ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICINE

DEPARTMENT OF ONCOLOGY, HEMATOLOGY AND NEUCLEAR MEDICINE

TREATMENT OUTCOMES AND PROGNOSTIC FACTORS IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER TREATED WITH DEFINITIVE CONCURRENT CHEMORADIOTHERAPY: A FOUR YEARS PROSPECTIVE STUDY IN TASH ONCOLOGY CENTER, ADDIS ABEBA, ETHIOPIA

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FINAL THESIS REPORT TO BE SUBMITTED TO DEPARTMENT OF CLINICAL ONCOLOGY, HEMATOLOGY AND NEUCLEAR MEDICINE, FACULTY OF MEDICAL SCIENCES, INSTITUTE OF HEALTH, ADDIS ABABA UNIVERSITY AS PARTIAL FULFILLMENT OF SPECIALITY IN CLINICAL ONCOLOGY

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December 2025

Adiss Ababa, Ethiopia

Abstract

Background: locally advanced cervical cancer continues to be a major cause of morbidity and mortality among women, with concurrent chemoradiation (CCRT) being the recomended treatment for locally advanced disease. However, prospective data on treatment outcomes and prognostic factors remain limited in Ethiopia specially in the LINAC era.

Methods: A prospective study of locally advanced cervical cancer patients who received definitive CCRT from January 2022 to July 2025 was employed. Survival outcome was estimated by using Kaplan-Meier curves. Univariant and multivariant cox proportional model was employed to evaluate the effect of various factors on RR, DFS and OS.

Results: Between January 1/2022 and July1/202*5*, a total of 167 patients diagnosed with locally advanced cervical cancer managed with curative-intent radiotherapy were enrolled. The median age of patients was 53.5 year (IQR 45–62). In this study 66.5% of patients received a brachytherapy boost while an EBRT boost was used in 18.5% of cases. Concurrent chemotherapy was administered in 64.5% of patients. Of 167 patients, 118 (70.7%) achieved complete response (CR) at 3 months. Among the 118 patients analysed, 69.5% experienced no recurrence during the follow-up period. Recurrence was observed in 30.5%. The 2-year overall survival (OS) was 73%, and the 2-year disease free survival (DFS) was 71% based on the Kaplan–Meier estimates. Late radiation-induced adverse events were documented in 82 patients (49.1%). No late toxicity was reported for 59 patients (35.3%), while the status was unknown or not assessable for 26 patients (15.6%).

Conclusion: This prospective study shows that definitive radiotherapy with concurrent chemotherapy and brachytherapy provides clinically meaningful response rates, survival outcomes, and manageable toxicity profiles for patients with locally advanced cervical cancer treated at Tikur Anbesa Specialized Hospital in the LINAC era. The observed two-year overall and disease-free survival rates align with existing evidence supporting of concurrent chemoradiotherapy as the standard of care in this setting.

Keywords: Locally advanced cervical cancer, Concurrent chemoradiotherapy, Recurrence or metastasis, Prognostic factors

Approval Sheet

This is to certify that the thesis entitled “Treatment outcome and prognostic factor in patient with locally advanced cervical cancer treated concurrent chemoradiotherapy: a four year prospective study in TASH oncology center” is submitted in partial fulfillment of the requirements for the Specialization Certificate in clinical oncology to the department of clinical oncology, hematology and nuclear medicine, Addis Ababa University college of health science and has been carried out by Dr Elsabet Abnew under my supervision. Therefore, I recommend that the student has fulfilled the requirements and hence hereby can submit the Thesis to the department.

Dr Sonia Worku (Consultant Oncologist)

Signature …….

Date……

Acknowledgment

First and foremost, I would like to express my deepest gratitude to Adiss Abeba university, Institute of Health, Faculty of Health sciences and School of Medicine for giving me the opportunity and resource to carry out this study. I am also thankful to my advisor, Dr. Sonia Worku for her continuous guidance, support, and encouragement throughout the development of this research. I would also like to acknowledge the department of clinical oncology, hematology and nuclear medicine for their cooperation and assistance during data collection and patient care. My heartfelt thanks go to the patients who participated in this study, without their cooperation, this research could not have been achieved. Finally, I extend my appreciation to my colleagues for their continuous support, involvement in data collection and patient follow up throughout the study.

Abbreviations

BRT	Brachytherapy
CC	Cervical cancer
CCRT	Concurrent chemoradiotherapy
CRP	Chronic radiation proctitis
CTCAE	Common Terminology Criteria for Adverse Event
DFS	Disease free survival
3DCRT	3-Dimensional conformal radiotherapy
DMFS	Distant metastasis free survival
2DRT	2-Dimensional radiotherapy
EBRT	External beam radiotherapy
EFS	Event free survival
EAPC	Estimated Annual Percentage Change
FIGO	International Federation of Obstetrics and Gynecology
HR	Hazard ratio
IARC	International Agency for Research
IG-IMRT	Image-guided intensity modulated radiation therapy
IGABT	Image-guided adaptive brachytherapy
LACC	Locally advanced cervical cancer
LINAC	Linear accelerator
LRFS	locoregional failure free survival
SIB	Simultaneous integrated boost
OAR	Organs at risk
OR	Odd ratio
ORR	Overall response rate
OS	Overall survival
RECIST	Response Evaluation Criteria in Solid Tumor
RFS	Recurrence free survival
TASH	Tikur Anbesa specialized hospital

TPS	Treatment planning system
USG	Ultrasound Sonography
VMAT	Volumetric arc therapy

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Chapter One: Introduction

1.1 Background

Worldwide, cervical cancer represents a significant proportion of malignancies affecting the female reproductive system, contributing to 3.1% of cancer incidence and 3.4% of cancer-related deaths(1). In 2019, the age-standardized incidence rate (ASIR) and mortality rate was estimated at approximately 8.91 and 2.9 per 100,000 women developed countries respectively (2).

In the developing world, it accounts for 12% of all cancers of women. Over two-thirds of patients with CC have locally advanced disease at the time of diagnosis (3)

In Ethiopia, Cervical cancer is the second most common and the second leading cause of cancer death(4).The incidence and prevalence of the disease have been rising in these two decade(4,5). Although prevention and early detection are the gold standards for early diagnosis and treatment, in Ethiopia there is relatively poor awareness and limited understanding about cervical cancer and among poor CC screening coverage (13%)(4). Therefore, most women are diagnosed at advanced stages (55.2% stage IIIb or higher). Only 12.1% presented with an early FIGO stage of I-IIa, making them candidate for surgery (6).

For patients with locally advanced cervical cancer (LACC) defined as stage IB3 to IVA according to the FIGO 2018 staging system, radical concurrent chemoradiotherapy (CCRT) followed by brachytherapy is recommended (7–9). The 5-year overall survival (OS) rate of patients with FIGO stage II, stage III, and stage IV CC are 65–69%, 40–43%, and 15–20%, respectively. For elderly patients who refuse brachytherapy or are not amenable to brachytherapy, intensity-modulated radiation therapy with simultaneous integrated boost (SIB) to macroscopic disease can be utilized, as an alternative (10).

Under the standard treatment scheme, the local control and OS rates of LACC were approximately 80% and 60%, respectively (11,12) However,30-40% of patients experienced disease progression after CCRT and has poor prognosis (13). There have been significant advancements in the treatment of cervical cancer in recent years

especially for LACC, to improve survival and prognosis(14,15). Extensive research has demonstrated the short- and long-term effectiveness of concurrent chemoradiotherapy (CCRT) for locally advanced cervical cancer (LACC), as well as its benefits compared with other treatment strategies and its associated prognostic factors.

Recent studies show short-course induction chemotherapy followed by chemoradiotherapy significantly improves survival of patients with locally advanced cervical cancer, appears to be a promising therapeutic strategy that could be applied in the treatment of LACC patients (16)

Prognostic factors for LACC include stage, grade, histologic type, positive lymph node, age and performance status(7,17). Cell type, depth of tumor invasion, hemoglobin level, leukocytosis, lymph-vascular space invasion, neutrophil-to-lymphocyte ratio, parametrial invasion, platelet-to-lymphocyte ratio, resection margin, squamous cell carcinoma antigen level, thrombocytosis, tumor size, and tumor volume were clinicopathological factors influencing OS and EFS of CC patients(18).

In the TASH oncology center for the last 20 yrs before January 2021, we treated LACC patients with CCRT with cobalt 2DRT technique plus BRT. Since 2021 we have been treating this patient with CCRT with LINAC 3DCRT.

While CCRT plus BRT has shown promising outcomes in localized cervical cancer, but treatment outcome and prognosis vary, therefore there is still a need to understand the treatment outcomes and evaluate prognostic factors specific to locally advanced cases. Identifying these factors can help clinicians tailor treatment strategies, optimize patient selection, and improve overall survival rates.

Previous studies have assessed therapeutic outcomes and prognostic determinants in cervical cancer patients; however, the specific analysis of CCRT plus BRT in locally advanced cases at the TASH Oncology Center in the Linac era remains limited. Previous studies were conducted in the 2DRT cobalt (Pre - 3DCRT) era and to my knowledge there are no recent studies on the treatment outcome and prognostic factor of LA cervical cancer patients treated with 3DCRT plus BRT. Therefore, conducting a comprehensive analysis of treatment outcomes and prognostic factors within this specific context will provide valuable insights into the effectiveness of this treatment approach. Further in-depth exploration of the treatment outcomes and prognostic factors in patients with LACC treated with advanced RT technique is a key imperative

to assess the efficacy of treatment and design a tailed treatment strategy and compare standard treatment outcomes with other countries.

1.2 Statement of the problem

Locally advanced cervical cancer remains a critical health challenge in Ethiopia, as the majority of women present with advanced disease (55.2% at stage IIIb or higher), while only a small proportion (12.1%) are diagnosed at early FIGO stages (I–IIa), allowing for surgical intervention(19). CCRT plus BRT is the standard management of locally advanced cervical cancer (20).

The outcome of LACC is sub-optimal with a long-term survival rate of 60%, and emphasizes the need to identify prognostic factors and investigate new treatment strategies for these patients to improve treatment outcomes and improve survival. Several studies investigated the specific treatment outcomes and prognostic factors associated with this therapeutic approach and reported that treatment outcomes can vary based on different treatment modalities and factors (21,22).

Currently, there is limited research focusing on the analysis of treatment outcomes and prognostic factors following CCRT with or without BRT in the context of Ethiopia specifically in the post-cobalt era(4). Therefore, there is a need to investigate the specific treatment outcomes and prognostic factors associated with this therapeutic approach in TASH.

This study aims to bridge this gap by conducting a comprehensive analysis of the treatment outcomes and prognostic factors after definitive CCRT with or without BRT for locally advanced cervical cancer patients in the post-2DRT era at TASH Oncology Center from 2022 to 2025. By identifying the factors that influence treatment outcomes, this study can play a role in the development of more personalized and effective treatment strategies for locally advanced cervical cancer patients in the TASH Oncology Center and beyond.

1.3 Significance of the study

The significance of this prospective study on evaluating the treatment outcomes and prognostic factors after definitive CCRT with or without BRT for locally advanced cervical cancer patients is multi-fold.

Firstly, cervical cancer causes a significant burden in LMIC including Ethiopia, and a combination of CCRT and BRT is the standard treatment for LACC, which is a prevalent stage at presentation of cervical cancer patients in these countries. Several studies in other countries conducted and reported the efficacy and optimal treatment outcomes of LACC patients treated with CCRT and BRT.

Second, this is the 1st study conducted in the 3DCRT era in Ethiopia that will evaluate key treatment outcomes including local control rate, overall survival, disease-free survival, and incidence of late toxicities which are crucial for assessing the clinical benefit and tolerability of the treatment regimen. By analyzing these outcomes, the study will provide important insights into the clinical outcomes and toxicity pattern of CCRT plus BRT for the management of locally advanced cervical cancer patients in the context of the TASH Oncology Center in the 3DCRT era.

Additionally, by analyzing prognostic factors associated with treatment outcomes, the study can potentially facilitate the development of personalized treatment approaches tailored to the individual needs of patients, thereby optimizing the effectiveness of therapy.

Overall, the findings of this study will have the potential to enhance healthcare professionals understanding of this specific treatment modality and its impact on locally advanced cervical cancer patients, ultimately leading to the advancement of medical knowledge and helping healthcare professionals make more informed treatment decisions, and contributing to improved patient outcomes and quality of life.

Chapter Two: Literature Review

Epidemiology of cervical cancer

Cervical cancer (CC) is a significant public health concern in Ethiopia, with a steady increase in incidence and prevalence over the last two decades (5). A study conducted in TASH between 1997 and 2012, there were a total of 16,622 new cancer cases, and 31.8% of all cancer cases, and the most affected women age group was 40-49 years(5). Similarly, multiple studies found that the majority of Ethiopian women presented with advanced stages (49 -65 % stage III & IV), with only 12.1% eligible for surgery due to early-stage diagnosis(6,19,23)

Treatment pattern and outcomes of LACC

Management of Locally Advanced Cervical Cancer (LACC) poses significant challenges and the current standard treatment is concurrent cisplatin-based chemoradiation (CCRT). Multiple studies have investigated the effectiveness of CCRT plus brachytherapy (BRT) in LACC. For instance, A large meta-analysis evaluated CCRT versus radiation therapy (RT) alone in locally advanced cervix cancer and found that CCRT improved complete response (CR (+ 10.2%), local-regional control (LRC (+ 8.4%), and overall survival (OS (+ 7.5%) compared to RT alone, revealed that CRT certainly improves the therapeutic outcomes in LACC with progression-free survival (PFS) and OS rates of approximately 58% and 66%, respectively (12).

Similarly, additional study reported a 5years overall survival rate of CC patients treated with CCRT plus BRT are 65–69%, 40–43%, and 15–20% in FIGO stage II, stage III, and stage IV, respectively (8).

Regarding treatment outcomes Of LACC patients treated with CCRT plus BRT, previous research has highlighted the significance of local tumor control, disease-free survival, and adverse events. However, despite this improvement, outcomes in these diseases remain sub-optimal, with a 5-year progression-free survival and overall survival rates of approximately 60% *(8,12)*.

The suboptimal results have prompted investigators to search other novel strategies of combined modality therapies, including modified chemotherapy (CT) schedules, targeted agents, and immuno-modulation. In addition, there is need for detailed investigation and identification of prognostic factors to design personalized treatment strategies to improve the treatment outcomes and survival of LACC patients.

Prognostic factor affecting treatment outcome in LACC

Several studies have identified potential prognostic factors for treatment outcomes in LACC patients. A retrospective study of 127 patients with locally advanced cervical cancer demonstrated that tumor size ≥6 cm was associated with shorter local-regional failure-free survival (LRFS) and overall survival (OS). Adenocarcinoma histology and positive lymph nodes were also associated with shorter distant metastasis-free survival (DMFS). This study also reports patients treated with consolidation chemotherapy had longer DMFS and OS compared with patients who were not treated with consolidation chemotherapy, although the difference was not significant (24).

Similarly, A study in China identified that, among various clinical factors and radiation doses, pre-treatment local lymph node metastasis was the significant independent risk factor for short- and long-term outcomes (22). Additional studies also identified metastasis to lymph nodes were independent prognostic factors for LACC (21,25).

Other studies have reported that patients with squamous cell carcinoma have better short-term treatment response, overall survival (OS), and disease-free survival (DFS) than those with adenocarcinoma (26–28). Tumor diameter has been shown to independently predict clinical outcomes in patients with locally advanced cervical cancer (29). The recurrence rate of LACC patients ranges from 20% to 30%. The most common recurrence pattern is distant recurrence with lymph node metastasis (30,31).

Additional prognostic factor identified in comparative study which demonstrated the survival benefit of incorporating brachytherapy into concurrent chemoradiotherapy for locally advanced cervical cancer(32). 5-year overall survival was significantly higher for patients receiving an intracavitary brachytherapy boost (82% vs 58%) compared with those treated with external beam radiotherapy boost alone, RFS was also significantly higher in patient who received brachytherapy (79% vs 38%). Omission of brachytherapy associated with a significantly increased risk of recurrence(32)

Treatment outcomes and challenges Ethiopian context

The overall survival rate was lower in Ethiopia compared to high- and middle-income countries (19,23). The reported 1- and 2-year overall survival of 90.4% and 73.6% respectively. In a facility-based retrospective cohort study at the TASH oncology center 5-year overall survival rate was 38.62%(19). The study identified factors associated with increased mortality risk including advanced FIGO stage, baseline anemia, comorbidity, substance use, advanced age, and treatment modality(19). Non-substance users and patients diagnosed at early stages had better survival rates and longer median survival times than substance users and those diagnosed at advanced stages(19).The cumulative survival rate of early stage (I&II) disease was 81.04% and 67.94% respectively, and for those diagnosed at advanced stage (III&IV) 23.33 and 20.03% respectively (19).

The above studies identified several challenges including a lack of awareness about the disease, wrong diagnosis in lower health facilities, economic constraints, and limited access to screening and treatment facilities, that contribute to late diagnosis and poor survival rates in cervical cancer patients in Ethiopia. Addressing the challenges associated with late diagnosis and improving access to screening and treatment facilities are essential to combat cervical cancer in Ethiopia.

In conclusion the management of LACC remains challenging, with sub-optimal outcomes despite the use of concurrent cisplatin-based chemoradiation. Novel strategies, including modified chemotherapy schedules and targeted agents, are being explored to enhance therapeutic efficacy, and the identification of poor prognostic factors, including tumor size, histology, and lymph node status, is needed to improve treatment outcomes and identify effective strategies for patients with high-risk diseases.

Over view of late radiation toxicity in LACC after CCRT

Studies have reported the development of Chronic radiation proctitis (CRP) as a common complication following radiotherapy for cervical cancer (33). Peng et al. (2022) reported the incidence of mild CRP (Grades 1-2) was around 21%, while severe CRP (Grades 3-4) occurred in approximately 5% of patients. Dosimetry analysis revealed that patients with severe CRP had an average rectal cumulative D2cm3 of 73.4 Gy, which was 3.9 Gy higher than those without CRP(22). This study emphasized the

importance of fully considering and limiting rectal D2cm3 during radiotherapy planning to minimize the risk of CRP.

Treatment of cervical cancer has improved significantly in recent years, particularly for LACC. The combination of VMAT, cisplatin-based chemotherapy, and IGABT has been associated with favorable overall response and overall survival in previous studies. Compared with 3-dimensional conformal radiation therapy and conventional 2-dimensional brachytherapy, IG-IMRT and IGABT offer improved treatment efficacy in cervical cancer. (34–37).

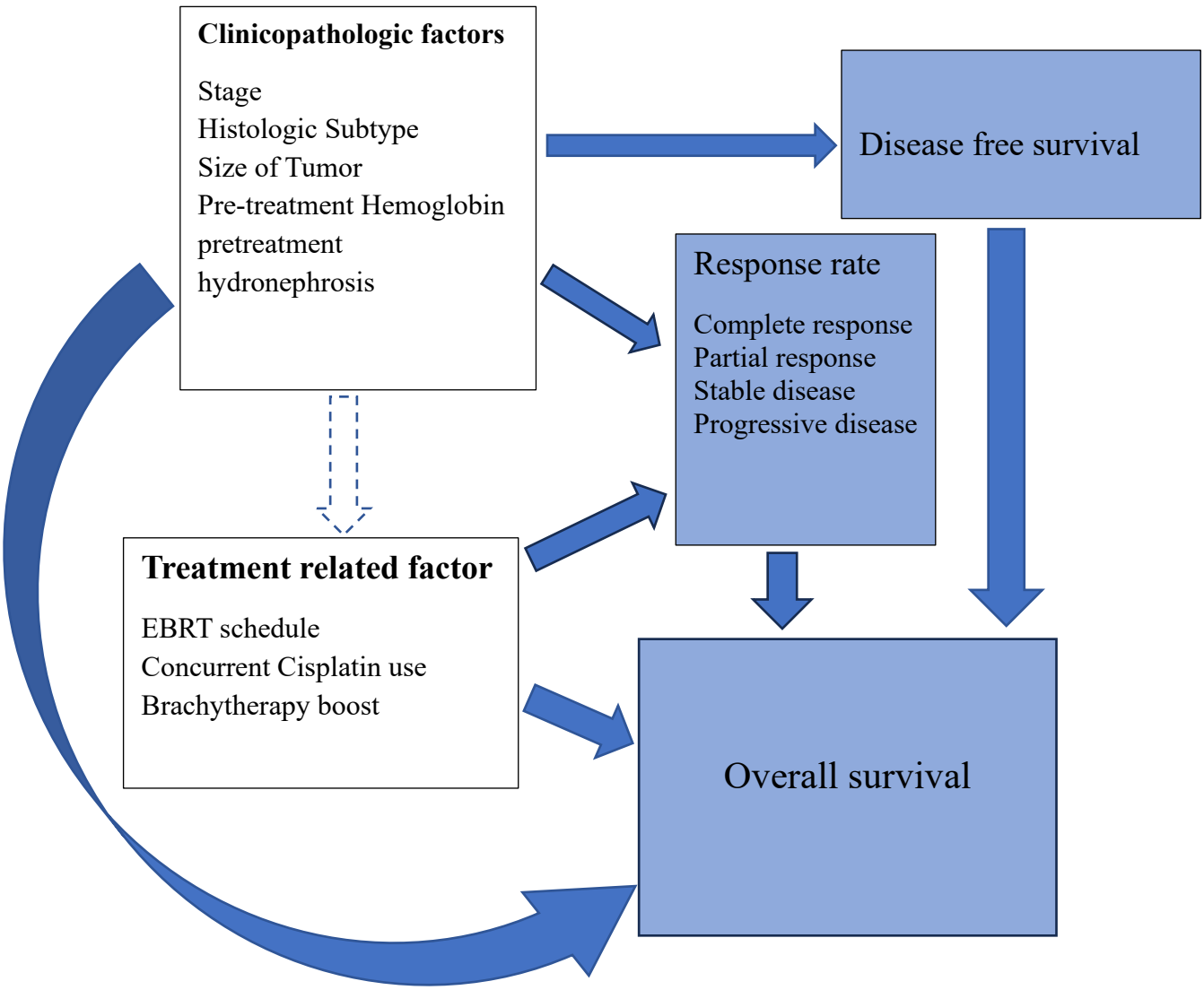
Overall, While the literature provides valuable insights regarding the effectiveness of CCRT plus BRT for locally advanced cervical cancer patients' treatment, there remains limited data specific to the TASH Oncology Center specifically in the post-2DRT era regarding treatment outcomes and prognostic factors in locally advanced cervical cancer patients treated with CCRT plus BRT. Therefore, there is an urgent need for research at the TASH Oncology Center to assess treatment outcomes and identify prognostic factors associated with improved survival.

To bridge this gap, a prospective observational cohort study was conducted among patients receiving LINAC-based radiotherapy between 2022 and 2025. By evaluating treatment outcomes and identifying prognostic factors, this research intends to enhance patient care and refine treatment strategies at the TASH Oncology Center.

The findings from this study will contribute to the existing knowledge base and improve the understanding of treatment outcomes and prognostic factors in LACC patients treated with CCRT plus BRT in the hospital and beyond.

Conceptual Frame work

Figure 1- Conceptual framework



Chapter Three: Objectives

3.1 General objective

To evaluate treatment out comes and identify prognostic factors in locally advanced cervical cancer patients treated with CCRT at TASH oncology center. Addis Ababa, Ethiopia.

3.2 Specific Objectives

- To analyze the survival (DFS and OS) of patients with locally advanced cervical cancer treated with definitive CCRT.
- To evaluate the tumor overall response rate (ORR) of patients with locally advanced cervical cancer treated with definitive CCRT.
- To investigate the prognostic (patient and treatment-related) factors associated with survival.

Chapter Four: Methodology

4.1 Study design

Single institution prospective study

4.2 Study area and period

Study area

The study was conducted at the TASH (Tikur Anbessa Specialized Hospital) Oncology Center in Addis Ababa, Ethiopia. Addis Ababa is the capital city of Ethiopia. Tikur Anbessa Hospital is one of Ethiopia's leading tertiary care centers, serving as a national referral hospital for complex cases and providing specialized care to patients from across the country, with a population of over 120 million. The Hospital provides health services for approximately 25 thousand inpatients and 400 thousand outpatients in a year with a bed capacity of 700.

Study period

The study was conducted from January 2022 to December 2025.

4.3 Sources of Data

Data for this study was collected from patient charts, logbooks, TPS. Follow-up data were obtained during scheduled clinic visits, phone interviews and through review of institutional databases (I-care).

Source Population

The source population consisted of all locally advanced cervical cancer patients who attended the radiotherapy unit of TASH listed in the cancer registry at TASH's Radiotherapy Center.

Study population

The study population included all patients with locally advanced cervical cancer who completed CCRT with or without subsequent brachytherapy at TASH Radiotherapy Center during study period.

4.4 Eligibility Criteria

Inclusion criteria

- Stage IB3, IIA2-IVA cervical cancer (according to the 2018 FIGO staging guidelines).
- Pathological confirmed histology of squamous cell carcinoma, adenocarcinoma, or Adeno-squamous carcinoma.
- No previous history of major surgery and pelvic radiotherapy.
- Adequate staging workup.

Exclusion criteria

- Other synchronous malignant tumors.
- Patient without 3-to-6-month post treatment response assessment.

4.5 Sample size determination and sampling technique

We use 95% CI, alpha 0.05,Power 80%(1-B 0.8) , Margin of error (8%):

CCRT : LACC disease control rate (65-80%), over all recurrence (35 % SD= 0.35) and OS (60%) (17).

Missed data/lost follow up assumed to be 10%

N = 295……due to resource constraints, we are able to include 167 patients only.

Sampling technique

A consecutive sampling technique was employed to recruit study participants until the achievement of the expected sample size within the given study period.

4.6 Study variables

Independent Variables

1. Clinicopathological factors
    - Stage of the disease
    - Tumor Size
    - Histologic type
    - Pre-treatment Hemoglobin
    - Pretreatment hydronephrosis

2. Treatment related factors
    - EBRT schedule
    - Concurrent cisplatin received or not
    - Brachytherapy boost

Dependent variables

- Disease free survival
- Overall survival (OS)
- Response Rate (RR)

4.7 Operational definition

- **Stage of Cancer**: The stage of locally advanced cervical cancer, according to the 2018 International Federation of Gynecology and Obstetrics (FIGO) staging system.
- **Tumor Size**: The largest diameter of the primary tumor measured in centimeter during pelvic examination or imaging.
- **Histology:** The histological subtype of cervical cancer (squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma) based on histopathological examination of the cervical biopsy specimen obtained prior to initiation of treatment.

- **Pretreatment hemoglobin**: hemoglobin level(mg/dl) measured within 2 weeks before initiation of radiotherapy. For patient who received blood transfusion, hemoglobin level after transfusion was taken.
- **Pretreatment hydronephrosis**: radiologic evidence of unilateral or bilateral dilation of renal pelvis and/or calyces documented in USG, CT or MRI prior to radiotherapy.
- **Comorbidity**: Any pre-existing medical conditions or comorbidities that may impact treatment outcomes.
- **EBRT schedule**: the prescribed total dose and fractionation delivered to the pelvis. Patients received either **conventional fractionation** (1.8–2.0 Gy per fraction) or **hypo fractionated schedules** (>2.0 Gy per fraction), delivered once daily, five days per week using LINAC.
- **Response Rate**: The proportion of patients achieving a complete response, partial response, stable disease, or progressive disease after the CCRT
- **Short-Term Efficacy:** Tumor response - Imaging to assess the efficacy of treatment 3 months after treatment according to the Response Evaluation Criteria in Solid Tumors (RECIST version 1.1).
- **Complete response (CR):** defined as complete disappearance of the lesions for more than 4wks.
- **Partial response (PR)**: defined as a ≥30% decrease in the lesion diameter for more than 4 weeks.
- **Stable disease (SD):** defined as a <30% decrease or a <20% increase in the lesion diameter.
- **Progressive disease (PD)**: defined as a ≥20% increase in the lesion diameter and an increase in the absolute value by ≥5 cm or the appearance of new lesions.
- **Complete response (CRR) rate:** was calculated as the percentage of patients achieving complete response.
- **Non complete response:** included patients with partial response, stable disease or progressive disease.
- **Overall survival (OS):** defined as the length of time from the start of treatment until death from any cause or lost to follow up.

- **Disease free survival:** defined as the time from the beginning of treatment to local/regional and /or metastasis recurrence, or death for any reason or the last follow-up.
- **Distant metastasis (DM)-free survival:** defined as the time from the beginning of treatment to the first distant metastasis or death for any reason.
- **Locoregional recurrence (LR)-free survival:** defined as the time from the beginning of treatment to the first loco-regional recurrence.
- **Late Adverse Events**: treatment-related adverse event affecting the gastrointestinal or genitourinary systems that occurred ≥90 days after completion of radiotherapy or occur within 90 days of start of radiotherapy but persists more than 90 days, and was graded according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.

4.8 Data collection procedure

Recruitment strategy and screening

Potential participant was identified by the research team by reviewing electronic medical records number (I-Care), treatment planning systems (TPS), logbooks and screened for eligibility. Eligible patients were approached by the research team in clinic. The nature, purpose and observational nature of the study was explained in detail. Verbal informed consent was taken for each patient.

Baseline data of all respective patients that fulfill inclusion criteria was reviewed, and the clinicopathological factors such as demographic information (e.g. age), clinical characteristics (e.g. stage of cancer, tumor size, histology) was collected from I-care, log books and charts. The treatment details (e.g., total dose, dose per fraction and duration of CCRT and BRT) was sought from EBRT and BRT TPS.

Follow up and procedures

The data collection team (Data collector and chart finders) were trained by the principal investigator about the purpose of the study and data extraction techniques. Response assessment using MRI, CT SCAN and USG were done within 3 to 6 months after completion of radiotherapy. Follow-up information was gathered by reviewing patient

records (EMRs), phone calls, and interviews to evaluate treatment outcomes such as response rates (RR), progression-free survival (PFS), and overall survival (OS).

Follow-up was conducted by hospital re-examinations and telephone calls. Reexaminations were performed every 1-3 months in the 1st year, every 6 months in the 2nd to 4th years. Late radiation toxicity was assessed according to Common Terminology Criteria for Adverse Events (CTCAE) v5.0.

All relevant data were recorded and retrieved for each participant using a structured data collection questionnaire, which was pretested prior to the study. Patients who do not experience the event of interest (recurrence or death) by the end of the follow-up period was censored at their last date of known contact. Patients lost to follow-up or who withdraw consent was also censored at the last date they were known to be event-free. The collected data was checked for completeness by the principal investigator and entered into Microsoft excel which subsequently exported to SPSS version 27 for analysis.

4.9 Data Analysis

The original data collected in Microsoft Excel, was reviewed to ensure completeness and consistency before being exported to SPSS® version 27. Descriptive statistics was used to summarize patient characteristics, treatment factors, and treatment outcomes with categorical variables presented as frequencies and percentages, and continuous variables described using the mean and standard deviation (SD) or median and interquartile range (IQR). Univariate logistic regression analysis was performed to assess the association between each potential prognostic factor and treatment outcome. Variables with a p-value less than 0.25 in the univariate analysis were subsequently included in the multivariate logistic regression model. The Kaplan-Meier method and Cox risk regression model were used for the analysis of DFS and OS. $P < 0.05$ was considered statistical significance. SPSS v27 software used for statistical analysis.

4.10 Ethical considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki. An institutional review board of TASH approved the study before data collection. During patient enrollment informed consent was taken for each patient.

Chapter Five: Results

Between January 1/2022 and December 1/2025, a total of 198 patients with locally advanced cervical cancer who received definitive radiotherapy with or without concurrent chemotherapy were enrolled in the prospective single-arm study. Patients who are lost to follow up before response assessment were excluded from final analysis (n=24). Furthermore, patients without histological confirmation (n = 2), with synchronous malignancies (n = 3), and those who declined further participation or withdrew consent (n = 2) were excluded. The final analysis included 167 patients with complete baseline data and evaluable treatment response.

5.1 Socio-demographic and disease characteristics

In this study the median age of patients was 53.5 year (IQR 45–62). Most patients had good functional status, with ECOG performance status 1 in 94% and ECOG performance status 2 in 3%. The baseline (before treatment) mean haemoglobin was 12.85 ± 1.79 g/dL, and the median renal function (RFT/Cr) was 0.70 (IQR 0.50-0.80). 46.7% or more has one or more comorbidity. 81.4% of patients have largest tumour diameter of >4cm while 18.6% has ≤ 4cm. Among patients living with HIV, 96% were receiving HAART. Of the 167 patients assessed, 11.8% had hydronephrosis, and of these, 95% developed it before treatment initiation (table 1).

Table 1: Socio-demographic and disease characteristics

Patient characteristics (N=61)	Frequency (n)	%
Comorbidity		
HIV	33	19.5
HTN (Hypertension)	27	16.0
Hydronephrosis	20	11.8

DM (Diabetes Mellitus)			9	5.3
Other Conditions*			5	3
Cardiac (heart disease)			2	1.2
ARF			1	0.6
CRF			1	0.6
Stent/PCN Placement				
yes			10	50.0
No			10	50.0
Histologic type				
Squamous Cell Carcinoma (SCC)			149	89.2
Adenocarcinoma (ADC)			16	9.6
Adeno-squamous Carcinoma (ASC)			2	1.2
FIGO 2018 Stage				
Stage I	IB		3	1.8
Stage II	IIA		6	3.6
	IIB		77	46.1
Stage III	IIIA		7	4.2
	IIIB		10	6.0
	IIIC	C1	39	23.3
		C2	3	1.8
Stage IV	IVA		21	12.6
Unknown	-		3	1.8
Tumer size in CM	Tumer size <4cm		32	19.8
	Tumer size ≥4cm		135	80.2

*The "Other Comorbidities" category includes cases of Asthma, CKD, D VT, and Stroke.

5.2 Radiation Dose and technique

The mean prescribed external beam radiotherapy (EBRT) dose was 42.3 Gy (SD = 3.8), delivered in an average of 17.7 fractions (SD = 5.3). The mean overall EBRT treatment duration was 33.2 days (SD = 17 days). Radiotherapy was delivered using 3DCRT in 98.8% of patients. An EBRT boost was used in 18.5% of cases, and the boost technique was sequential in all patients. The median radiotherapy interruption was 5 days (IQR = 2–10).

In this study 66.5% of patients received a brachytherapy boost. The mean interval between the completion of external beam radiotherapy (EBRT) and the start of brachytherapy was 22 days (SD = 18 days). Brachytherapy was delivered with a mean prescribed dose of 7.8 Gy per fraction (SD = 0.5 Gy) over an average of 3.0 fractions (SD = 0.4). The mean dose to Point A achieved 99.1% of the prescribed dose (SD = 4.2%), corresponding to a mean equivalent dose in 2 Gy fractions (EQD2) of 76.7 Gy (SD = 5.5). Among patients receiving brachytherapy, the overall treatment duration averaged 8.9 weeks (SD = 3.1 weeks).

5.3 Chemotherapy utilization and regimen

Chemotherapy was administered prior to radiotherapy in 13.8% of patients (n = 23). Among these patients, the most frequently delivered number of chemotherapy cycles was six, observed in 43.5% of cases, followed by three cycles in 39.1%. A smaller proportion of patients received one cycle (13.0%) or five cycles (4.3%). the median duration from chemotherapy completion to start of RT was 90 day (IQR 25.5-118) The most common chemotherapy regimen used was Carboplatin/paclitaxel (39%). Post-radiotherapy chemotherapy was given to 4.8% of patients, primarily for residual disease (87.5%) and, less commonly, for progressive disease (12.5%). The mean interval from the completion of radiotherapy to the initiation of post-radiotherapy chemotherapy was 86 days, ranging from 7 to 150 days.

Concurrent chemotherapy was administered in 64.5% of patients. Among these, 26.2% received weekly cisplatin at a dose of 40–50 mg/m², while 62.2% received of 30 to 35 mg/m². The mean number of concurrent chemotherapy cycles was 2.3, with a range of 1 to 5 cycles.

5.4 Response following chemoradiotherapy at 3,6 months and recurrence rate

Tumour response after chemoradiotherapy is shown at 3 months. Most patients achieved complete response at each time point, while a smaller proportion had partial response, stable disease, or progressive disease (see table 2). Of 167 patients, 118 (70.7%) achieved complete response (CR) at 3 months, of whom 98 (83.1%) maintained CR at 6 months. Late conversion to CR occurred in 19.2% of partial responders and 20.0% of patients with stable disease. Disease progression by 6 months was observed in 30.8% of partial responders and 33.3% of patients with stable disease.

To assess factors predicting complete response versus non complete response, univariable binary logistic regression was performed. Variables including tumour size, disease stage, pre-treatment hydronephrosis, brachytherapy boost status, baseline haemoglobin level, RT schedule, and histologic type demonstrated p-values < 0.25 and were thus included in a subsequent multivariable binary logistic regression model. In the final adjusted model, brachytherapy boost remained a statistically significant predictor of complete response (OR = 2.0, $p = 0.047$).

Among the 118 patients analysed, 69.5% experienced no recurrence during the follow-up period. Recurrence was observed in 30.5%. The most common pattern of failure was isolated local recurrence, occurring in 10.2%. Pelvic organ or pelvic side-wall recurrence was noted in 4 patients (3.4%). Distant metastasis (DM) alone occurred in 7 patients (5.9%), while combined local and distant recurrence was seen in 3 patients (2.5%). Other recurrence patterns, including locoregional, para-aortic nodal, and mixed locoregional-distant failures, were uncommon.

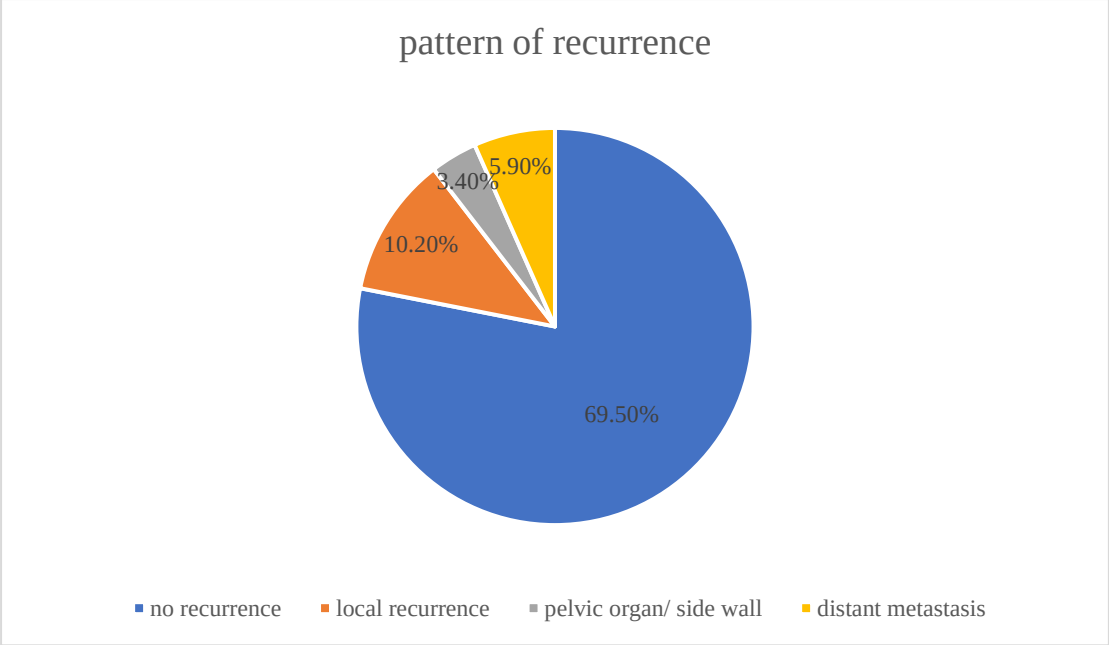


Figure 2 : pattern of recurrence in locally advanced cervical ca after CCRT at TASH

Table 2: Response following chemoradiotherapy at 3, 6, and 12 months

Assessment Time	Response	Frequency (n)	Percentage (%)
At 3 months (N=)167	CR	118	70.7
	PR	26	15.6
	SD	15	9
	PD	6	3.6
	N/A*	2	1.2
At 6 months (N=132)	CR	106	63.5
	PR	12	7.2
	SD	11	6.6
	PD	28	16.8
	N/A*	10	6

Abbreviations: CR = Complete Response; PR = Partial Response; SD = Stable Disease; PD = Progressive Disease; *N/A = not applicable (patients died before evaluation time, patient drop out from follow up or evaluation time is not reached).

5.5 Survival outcome

The mean follow-up for the study was 23 months. The minimum and maximum follow up time is 2 month and 46 months respectively.

The 2-year overall survival (OS) rate was 73%, and the 2-year disease free survival (DFS) rate was 71% based on the Kaplan–Meier estimates. The median survival time was not reached during the study period. The 2-year overall survival (OS) rate was significantly higher among patients who received brachytherapy (BT) boost compared with those who did not (81% vs. 59%, log-rank p = 0.008).

Similarly, the 2-year disease free survival (DFS) was superior in the BT-boost group (78% vs. 56%, log-rank p = 0.02). Patients receiving concurrent chemotherapy had significantly better survival outcomes compared to those who did not. The 2-year overall survival (OS) rate was 80% in the chemotherapy group versus 62% in the no-chemotherapy group (p = 0.014). Similarly, 2-year disease free survival (DFS) was markedly higher with concurrent chemotherapy (78% vs. 58%; p = 0.021).

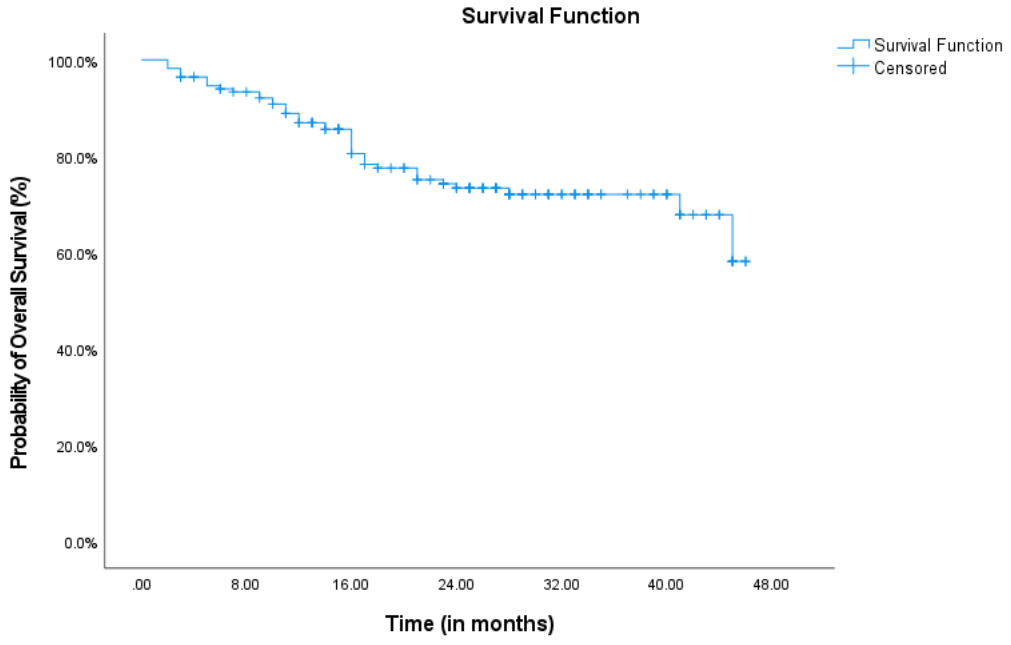


Figure 3: Kaplan-Meier overall survival curve of locally advanced cervical ca, for the overall patients at TASH

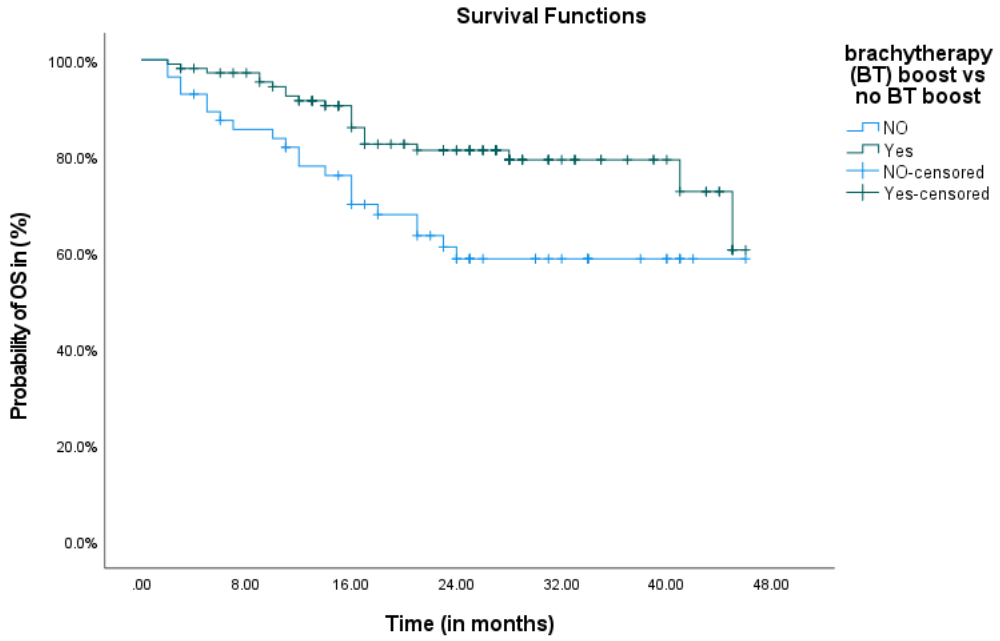


Figure 4: Kaplan-Meier overall survival curve of locally advanced cervical ca, for brachytherapy boost vs no brachytherapy boost

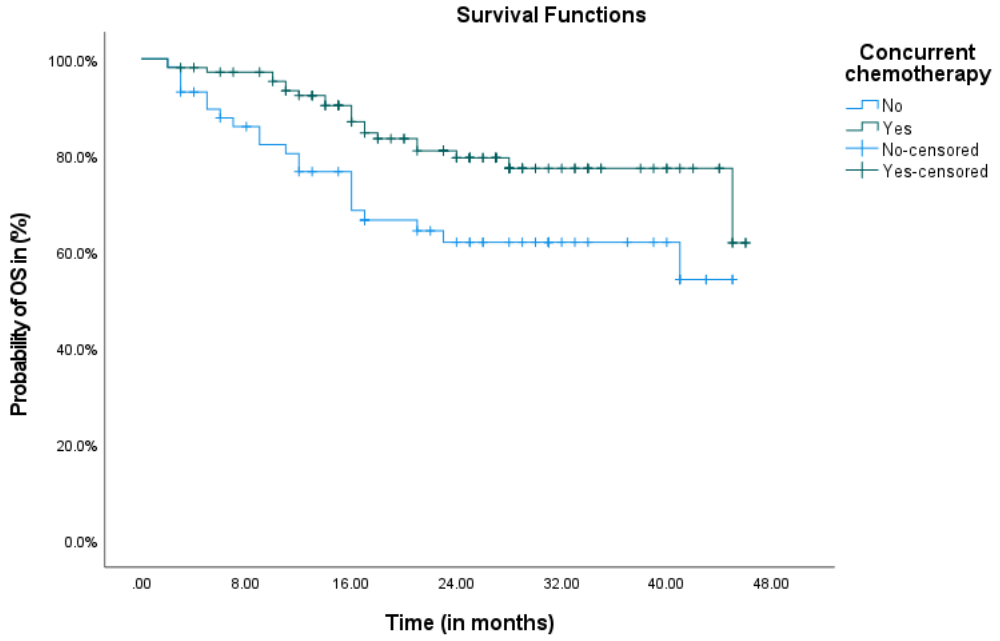


Figure 5: Kaplan-Meier overall survival curve of locally advanced cervical ca, for patient received concurrent chemotherapy vs no chemotherapy.

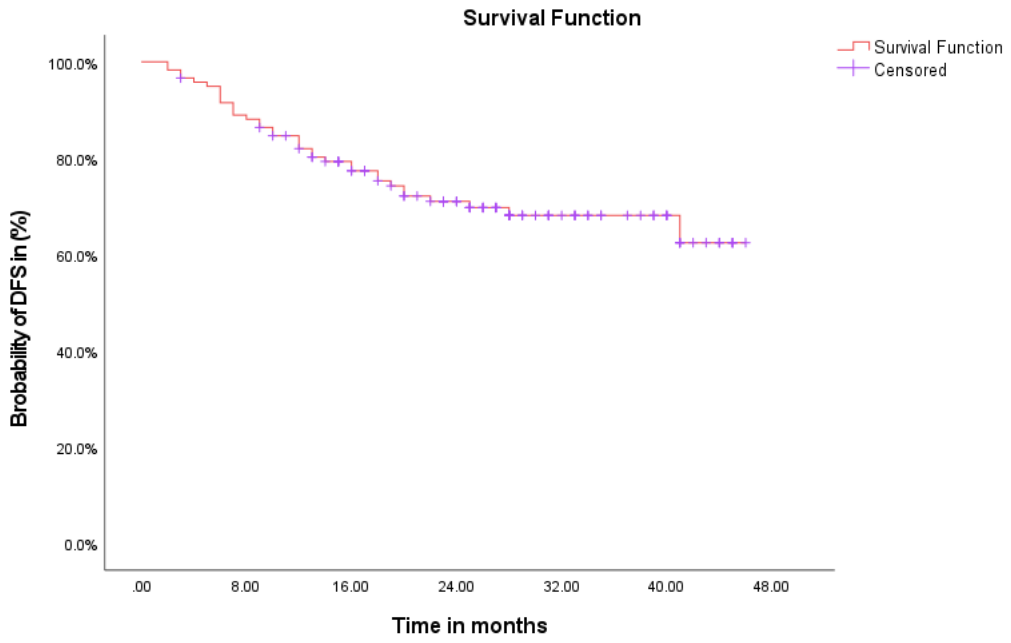


Figure 6: Kaplan-Meier DFS curve of locally advanced cervical ca, in overall population

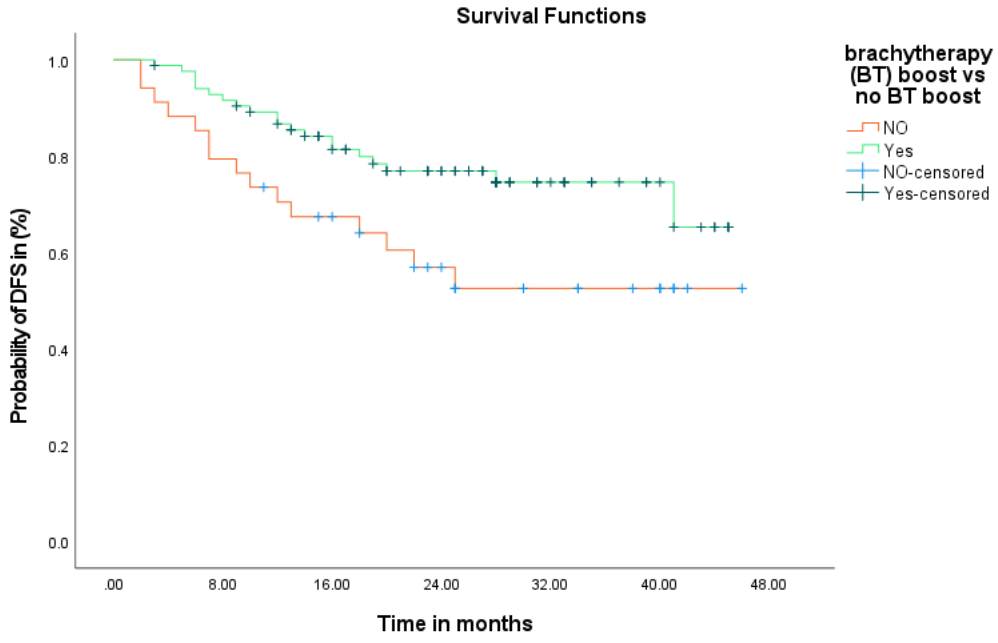


Figure 7: Kaplan-Meier DFS curve of advanced cervical ca, for brachytherapy boost vs no brachytherapy boost

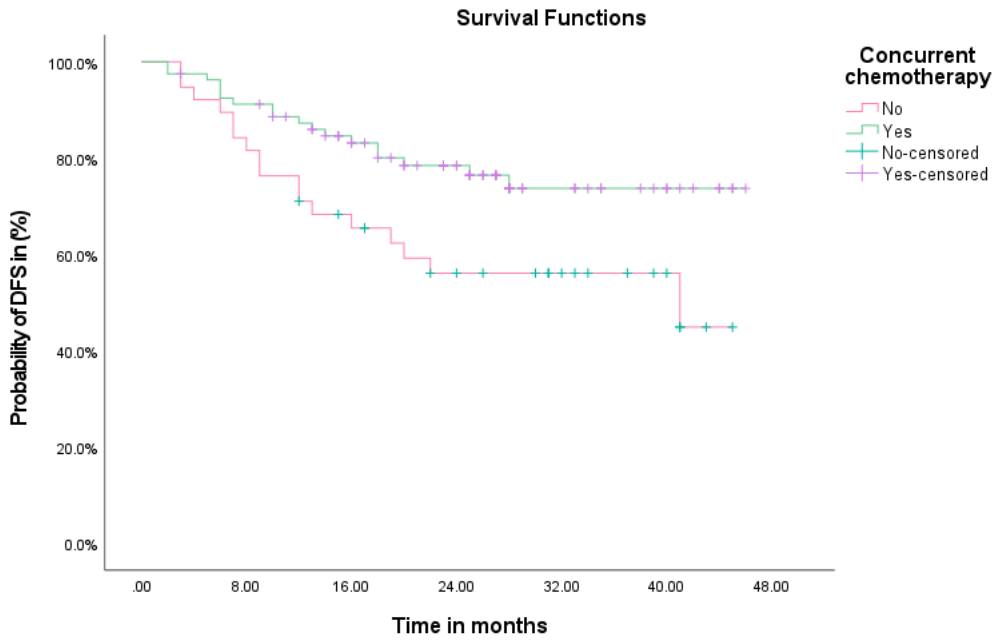


Figure 8: Kaplan-Meier DFS curve of advanced cervical ca, for patient received concurrent chemotherapy vs no chemotherapy

5.6 Prognostic factors

Predictor of overall survival

On univariable analysis stage of disease, baseline haemoglobin, pretreatment hydronephrosis, brachytherapy use, tumour response at 3-month, largest tumour diameter in centimetre, histologic type, concurrent chemotherapy, EBRT schedule were analysed for possible prognostic factor for overall survival. From these variable baseline haemoglobin, pretreatment hydronephrosis, brachytherapy use, tumour response, stage and largest tumour diameter in centimetre were a candidate for final analysis with a candidate for final analysis with P<= 0.25.

In the multivariate Cox model, complete response (CR) and largest tumour diameter was independent predictor of survival, with CR patients showing a 68% lower mortality risk (HR = 0.32; 95% CI: 0.15–0.68; p = 0.003) and each 1cm increment in largest tumour diameter will increase the risk of death by 1.3 times (1-1.7, p-value: 0.016). Although hydronephrosis, baseline haemoglobin, and receipt of brachytherapy (BRT) did not reach statistical significance, BRT demonstrated a clinically meaningful trend toward improved outcomes (HR = 1.91; p = 0.085), suggesting a potential survival advantage for patients receiving the boost.

Predictors of DFS

Univariable analysis for base line haemoglobin, stage of disease, pre-treatment hydronephrosis, brachytherapy use, EBRT schedule, largest tumour diameter, histologic type and concurrent chemotherapy were analysed for possible prognostic factor for DFS. Among this these variable baseline haemoglobin, pre-treatment hydronephrosis, stage, brachytherapy use, concurrent chemotherapy use and largest tumour diameter were a candidate for final analysis with P<= 0.25.

In the multivariable analysis, the use of a brachytherapy boost was associated with improved DFS, corresponding to a 37% lower risk of recurrence (HR=0.63, 95% CI: 0.29-1.34), though this association did not reach statistical significance (p=0.23). Concurrent chemotherapy also showed a strong association with prolonged DFS, suggesting an approximately 50% reduction in recurrence risk (HR=0.50, 95% CI: 0.25–1.01; p=0.054). In contrast, pre-treatment hydronephrosis, largest tumour diameter, and FIGO stage were not significantly associated with DFS outcomes in the adjusted model.

Table 3. Multivariable Cox regression analysis for overall survival

Variable	**Category**	**Patient numbers (N)**	**HR (95% CI), OS**	**P-value**
Tumor Response (3-month)	Complete response	118	0.32(0.15, 0.68)	0.003
	Non-complete response	48	1 (Reference)	
Largest tumor diameter (cm)	-	-	1.3(1.0-1.7)	0.016
BRT received	No	56	1.91(0.92, 4.00)	0.085
	Yes	111	1 (Reference)	_
Hb	(per unit increase)	-	0.86 (0.70, 1.06)	0.151
Pre-treatment Hydronephrosis	Yes	20	0.50 (0.20, 1.22)	0.125
	no	147	1 (Reference)	_

Concurrent chemotherapy use	Yes	109	0.6(0.3-1.2)	00.21
	No	57	1 (Reference)	

Note. CR = Complete Response; BRT = Brachytherapy; Hb =Haemoglobin

5.7 Radiation Induced late toxicity

Late radiation-induced adverse events were documented in 82 patients (49.1%). No late toxicity was reported for 59 patients (35.3%), while the status was unknown or not assessable for 26 patients (15.6%). For the 82 patients who developed a late radiation-induced toxicity, the median time from the end of radiotherapy to onset was 6.0 months (IQR: 5.0 – 9.0 months). Radiation-induced late adverse events (AEs) differed between patients who received brachytherapy (BRT) and those who did not. Among patients who did not receive BRT, 24 (42.9%) had no late AEs, while 18 (32.1%) experienced late AEs. Among those who received BRT, 35 (31.5%) had no late AEs and 64 (57.7%) developed late AEs.

Late organ-specific toxicities were assessed, with rectal toxicity being the most frequent, occurring in 44.9% of patients, while 54.1% were unaffected. Bladder toxicity was less common, affecting 15.0% of patients, absent in 85%. Concurrent late bladder and rectal toxicity was observed in 18 patients, representing 10.8% of the entire cohort. Among patients who developed bladder toxicity, the majority (72.0%) also experienced rectal toxicity. Conversely, approximately one-quarter (24.0%) of patients with rectal toxicity had concurrent bladder toxicity.

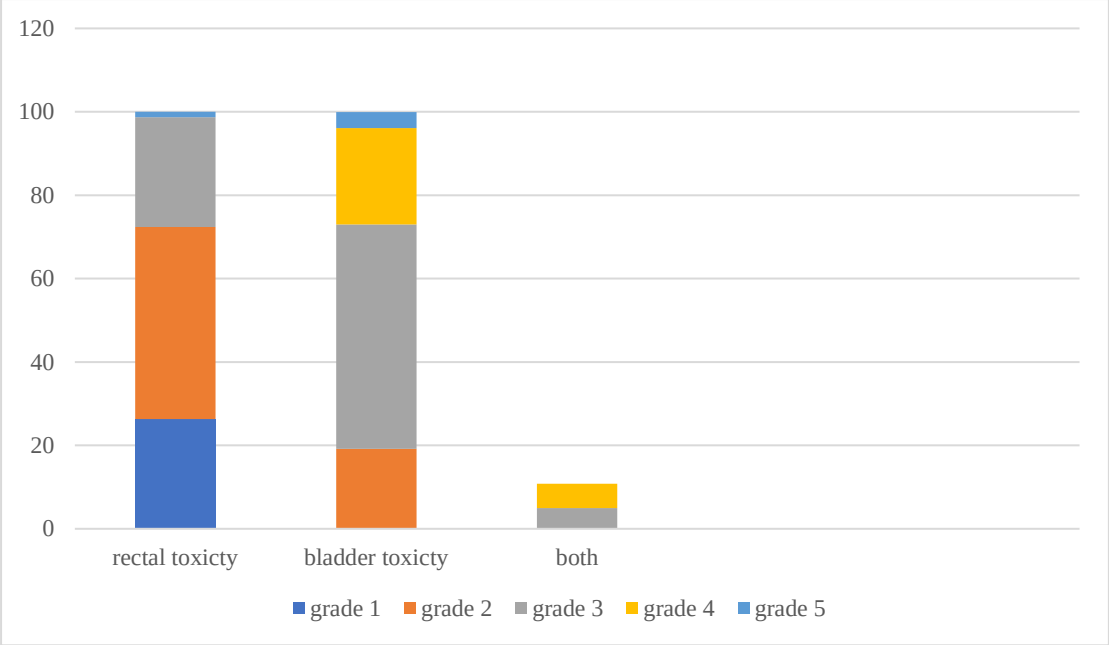


Figure 9: Radiation toxicity with CTCAE grade

Chapter Six: Discussion

This prospective study investigated treatment outcomes, prognostic factors, and late toxicities among women with locally advanced cervical cancer treated with definitive radiotherapy, with or without concurrent chemotherapy, at Tikur Anbesa Specialized Hospital in the LINAC era.

The demographic and disease characteristics assessed in this cohort are consistent with the known epidemiology of cervical cancer in Ethiopia and similar low-resource settings. The median age in the fifth decade of life, predominance of squamous cell carcinoma, and the high proportion of FIGO stage IIB–IVA disease reflects delayed presentation and limited population-based screening(6,19,23). The high tumor burden at presentation further emphasizes the structural barriers to early diagnosis.

The complete response rate of approximately 71% at three months and the two-year overall and disease-free survival rates exceeding 70% demonstrate that satisfactory outcomes can be accomplished using 3D conformal radiotherapy combined with brachytherapy and concurrent chemotherapy. These findings are comparable to other reports from low- and middle-income countries and consistent with international data demonstrating two-year overall survival rates ranging from 65–75% for locally advanced disease treated with concurrent chemoradiotherapy (8,12). Nonetheless, outcomes remain inferior to those reported from centers employing image-guided adaptive brachytherapy and intensity-modulated techniques, emphasizing a persistent technology gap (22,35).

Brachytherapy boost emerged as a key factor in determining both treatment response and survival. Patients receiving brachytherapy achieved significantly higher two-year overall survival and disease-free survival than those who did not. This observation strongly reinforces the irreplaceable role of brachytherapy in attaining optimal local control and survival, as consistently highlighted in international guidelines and large cohort studies (9,35). The observed underutilization of brachytherapy reflects real-world challenges related to access, logistics, and patient-related factors.

Concurrent chemotherapy was also associated with favorable survival outcomes. Patients treated with cisplatin-based chemoradiotherapy has superior overall and disease-free survival compared with radiotherapy alone, in line with evidence from randomized trials and meta-analyses demonstrating the survival advantage of concurrent chemotherapy (3,12,13). However, the low number of chemotherapy cycles administered underscores challenges related to treatment tolerance, comorbidities, and resource constraints.

Tumor size and early response to treatment were the strongest independent prognostic factors for overall survival. Larger tumor size was associated with increased mortality risk, confirming previous studies that identified bulky disease as a key adverse prognostic factor(24,29). Complete response at three months was associated with a significant reduction in mortality risk, highlighting the predictive value of early response assessment and the importance of close post-treatment surveillance (11,28).

The patterns of failure were predominantly local recurrence, followed by distant metastasis, consistent with the natural course of locally advanced cervical cancer treated with conventional radiotherapy technique(30,31). This emphasizes the need for further optimization of local therapy with timely brachytherapy and improved treatment planning.

Nearly half of the cohort experienced late radiation-induced toxicities, with rectal toxicity being the most frequent. This rate of late morbidity contrasts with the lower incidence of severe (Grade 3‑4) chronic gastrointestinal (4.1%) and genitourinary (2.7%) toxicity reported in a study of elderly cervical cancer patients (≥70 years) treated with radical radiotherapy or concurrent chemoradiotherapy (25).

Strengths of the Study

This study has several notable strengths. The prospective design allowed standardized evaluation of treatment response and late toxicity, reducing recall as well as documentation bias frequently seen in retrospective analyses. The study provides contemporary real-world data from the LINAC era in Ethiopia, addressing a important evidence gap in sub-Saharan Africa. Comprehensive evaluation of prognostic factors and reporting of late toxicities add further value, as these outcomes are often under-reported in similar settings.

Limitations of the Study

While these has many strengths, several limitations should be acknowledged. The single-center design may not be generalizable across institutions. The follow-up duration, while sufficient for early survival assessment, may underestimate late recurrences, long term survival and very late toxicities. Outcomes could have been influenced by limited use of advanced radiotherapy techniques and incomplete chemotherapy delivery. Additionally, detailed dosimetric parameters and molecular prognostic factors were also not analyzed.

Conclusion

This prospective study evaluated that definitive radiotherapy with concurrent chemotherapy and brachytherapy provides clinically meaningful response rates, survival outcomes, and manageable toxicity profiles for patients with locally advanced cervical cancer treated at Tikur Anbesa Specialized Hospital in the LINAC era. The demonstrated two-year overall and disease-free survival rates rates align with existing evidence supporting concurrent chemoradiotherapy as the standard of care in this setting.

Brachytherapy boost and concurrent chemotherapy were the most important determinants of improved treatment response and survival, reflecting their central role in the management of locally advanced cervical cancer. Tumor size at presentation and early treatment response were the strongest independent prognostic factors, emphasizing the importance of early assessment and risk stratification.

Despite these favorable outcomes, a substantial burden of disease recurrence and late radiation-related toxicity observed. These findings highlight the need to improve comprehensive chemoradiotherapy services, optimize radiotherapy delivery, and gradually adopt image-guided and intensity-modulated techniques. Continued investment in technology, supportive care, and early detection strategies will be important to further improve survival and quality of life for women with cervical cancer in Ethiopia and similar resource-limited settings.

Recommendations

Based on the findings of this study, the following recommendations are proposed:

1. Access to timely and high-quality brachytherapy services should be prioritized, as it is critical for local control and survival.
2. Efforts should be made to improve delivery and completion of concurrent chemotherapy through optimized supportive care and patient selection.
3. Optimize technique of radiotherapy delivery, improve radiotherapy toxicity prevention and monitoring.
4. Gradual adoption of advanced radiotherapy and image-guided brachytherapy techniques should be pursued as resources permit.

Future research should focus on longer follow-up, incorporation of dosimetry and molecular factors, and evaluation of survivorship and quality-of-life outcomes.

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Chapter Seven: References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May;71(3):209–49. doi:10.3322/caac.21660 PubMed PMID: 33538338.

2. Zhang X, Zeng Q, Cai W, Ruan W. Trends of cervical cancer at global, regional, and national level: data from the Global Burden of Disease study 2019. BMC Public Health. 2021 Dec 1;21(1). doi:10.1186/s12889-021-10907-5 PubMed PMID: 33975583.

3. Shrivastava S, Mahantshetty U, Engineer R, Chopra S, Hawaldar R, Hande V, et al. Cisplatin chemoradiotherapy vs radiotherapy in FIGO stage IIIB squamous cell carcinoma of the uterine cervix a randomized clinical trial. JAMA Oncol. 2018 Apr 1;4(4):506–13. doi:10.1001/jamaoncol.2017.5179 PubMed PMID: 29423520.

4. Derbie A, Mekonnen D, Nibret E, Misgan E, Maier M, Woldeamanuel Y, et al. Cervical cancer in Ethiopia: a review of the literature. Cancer Causes & Control. 2023;34(1):1–11. doi:10.1007/s10552-022-01638-y

5. Migbaru Abate S. Trends of Cervical Cancer in Ethiopia. 2015. doi:10.4172/2475-3173.1000103

6. Begoihn M, Mathewos A, Aynalem A, Wondemagegnehu T, Moelle U, Gizaw M, et al. Cervical cancer in Ethiopia-predictors of advanced stage and prolonged time to diagnosis. Infect Agent Cancer. 2019 Nov 11;14(1). doi:10.1186/s13027-019-0255-4

7. Cohen PA, Jhingran A, Oaknin A, Denny L. Cervical cancer. The Lancet. 2019 Jan 12;393(10167):169–82. doi:10.1016/S0140-6736(18)32470-X

8. Verma J, Monk BJ, Wolfson AH. New Strategies for Multimodality Therapy in Treating Locally Advanced Cervix Cancer. Semin Radiat Oncol. 2016;26(4):344–8. doi:https://doi.org/10.1016/j.semradonc.2016.05.003

9. Abu-Rustum NR, Yashar CM, Arend R, Barber E, Bradley K, Brooks R, et al. NCCN GUIDELINES® INSIGHTS Cervical Cancer, Version 1.2024. JNCCN Journal of the National Comprehensive Cancer Network. 2023 Dec 1;21(12):1224–33. doi:10.6004/jnccn.2023.0062 PubMed PMID: 38081139.

10. Mazzola R, Ricchetti F, Fiorentino A, Levra NG, Fersino S, Di Paola G, et al. Weekly Cisplatin and Volumetric-Modulated Arc Therapy With Simultaneous Integrated Boost for Radical Treatment of Advanced Cervical Cancer in Elderly Patients: Feasibility and Clinical Preliminary Results. Technol Cancer Res Treat. 2017 Jun 1;16(3):310–5. doi:10.1177/1533034616655055 PubMed PMID: 27402633.

11. Todo Y, Watari H. Concurrent chemoradiotherapy for cervical cancer: Background including evidence-based data, pitfalls of the data, limitation of treatment in certain groups. Chinese Journal of Cancer Research. AME Publishing Company; 2016. p. 221–7. doi:10.21147/j.issn.1000-9604.2016.02.10

12. Datta NR, Stutz E, Liu M, Rogers S, Klingbiel D, Siebenhüner A, et al. Concurrent chemoradiotherapy vs. radiotherapy alone in locally advanced cervix cancer: A systematic review and meta-analysis. Gynecol Oncol. 2017 May 1;145(2):374–85. doi:10.1016/j.ygyno.2017.01.033

13. Vale C, Tierney JF, Stewart LA, Brady M, Dinshaw K, Jakobsen A, et al. Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: A systematic review and meta-analysis of individual patient data from 18 randomized trials. Journal of Clinical Oncology. 2008 Dec 10;26(35):5802–12. doi:10.1200/JCO.2008.16.4368 PubMed PMID: 19001332.

14. Marchetti C, Fagotti A, Tombolini V, Scambia G, De Felice F. Survival and toxicity in neoadjuvant chemotherapy plus surgery versus definitive chemoradiotherapy for cervical cancer: A systematic review and meta-analysis. Cancer Treat Rev. 2020;83:101945. doi:https://doi.org/10.1016/j.ctrv.2019.101945

15. Marchetti C, Francesca De F, Pinto A Di, Romito A, Musella A, Palaia I, et al. Survival nomograms after curative neoadjuvant chemotherapy and radical surgery for stage IB2-IIIB cervical cancer. Cancer Res Treat. 2018 Jan 1;50(3):768–76. doi:10.4143/crt.2017.141 PubMed PMID: 28724282.

16. McCormack M, Eminowicz G, Gallardo D, Diez P, Farrelly L, Kent C, et al. Induction chemotherapy followed by standard chemoradiotherapy versus standard chemoradiotherapy alone in patients with locally advanced cervical cancer (GCIG INTERLACE): an international, multicentre, randomised phase 3 trial. The Lancet. 2024 Oct 19;404(10462):1525–35. doi:10.1016/S0140-6736(24)01438-7 PubMed PMID: 39419054.

17. Parulekar M, Kim MK, Noh JJ, Suh DH, Kim K, Kim YB, et al. Clinicopathological Factors Affecting Prognosis in Patients with Advanced Cervical Cancer Undergoing Concurrent Chemoradiation Therapy. Cancers (Basel). 2025 Sep 1;17(18). doi:10.3390/cancers17183042

18. Kang S, Wu J, Li J, Hou Q, Tang B. Prognostic Significance of Clinicopathological Factors Influencing Overall Survival and Event- Free Survival of Patients with Cervical Cancer: A Systematic Review and Meta-Analysis. Medical Science Monitor. International Scientific Information, Inc.; 2022. doi:10.12659/MSM.934588 PubMed PMID: 35260545.

19. Wassie M, Argaw Z, Tsige Y, Abebe M, Kisa S. Survival status and associated factors of death among cervical cancer patients attending at Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia: A retrospective cohort study. BMC Cancer. 2019 Dec 16;19(1). doi:10.1186/s12885-019-6447-x PubMed PMID: 31842805.

20. Liu J, Tang G, Zhou Q, Kuang W. Outcomes and prognostic factors in patients with locally advanced cervical cancer treated with concurrent chemoradiotherapy. Radiation Oncology. 2022 Dec 1;17(1). doi:10.1186/s13014-022-02115-1 PubMed PMID: 35978412.

21. Pinto PJJ, Chen MJ, Santos Neto E, Faloppa CC, De Brot L, Guimaraes APG, et al. Prognostic factors in locally advanced cervical cancer with pelvic lymph node metastasis. International Journal of Gynecological Cancer. 2022 Mar 1;32(3):239–45. doi:10.1136/ijgc-2021-003140 PubMed PMID: 35256409.

22. Peng QH, Chen K, Li JY, Chen L, Ye WJ. Analysis of Treatment Outcomes and Prognosis After Concurrent Chemoradiotherapy for Locally Advanced Cervical Cancer. Front Oncol. 2022 Jul 6;12. doi:10.3389/fonc.2022.926840

23. Kantelhardt EJ, Moelle U, Begoihn M, Addissie A, Trocchi P, Yonas B, et al. Cervical Cancer in Ethiopia: Survival of 1,059 Patients Who Received Oncologic Therapy. Oncologist. 2014 Jul 1;19(7):727–34. doi:10.1634/theoncologist.2013-0326 PubMed PMID: 24951611.

24. Queiroz ACM, Fabri V, Mantoan H, Sanches SM, Guimarães APG, Ribeiro ARG, et al. Risk factors for pelvic and distant recurrence in locally advanced cervical cancer. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2019 Apr 1;235:6–12. doi:10.1016/j.ejogrb.2019.01.028

25. Wang SC, Lin LC, Kuo YT, Lin YW. Radiographic number of positive pelvic lymph nodes as a prognostic factor in cervical cancer treated with definitive concurrent chemoradiotherapy or intensity-modulated radiotherapy. Front Oncol. 2018;8(NOV). doi:10.3389/fonc.2018.00546

26. Hu K, Wang W, Liu X, Meng Q, Zhang F. Comparison of treatment outcomes between squamous cell carcinoma and adenocarcinoma of cervix after definitive radiotherapy or concurrent chemoradiotherapy. Radiation Oncology. 2018 Dec 17;13(1). doi:10.1186/s13014-018-1197-5 PubMed PMID: 30558636.

27. Intaraphet S, Kasatpibal N, Søgaard M, Khunamornpong S, Patumanond J, Chandacham A, et al. Histological type-specific prognostic factors of cervical small cell neuroendocrine carcinoma, adenocarcinoma, and squamous cell carcinoma. Onco Targets Ther. 2014 Jul 1;7:1205–14. doi:10.2147/OTT.S64714

28. Kang JH, Cho WK, Yeo HJ, Jeong SY, Noh JJ, Shim JI, et al. Prognostic significance of tumor regression rate during concurrent chemoradiotherapy in locally advanced cervix cancer: Analysis by radiation phase and histologic type. J Clin Med. 2020 Nov 1;9(11). doi:10.3390/jcm9113471

29. Chen W, Xiu S, Xie X, Guo H, Xu Y, Bai P, et al. Prognostic value of tumor measurement parameters and SCC-Ag changes in patients with locally-advanced cervical cancer. Radiation Oncology. 2022 Dec 1;17(1). doi:10.1186/s13014-021-01978-0 PubMed PMID: 35012582.

30. de FOUCHER T, Bendifallah S, Bricou A, Lavoue V, Varinot J, Canlorbe G, et al. Patterns of recurrence and prognosis in locally advanced FIGO stage IB2 to IIB cervical cancer: retrospective multicentre study from the FRANCOGYN Group. Short version of title: Recurrence and prognosis for locally advanced cervical cancer. 2018. Report.

31. Kilic C, Kimyon Comert G, Cakir C, Yuksel D, Codal B, Kilic F, et al. Recurrence pattern and prognostic factors for survival in cervical cancer with lymph node metastasis. Journal of Obstetrics and Gynaecology Research. 2021 Jun 1;47(6):2175–84. doi:https://doi.org/10.1111/jog.14762

32. Delgado D, Figueiredo A, Mendonça V, Jorge M, Abdulrehman M, De Pina MF. Results from chemoradiotherapy for squamous cell cervical cancer with or without intracavitary brachytherapy. J Contemp Brachytherapy. 2019;11(5):417–22. doi:10.5114/jcb.2019.88116

33. Tabaja L, Sidani SM. Management of Radiation Proctitis. Dig Dis Sci. 2018;63(9):2180–8. doi:10.1007/s10620-018-5163-8

34. Liang YQ, Feng SQ, Xie WJ, Jiang QZ, Yang YF, Luo R, et al. Comparison of survival, acute toxicities, and dose–volume parameters between intensity-modulated radiotherapy with or without internal target volume delineation method and three-dimensional conformal radiotherapy in cervical cancer patients: A retrospective and propensity score-matched analysis. Cancer Med. 2022 Jan 1;11(1):151–65. doi:10.1002/cam4.4439 PubMed PMID: 34821082.

35. Pötter R, Tanderup K, Schmid MP, Jürgenliemk-Schulz I, Haie-Meder C, Fokdal LU, et al. MRI-guided adaptive brachytherapy in locally advanced cervical cancer (EMBRACE-I): a multicentre prospective cohort study. Lancet Oncol. 2021 Apr 1;22(4):538–47. doi:10.1016/S1470-2045(20)30753-1

36. Tiwari R, Narayanan GS, Narayanan S, Suresh Kumar P. Long-term effectiveness and safety of image-based, transperineal combined intracavitary and interstitial brachytherapy in treatment of locally advanced cervical cancer. Brachytherapy. 2020 Jan 1;19(1):73–80. doi:10.1016/j.brachy.2019.10.003 PubMed PMID: 31813739.

37. Klopp AH, Yeung AR, Deshmukh S, Gil KM, Wenzel L, Westin SN, et al. JOURNAL OF CLINICAL ONCOLOGY Patient-Reported Toxicity During Pelvic Intensity-Modulated Radiation Therapy: NRG Oncology-RTOG 1203. J Clin Oncol. 2018;36:2538–44. doi:10.1200/JCO

Annexes

Annex I: Data collection tool and verbal consent form

Demographics and clinical characteristics.		
MRN		
Age		
ECOG PS base line		
Hg level before start of RT		

Cr/GFR base line and current		
Comorbidity	DM	
	HTN	
	CVD	
	HIV	
	AKI	
	CKD	
	Hydronephrosis	
	Other specify_____	
	None	
If yes for hydronephrosis specify the grade and kidney affected and Cr/GFR(before /after stenting and current) and the timing of development of hydronephrosis relative to start of RT (before RT or after RT)		
Type of treatment received and timing of treatment for hydronephrosis relative to start of RT (before RT or after RT)		
If yes for HIV	Time since diagnosis	

	HAART	
	CD4 count	
	Viral load	
Histology type	SCC	
	ADC	
	ADSC	
	Other specify	
T-stage	Tis	
	T1	
	T2	
	T3	
	T4a	
	Tx	
N-stage	N0	
	N1	
	N2	
	Nx	
Group stage/TNM		
The size of the primary tumor.(if available)		
RT technique	3DCRT	
	VMAT	
	IMRT	
	Other specify	
Total prescribed EBRT dose and fraction		

number to the PTV comb(Total)		
Boost dose of EBRT(PTV boost)	A.Boost to the primary tumor(PTV 1)	
	B.Boost to the PTV 1 and PTV 2	
	C.Boost to PTVGTV node(PTVn boost)	
	D.None	
	F.Unknown	
Dose of boost RT		
Technique of RT used for boost delivery	A.SIB	
	B.Sequential	
	C.other specify_____	
If boost is given either of the above please specify the reason of EBRT boost	A.For GTV N	
	B.Inadequate pelvis/cervixs/uterus(myoma) for BRT	
	C.Bulky tumor that had poor response to EBRT and not appropriate for BRT Tx	
	D.BRT treatment was not functional/pt not afford BRT payment	
	E.Unknown	
	F.Other please specify_____	
Rectal dose from EBRT	A.V50Gy < 50% (percentage of rectum received doses >50Gy is < 50 %).	
	B.V60Gy < 35%	
	C.V65Gy < 25%	
	D.V70Gy < 20%	
	F.V75Gy <15%	
	G,Dmax	

	H. Other please specify the dose and volume received by rectum respectively from above I. V50Gy_____% II. V60Gy_____% III. V65Gy_____% IV. V70Gy _____% V. V75Gy _____% VI. Dmax _____Gy	
Bladder dose from EBRT	A.V45Gy < 15 to 30%	
	B.V40Gy <= 40% to 55%	
	C.Dmax <= 50Gy	
	D. Other please write the specific dose and volume respectively from above I. V40Gy in % II. Dmax in Gy III. V45Gy in % IV. V50Gy in %	
Small bowel dose from EBRT	A.V40Gy < 30%	
	B.V50 <5%	
	B.Dmax <= 50Gy	
	C.D60cc <=45Gy	
	D.D100cc <= 40Gy	
	E.D180cc <= 35Gy	

	F. Other please specify the specific dose and volume respectively from the above choices I. V40Gy in % II. V50Gy in % III. Dmax in Gy IV. D60cc in Gy V. D100cc in Gy VI. D180cc in Gy		
EBRT over all treatment time (total duration in days)			
RT interruption	Yes		
	No		
Duration of RT interruption			
Reason of RT interruption	Acute treatment toxicities		
	Refusal of treatment		
	Machine down of any reason		
	Other, specify		
BRT	Dose per fraction		
	Total dose of BRT		
BRT OTT			
OTT for both BRT and EBRT			
BRT Dose deviled to point A (%)			
	A. <= 65% of point A dose		
	B.>65 % of point A dose		

BRT Effective dose to Rectal tissue (% of point A dose)	C.Unknown	
	Please the specific % of point A dose received by rectal tissue_____	
BRT Effective dose to Bladder tissue (% of dose of point A)	A.<=75 % of point A dose	
	B.> 75 % of point A dose	
	C.Unknown	
	Please the specific % of point A dose received by Bladder tissue_____	
Point B dose if available		
Duration from end of EBRT to start of BRT		
Combined(Total) proscribed dose to point A from HDR BRT plus EBRT[(to an LDR equivalent(Gy)].	A.<80Gy	
	B.>85Gy	
	C.80 to 85Gy	
	D.85 to 90Gy	
	E.>90 Gy	
	F.Other specify the dose(Gy) _____	
Combined(cumulative) BRT & EBRT dose to rectum(Gy)(EQD2)	A.EQD2(Gy) <= 75Gy	
	B.> 75Gy	
	C.Unknown	
	Please write the specific EQD2 dose of combined RT received by rectum in Gy _____	
Combined(cumulative) BRT & EBRT dose to Bladder	A.EQD2(Gy) <=80Gy	
	B.EQD2(Gy) >80Gy	
	C.unknown	

(Gy)(EQD2)(a/b ratio of 3)	Please write the specific EQD2 dose of combined RT received by Bladder in Gy _____	
Chemotherapy before RT	Yes	
	No	
If yes for CT regimens drugs		
Number of cycles of CT		
Time duration from the start of RT after completion of CT in days		
Post RT chemotherapy	Yes	
	No	
Reason for post RT CT and number of cycle		
Time of Start of post RT CT after end of RT		
Concurrent chemotherapy	Yes	
	No	
Schedule and dose of concurrent CT received	30mg/m2 /wkly	
	40mg/m2 /wkly	
	80-100mg/m2 /3wkly	
	80mg/m2/ 3wkly	
Total number of cycles of concurrent chemotherapy		
Short-term effects	CR	

	PR	
	SD	
	PD	
	Unknown	
Follow up imaging finding at 3/6/12/18/24month		
Type of imaging modality done for each follow up visits		
Radiation-induced late AEs	Yes	
	No	
If yes for RI late adverse effects Time of development of late adverse effect after end of RT		
Radiation-induced late rectal AEs	Yes	
	No	
Patient symptom from late rectal AEs		
Imaging or endoscopy done to dx rectal sm	Yes	
	No	
Finding from endoscopy or imaging for rectal sm		
Type of Late RI Rectal AEs	A.Rectal hemorrihage/bleeding	
	B.Proctitits/mucositis	
	C.Rectal fissue	

	D.Rectal fistula/perforation	
	F.Rectal stenosis/Obstruction	
	G.Rectal ulceration	
	H.Rectal pain	
	I.Rectal necrosis	
	J.other specify_____	
Treatment type received or receiving		
Current status from late rectal AEs	Reliefed	
	worsning	
	No improvement	
Grade of rectal Late AEs(based on the CTCAE 5 see annex 3)	G1-	
	G2-	
	G3-	
	G4-	
	G5	
Grade of RI-Late bladder AEs(CTCAE- 5 see Annex 3)	G1-	
	G2-	
	G3-	
	G4_	
	G5-	
	Unknown	
Patient symptom from late bladder toxicity		
Type of Late RI Bladder AEs	A.Urinary tract pain	
	B.Urinary urgency/frequency	
	C.Urinary incontinent	
	D.Urinary retention	

	E.Cystitis non infections	
	F.UT perforation	
	G.Hematturia	
	H.UT abstraction	
	I.UT fistula	
	J.Other specify_____	
Treatment type received or receiving for late bladder toxicity		
Current patient status from bladder symptom	Reliefed	
	worsning	
	No improvement	
Patient develop late RI small bowel toxicity	A.Yes	
	B.No	
	C.Unknown	
If yes for the above what are the type/s of Late adverse effect of small bowel developed	A.SI abstraction/stenosis	
	B.SI Mucositis	
	C.SI perforation	
	D.Ileus	
	E.SI ulceration	
	F.intra abdominal hemorrahage	
	G.Other _____	
Grade of late small bowel AEs developed(see Annex-3)	G1-	
	G2-	
	G3-	
	G4-	
	G5-	
	G0-	

Current symptom of patient from late small bowel toxicity	A. Similar(No improvement) with the initial symptoms	
	B.Worsning	
	C.Releifed	
	D.Other_____	
Type of treatment the patient received or receiving for small bowel adverse effect treatment		
Investigation Type done to diagnosis the small bowel AEs and the Findings(write)		
Tumor recurrence developed	yes	
	No	
Means of diagnosis of tumor recurrence	A.Sign and symptom developed	
	B.Incidental finding from followup imaging	
	C.specify the sign or symptom pt developed during recurrence	
	D.Initially was not CR /persistent disease	
If yes for tumor recurrence time of recurrence after end of RT		
	Local (Cx,Ux,Vx,)	

	LRR other than above mentioned local recurrence(rectal,bladder,pelvic side wall,pre-sacral space)	
If yes for tumor recurrence specific site of recurrence	Par-aortic LN	
	Inguinal LN	
	Pelvic LN	
	Distant metastatic recurrence	
	More than one of the above site please list it	
	Other specify	
Distant metastasis developed	Lung	
	Liver	
	Bone	
	If more than 1 sites specify	
	Other specify	
	None(no DM developed)	
Patient alive	Yes	
	No	
	Other specify	
If patient is not alive reason of not alive	Dead	
	Lost follow up/unanswered call	
	Other reason specify	
If the patient died reason for death		
Time after end of RT the patient not alive in any reason of above		

Addis Ababa University college of Health Science Department of Clinical Oncology, hematology and nuclear medicine

Verbal consent form English version

I care number	
Study title	Prospective Study of Locally Advanced Cervical Cancer Treated with Concurrent Chemoradiation
Investigator	Dr Elsabet Abnew Yirga
Introduction	Hello, my name is Dr Elsabet, I am conducting a study about cervical cancer treatment. I would like to enroll you in this study to understand treatment outcomes, side effects, and factors that may affect recovery
Purpose	To study about treatment results, side effects, and disease recurrence to help improve care for future patients.
What will happen	I will record information about your treatment, any side effects or toxicities, and if the cancer comes back. You will receive the **same standard treatment**; nothing extra is required for this study.
Risk and benefit	There is no additional risk since there is no intervention and your treatment is standard. The study may not provide direct benefit to you, but your participation may help improve care for future patients
privacy	Your information will be confidential, and your name will **not** appear in any reports or publications.

Voluntary Participation	You can withdraw or stop participating at any time without affecting your care.
Consent Question (Verbal)	Do you agree to let us use your treatment and follow-up information for this study? ☐ Yes ☐ No

Investigator Name & Signature: _____
Date: _____

Annex II: Common Terminology Criteria for Adverse Events (CTCAE) v5.0

Publish Date: November 27, 2017

Grades

- Grade refers to the severity of the AE. The CTCAE displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:
  - Grade 1 Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
  - Grade 2 Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*.
  - Grade 3 Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**.
  - Grade 4 Life-threatening consequences; urgent intervention indicated.
  - Grade 5 Death related to AE.
- Activities of Daily Living (ADL)
  - *Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
  - **Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

Renal and urinary disorders					
CTCAE Term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
Bladder perforation	-	Invasive intervention not indicated	Invasive intervention indicated	Life-threatening consequences; organ failure; urgent operative intervention indicated	Death
Definition: A disorder characterized by a rupture in the bladder wall. **Navigational Note:** -					
Bladder spasm	Intervention not indicated	Antispasmodics indicated	Hospitalization indicated	-	-
Definition: A disorder characterized by a sudden and involuntary contraction of the bladder wall. **Navigational Note:** -					
Cystitis noninfective	Microscopic hematuria; minimal increase in frequency, urgency, dysuria, or nocturia; new onset of incontinence	Moderate hematuria; moderate increase in frequency, urgency, dysuria, nocturia or incontinence; urinary catheter placement or bladder irrigation indicated; limiting instrumental ADL	Gross hematuria; transfusion, IV medications, or hospitalization indicated; elective invasive intervention indicated	Life-threatening consequences; urgent invasive intervention indicated	Death
Definition: A disorder characterized by inflammation of the bladder which is not caused by an infection of the urinary tract. **Navigational Note:** -					

Hematuria	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; urinary catheter or bladder irrigation indicated; limiting instrumental ADL	Gross hematuria; transfusion, IV medications, or hospitalization indicated; elective invasive intervention indicated; limiting self care ADL	Life-threatening consequences; urgent invasive intervention indicated	Death
Definition: A disorder characterized by laboratory test results that indicate blood in the urine. **Navigational Note:** -					
Urinary fistula	-	Symptomatic, invasive intervention not indicated	Invasive intervention indicated	Life-threatening consequences; urgent invasive intervention indicated	Death
Definition: A disorder characterized by an abnormal communication between any part of the urinary system and another organ or anatomic site. **Navigational Note:** -					
Urinary frequency	Present	Limiting instrumental ADL; medical management indicated	-	-	-
Definition: A disorder characterized by urination at short intervals. **Navigational Note:** -					
Urinary incontinence	Occasional (e.g., with coughing, sneezing, etc.), pads not indicated	Spontaneous; pads indicated; limiting instrumental ADL	Intervention indicated (e.g., clamp, collagen injections); operative intervention indicated; limiting self care ADL	-	-
Definition: A disorder characterized by inability to control the flow of urine from the bladder.					
Urinary retention	Urinary, suprapubic or intermittent catheter placement not indicated; able to void with some residual	Placement of urinary, suprapubic or intermittent catheter placement indicated; medication indicated	Elective invasive intervention indicated; substantial loss of affected kidney function or mass	Life-threatening consequences; organ failure; urgent operative intervention indicated	Death
Definition: A disorder characterized by accumulation of urine within the bladder because of the inability to urinate. **Navigational Note:** -					
Urinary tract obstruction	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic but no hydronephrosis, sepsis, or renal dysfunction; urethral dilation, urinary or suprapubic catheter indicated	Altered organ function (e.g., hydronephrosis or renal dysfunction); invasive intervention indicated	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by blockage of the normal flow of contents of the urinary tract. **Navigational Note:** -					
Urinary tract pain	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self care ADL	-	-
Definition: A disorder characterized by a sensation of marked discomfort in the urinary tract. **Navigational Note:** -					
Urinary urgency	Present	Limiting instrumental ADL; medical management indicated	-	-	-
Definition: A disorder characterized by a sudden compelling urge to urinate. **Navigational Note:** -					

Gastrointestinal disorders					
CTCAE Term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
Lower gastrointestinal hemorrhage	Mild symptoms; intervention not indicated	Moderate symptoms; intervention indicated	Transfusion indicated; invasive intervention indicated; hospitalization	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by bleeding from the lower gastrointestinal tract (small intestine, large intestine, and anus). **Navigational Note:** -					
Malabsorption	-	Altered diet; oral intervention indicated	Inability to aliment adequately; TPN indicated	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by inadequate absorption of nutrients in the small intestine. Symptoms include abdominal marked discomfort, bloating and diarrhea. **Navigational Note:** -					

Proctitis	Rectal discomfort, intervention not indicated	Symptomatic (e.g., rectal discomfort, passing blood or mucus); medical intervention indicated; limiting instrumental ADL	Severe symptoms; fecal urgency or stool incontinence; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by inflammation of the rectum. **Navigational Note:** -					
Rectal fissure	Asymptomatic	Symptomatic	Invasive intervention indicated	-	-
Definition: A disorder characterized by a tear in the lining of the rectum. **Navigational Note:** -					
Rectal fistula	Asymptomatic	Symptomatic, invasive intervention not indicated	Invasive intervention indicated	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by an abnormal communication between the rectum and another organ or anatomic site. **Navigational Note:** -					
Rectal hemorrhage	Mild symptoms; intervention not indicated	Moderate symptoms; intervention indicated	Transfusion indicated; invasive intervention indicated; hospitalization	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by bleeding from the rectal wall and discharged from the anus. **Navigational Note:** -					
Rectal mucositis	Asymptomatic or mild symptoms; intervention not indicated	Symptomatic; medical intervention indicated; limiting instrumental ADL	Severe symptoms; limiting self care ADL	Life-threatening consequences; urgent operative intervention indicated	Death
Definition: A disorder characterized by ulceration or inflammation of the mucous membrane of the rectum. **Navigational Note:** -					
Rectal necrosis	-	-	Tube feeding or TPN indicated; invasive intervention indicated	Life-threatening consequences; urgent operative intervention indicated	Death
Definition: A disorder characterized by a necrotic process occurring in the rectal wall. **Navigational Note:** -					
Rectal obstruction	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; altered GI function; limiting instrumental ADL	Hospitalization indicated; invasive intervention indicated; limiting self care ADL	Life-threatening consequences; urgent operative intervention indicated	Death
Definition: A disorder characterized by blockage of the normal flow of the intestinal contents in the rectum. **Navigational Note:** -					
Rectal pain	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self care ADL	-	-
Definition: A disorder characterized by a sensation of marked discomfort in the rectal region. **Navigational Note:** -					
Rectal perforation	-	Invasive intervention not indicated	Invasive intervention indicated	Life-threatening consequences; urgent operative intervention indicated	Death
Definition: A disorder characterized by a rupture in the rectal wall. **Navigational Note:** -					
Rectal stenosis	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; altered GI function	Severely altered GI function; tube feeding or hospitalization indicated; elective operative intervention indicated	Life-threatening consequences; urgent operative intervention indicated	Death
Definition: A disorder characterized by a narrowing of the lumen of the rectum. **Navigational Note:** -					
Rectal ulcer	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; altered GI function (e.g., altered dietary habits, vomiting, diarrhea)	Severely altered GI function; TPN indicated; elective invasive intervention indicated	Life-threatening consequences; urgent operative intervention indicated	Death
Small intestinal mucositis	Asymptomatic or mild symptoms; intervention not indicated	Symptomatic; medical intervention indicated; limiting instrumental ADL	Severe pain; interfering with oral intake; tube feeding, TPN or hospitalization indicated; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by ulceration or inflammation of the mucous membrane of the small intestine. **Navigational Note:** -					
Small intestinal obstruction	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; altered GI function; limiting instrumental ADL	Hospitalization indicated; invasive intervention indicated; limiting self care ADL	Life-threatening consequences; urgent operative intervention indicated	Death
Definition: A disorder characterized by blockage of the normal flow of the intestinal contents of the small intestine. **Navigational Note:** -					
Small intestinal perforation	-	Invasive intervention not indicated	Invasive intervention indicated	Life-threatening consequences; urgent operative intervention indicated	Death
Definition: A disorder characterized by a rupture in the small intestine wall. **Navigational Note:** -					
Small intestinal stenosis	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; altered GI function	Symptomatic and severely altered GI function; tube feeding, TPN or hospitalization indicated; non-emergent operative intervention indicated	Life-threatening consequences; urgent operative intervention indicated	Death
Definition: A disorder characterized by a narrowing of the lumen of the small intestine. **Navigational Note:** -					
Small intestine ulcer	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; altered GI function; limiting instrumental ADL	Severely altered GI function; TPN indicated; elective invasive intervention indicated; limiting self care ADL	Life-threatening consequences; urgent operative intervention indicated	Death
Definition: A disorder characterized by a circumscribed, erosive lesion on the mucosal surface of the small intestine. **Navigational Note:** -					

Ileal ulcer	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; altered GI function	Severely altered GI function; TPN indicated; elective invasive intervention indicated	Life-threatening consequences; urgent operative intervention indicated	Death
Definition: A disorder characterized by a circumscribed, erosive lesion on the mucosal surface of the ileum. **Navigational Note:** -					
Ileus	Asymptomatic and radiologic observations only	Symptomatic; altered GI function; bowel rest indicated	Severely altered GI function; TPN indicated; tube placement indicated	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by failure of the ileum to transport intestinal contents. **Navigational Note:** -					
Intra-abdominal hemorrhage	-	Moderate symptoms; intervention indicated	Transfusion indicated; invasive intervention indicated; hospitalization	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by bleeding in the abdominal cavity. **Navigational Note:** -					