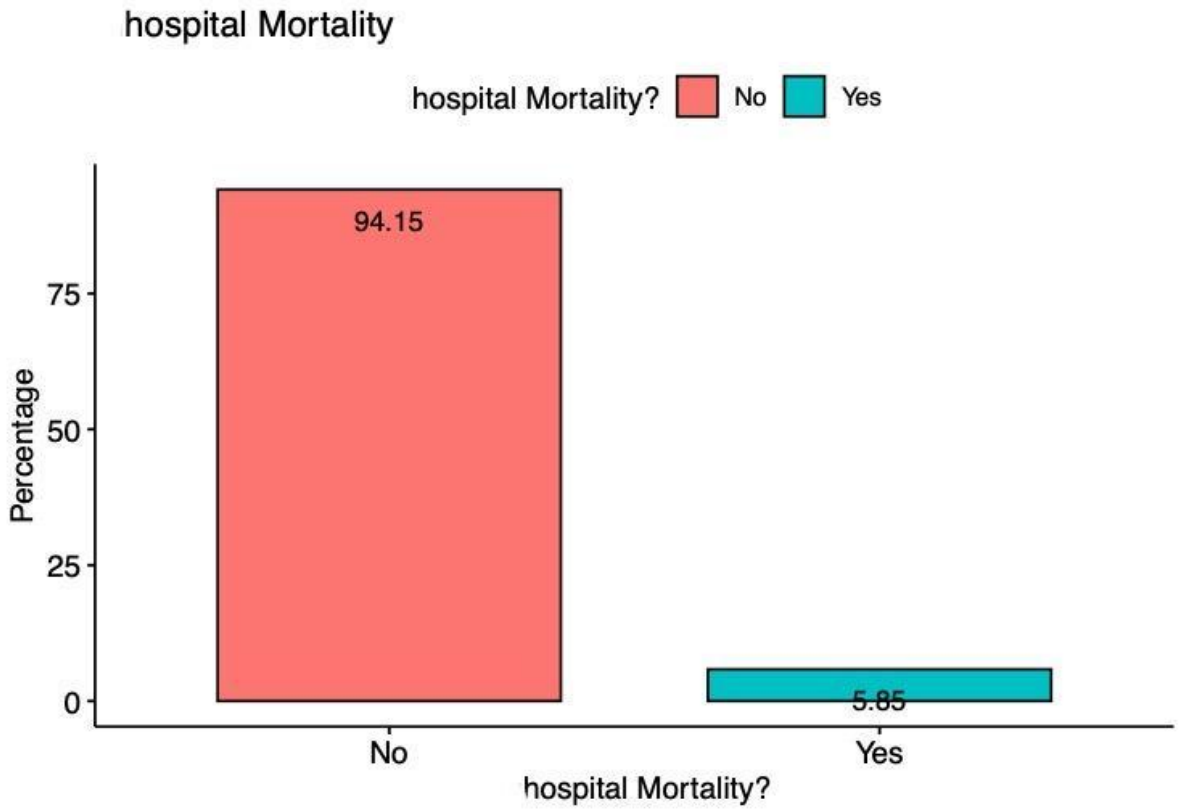


BIVARIATE ANALYSIS

Hospital Mortality

There was an overall hospital mortality rate of 5.85 % (n=13) for all patients that underwent esophagectomies.

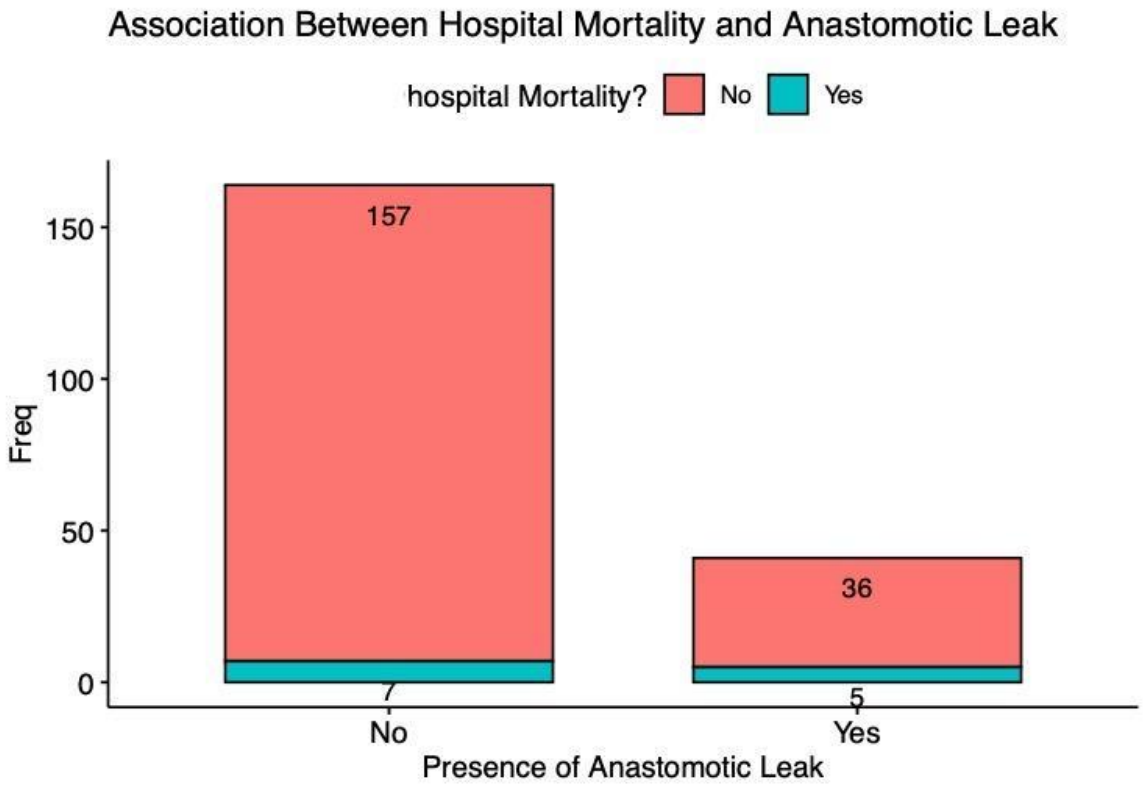
Figure 8:A Bar Plot showing the overall mortality rate



CEGAL and Hospital Mortality

There were 5 Hospital mortalities among the 41 patients that developed CEGAL and 7 in the group that had no CEGAL. Analysis revealed no association between CEGAL and increased risk of Hospital Mortality.**(p=0.118)**

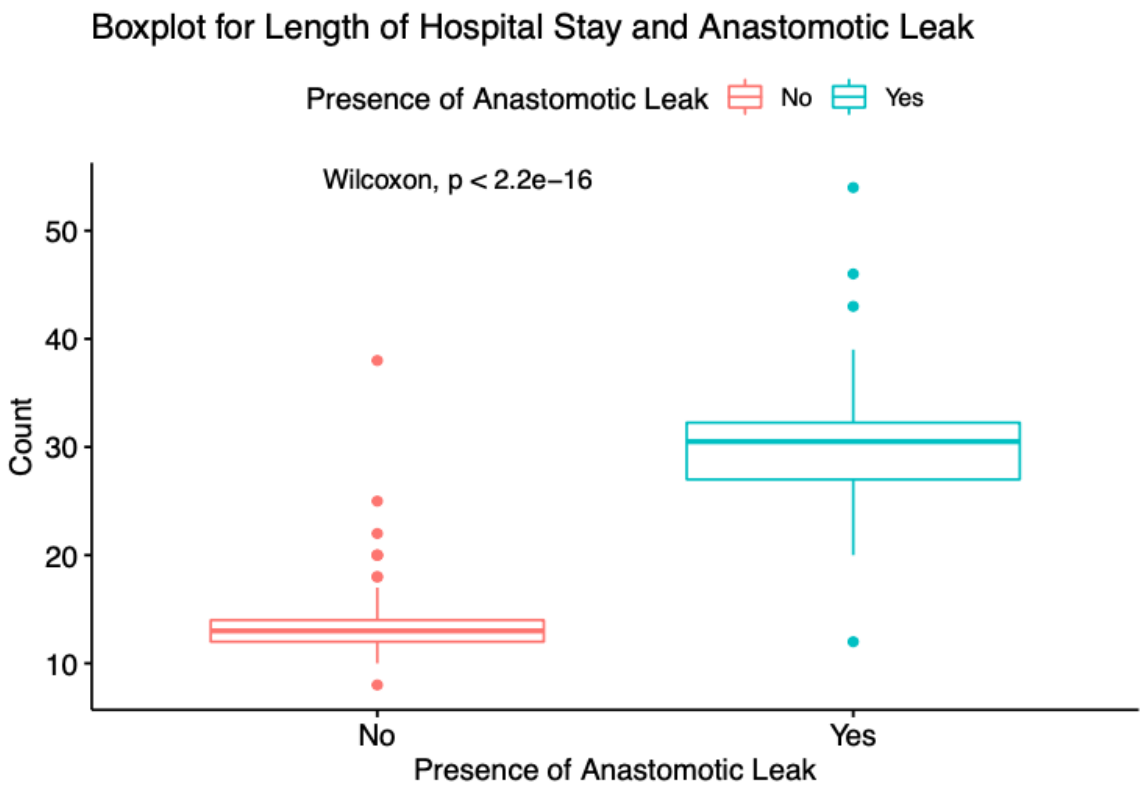
Figure 9: A Bar Plot showing the frequency of Hospital Mortality



Length Of Hospital Stay

For patients that did not develop CEGAL the mean length of hospital stay was 13.3 days with a median of 13 days. However, for patients with CEGAL, the mean length of hospital stay was 31.1 days with a median of 30.5 days. Analysis showed a clear association between CEGAL and increased length of hospital stay **(p<0.0001)**

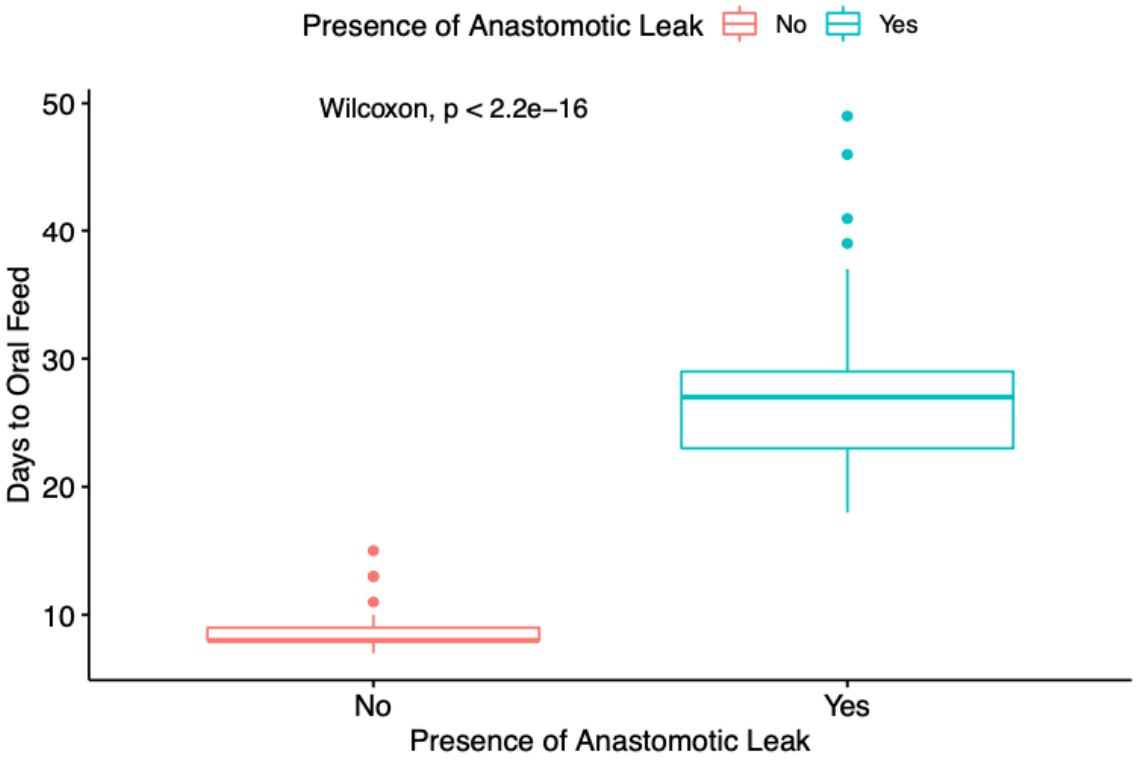
Figure 10 : A Box Plot Showing Association between CEGAL and Length of Hospital stay



Time to Oral feeding

Patients that did not develop CEGAL had a shorter time to oral feeding, a mean time of 8.34 days and a median of 8 days . For patients with CEGAL initiation of oral feeds was delayed with a mean of 27.9 days and a median of 27 days . Analysis showed that the presence of CEGAL significantly increased time to oral intake **(p<0.0001).**

Figure 11 : A Box Plot showing the Time to initiation of oral feeds.



SUMMARY OF BIVARIATE ANALYSIS

Results of the bivariate analysis indicate that the presence of CEGAL does not significantly increase the risk of Hospital mortality (p=0.118). However Presence of CEGAL significantly increased length of hospital stay (p<0.0001) and time to initiation of oral feeds(p<0.0001).

Table 6 : Summary of Bivariate Analysis

	CEGAL	**No CEGAL**	**P value**
Mortality	5	7	0.118
Length of Hospital stay(Median)	30.5	13	< 0.0001
Time to oral feeds(Median)	27	8	< 0.0001

DISCUSSION

CEGAL is a common complication of oncologic esophagectomy anastomosis with significant morbidity and mortality[9-17].

The incidence of this problem, and associated complications is not known in Kenya due to lack of adequate data on the subject since no study has looked into cervical anastomosis and associated outcomes e.g. time to oral intake and need for surgical intervention after leak. In this study we set out to determine the incidence of cervical esophago-gastric anastomotic leak and the early outcomes associated with CEGAL.

The incidence of cervical esophago-gastric anastomotic leak (CEGAL) widely varies in published reports. Most authors give a range of between 5-25% [9]. In this study we found an incidence of 20% which falls within the above range. A 2013 publication from a 8 year retrospective study done in Spain reported an incidence of 23.3%[11] . Our data therefore indicates that the incidence of CEGAL at KNH is similar to other institutions globally.

The morbidity and mortality associated specifically with CEGAL has not been widely studied. The outcome parameters that have been studied include, mortality rate, length of hospital stay, duration of ICU stay, time to oral feeding and need for surgical intervention.[9,11,16,21,23,24,] . The outcome parameters studied in this research were; Hospital mortality, length of hospital stay, need for surgical intervention and time to oral feeding.

Few studies have looked at the need for surgery in the management of CEGAL. Tabatabai et al., found 69 % need for surgery[9] whereas a meta analysis by Verstegen et al., reported it at 17%[21]. Data from this study identified a 12% need for surgical management for CEGAL. This implies that most patients recovered spontaneously with conservative management.

Analysis of data from this study shows a clear association between development of CEGAL and increased length of hospital stay ($p<0.0001$) with a median of 30.5 days.This is

consistent with other studies that have looked at this parameter. Larburu et al., published a median stay of 28.5 days [11] and Verstegen et al., 22 days[21]. This illustrates the negative financial impact of CEGAL on health care resources as further elaborated by Agazarian et al.[25]

There are conflicting published reports on the association between presence of CEGAL and increased risk of Hospital mortality. Schurchert et al., Larburu et al., and Verstegn et al., all published an associated risk of 3.3%, 5.5% and 8% respectively.[23,11,21] Where as Tabatabai et al., Aminian et al., and Van Rossum et al., found no association. [9,16,24]. Data from this study showed no association between the presence of CEGAL and increased Hospital mortality (p=0.118). This implies that in our setting the development of a cervical anastomotic leak does not significantly increase the patients' risk of mortality.

Published reports indicate that the overall mortality following esophagectomy with a cervical anastomosis ranges from 0-5% [16,26,27,28]. Schieman et al., reported an overall mortality of 5% for patients undergoing Transhiatal esophagectomy and 4.32% for Mckeowns esophagectomy[28]. Data from this study shows the overall mortality at KNH to be 5.83% which is within acceptable range. Metzger et al,. reported that 20 esophagectomies per year is the figure required for an institution to be a high volume center with an average mortality rate of 4.9%[29] Using this criteria KNH can be classified as a high volume center with low mortality rates.

Data from this study shows an association between presence of CEGAL and delay in resumption of oral intake ($p<0.0001$). Median time to resumption of oral feeds in patients without a leak was 8 days whereas in patients that developed CEGAL,time to oral intake was increased to a median of 27 days. This is consistent with data from Van Rossum et al., who published a clear association between CEGAL and increased time to oral intake[24].

Conclusion

CEGAL is a common complication of esophagectomy world wide. However in our setting there is no association between the presence of CEGAL and increased risk of Hospital perioperative mortality. Data analysis also showed that CEGALs are mainly managed conservatively and recover spontaneously without surgical intervention in the majority of cases.

On the other hand, the presence of CEGAL increases the length of hospital stay which has an impact on the overall cost of treatment. CEGALs also lead to a delay in resumption of oral intake which has an impact on the patients' quality of life.

Limitations of the Study

The study relied on data from a single center, a multicenter study would be more representative and offer clearer and more acceptable results on the incidence and outcomes of CEGAL. As a retrospective study it has an inferior level of evidence compared with prospective studies.

Recommendations

1. The detection/diagnosis of CEGALs seem to be clinical and mainly between post operative day 8 - 9 . Thus medical practitioners taking care of these patients should have a high index of suspicion to detect CEGAL during that period.
2. Follow up study to elaborate on the risk factors contributing to the development of CEGAL would reveal modifiable factors that will reduce the incidence of CEGAL at our institution.
3. Long Term follow up of patients with CEGAL to review their long term complications/outcomes and in particular the association between CEGAL and stricture formation.

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APPENDICES

Appendix 1: Data collection tool

Study title: THE INCIDENCE AND EARLY OUTCOMES OF CERVICAL ESOPHAGOGASTRIC ANASTOMOTIC LEAKS FOLLOWING ESOPHAGECTOMY FOR CANCER AT KENYATTA NATIONAL HOSPITAL

Form Number _____

Age _____ years

Sex: Male / Female

Tumor histological type: adenocarcinoma / squamous cell carcinoma/other

What is the location of the tumor? Midthoracic/distal thoracic/GE junction

Has the patient undergone neoadjuvant treatment?: yes/no

Date of surgery: day / month / year

What is the type of surgery done? Mckeowns/Transhiatal

Is there presence of anastomotic leak?: yes / no

What is the date of the diagnosis of the anastomotic leak?: day / month / year

If there was a leak, what was the type of management: operative / non-operative

Date of initiation of oral feeds: day/ month/year

In hospital mortality: yes / no

Date of death: day / month / year

Date of discharge: day/month/year

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