

**ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCE
SCHOOL OF MEDICINE**



**ASSESSMENT OF ADEQUACY OF SURGICAL RESECTION FOR COLORECTAL CANCER
AT TIKUR ANBESSA SPECIALIZED HOSPITAL FROM 2016-2019, ADDIS ABABA,
ETHIOPIA**

BY: YONAS NIBRET (MD)

**A THESIS TO BE SUBMITTED TO THE ADDIS ABABA UNIVERSITY
SCHOOL OF MEDICINE DEPARTMENT OF SURGERY IN PARTIAL
FULFILLMENT OF THE REQUIREMENTS FOR A SPECIALITY
CERTIFICATE IN GENERALSURGERY**

**OCTOBER 2020
ADDIS ABEBA, ETHIOPIA**

ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCE SCHOOL OF MEDICINE

**ASSESSMENT OF ADEQUACY OF SURGICAL RESECTION FOR COLORECTAL CANCER
AT TIKUR ANBESSA HOSPITAL FROM 2016-2019, ADDIS ABABA, ETHIOPIA**

BY: YONAS NIBRET (MD)

ADVISORS: NEBYOU SEYOUM (MD, ASSOCIATE PROF. OF SURGERY)

PROFESSOR BERHANU KOTISSO (MD, PROFESSOR OF SURGERY)

OCTOBER 2020

ADDIS ABABA, ETHIOPIA

Approval by the Board of Examiners

This thesis by Yonas Nibret is accepted in its present form by the board of examiners as satisfying the thesis requirement for the specialty certificate in general surgery

Examiner: full name _____

Research advisors

1. Dr. Nebyou Seyoum (MD, Associate prof. Of surgery)
2. Professor Berhanu Kotisso (MD, Professor of surgery)

ACKNOWLEDGMENT

I would like to provide my heart full gratitude to my advisers Dr. Nebyou Seyoum (MD, Associate prof. of surgery) and professor Berhanu Kotisso (MD, professor of surgery) for their fruitful advice, valuable comments, and cooperation in preparing this research.

I would also like to thank my family with their continuous support and my brother Mr. Biresaw Wassihun (BSc, MPH) for helping me with the details.

Table of Contents

ACKNOWLEDGMENT	III
List of tables.....	VI
List of Figures	VII
Abbreviations	VIII
Abstract.....	IX
1. Introduction.....	1
1.1. Background	1
1.3. Significance of the study	4
2. Literature review	5
2.1. The burden of colorectal cancer.....	5
2.2. Adequacy of surgical resection of colorectal cancer.....	5
3. OBJECTIVES	9
3.1. General Objective	9
3.2. Specific Objectives.....	9
4. METHODS AND MATERIALS	10
4.1. Study area and period.....	10
4.2. Study design	10
4.3. Population.....	10
4.3.1. Source population	10
4.3.2. Study population	10
4.3.3. Study unit.....	10
4.4. Sample size and sampling technique.....	10
4.5. Inclusion and exclusion criteria	10
4.5.1. Inclusion criteria.....	10
4.6. Study Variables.....	11
4.7. Operational Definitions.....	11
4.8. Data Collection Procedure	11
4.9. Data processing and Analysis	11
4.10. Data quality assurance	12
4.11. Ethical Consideration	12
4.12. Dissemination of the result.....	12
5. Result.....	13

6. Discussion	20
7. Conclusion and recommendations	21
8. Limitations of the study	22
9. References	29

List of tables

Table 1 socio-demographic characteristics of a study participant in Addis Ababa TikurAnbessa Specialized hospital.	13
Table 2 Clinical characteristics of a study participant in Addis Ababa TikurAnbessa Specialized hospital	14
Table 3. pathological report of margin status in Addis Ababa TikurAnbessa Specialized hospital	16
Table 4 factors associated with adequacy of LN harvested in Binary logistic regression (n=85)	18
Table 5 Factors Associated with the radial margin	19

List of Figures

Figure 1 Location of tumor among study participant in Addis Ababa TikurAnbssa Specialized hospital	13
Figure 2. length of colon resected in CM.....	16
Figure 3. number of LN harvested.....	17

Abbreviations

APR	Abdominal Perineal Resection
AJCC	American Joint Committee on Cancer
CRC	Colorectal Cancer
Ca	Cancer
CRM	Circumferential Resection Margin
LN	Lymph Node
TME	Total Mesorectal Excision

Abstract

Background: Colorectal carcinoma is a malignant neoplasm of the colon and rectum. It is the most common malignancy of the gastrointestinal tract. The enbloc removal of the presenting malignancy, to include adequate margins plus the lymphatic nodal basin, remains the hallmark of surgical treatment for cure. Adequate lymph node evaluation is required for proper staging of colorectal cancer, and the number of lymph nodes examined is associated with survival

Objectives: To determine the adequacy of surgical resection of patients operated for colorectal cancer at Tikur Anbessa Specialized Hospital.

Methods: A retrospective cross-sectional study was conducted by a review of the medical records of all patients who had undergone resection of colorectal cancer at Tikur Anbessa Specialized hospital from January 1, 2016 to December 31, 2019. The data was obtained from the patient's record review; data was collected using a pretested questionnaire and checklist. Data were checked and entered into Epi data version 3.1 then exported to statically package for social science version 24 for analysis.

Result: From the total of study participants above the half 48(53.3%) are male, with male to female ratio of 1.14:1. The majority 44(48.9%) of study participants were found in the age groups of <50 years followed by 50-64 years 26(28.9%).The mean of LN harvested was 10.35(SD \pm 7.86) with a maximum of 41 and a minimum of 0.And only40% of patients had Adequate LN harvested (\geq 12). female patients were 2.12 times more likely to have adequate LN harvested as compared to male patients with AOR=2.12(1.49-3.96). Similarly, patients found in the age group of \geq 65 were less likely to have adequate LN harvested as compared to patients found in the age group of <50 years with AOR=1.22 (1.60-4.88). Those patients with an age group of \geq 65 years were 2.04 times more likely to have radial Margin involvement as compared to others, while fixed tumors are 2.81 times more likely to have radial margin involvement relative to mobile tumors.

Conclusion: In this retrospective study, we described the adequacy of nodal harvest in colorectal cancer and evaluated possible factors that may affect the adequacy nodal harvest. Only 40 % of the patients in this study have adequate nodal harvest based on current guidelines. Younger patients less than 50 years of age and female patients were associated with improved nodal harvest. In this study, age \geq 65 years and fixed tumors are more likely to have radial margin involvement.

Keywords. Adequacy, resection, colorectal cancer, Ethiopia

1. Introduction

1.1. Background

Colorectal cancer refers to cancer in the colon or rectum. Cancer starts as small growths occurring in the mucosal layer of the colon(1). These small growths are known as polyps; they are benign (non-cancerous). Over a few years, the polyps may grow to become malignant (cancerous) tumors referred to collectively as colorectal cancer(2)

Colorectal cancer (CRC) is one of the most common types of cancer worldwide. CRC is the third most common type of cancer in males and the second in females(3). CRC accounts for 8 % of all cancer deaths and is the fourth most common cause of death in Central and Eastern Europe. It occurs in hereditary, sporadic, or familial forms(3, 4)

The presenting symptoms of colorectal cancer vary depending on the site of cancer and stage of the disease(5). Patients may present with symptoms of alteration in bowel habit, intestinal obstruction, pain with an abdominal mass, unexplained reduction in weight, the presence of blood in the stool, or anemia(5, 6). Patients with colorectal cancer on the right side of the colon usually have symptoms of anemia, loss of weight, or abdominal pain. Patients with cancer in the left side of the colon often have an alteration in bowel habit or rectal bleeding(7)

Surgical resection offers the only opportunity for a cure as well as affording significant palliation in patients with advanced disease. Surgical management should encourage adequate resection for cure or palliation rather than bypass or diversion(8). The en bloc removal of the presenting malignancy, to include adequate margins plus the lymphatic nodal basin, remains the hallmark of surgical treatment for cure. Adequacy of resection is now generally accepted to include a 10-cm proximal bowel margin and at least a true 2-cm distal margin along with complete resection of the primary and secondary nodal basin, based on the blood supply of the involved bowel segment(8, 9). Adequate lymph node evaluation is required for proper staging of colorectal cancer, and the number of lymph nodes examined is associated with survival. According to current guidelines, the recommended minimum number of lymph nodes examined to ensure adequate sampling is 12 LNs(9). Because detection of any positive lymph node is critical for predicting patient outcomes, an adequate number of lymph nodes must be examined. Inadequate lymph node sampling has serious implications. It can lead to positive lymph nodes being missed and to patients being inappropriately classified as having lymph node-negative disease

. Such patients may not be allowed to benefit from adjuvant therapy(10). Besides, inadequate lymph node sampling may fail to remove involved lymph nodes, thus increasing the risk of local recurrence; it may also be a marker of poor-quality surgical or pathologic care, both of which are associated with worse long-term outcome for colorectal cancer patients(11)

Cancer is the leading cause of death globally, surpassing mortality rates of tuberculosis, malaria, and HIV/AIDS combined, and it is quietly taking center stage(12, 13)

In Ethiopia, CRC is the third most prevalent cancers among the entire adult population, and patients often present with advanced stages of cancer(14)

In Africa, data for the adequacy of surgical resection of colorectal cancer is scanty. In Ethiopia, to the best of our knowledge, there is no published study on the adequacy of surgical resection of colorectal cancer. For these reasons, this study determined the adequacy of surgical resection of colorectal cancer at Tikur Anbessa specialized hospital from 2016-2019, Addis Ababa, Ethiopia

1.2. Statement of the problem

Colorectal cancer is a cancer of the large intestine. It can be either colon cancer or rectal cancer based on the site where the cancer originates and they are collectively referred as colorectal cancer (CRC)(15, 16). About 1,096,000 new cases of colon cancer are estimated to be diagnosed in 2018, while about 704,000 new cases of rectal cancer are expected. Together, these comprise 1.8 million new cases of CRC(17). The enbloc removal of the presenting malignancy, to include adequate margins plus the lymphatic nodal basin, remains the hallmark of surgical treatment for cure. Adequacy of resection is now generally accepted to include a 10-cm proximal bowel margin and at least a true 2-cm distal margin along with complete resection of the primary and secondary nodal basin, based on the blood supply of the involved bowel segment. Adequate lymph node evaluation is required for proper staging of colorectal cancer, and the number of lymph nodes examined is associated with survival(8). According to current guidelines, the recommended minimum number of lymph nodes examined to ensure adequate sampling is 12. Inadequate lymph node sampling has serious implications. It can lead to positive lymph nodes being missed and to patients being inappropriately classified as having lymph node-negative disease(18, 19). Such patients may not be allowed to benefit from adjuvant therapy. Besides, inadequate lymph node sampling may fail to remove involved lymph nodes, thus increasing the risk of local recurrence; incomplete removal of the tumor is the main cause of local recurrence in rectal carcinomas (9, 19, 20). CRC is the third most commonly diagnosed cancer and the most cause of cancer-related death worldwide and remains one of the killer cancers in the world. Its problem is predictable to increase. Even though this increasing burden in Africa CRC continues to receive a relatively low public health, priority (21-23)

The adequacy of surgical resection of colorectal cancer has been studied in the developed world. Owing to differences in disease patterns and resource availability, the findings of studies conducted in the developed world might not be an accurate reflection of the experience of colorectal cancer resection inEthiopia. For these reasons, this study was conducted to determinethe adequacy of surgical resection of colorectal cancer at Tikur Anbessa hospital from 2016-2019, Addis Ababa, Ethiopia

1.3. Significance of the study

CRC continues to be one of the commonest malignancies worldwide. This study has the following significances

- ✚ Helps to give basic data and information about the adequacy of surgical resection of colorectal cancer in Tikur Anbessa Specialized Hospital.
- ✚ The study will also identify factors affecting the adequacy of surgical resection of colorectal cancer
- ✚ This study may help to design management protocol for a patient with resectable colorectal cancer
- ✚ It will be used as a baseline for future research

2. Literature review

2.1. The burden of colorectal cancer

CRC is the third most commonly diagnosed cancer in males and the second in females worldwide. It accounts for over 9 % of all cancer incidence, with an estimated 1.4 million cases occurring in 2012 (3)

There is wide geographical variation in incidence across the world, with almost 55 % of the cases occurring in more developed countries(3). These geographic differences may be attributable to different dietary and environmental exposures that are imposed upon a background of genetically determined susceptibility(24)

Countries with the highest incidence rates include Australia, New Zealand, Europe, and Northern America. Conversely, incidence rates are low in Africa, South-Central Asia, and Central America(25, 26)

In Ethiopia according to the Addis Ababa cancer registry, it is the first in males and fourth in females (14). Its presenting symptoms of colorectal cancer vary depending on the site of cancer and stage of the disease. Patients may present with symptoms of alteration in bowel habit, intestinal obstruction, pain with an abdominal mass, unexplained reduction in weight, the presence of blood in the stool, or anemia(27)

Patients with colorectal cancer on the right side of the colon usually have symptoms of anemia, loss of weight, or abdominal pain. Patients with cancer in the left side of the colon often have an alteration in bowel habit or rectal bleeding(28)

2.2. Adequacy of surgical resection of colorectal cancer

Surgical resection offers the only opportunity for a cure as well as affording significant palliation in patients with advanced disease. Surgical management should encourage adequate resection for cure or palliation rather than bypass or diversion. The en bloc removal of the presenting malignancy, to include adequate margins plus the lymphatic nodal basin, remains the hallmark of surgical treatment for cure. Adequacy of resection is now generally accepted to include a 10-cm proximal bowel margin and at least a true 2-cm distal margin along with complete resection of the primary and secondary nodal basin, based on the blood supply of the involved bowel segment. Adjuvant use of chemotherapy and radiation therapy also offer significant bonuses in the treatment of rectal carcinoma(29, 30)

Identification of ≥ 12 lymph nodes in resected colon cancer specimens has been endorsed as a quality indicator. Anatomic location, colorectal surgical training, and case volume was strongly correlated with the number of lymph nodes identified. Colon cancer patients who have metastases to regional lymph nodes (stage III) have worse survival than patients without metastases (stages I and II), and randomized trials prove that such patients benefit from adjuvant systemic therapy.¹⁻⁵ The accuracy of lymph node staging depends on the adequacy of surgical resection and identification of lymph node metastases by the pathologist. Therefore, identification and evaluation of all lymph nodes in an appropriately resected specimen is critical for accurate staging to direct therapy. A variety of studies, including nested cohorts from large randomized trials, and population-based and single-institution studies, demonstrate that the number of lymph nodes identified in resected colon cancer specimens is predictive of survival (9, 31, 32)

The surgeon with the highest volume of resections, who completed a fellowship in colorectal surgery, had a higher average number of lymph nodes found in his resections than each of the 3 general surgeons. The average and median numbers of lymph nodes were ≥ 12 for all anatomic sites, but the range was 57% to 83% for resections in which ≥ 12 lymph nodes were identified. Collectively, lesions of the right side of the colon were associated with more lymph nodes and a higher percentage, in which ≥ 12 lymph nodes were identified, than left-sided lesions (9, 32).

2.3 Factors Associated with Adequacy of surgical resection of colorectal cancer

A retrospective study conducted showed that the highest average numbers of lymph nodes were identified in ascending colon resections, a figure that was higher than cecum, sigmoid colon, and descending colon, but not higher than a transverse colon or splenic or hepatic flexures. For right-sided lesions, the rates of partial colectomy rather than hemicolectomy were 35 of 131 (25.4%) for cecal cancers compared with 24 of 120 (16.1%) for ascending colon lesions ($P = .067$). There were differences in lymph node identification by age: resections from patients < 60 years of age were more likely to have ≥ 12 lymph nodes identified, but there were no differences in the percentages among the 60- to 69-, 70- to 79-, and > 80 -year age cohorts. There were more lymph nodes identified, and higher proportions of resections containing ≥ 12 lymph nodes, from patients with the regional disease (T3 or T4 local extension and/or lymph node metastases) than patients who had either local disease (T1 or T2) or distant metastases. In each stage of the disease, The ≥ 12 -lymph node threshold was associated with better survival for patients with stage I or stage II disease, but not stage III or IV (9, 34)

The stage is the strongest predictor of survival for patients with colorectal cancer. Accurate staging also is critical for appropriate patient management(35). Incomplete removal of the tumor is the main cause of local recurrence in rectal carcinomas; this often occurs at the lateral aspects devoid of the peritoneum. LRM involvement in 20% of these unselected cases of rectal carcinoma and the subsequent local recurrence in 53.3% of patients showed that incomplete surgical resection is a significant factor in local recurrence(36).

Total mesorectal excision offers the lowest reported rates of local recurrence for rectal cancer. Routine excision of the intact mesorectum during resection of cancers of the mid and lower rectum has resulted in the lowest incidence of local recurrence ever reported. A circumferential resection margin of less than 1 mm is considered involved(18,19)

A study conducted by Johnson et al showed that the presence of nodal metastasis is a critical component of staging in colorectal cancer. Accurate assessment of nodal status requires sufficient node sampling, Identification of 12 or more lymph nodes were considered an adequate nodal harvest based on the current American Joint Committee on Cancer recommendations(19).

There was a strong association between the length of the bowel and the number of lymph nodes identified (P 0.005). The prognostic and adjuvant therapy-related consequences of nodal metastases make the accurate assessment of lymph node status an essential component of colorectal cancer staging. The overall rate of nodal metastases (38%) was comparable to that reported in the literature using standard manual techniques for gross examination of the specimens. Right-sided resections, high surgeon volume, and examination of gross specimens by a staff pathologist were associated with improved nodal harvest(37). Nodal status is recognized as an important prognostic factor(38).

Studies suggest that the greater the number of lymph nodes examined in a surgical specimen, the higher the incidence of finding nodes positive for cancer. It has also been suggested that increased survival is associated with a lower percentage of positive lymph nodes examined. In patients with rectal cancer who receive high-dose neoadjuvant chemo-radiation followed by TME, less than 12 lymph nodes in the surgical specimen can be expected in 72% of the cases(9)

Advanced tumor stage was statistically significantly associated with adequate lymph node evaluation(9). In no metastatic colorectal cancer, lymph node status is the strongest pathologic predictor of patient outcome. Approximately 68% of patients with no lymph node involvement will survive 5 years, compared with only 40% of those with lymph node metastases.

Irrespective of tumor stage, younger patients were statistically significantly more likely than older patients to receive adequate lymph node evaluation (9).

3. OBJECTIVES

3.1.General Objective

To determine the adequacy of surgical resection for colorectal cancer in Tikur Anbessa Specialized Hospital, Addis Ababa University from January 2016 to December 2019.

3.2.Specific Objectives

- ✚ To determine the status of surgical margins of resected colorectal cancer
- ✚ To determine the number of LN harvested and their status
- ✚ To determine factors affecting the adequacy of surgical resection of colorectal cancer
- ✚ To determine common types of surgery performed for colorectal cancer.
- ✚ To determine the intra-operative finding of colorectal cancer.

4. METHODS AND MATERIALS

4.1. Study area and period

The study was conducted in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. From January 1st, 2016 to December 31st, 2019.

4.2. Study design

A hospital-based retrospective cross-sectional study design was conducted

4.3. Population

4.3.1. Source population

All patients who had undergone resection of colorectal cancer in Tikur Anbessa Specialized Hospital

4.3.2. Study population

All patients undergone resection of colorectal cancer in Tikur Anbessa Hospital and they fulfilled the inclusion criteria.

4.3.3. Study unit

Individual patient

4.4. Sample size and sampling technique

All cases managed by resection of colorectal cancer during the study period were included. A medical record number of all resection of colorectal cancer patients in the study period were retrieved from Jan 1st, 2016 – Dec 31st, 2019. and resection of colorectal cancer was performed for 122 patients (115 on elective and 7 on emergency base). Of these 90 complete charts were retrieved with a retrieval rate of 74%.

4.5. Inclusion and exclusion criteria

4.5.1. Inclusion criteria

- All patients who undergone resection for colorectal carcinoma in the study period who has a complete pathology report.

4.5.2. exclusion criteria

- Patients who did not fill the inclusion criteria like havening incomplete charts or incomplete pathology reports were excluded.
- Those patients who undergone only diversion colostomy or internal bypass without resection of the colorectal cancer were excluded.

4.6. Study Variables

4.6.1. Independent Variables

- Age
- Sex
- Location of tumor
- Clinical stage
- Neoadjuvant therapy
- Type of surgery
- Surgeons level of training
- Intra-operatively, the status of the mass
- Intra-operatively, the presence of LAP

4.6.2. Dependent Variables

- ✚ Length of colon resected
- ✚ Status of the proximal margin
- ✚ Status of the distal margin
- ✚ Status of radial margin
- ✚ Number of LN harvested
- ✚ Number of positive LNs

4.7. Operational Definitions

Colorectal cancer is defined as biopsy-proven cancer of the colon or rectum.

4.8. Data Collection Procedure

The data were collected by five medical interns who have some knowledge about the disease and can retrieve chart. A structured and pre-prepared format was used. Training was given for data collectors on the objective, the relevance of the study and confidentiality of information and steps on how to collect and transfer data from the patient's chart, and the principal investigator supervised each as required during the data collection.

4.9. Data processing and Analysis

The collected data were entered using Epi data version 3.1 and analyzed using SPSS (Statistical Package for Social Science) version 24 software. Descriptive statistics such as frequency, percentage, mean, standard deviation were used to describe and summarize the data. A statistical significance test was applied to compare the adequacy of surgical resection of colorectal cancer at a p-value less than 0.05

4.10. Data quality assurance

During data collection, the principal investigator checked the completeness, ambiguous suspicions, and checked on the spot. Before feeding the information into the computer, it was checked for completeness and accuracy; then it was fed into the computer and be analyzed and interpreted.

4.11. Ethical Consideration

Data collection was started after permission has been obtained from IRB of college of health sciences Addis Ababa University and the card room. To ensure smooth and effective participation of card room personnel, the objective of the study was thoroughly explained and confidentiality is secured.

4.12. Dissemination of the result

The finding of this result will be disseminated through publication (local or international journals) or presentationsat conferences. A copy of it will be given to AAU, department of Surgery and other concerned bodies so that they can use the results for planning and implementation to prevent morbidity and mortality related to colorectal cancer.

5. Result

5.1 Socio-demographic characteristics of study participants

From the total of study participants above half 48(53.3%) were males and 42(46.7) were females with male to female ratio of 1.14:1 .The majority 44(48.9%) of study participants were found in the age groups of <50 years followed by 50-64 years 26(28.9%) (Table 1.)

Table 1 Socio-demographic characteristics of a study participant in Addis Ababa TikurAnbssa Specialized hospital

Variables	Frequency	Percentage
Sex		
Male	48	53.3
Female	42	46.7
Age		
<50	44	48.9
50-64	26	28.9
≥65	20	22.2

5.1. Clinical Characteristics of study participants

From the total of 90 patients in majority 24(26.7%) of the tumor was located in the rectum followed by sigmoid colon 21(23.3%) figure 1

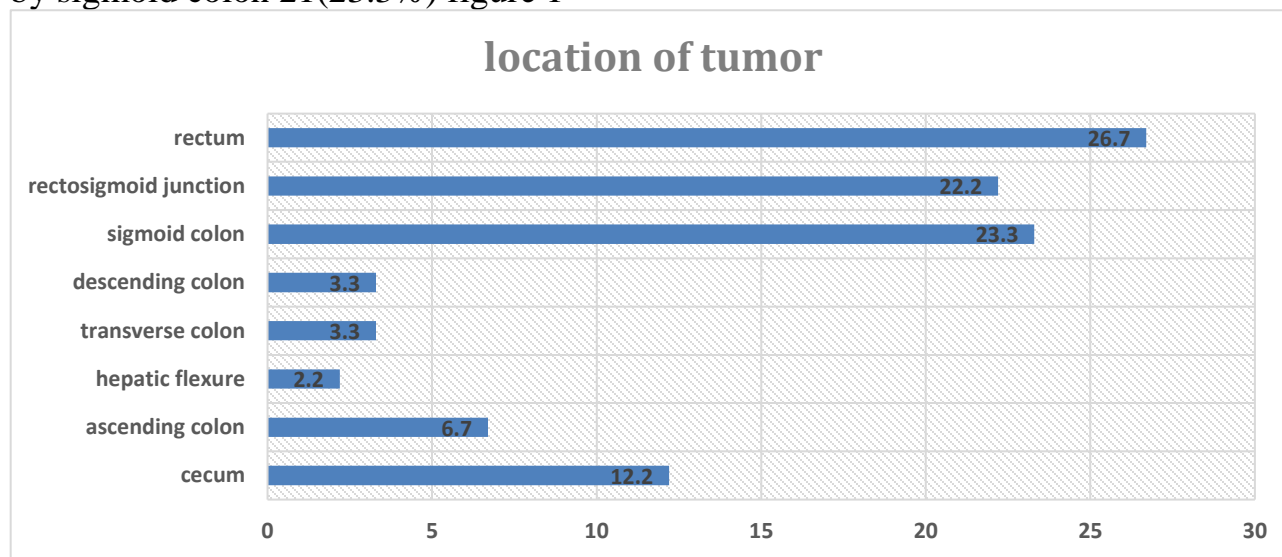


Figure 1 Location of tumor among study participant in Addis Ababa TikurAnbssa Specialized hospital

In this study majority 44 (48.9%) of patients were found in the clinical stage III and 11(12%) were found in stage II. However, 29(32.2%) of the patient stage was not documented. Only 1% of patients had neoadjuvant chemotherapy and 89(98.9) have no neoadjuvant chemotherapy or radiotherapy. The types of surgery

performed in majority 26(28.9%) were anterior resection followed by sigmoidectomy 20(22.2%).Almost all 80 (88.9%) surgeries were done by consultant Surgeons and only 10(11.1%) of surgery was performed by 4th-year residents. Almost all 87(96.7%) of surgery was done electively. Besides, the intra-operative status of the mass showed that the majority 48(53.3%) of patients have mobile mass and 27(30.0%) were fixed mass followed by 15(16.7%) of patients the status of mass was not documented (Table 2)

Table 2 *Clinical characteristics of a study participant in Addis Ababa Tikur Anbessa Specialized hospital*

Variables	Frequency	Percentage
Clinical stage		
Stage I	1	1.1
Stage II	11	12.2
Stage III	44	48.9
Stage IV	5	5.6
Not Documented	29	32.2
Neoadjuvant therapy		
Chemotherapy	1	1.1
None	89	98.9
Types of surgery performed		
enblock resection	2	2.2
right hemicolectomy	21	23.3
left hemicolectomy	5	5.6
Sigmoidectomy	20	22.2
anterior resection	26	28.9
APR	16	17.8
Surgery is done by		
Consultant Surgeon	80	88.9
Year 4 resident	10	11.1
Urgency of surgery		
Emergency	3	3.3
Elective	87	96.7

intra-operatively the status of the mass		
Mobile	48	53.3
Fixed	27	30.0
Not documented	15	16.7
Intra-operatively, palpable LN status		
Present	26	28.9
Absent	24	26.7
Not documented	40	44.4
location Right vs left side		
the cecum,ascending colon, hepatic flexure, transverse colon	22	24.4
splenic flexure, descending colon, sigmoid colon, rectosigmoid junction	44	48.9
Rectum	24	26.7
the length of colon resected in CM Mean=26.2		
≤26.2	26	28.9
>26.2	64	71.1

5.2. The pathology report of the length of colon resected in CM

In the finding, the length of colon resected in CM had a mean of 26.2 (SD±10.7) with a minimum of eight and a maximum of 59 respectively. The majority 64(71.1%) of were > 26.2 lengths of colon resected in CM and 26(28.9%) were ≤ 26.2 lengths of colon resected in CM (**Figure 2**)

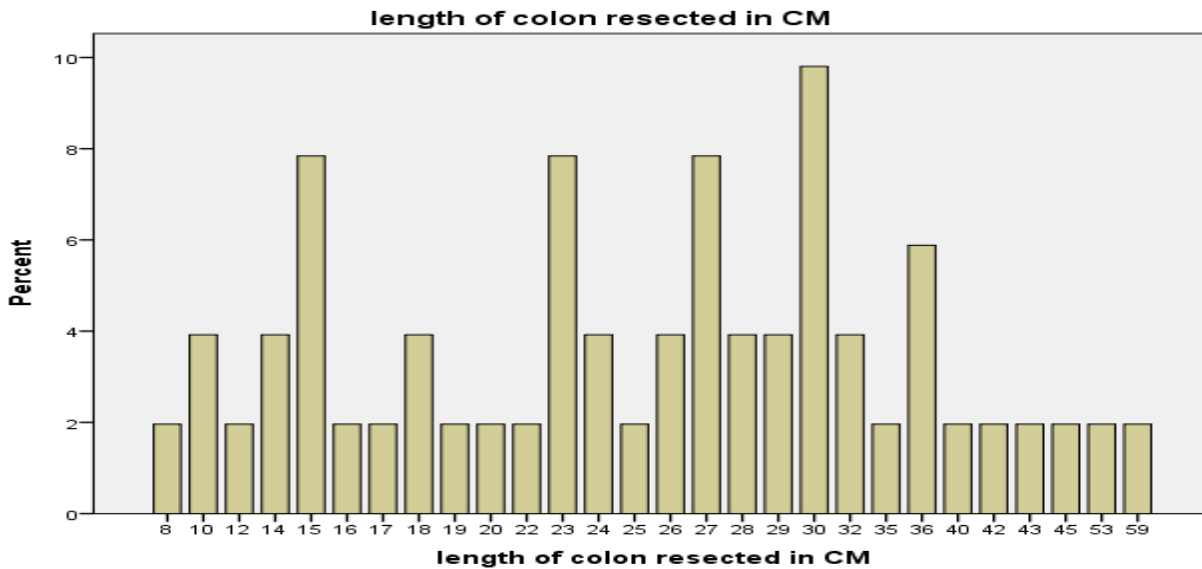


Figure 2. length of colon resected in CM

5.3. The pathology report of margin status

The finding of this study showed that the majority 79 (87.8%) of proximal margin were free and similarly 79(87.5%) of distal margin were free followed by two (2.2%) involved and, nine (10%) were not documented. Besides, the radial margin showed that above half 61(67.8%) were free and 13(14.4%) were involved but 16(17.8%) were not documented.

In this finding, the mean of LN harvested was 10.35(SD ±7.86) with maximum of 41 and a minimum of 0 (Table 3).

Table 3. pathological report of margin status in Addis Ababa TikurAnbssa Specialized hospital

Proximal margin	Frequency	Percentage
Free	79	87.8
Involved	0	0
Not documented	11	12.2
Distal margin		
Free	79	87.8
Involved	2	2.2
Not documented	9	10.0
Radial margin		
Free	61	67.8

Involved	14	14.4
Not documented	16	17.8
The number of LN harvested		
Not adequate LN harvested (0-11)	51	60
Adequate LN harvested (≥ 12)	34	40

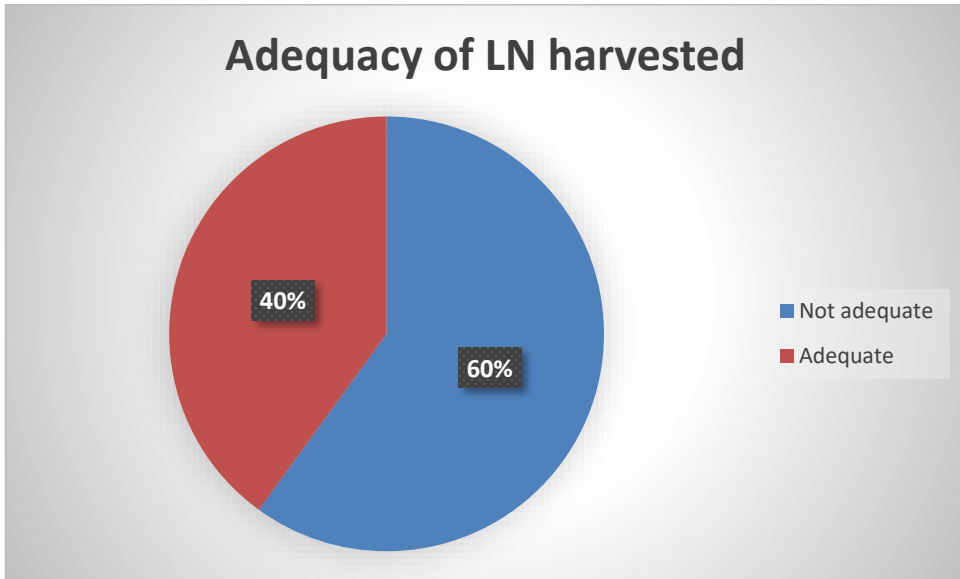


Figure 3. Number of LN harvested

5.4. Factors Associated with the adequacy of LN harvested

In binary logistic regression, variables such as sex and age were factors associated with the adequacy of LN harvested. Similarly, in multivariable analysis after controlling confounding variables age and sex were associated with the adequacy of LN harvested.

Those female patients were 2.12 times more likely to have adequate LN harvested as compared to those male patients with AOR=2.12(1.49-3.96) Similarly, patients found in the age group of ≥ 65 were less likely to have adequate LN harvested as compared to patients found in the age group of < 50 years with AOR= 1.22 (1.60-4.88). and patient with longer (> 26.2 CM) resected colon are more likely to have adequate LN harvest compared to those with shorter colon resected with AOR= 1.39(1.49-3.96)

Table 4 factors associated with adequacy of LN harvested in Binary logistic regression (n=85)

Variables	LN harvested		COR with 95% CI	AOR with 95% CI	P-Value
	Not Adequate (0-11)	Adequate (≥12)			
Sex					
Male	31	13	1	1	
Female	20	21	2.50(3.11-9.21)	2.12(1.49-3.96)*	0.04
Age					
<50	20	21	1	1	
50-64	16	9	0.53(0.19-1.49)	0.57(0.19-1.69)	
≥65	15	4	0.25(0.07-0.89)*	1.22 (1.60-4.88)*	0.03
Intra-operative status					
Mobile	26	21	1	1	
Fixed	17	8	0.58(1.21-6.61)*	0.41(0.13-1.26)	0.12
Not documented	8	5	0.77(0.22-2.72)	0.67(0.17-2.68)	
Length of colon					
Less than or equal to 26.2	17	9	1	1	
Greater than 26.2	34	25	1.38(0.53-3.62)	1.39(1.49-3.96)*	0.05

Key *significance

Factors Associated with a radial margin

The finding of the multivariable analysis showed that radial margin status has an association with age and Intra-operative status. Those patients with an age group of ≥65 years were 2.04 times more likely associated with radial Margin involvement as compared to those < 50 years of age, and fixed tumors are 2.81 times more likely to have radial margin involvement as compared to mobile tumors with AOR= 2.81(4.21-8.35)

Table 5. Factors Associated with the radial margin

Variables	Radial Margin		COR with 95% CI	AOR with 95% CI	P-Value
	Free	Involved			
Sex					
Male	30	7	1	1	
Female	31	6	0.82(0.23-0.78)*	0.23(0.91-2.41)	
Age					
<50	29	9	1	1	
50-64	21	3	0.46(0.2.5-5.02)	0.27(0.28-7.09)	
≥65	11	1	0.63(0.21-3.36)	2.04(2.31-7.98)*	0.03
Intraoperative status					
Mobile	38	3	1	1	
Fixed	14	10	9.04(3.23-9.21)*	2.81(4.21-8.35)*	0.02
Not documented	9	0	0.15(0.21-4.23)	0.13(0.26-4.27)	
Length of colon					
Less than or equal to 26.2	18	4	1	1	
Greater than 26.2	43	9	0.94(0.24-5.12)	1.42(0.92-2.34)	

6. Discussion

Lymph node status is the strongest predictor of long-term outcome in patients with nonmetastatic colorectal cancer. Moreover, the current AJCC recommends that we need to harvest at least 12 LNs to determine the status of lymph node .and it in turn is used to decide the need for adjuvant chemo radiotherapy (9).

The purpose of this study was to determine the adequacy of colorectal cancer resection by determining factors associated with resection margin status and adequacy of lymph node harvest.

In this study, the mean (SD) of LNs harvested was 10.4 LNs(7.8) with a minimum of 0 and a maximum of 41 LNs. Which is comparable with other studies, Baxter et al, Marks et al, Tekkis et al, who reported a mean of 9, 10.1, and 11.7 harvested LNs respectively, and slightly higher than Johnson et al who showed a mean 8.3 LNs but lower than Jakob et al and Dillman et al who reported 12.7 and 14.5 LNs, this may be because both of them didn't include rectal ca, which in different studies, is associated with lower rate LN harvest compared to colonic ca.

The finding of this study also showed that only 40% of patients had Adequate LN harvested (≥ 12). This was similar to the study done by Baxter et al which showed that only 37% had adequate LN harvest. But significantly better than Marks et al and Johnson et al who reported only 28% and 22.4% of adequate LN harvest.

In binary logistic regression, variables such as sex , age and length of colon resected were factors associated with the adequacy of LN harvested.

Similarly, in multivariable analysis after controlling confounding variables age, sex and length of colon resected were associated with adequacy of LN harvested

Those female patients were 2.12 times more likely to have adequate LN harvested as compared to those male patients. The age group of ≥ 65 were less likely to have adequate LN harvested as compared to patients found in the age group of < 50 years. This finding was similar to another study which showed that there were differences in lymph node identification by age, young patients have a higher chance of adequate LN harvest.(9,20, 31,32, 34). This maybe because surgeons tend to do more aggressive surgery for younger patients who has a longer life expectancy compared to elderly patients.

In this study,stage of the disease has no statistically significant association with adequate lymph node harvest, but the finding of other literature showed that the tumor stage was statistically significantly associated with adequate lymph node harvest,i.e. as the stage of disease increases the probability of

adequate LN harvest increases (9, 31, 32).

The discrepancy might be due to the difference in sample size and study period because the previous study includes large sample size and this study includes only a small sample size. Moreover, another reason maybe for 32% of our patients, the stage was not documented.

In this study, the length of the colon has association with the adequacy of colorectal resection similar to other studies which showed that there was a strong association between the length of bowel and the number of lymph nodes identified(37-38).

In this study location of the tumor has no statistically significant association with the adequacy of LN harvest, but other literature shows that right side tumors have a better LN harvest than the left side and rectal cancers.(9,19,). This maybe because in this study majority of cases are left side and rectal and it maybe year 4 residents did only right side resections.

These study findings showed the majority (87.8%, 87.5% and, 67.8%) of proximal, distal, and radial surgical margins were free respectively. Also, 2.2% of distal and 14.4% of radial margin were involved. O.L Ng et al reported 20% radial margin involvement in rectal cancer resections.

In this study radial margin status has an association with age and Intra-operative status of the mass. Those patients with an age group of ≥ 65 years were 1.88 times more likely to have radial Margin involvement as compared to others, while fixed tumors are 4.48 times more likely to have radial margin involvement relative to mobile tumors.

7. Conclusion and recommendations

In this retrospective study, we described the adequacy of nodal harvest in colorectal cancer and evaluated possible factors that may affect the adequacy nodal harvest. Only 40 % of the patients in this study have adequate nodal harvest based on current guidelines. Younger patients less than 50 years of age and female patients were associated with improved nodal harvest.

In this this study age ≥ 65 years and fixed tumors are more likely to have radial margin involvement. Besides, appropriate documentation will be needed because some of the data were not fully documented.

Further retrospective cohort study will be needed, by including a large sample size to evaluate other possible factors including patient, pathologist, and surgeon factors that affect the adequacy of the LN harvest.

8. Limitations of the study

The potential limitations of this study are that it can't be truly representative of the general population because it was done in a single institution. It also did not assess pathological factors like the level of training of pathologists and specimen processing methods.

ANNEX 2: QUESTIONNAIRE

Addis Ababa University College of health sciences.

Questionnaire for retrospective analysis of the adequacy of surgical resection of colorectal cancer

1. Patient card number _____

2. Sex

A. Male B. Female

3. Age

A. <50 years B. 50-64 years C. ≥65 years

4. Location of the tumor

- A. Cecum
- B. Ascending colon
- C. Hepatic flexure
- D. Transverse colon
- E. Splenic flexure
- F. Descending colon
- G. Sigmoid colon
- H. Recto-sigmoid junction
- I. Rectum

5. Clinical stages of the disease

A. stage I B. stage II C. Stage III
D. stage IV E. not documented

6. What neoadjuvant therapy did the patient take?

A. chemotherapy B. radiotherapy C. chemoradiotherapy D. none

7. Type of surgery done

- A. Enblock resection of the mass
- B. Right hemicolectomy
- C. Transverse colectomy
- D. Left hemicolectomy
- E. Sigmoidectomy
- F. Anterior resection
- G. APR

8. Surgery is done by
- A. Consultant surgeon
 - B. R4 C. R3 D. R2 E. R1

9. Surgery is done on (urgency of surgery)
- A. Emergency base
 - B. Elective base

10. Intra-operatively, the status of the mass.
- A. Mobile
 - B. Fixed
 - C. Not mentioned

11. Intra-operatively, palpable LAP
- A. Present
 - B. Absent
 - C. Not mentioned

Pathology report

12. Length of the colon resected (in CM).....

13. Status of Proximal margin

- A. Free B. involved C. not documented

14. Status of Distal margin

- A. free B. involved C. not documented

15. Status of Radial (circumferential) margin

- A. Free B. involved C. not documented

16. A number of the LN harvested.....

17. A number of the positive LN.....

ANNEX 3: DUMMY TABLES

Table 1: Sociodemographic characteristics of patients with CRC treated surgically in BLH from 2014-2018.

Characteristics		Numbers	Percentage
Age(years)	<50		
	50-64		
	>=65		
	Total		
Sex	Male		
	Female		
	Total		

Table 2: Location of the tumor

Location	Number	Percentage
Cecum		
Ascending colon		
Hepatic flexure		
Transverse colon		
Splenic flexure		
Descending colon		
Sigmoid		
Rectosigmoid junction		
Rectum		

Table 3: level of training of the person performing the surgery.

	Numbers	Percentage
Consultant surgeon		
R4		
R3		
R2		
R1		

Table 4: surgery is done on an emergency or elective base

	Numbers	Percentage
Emergency		
Elective		

Table 5: type of surgery done

Clinical findings	Number	Percentage
Right hemicolectomy		
Transverse colectomy		
Left hemicolectomy		
Sigmoidectomy		
Anterior resection		
APR		

Table 6: interop status of the mass.

status of the mass	Number	Percentage
Mobile		
Fixed		
Not documented		

Table 7: interop palpable LAP

Palpable LAP	Number	Percentage
Absent		
Present		
Not documented		

Table 8: Status of the proximal margin

Proximal margin	Number	Percentage
Free		
Involved		
Not documented		

Table 9: Status of the distal margin

Distal margin	Number	Percentage
Free		
Involved		
Not documented		

Table 10: status of radial (circumferential) margin

Radial margin	Number	Percentage
Free		
Involved		
Not documented		

Table 11: number of LNs harvested

Number of LN	Number	percentage
0- 11		
>/= 12		

9. References

1. Watanabe T, Itabashi M, Shimada Y, Tanaka S, Ito Y, Ajioka Y, et al. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2010 for the treatment of colorectal cancer. *International journal of clinical oncology*. 2012;17(1):1-29.
2. Alteri R, Kramer J, Simpson S. Colorectal cancer facts and figures 2014-2016. Atlanta: American Cancer Society. 2014:1-30.
3. Favorite P, Carbone G, Greco M, Pirozzi F, Pirozzi REM, Corcione F. Worldwide burden of colorectal cancer: a review. *Updates in surgery*. 2016;68(1):7-11.
4. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods, and major patterns in GLOBOCAN 2012. *International journal of cancer*. 2015;136(5):E359-E86.
5. Cuffy M, Abir F, Audisio RA, Longo WE. Colorectal cancer presenting as surgical emergencies. *Surgical oncology*. 2004;13(2-3):149-57.
6. Ghazali AK. Modeling of survival and incidence for colorectal cancer in Malaysia: Lancaster University; 2018.
7. Simpson J, Scholefield JH. Treatment of colorectal cancer: surgery, chemotherapy, and radiotherapy. *Surgery (Oxford)*. 2008;26(8):329-33.
8. McGinnis LS. Surgical treatment options for colorectal cancer. *Cancer*. 1994;74(S7):2147-50.
9. Baxter NN, Virnig DJ, Rothenberger DA, Morris AM, Jessurun J, Virnig BA. Lymph node evaluation in colorectal cancer patients: a population-based study. *Journal of the National Cancer Institute*. 2005;97(3):219-25.
10. Retz M, Lehmann J, Szysnik C, Zwank S, Venzke T, Röder C, et al. Detection of occult tumor cells in lymph nodes from bladder cancer patients by MUC7 nested RT-PCR. *European urology*. 2004;45(3):314-9.
11. Ng IO, Luk IS, Yuen ST, Lau PW, Pritchett CJ, Ng M, et al. Surgical lateral clearance in resected rectal carcinomas. A multivariate analysis of clinicopathologic features. *Cancer*. 1993;71(6):1972-6.
12. Boutayeb A. The double burden of communicable and non-communicable diseases in developing countries. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 2006;100(3):191-9.
13. Kapczynski A. Addressing global health inequalities: An open licensing approach for university innovations. *Berkeley Tech LJ*. 2005;20:1031.
14. Memirie ST, Habtemariam MK, Asefa M, Deressa BT, Abayneh G, Tsegaye B, et al. Estimates of cancer incidence in Ethiopia in 2015 using population-based registry data. *Journal of global oncology*. 2018;4:1-11.

15. Siegel RL, Torre LA, Soerjomataram I, Hayes RB, Bray F, Weber TK, et al. Global patterns and trends in colorectal cancer incidence in young adults. *Gut*. 2019;68(12):2179-85.
16. Peterse EF, Meester RG, Siegel RL, Chen JC, Dwyer A, Ahnen DJ, et al. The impact of the rising colorectal cancer incidence in young adults on the optimal age to start screening: microsimulation analysis I to inform the American Cancer Society colorectal cancer screening guideline. *Cancer*. 2018;124(14):2964-73.
17. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*. 2018;68(6):394-424.
18. Jeyarajah S, Sutton C, Miller A, Hemingway D. Factors that influence the adequacy of total mesorectal excision for rectal cancer. *Colorectal disease*. 2007;9(9):808-15.
19. Johnson PM, Malatjalian D, Porter GA. Adequacy of nodal harvest in colorectal cancer: a consecutive cohort study. *Journal of gastrointestinal surgery*. 2002;6(6):883-90.
20. Tekkis PP, Smith JJ, Heriot AG, Darzi AW, Thompson MR, Stamatakis JD, et al. A national study on lymph node retrieval in resectional surgery for colorectal cancer. *Diseases of the colon & rectum*. 2006;49(11):1673-83.
21. Collaborators G. Global, regional and national levels of age-specific mortality and 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2015;385(1):1990-2015.
22. Irabor DO. Emergence of colorectal cancer in West Africa: accepting the inevitable. *Nigerian medical journal: journal of the Nigeria Medical Association*. 2017;58(3):87.
23. Farhood B, Raei B, Malekzadeh R, Shirvani M, Najafi M, Mortezaadeh T. A review of incidence and mortality of colorectal, lung, liver, thyroid, and bladder cancers in Iran and compared to other countries. *Contemporary Oncology*. 2019;23(1):7.
24. Saba PEM, Hassan AAK, Al-Sharkawy MAM, Refaat LM. Computed tomography perfusion imaging of colorectal cancer in correlation with tumor grades. *Journal of Current Medical Research and Practice*. 2020;5(3):290.
25. Boyle P, Langman MJ. ABC of colorectal cancer: Epidemiology. *Bmj*. 2000;321(Suppl S6).
26. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA: a cancer journal for clinicians*. 2015;65(2):87-108.
27. Jessup JM, Menck HR, Fremgen A, Winchester D. Diagnosing colorectal carcinoma: clinical and molecular approaches. *CA: a cancer journal for clinicians*. 1997;47(2):70-92.
28. Benedix F, Kube R, Meyer F, Schmidt U, Gastinger I, Lippert H, et al. Comparison of 17,641 patients with right-and left-sided colon cancer: differences in epidemiology, perioperative course, histology, and survival.

- Diseases of the Colon & Rectum. 2010;53(1):57-64.
29. Wasserman M, Baxter N, Rosen B, Burnstein M, Halverson AL. A systematic review of internet patient information on colorectal cancer surgery. *Diseases of the colon & rectum*. 2014;57(1):64-9.
 30. Minsky BD. Adjuvant therapy for rectal cancer—the transatlantic view. *Colorectal Disease*. 2003 Sep;5(5):416-22.
 31. Dillman RO, Aaron K, Heinemann FS, McClure SE. Identification of 12 or more lymph nodes in resected colon cancer specimens as an indicator of quality performance. *Cancer*. 2009;115(9):1840-8.
 32. Jakub JW, Russell G, Tillman CL, Lariscy C. Colon cancer and low lymph node count: who is to blame? *Archives of Surgery*. 2009;144(12):1115-20.
 33. Abrams JS, Reines HD. Increasing incidence of right-sided lesions in colorectal cancer. *The American Journal of Surgery*. 1979;137(4):522-6.
 34. Sun WY, Basch CE, Wolf RL, Li XJ. Factors associated with colorectal cancer screening among Chinese-Americans. *Preventive Medicine*. 2004;39(2):323-9.
 35. Compton CC, Greene FL. The staging of colorectal cancer: 2004 and beyond. *CA: a cancer journal for clinicians*. 2004;54(6):295-308.
 36. Hartley JE, Mehigan BJ, Qureshi AE, Duthie GS, Lee PW, Monson JR. Total mesorectal excision: assessment of the laparoscopic approach. *Diseases of the colon & rectum*. 2001;44(3):315-21.
 37. Marks J, Valsdottir E, Rather A, Nweze I, Newman D, Chernick M. Fewer than 12 lymph nodes can be expected in a surgical specimen after high-dose chemoradiation therapy for rectal cancer. *Diseases of the colon & rectum*. 2010;53(7):1023-9.
 38. Dehing-Oberije C, De Ruyscher D, van der Weide H, Hochstenbag M, Bootsma G, Geraedts W, et al. Tumor volume combined with several positive lymph node stations is a more important prognostic factor than TNM stage for the survival of non–small-cell lung cancer patients treated with (chemo) radiotherapy. *International Journal of Radiation Oncology* Biology* Physics*. 2008;70(4):1039-44.

DECLARATION

I, the undersigned, specialty student declare that this thesis is my original work in partial fulfillment of the requirement for the specialty certificate in general surgery.

Name: Yonas Nibret Signature: _____ Date -----

Place of submission: School of Medicine, Department of surgery, Addis Ababa University

Date of Submission: _____

This thesis work has been submitted to the Department of surgery, Addis Ababa University for examination with my approval as a university advisors.

Advisors: 1. Dr Nebyou seyoum (MD, Associate prof. Of surgery) Signature: _____ Date _____

2. Professor Berhanu Kotisso (MD, Professor of surgery) Signature _____ Date _____