

ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE
DEPARTMENT OF ONCOLOGY



**SURVIVAL OUTCOMES IN PATIENTS WITH BRAIN METASTASES
TREATED WITH WHOLE BRAIN RADIOTHERAPY : A
RETROSPECTIVE STUDY AT TIKUR ANBESSA SPECIALIZED
HOSPITAL , ETHIOPIA (2020–2024)**

BY: DR HENOK TESFAW (CLINICAL ONCOLOGY SENIOR RESIDENT)

RESEARCH PAPER SUBMITTED TO THE SCHOOL OF MEDICINE,
COLLEGE OF HEALTH SCIENCES, ADDIS ABABA UNIVERSITY IN
PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE SPECIALITY
CERTIFICATE IN CLINICAL ONCOLOGY.

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ADDIS ABABA , ETHIOPIA

ADVISOR'S APPROVAL SHEET

This is to certify that the thesis entitled “ survival outcomes in patients with brain metastases treated with whole brain radiotherapy: a retrospective study at tikur anbessa specialized hospital , ethiopia (2020–2024)” is submitted in partial fulfillment of the requirements for the specialization certificate in clinical oncology to the department of clinical oncology, addis ababa university college of health science and has been carried out by Dr Henok Tesfaw under my supervision. Therefore, i recommend that the student has fulfilled the requirements and hence hereby can submit the thesis to the departmen t.

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Declaration

I hereby declare that this research thesis is my original work and has not been presented by any other investigator and all the source materials used for this thesis have been duly acknowledged.

Dr. Henok Tesfaw (clinical Oncology senior resident)

Signature: _____

Date: _____

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ABSTRACT

Background : Brain metastases are the most common intracranial tumors in adults and are associated with poor prognosis. In low resource settings such as Ethiopia, wholebrain radiotherapy (WBRT) remains the primary treatment option for most patients due to limited access to stereotactic radiosurgery and neurosurgical services. However local evidence regarding survival outcomes and prognostic factors following WBRT is scarce.

Objective : To assess overall survival and identify prognostic factors influencing survival among patients with brain metastases treated with whole brain radiotherapy at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

Methods : A retrospective study was conducted among adult patients with radiologically confirmed brain metastases who received WBRT between April 2020 and April 2024. Data were extracted from medical records and radiotherapy logs using a standardized checklist. Overall survival was estimated using the Kaplan Meier method and group comparisons were performed using the log rank test. Univariable and multivariable Cox proportional hazards regression analyses were employed to identify independent predictors of survival.

Results : A total of 70 patients were included in the analysis. The median overall survival from initiation of WBRT was 4.7 months (95% CI: 3.7–5.7). The 6 month and 12month overall survival rates were 38% and 14%, respectively. On multivariable analysis, Karnofsky Performance Status (KPS) ≥ 70 was independently associated with improved survival, while delays in initiating WBRT beyond four weeks from diagnosis of brain metastases were associated with significantly worse survival outcomes.

Conclusion : Survival outcomes for patients with brain metastases treated with WBRT at Tikur Anbessa Specialized Hospital remain poor. Performance status and timely initiation of radiotherapy are key determinants of survival. Strengthening early diagnosis, streamlining referral pathways and improving access to timely radiotherapy may improve outcomes in this resource limited setting.

Keywords : Brain metastases , Whole brain radiotherapy , Overall survival , Prognostic factors, Ethiopia

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LIST OF ABBREVIATIONS AND ACRONYMS

AAU	Addis Ababa University
BM	Brain Metastases
CI	Confidence Interval
CNS	Central Nervous System
CT	Computed Tomography
ECOG	Eastern Cooperative Oncology Group
EGFR	Epidermal Growth Factor Receptor
GPA	Graded Prognostic Assessment
Gy	Gray
HA-WBRT	Hippocampal-Avoidance Whole-Brain Radiotherapy
HDI	Human Development Index
HER2	Human Epidermal Growth Factor Receptor 2
HR	Hazard Ratio
IQR	Interquartile Range
KPS	Karnofsky Performance Status
LMICs	Low- and Middle-Income Countries
MRI	Magnetic Resonance Imaging
NSCLC	Non-Small Cell Lung Cancer
OS	Overall Survival
PCI	Prophylactic Cranial Irradiation
RCC	Renal Cell Carcinoma
RCT	Randomized Controlled Trial
RPA	Recursive Partitioning Analysis
RT	Radiotherapy
RTOG	Radiation Therapy Oncology Group
SCLC	Small Cell Lung Cancer
SRS	Stereotactic Radiosurgery
TASH	Tikur Anbessa Specialized Hospital
WBRT	WholeBrain Radiotherapy

1. INTRODUCTION

1.1. Background

Cancer remains a significant global health issue in the 21st century . It caused nearly 10 million deaths in 2022 and is a leading cause of early death worldwide (1). The latest GLOBOCAN estimates show around 20 million new cancer cases each year. The most commonly diagnosed cancers are those of the lung, female breast , colorectum, and prostate (2). There are notable differences in how this burden is distributed globally. Age-standardized incidence rates can vary about five times across different regions. The highest rates are seen in very high Human Development Index (HDI) areas like Australia / New Zealand , with 507.9 cases per 100,000 in males. In contrast, the lowest rates are in places like Western Africa (97.1 per 100,000 in males) and South-Central Asia (103.3 per 100,000 in females) (2). Projections suggest that without major intervention , global cancer cases could rise to 35 million by 2050 , which is a 77% increase from the 2022 figures. This surge will largely result from an aging population and population growth (2). Low and medium HDI countries will feel this increase the most, with projected rises in cancer incidence of 142% and about 100% , respectively (2).

Brain metastases (BMs) are the most common intracranial tumors in adults. They occur in 20-40% of all cancer patients during their illness (3) . The rate of BMs is increasing because better systemic treatments prolong survival. This gives cancer cells more time to spread to the brain. Improved magnetic resonance imaging (MRI) also helps with early detection (4). The primary cancers that most often lead to BMs are lung cancer (especially non-small cell lung cancer), breast cancer, melanoma, and renal cell carcinoma (5). The development of BMs is a serious complication. It causes a significant drop in quality of life due to symptoms like headaches, seizures, cognitive issues , and focal deficits. It also indicates a poor prognosis (6).

The management of brain metastases is multimodal and includes neurosurgery , radiotherapy (RT) , systemic therapy (such as chemotherapy, targeted therapy, and immunotherapy) and best supportive care. Treatment choices depend on prognostic factors, especially the number of brain metastases, the status of extracranial disease , patient performance , and the molecular profile of the primary tumor (7). Whole brain radiotherapy (WBRT) has been a fundamental treatment for patients with multiple brain metastases for decades . It delivers radiation to the entire brain , effectively relieving neurological symptoms and controlling intracranial disease (8).

1.2. Statement of the Problem

Brain metastases are a significant complication in cancer patients , and advances in high-income countries have led to individualized, multimodal treatments combining systemic therapies with modern radiation techniques, resulting in improved survival and quality of life (9). Globally, the role of WBRT has changed . Its use has become more selective and is often reserved for patients with many metastases who are not suitable for focal therapies like stereotactic radiosurgery (SRS) or those with poor prognostic factors (10) . In high-income countries , the availability of SRS has improved outcomes for certain patients (11).

By contrast, in low- and middle-income countries (LMICs) particularly in Sub-Saharan Africa, including Ethiopia there remains a predominant reliance on WBRT for the management of brain metastases. In such low resource settings WBRT continues to serve as the primary, and often the only , treatment modality available. At Tikur Anbessa Specialized Hospital (TASH) , although WBRT is frequently used, prior to this study there was a notable lack of local data regarding patient outcomes following this treatment.

Preliminary unpublished data from a prospective cohort study at TASH (Dr. Semira) indicate that among 57 patients with brain metastases, the 1, 3, and 6 month survival rates were 82%, 55% , and 17%, respectively. The study found that breast cancer was the most common primary tumor to metastasize to the brain, and patients receiving WBRT had improved survival compared with those who did not. These findings underscore the need for systematically collected local data to better guide clinical decisions .

Before the present study, important questions remained unanswered : What is the overall survival (OS) of patients with brain metastases treated with whole brain radiotherapy (WBRT)? In this particular cohort, which patient or disease characteristics such as performance status, primary cancer type, number of metastases , and presence of extracranial disease significantly impact survival? Understanding these outcomes is essential for guiding clinical decisions, optimizing patient management, allocating resources effectively, and improving the quality of care, particularly in settings where WBRT is the primary available treatment.

The absence of local survival statistics also posed difficulties to organize the health system and raises ethical concerns when speaking with patients because the efficacy of the sole widely accessible treatment had not been evaluated (12) .

1.3. Justification of the Study

This study was conducted to establish a baseline understanding of how effective standard care is at our institution. The findings provide the first thorough look at survival outcomes for patients with brain metastases treated with whole brain radiotherapy at TASH. This data is important for

patient counseling. It provides patients and their families with relevant , evidence-based information on expected survival outcomes to help them make informed decisions.

In terms of clinical practice, the findings may help develop local treatment guidelines and identify which groups of patients derive the most or least benefit from this treatment. Additionally, the research provides solid data to support requests for resources, such as planning for long term stereotactic radiosurgery capabilities. Lastly, the significant dataset generated from this retrospective analysis can serve as a basis for future prospective research and clinical trials aimed at enhancing neuro-oncological treatment in Ethiopia. By carrying out this study, we contributed to national health objectives aimed at improving non-communicable disease outcomes and advancing cancer care in low-resource settings

2. LITERATURE REVIEW

The management of brain metastases has changed a lot over the past twenty years. The important diagnosis specific graded prognostic assessment (GPA) developed by Sperduto et al. offered a solid way to estimate survival based on individual patient factors , moving away from a one-size fits all approach (7, 13). This tool has been validated and improved to include molecular markers, like EGFR and HER2 status. This highlights the shift towards personalized medicine in neuro oncology (14).

The treatment options have grown significantly. For patients with a limited number of metastases, usually 1-4 , Level 1 evidence from randomized controlled trials (RCTs) has established stereotactic radiosurgery (SRS) alone as the standard of care. It provides similar overall survival while better preserving neurocognitive function compared to whole brain radiation therapy (WBRT) plus SRS (15, 16). This shift has caused a decline in the routine use of WBRT in high resource settings. Additionally, the role of WBRT has come under further scrutiny . Studies show that early WBRT does not improve overall survival compared to close monitoring with salvage therapy in patients with limited brain metastases (17).

The neurocognitive effects of WBRT are well known. The phase III NRG Oncology CC001 trial showed that hippocampal-avoidance WBRT (HA WBRT) combined with memantine significantly reduced the decline in neurocognitive function compared to standard WBRT with memantine (11). This has set HA-WBRT + memantine as a new standard for patients who need WBRT when the technology is available.

In resource limited environments, managing brain metastases (BM) and their outcomes is very different from what is seen in high-income countries. Studies from similar regions show a heavy reliance on whole brain radiotherapy (WBRT). This reliance stems from limited access to other treatments like neurosurgery and stereotactic radiosurgery (SRS), which leads to significantly worse survival rates.

Research from India highlights this issue. A retrospective review from Eastern India of 79 patients found a median overall survival (OS) of 7 months after WBRT. Survival rates varied by the primary site : lung cancer patients had a median OS of 6.5 months, while breast cancer patients had an OS of 8 months, which also depended on Recursive Partitioning Analysis (RPA) class (18, 19). In another study from North West India , the median OS was even lower at only 4 months for a group of 140 patients (20). Both studies identified lung and breast cancers as the most common primary tumors and confirmed that established factors such as RPA class, performance status and especially having a single metastasis are crucial for predicting outcomes in these regions.

More recently, a study from Indonesia showed that WBRT extended median survival to 6.9 months compared to 1.5 months for untreated patients, while surgery alone did not provide a significant benefit (21). This reinforces WBRT's role as a life extending treatment when other options are unavailable (21).

Similarly, a recent study from Nigeria further emphasized the palliative value of WBRT , reporting a median overall survival of 6 months, significant improvements in both physical and emotional functioning among survivors and identifying the Karnofsky Performance Status (KPS) as the most significant prognostic factor influencing survival (22).

These findings relate to a bigger issue faced by low and middle income countries (LMICs), as shown in a meta-analysis by O'Leary et al. on the neuro oncological situation in Africa (23). Their analysis of 28 studies involving 12,552 patients showed that breast cancer (41.33%) is the leading primary source of central nervous system (CNS) metastases in the continent , followed by lung cancer (14.85%). The high mortality rate (44.88%) and the fact that 21.29% of cases were diagnosed after death highlight delays in diagnosis and treatment . The study also pointed out severe shortcomings in diagnostic resources , with MRI being used in only 38.27% of cases, and noted significant regional differences in management and outcomes (23).

Overall these studies show that lower survival rates in LMICs result from late diagnosis, advanced disease at diagnosis and limited treatment options. They highlight the continued importance of prognostic factors like RPA and the extent of metastasis. Furthermore , they reveal a tough reality that WBRT is often the primary treatment option not because it is more effective, but because alternatives are lacking, often serving more to relieve symptoms than to

cure. This evidence is vital for understanding local outcomes and shaping future policies and clinical practices in resource limited situations.

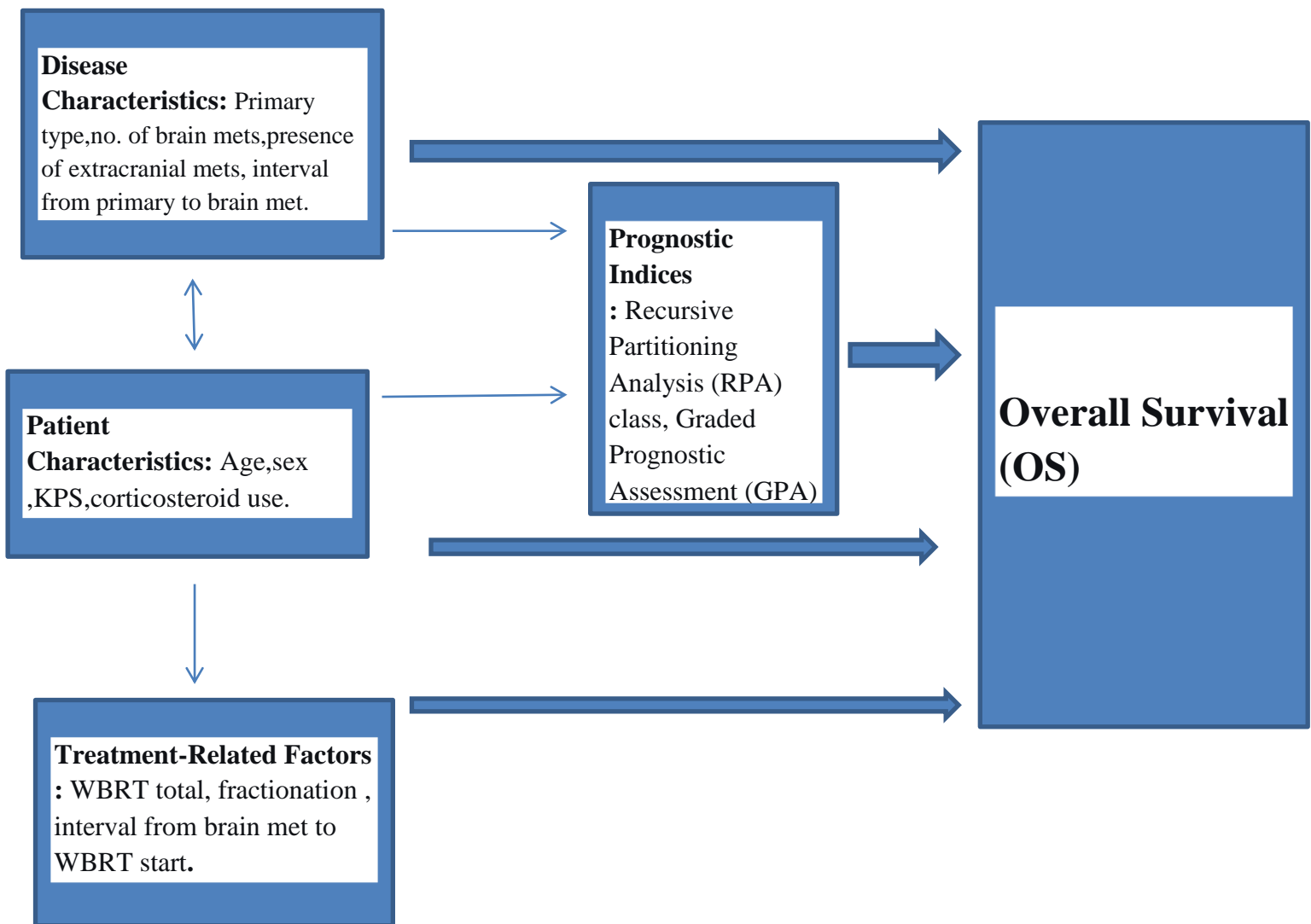


Figure 1: Conceptual Framework indicating possible relationship between Dependent and independent variables

3. OBJECTIVES

3.1. General Objective

- To assess survival outcomes and identify prognostic factors influencing overall survival in patients with brain metastases treated with Whole Brain Radiotherapy (WBRT) at Tikur Anbessa Specialized Hospital (TASH) between April 2020 and April 2024 .

3.2. Specific Objectives

1. To determine the survival outcomes for the cohort.
2. To identify factors affecting the survival outcomes of patients with brain metastases treated with Whole Brain Radiotherapy.
3. To apply standard prognostic indices (Recursive Partitioning Analysis (RPA) and Graded Prognostic Assessment (GPA)) where data permitted and to analyze their predictive value for survival in this cohort.

4. METHODS

4.1. Study setting and Period

This study was conducted at Addis Ababa University Oncology department (from October 7 2025 to December 15, 2025). 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.

4.2. Study Design

A retrospective study design was utilized.

4.3. Study Population

- **Source Population :** All adult patients with cancer diagnosed with brain metastases who presented at the TASH Oncology Department between April 2020 and April 2024.
- **Study Population :** All patients from the source population who received palliative Whole-Brain Radiotherapy (WBRT) at TASH and met the study's inclusion and exclusion criteria.

4.4. Inclusion and Exclusion Criteria

Inclusion Criteria

Patients met all of the following criteria:

1. Aged 18 years or older at the time of WBRT initiation.
2. Histologically or cytologically confirmed diagnosis of a solid malignant tumor (including carcinoma of unknown primary). Patients who had undergone neurosurgical resection for the current brain metastases before receiving WBRT were eligible.
3. New, radiologically confirmed (via CT or MRI) diagnosis of parenchymal brain metastasis(es).
4. Underwent at least one fraction of palliative WBRT at TASH between April 1, 2020, and April 1, 2024.
5. Possessed a medical record with sufficient retrievable data for analysis.

Exclusion Criteria

Patients were excluded based on any of the following criteria:

1. Received any prior cranial radiotherapy (e.g., prior WBRT or stereotactic radiosurgery).
2. Had leptomeningeal carcinomatosis as the only central nervous system manifestation at the time of WBRT planning (patients with concurrent parenchymal disease were eligible).
3. Received WBRT as prophylactic cranial irradiation (PCI) or for a primary brain tumor.
4. Initiated a new regimen of concurrent systemic therapy (including intrathecal chemotherapy, CNS-penetrating targeted therapy, or immunotherapy) within two weeks before or after starting WBRT (patients on a stable, ongoing regimen were eligible).

5. A pre-existing severe comorbid neurological condition (e.g., major stroke with persistent hemiplegia, advanced dementia) documented prior to the brain metastasis diagnosis that would independently confound survival assessment.
6. Had incomplete or missing medical records precluding adequate data collection.

4.5. Sample Size and Sampling Technique

Sample Size:

A census of all patients who met the inclusion criteria was included .

Sampling Technique:

A total population sampling approach was employed . All eligible patients identified from radiotherapy unit logs and medical records were included. This method minimized selection bias, ensured representativeness and was appropriate given the finite and accessible study population.

4.6. Study Variables

- **Dependent Variable**

- Overall Survival (OS)

- **Independent Variables**

- **Patient Characteristics** : Age , sex , Karnofsky Performance Status (KPS) , baseline corticosteroid use.
- **Disease Characteristics** : Primary cancer type , number of brain metastases , presence of extracranial metastases , interval from primary diagnosis to brain metastasis.
- **Treatment-Related Factors** : WBRT total dose , fractionation schedule , interval from brain metastasis diagnosis to WBRT start.
- **Prognostic Indices** : Recursive Partitioning Analysis (RPA) class, Graded Prognostic Assessment (GPA) score.

4.7. Operational Definitions

1. Overall Survival

- **Definition :** The duration of time from the start of Whole Brain Radiotherapy (WBRT) treatment to the date of death from any cause. For patients still alive at the time of analysis , survival was measured to the last confirmed date of follow-up.
- **Measurement :** Calculated in months from the WBRT start date to the date of death (event) or the last follow-up date (censored), using patient medical and follow up records.

2. Karnofsky Performance Status (KPS)

- **Definition :** A standardized score that quantifies a cancer patient's general functional capabilities and their ability to perform daily activities.
- **Measurement :** A numerical value between 0 (dead) and 100 (normal, no complaints) (**Annex 2**). For analysis , KPS was categorized into two groups (<70 and ≥ 70) based on established prognostic index cutoffs. This categorization aligned with both GPA scoring and RPA classification systems. As the Eastern Cooperative Oncology Group (ECOG) performance status is the standard metric documented at TASH, the KPS score was derived from the documented ECOG status using a validated conversion table (**Annex 3**)(24). The score was based on the assessment documented by the treating oncologist in the patient's record prior to the initiation of WBRT.

3. Number of Brain Metastases

- **Definition :** The total count of identifiable metastatic tumors within the brain.
- **Measurement :** The count of lesions identified on a contrast enhanced magnetic resonance imaging (MRI) scan, or computed tomography (CT) scan if MRI was contraindicated, performed closest to the time of WBRT planning. In cases where no recent imaging was available, the number of metastases was taken from the treating oncologist's documented assessment, ensuring that the source was clearly noted in the data extraction form. Categorized as 1, 2–3, or >3 for GPA scoring.

4. Presence of Extracranial Metastases

- **Definition :** The existence of metastatic disease outside of the brain at the time of brain metastasis diagnosis and WBRT planning.
- **Measurement :** Dichotomized as either "Present" or "Absent," based on a synthesis of all available imaging reports (e.g., CT, PET-CT, bone scan) within a period of 3 months prior to the start of WBRT. Where advanced imaging was unavailable , physician documentation of metastatic disease was accepted.

5. **WBRT Total Dose and Fractionation**

- **Definition :** The complete prescribed radiation dose for the WBRT course and its division into individual treatment sessions.
- **Measurement :** The total dose is recorded in Gray (Gy). The fractionation is recorded as the number of individual treatment sessions (fractions) delivered.

6. **Recursive Partitioning Analysis (RPA) Class**

- **Definition :** A prognostic classification system that groups patients based on age, Karnofsky Performance Status (KPS), and control of the primary cancer and extracranial metastatic disease.
- **Measurement :** Patients were assigned to Class I, II, or III using standard Radiation Therapy Oncology Group (RTOG) criteria applied to their clinical status (age, KPS, presence of extracranial metastases) at the time of WBRT(**Annex 4**) (19).

7. **Graded Prognostic Assessment (GPA) Score**

- **Definition :** A prognostic index that estimates survival for patients with brain metastases by weighting significant factors.
- **Measurement :** The original, non-diagnosis-specific GPA index was used for all patients (**Annex 5**). A cumulative score from 0.0 to 4.0 was calculated based on the following factors assessed at the time of WBRT: age, KPS, number of brain metastases, and presence of extracranial metastases. This decision was made for two key reasons: (1) feasibility, as the molecular data required for diagnosis specific GPA indices (e.g., Lung-molGPA) are not routinely available in our setting, and (2) to allow for the application of a uniform prognostic tool across the entire cohort, which includes diverse primary cancer types. The original GPA has been validated and widely used in similar resource limited contexts for these practical reasons (25).

4.8 Data Collection Methods and Procedures

Patient information was systematically extracted from three primary sources : electronic medical records (EMRs) , paper charts and departmental radiotherapy unit logs. To ensure data uniformity and reliability a standardized data extraction form (Annex 1) was employed. The extraction was conducted by trained oncology residents who underwent a dedicated training session. This training covered the precise definitions of all study variables, the protocol for converting Eastern Cooperative Oncology Group (ECOG) scores to Karnofsky Performance Status (KPS) and the methodologies for calculating the Recursive Partitioning Analysis (RPA) class and Graded Prognostic Assessment (GPA) score.

Data was collected across the following categories:

1. **Patient Identification and Follow up** : Unique patient study ID, vital status (alive/deceased), and dates of death or last confirmed followup.
2. **Demographics** : Age and sex.
3. **Clinical Status** : Karnofsky Performance Status (KPS) at the time of Whole Brain Radiotherapy (WBRT) initiation and baseline corticosteroid use (Yes/No).
4. **Disease Characteristics** : Primary cancer type, date of primary diagnosis, date of brain metastasis diagnosis, number of brain metastases and the presence of extracranial metastases.
5. **Treatment Characteristics** : WBRT start date, total radiation dose (Gy) and number of fractions delivered.
6. **Prognostic Scores** : Calculated RPA Class and GPA Score.
7. **Calculated Time Intervals** : Interval from primary cancer diagnosis to brain metastasis diagnosis and interval from brain metastasis diagnosis to the start of WBRT.

Procedure for Ascertaining Vital Status and Follow-up

Accurate determination of vital status and the last follow up date was critical for the calculation of Overall Survival (OS). A multi step procedure was implemented :

1. **Primary Ascertainment** :
Vital status (alive/deceased), date of death (if applicable), and all dates of clinical encounters were initially extracted from EMRs, paper charts and radiotherapy logs.
2. **Definition of Last Follow up Date** :
 - For **living patients**, the last follow up date was defined as the date of the most recent confirmed contact.

- If a recent clinic visit (within 1 month of the study period) was documented, the patient was considered alive and this visit date was used for censoring in survival analysis.
- If no recent visit was documented, an active confirmation process was initiated.

3. **Active Confirmation:**

- For patients without a recent documented visit or record of death, vital status was actively confirmed via a sensitive telephone call to the patient's listed family member or emergency contact.
- The caller identified themselves as a research team member, explained the purpose of the follow up in the context of the study and respectfully confirmed the patient's current status and if applicable the date of death.
- A confirmed living status provided a new, verified last follow-up date for censoring.

4. **Lost to Follow-up Classification:**

- A patient was classified as "lost to follow-up" only after exhaustive contact attempts (e.g., unreachable phone numbers, no response to calls) had failed.
- In such cases the date of their last documented clinical encounter from the records was used as the censoring date for survival analysis.

4.9 Data Management

All collected data was entered into a secure, password protected database created using statistical software. To maintain strict patient confidentiality, a unique study identification number was assigned to each participant , no personally identifiable information (PII) was entered into the analysis database.

Physical data collection sheets (hard copies) were stored securely in a locked cabinet within the principal investigator's office. Electronic data was stored exclusively on an encrypted computer. Access to both physical and electronic data was restricted to authorized members of the research team only

4.10 Data Analysis

Data Cleaning and Coding :

- Data was entered, coded and checked for accuracy and consistency.

Descriptive Statistics :

- Continuous variables were summarized using mean \pm SD or median (IQR), and categorical variables were summarized using frequencies and percentages.

Survival Analysis :

- Overall survival (OS) was estimated using the Kaplan Meier method.
- Median survival with 95% confidence intervals was reported.
- Group comparisons were performed using the log-rank test (KPS category).

Prognostic Factor Analysis :

- Prognostic factors were analyzed using univariate Cox regression to estimate hazard ratios (HR) with 95% confidence intervals , and multivariate Cox regression included variables that were significant in univariate analysis.

Software and Significance:

- Analyses were conducted using SPSS.
- A p-value < 0.05 was considered statistically significant.

4.11. Ethical statement

Ethical clearance and approval for the study were obtained from the Institutional Ethics Review Board of the Health Institute, Addis Ababa University. Permission was obtained from AAU administration, and patient privacy was maintained.

4.12. Dissemination plan

The findings of this study will be presented to the department of Clinical Oncology for thesis defense. Summary report will be submitted to AAU and result will also be communicated to clinicians who treat the patient to identify factors that could be focused on to improve outcome in this setting. Effort will be made to publish the findings in peer reviewed journals.

5. RESULTS

5.1. Baseline Patient Characteristics

Between April 1, 2020, and April 1, 2024, a total of 110 patients were identified from the radiotherapy unit logbook at Tikur Anbessa Specialized Hospital (TASH). Following the application of pre-defined inclusion and exclusion criteria, 70 eligible patients with radiologically confirmed brain metastases (BMs) who received whole-brain radiotherapy (WBRT) were included in this retrospective study.

Forty patients were excluded for the following reasons : 25 had incomplete medical records , 8 received radiotherapy as primary treatment for a brain tumor , 5 presented with leptomeningeal carcinomatosis as their only central nervous system manifestation, and 2 initiated a new concurrent targeted therapy regimen within two weeks of starting WBRT.

The demographic and clinical characteristics of the final patient cohort are summarized in **Table 1**. Half of the patients (50.0%, n=35) were under 50 years of age, 30.0% (n=21) were aged 50–60 years, and 20.0% (n=14) were older than 60 years. The majority of patients were female (68.6%, n=48), reflecting the high prevalence of breast cancer as a primary tumor source.

Karnofsky Performance Status (KPS) was ≥ 70 in 57.1% (n=40) of patients , while 42.9% (n=30) had a KPS < 70 . Baseline corticosteroid use was common with 90.0% (n=63) of patients receiving steroids prior to or during WBRT.

Breast cancer was the most frequent primary malignancy (45.7%, n=32) followed by non-small cell lung cancer (NSCLC) (28.6%, n=20). Other primary tumors included renal cell carcinoma (7.1%, n=5) , melanoma (7.1%, n=5) , small cell lung cancer (SCLC) (4.3%, n=3) and other cancers (7.1%, n=5).

Most patients presented with a high intracranial disease burden: 58.6% (n=41) had ≥ 4 brain metastases, while 14.3% (n=10) had a single metastasis. Extracranial metastases were present in 85.7% (n=60) of patients. Brain metastases developed within 6 months of the primary cancer diagnosis in 52.8% (n=37) of cases. The interval from BM diagnosis to initiation of WBRT was ≤ 2 weeks for 35.7% (n=25) , 2–4 weeks for 48.6% (n=34) and > 4 weeks for 15.7% (n=11).

According to Recursive Partitioning Analysis (RPA), 10.0% (n=7) were Class I, 47.1% (n=33) Class II and 42.9% (n=30) Class III. Graded Prognostic Assessment (GPA) scores were 0–1.0 in 54.3% (n=38), 1.5–2.5 in 44.3% (n=31), and 3.0 in 1.4% (n=1).

Table 1. Baseline patient and disease characteristics (N=70)

Characteristic	Frequency (n)	Percentage (%)
Age (years)		
<50	35	50.0
50–60	21	30.0
>60	14	20.0
Sex		
Female	48	68.6
Male	22	31.4
Karnofsky Performance Status (KPS)		
<70	30	42.9
≥70	40	57.1
Baseline Corticosteroid Use		
Yes	63	90.0
No	7	10.0
Primary Cancer Type		
Breast cancer	32	45.7
Lung (NSCLC)	20	28.6
Renal cell carcinoma	5	7.1

Characteristic	Frequency (n)	Percentage (%)
Melanoma	5	7.1
Lung cancer (SCLC)	3	4.3
Other	5	7.1
Number of Brain Metastases		
1	10	14.3
2–3	19	27.1
≥4	41	58.6
Extracranial Metastases		
Yes	60	85.7
No	10	14.3
Interval: Primary DX to BM DX		
<6 months	37	52.8
7–24 months	16	22.9
≥24 months	17	24.3
Interval: BM DX to WBRT Start		
≤2 weeks	25	35.7
2–4 weeks	34	48.6

Characteristic	Frequency (n)	Percentage (%)
>4 weeks	11	15.7
RPA Class		
Class I	7	10.0
Class II	33	47.1
Class III	30	42.9
GPA Score		
0–1.0	38	54.3
1.5–2.5	31	44.3
3.0	1	1.4

Abbreviations: BM, brain metastases; DX, diagnosis; GPA, Graded Prognostic Assessment; KPS, Karnofsky Performance Status; NSCLC, non-small cell lung cancer; RCC, renal cell carcinoma; RPA, Recursive Partitioning Analysis; SCLC, small cell lung cancer; WBRT, whole-brain radiotherapy.

5.2. Treatment Details

The majority of patients (91.4% , n=64) received a hypofractionated WBRT regimen of 20 Gy in 5 fractions. A smaller proportion (8.6% , n=6) received 30 Gy in 10 fractions. Prior neurosurgical intervention was rare with only one patient (1.4%) undergoing resection before WBRT.

A risk-adapted treatment strategy was observed : all 63 patients with poorer prognosis (RPA Class II/III) received short course palliative radiation (20 Gy/5 fractions). In contrast 85.7% (6 of 7) of favorable-prognosis RPA Class I patients received a longer course (30 Gy/10 fractions) (**Figure 2**) .

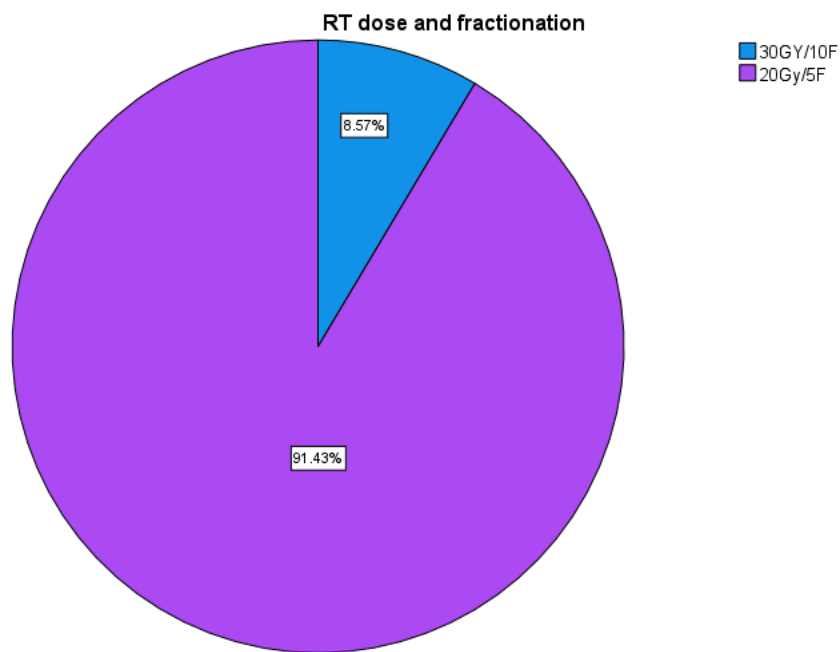


Figure 2. Whole-brain radiotherapy dose–fractionation patterns among study patients

5.3. Survival Outcomes

By the end of the study period, 90% (n=63) of patients had died. The median overall survival (OS) from the start of WBRT was **4.7 months** (95% confidence interval [CI]: 3.7–5.7 months). The 6 month OS rate was 38% and the 12 month OS rate was 14% (**Figure 3**).

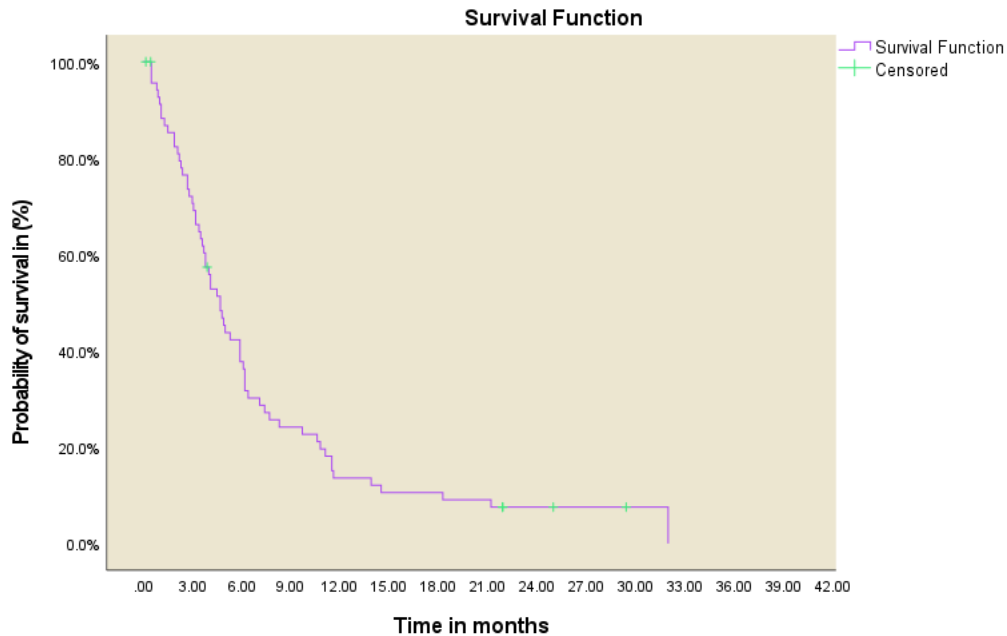


Figure 3. Kaplan–Meier curve showing overall survival of the cohort

5.4. Survival Stratified by Performance Status

Overall survival differed significantly by KPS. Patients with KPS ≥ 70 had a median OS of **6.4 months** (95% CI: 4.9–7.9 months) compared to **2.4 months** (95% CI: 1.6–3.2 months) for those with KPS < 70 (logrank $p < 0.001$). The 6-month OS rates were 58% for KPS ≥ 70 versus 5% for KPS < 70 . At 12 months survival was 20% for KPS ≥ 70 and 5% for KPS < 70 (**Figure 4**).

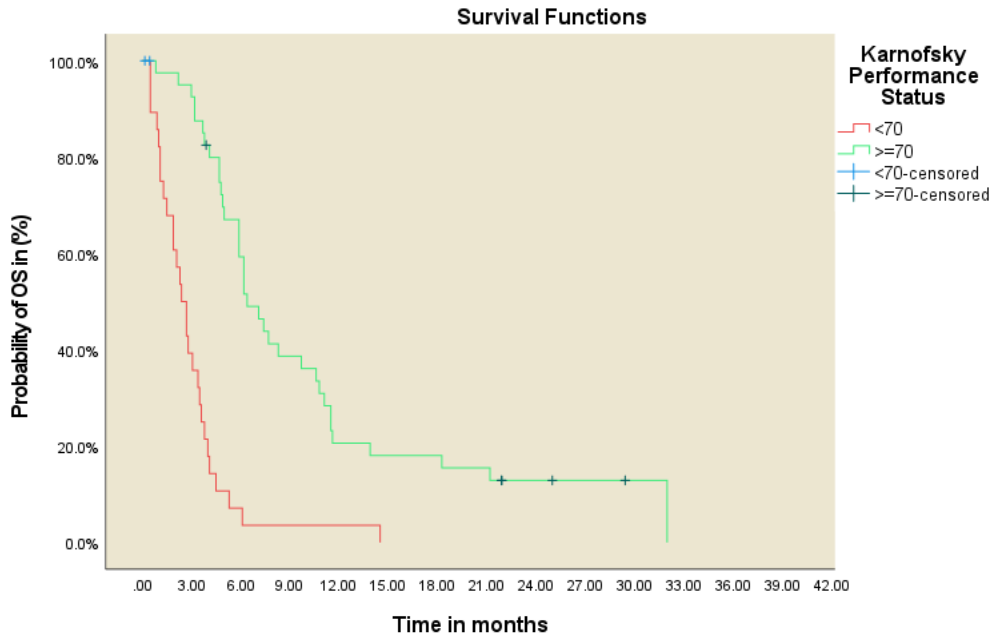


Figure 4 . Kaplan–Meier estimates of overall survival stratified by Karnofsky Performance Status

5.5. Prognostic Factors for Overall Survival: Univariable Analysis

In univariable Cox regression analysis (**Table 2**) several factors were significantly associated with survival :

- **KPS $\geq 70\%$** was strongly associated with improved survival (HR = 0.10 , 95% CI: 0.05–0.22, $p < 0.001$).
- **RPA Class III** (vs. Class I) was associated with worse survival (HR = 6.70 , 95% CI: 2.6–16.9, $p < 0.001$).
- **Delayed WBRT initiation (>4 weeks after BM diagnosis)** was associated with significantly worse outcomes (HR = 6.50 , 95% CI: 2.7–15.3, $p < 0.001$).
- **Higher GPA score (1.5–2.5 vs. 0–1.0)** predicted better survival (HR = 0.38 , 95% CI: 0.22–0.64 , $p < 0.001$).
- **Longer interval from primary diagnosis to BM (>6 months)** was protective (HR = 0.34–0.39, $p = 0.002$).
- **Primary tumor type** : Breast cancer histology predicted better survival (HR = 0.40, 95% CI: 0.2–0.70, $p = 0.004$), while SCLC (HR = 9.7 , 95% CI: 2.4–38, $p < 0.001$) and melanoma (HR = 5.3, 95% CI: 1.7–16, $p = 0.003$) predicted poorer survival compared to NSCLC.

5.6. Prognostic Factors for Overall Survival: Multivariable Analysis

In the multivariable Cox regression model (**Table 2**), adjusting for all significant univariable factors, only two variables remained independent predictors of OS:

1. **KPS $\geq 70\%$** (HR = 0.10, 95% CI: 0.016–0.67, p = 0.017).
2. **Time from BM diagnosis to WBRT initiation:**
 - Delay of 2–4 weeks: HR = 2.02 (95% CI: 1.02–4.0, p = 0.043)
 - Delay of >4 weeks: HR = 7.08 (95% CI: 2.47–20.30, p < 0.001)

Other factors, including RPA class, GPA score, primary tumor type, and interval from primary to BM diagnosis, were no longer statistically significant in the multivariable model, suggesting their effects were confounded by or mediated through performance status and treatment timing.

Table 2. Univariable and multivariable Cox regression analysis for overall survival

Variable	Category	Univariable HR (95% CI)	p- value	Multivariable HR (95% CI)	p- value
KPS	<70% (Ref)	1.00	–	1.00	–
	$\geq 70\%$	0.10 (0.05– 0.22)	<0.001	0.10 (0.016– 0.67)	0.017
RPA Class	Class I (Ref)	1.00	–	1.00	–
	Class II	1.52 (0.62– 3.30)	0.31	1.17 (0.41–3.33)	0.76
	Class III	6.70 (2.6–16.9)	<0.001	1.47 (1.05–4.22)	0.50
GPA Score	0–1.0 (Ref)	1.00	–	1.00	–
	1.5–2.5	0.38 (0.22–	<0.001	0.40 (0.18–0.91)	0.80

Variable	Category	Univariable HR (95% CI)	p- value	Multivariable HR (95% CI)	p- value
		0.64)			
	3.0	0.34 (0.04– 2.53)	0.21	0.65 (0.06–6.85)	0.72
Interval Primary to BM	≤6 mo (Ref)	1.00	–	1.00	–
	6–24 mo	0.39 (0.22– 0.72)	0.002	0.78 (0.36–1.66)	0.52
	>24 mo	0.34 (0.17– 0.67)	0.002	0.59 (0.22–1.55)	0.28
Interval BM to WBRT	≤2 wk (Ref)	1.00	–	1.00	–
	2–4 wk	1.50 (0.9–2.7)	0.09	2.02 (1.02–4.0)	0.043
	>4 wk	6.50 (2.7–15.3)	<0.001	7.08 (2.47– 20.30)	<0.001
Primary Cancer	NSCLC (Ref)	1.00	–	1.00	–
	SCLC	9.70 (2.4–38)	<0.001	3.21 (0.81– 14.30)	0.093
	Breast	0.40 (0.2–0.70)	0.004	0.61 (0.28–1.33)	0.27
	RCC	2.40 (0.8–7.0)	0.087	1.85 (0.58–5.93)	0.29

Variable	Category	Univariable HR (95% CI)	p- value	Multivariable HR (95% CI)	p- value
	Melanoma	5.30 (1.7–16)	0.003	6.50 (0.71–24.6)	0.06
	Other	0.60 (0.2–1.8)	0.30	0.96 (0.27–3.34)	0.94

Abbreviations: BM, brain metastasis; CI, Confidence Interval; HR, Hazard Ratio; KPS, Karnofsky Performance Status; NSCLC, Non-Small Cell Lung Cancer; RCC, Renal Cell Carcinoma; RPA, Recursive Partitioning Analysis; SCLC, Small Cell Lung Cancer; WBRT, Whole-Brain Radiotherapy.

6. DISCUSSION

This is the first retrospective study which focuses on survival results and prognostic markers for patients with brain metastases on whole brain radiotherapy at Tikur Anbessa Specialized Hospital Ethiopia, a setting of care typical in many resource limited healthcare systems in Sub Saharan Africa. Our results emphasize both the palliative value of WBRT and the significant difference patient performance status and systemic time delays in treatment initiation make to survival.

6.1. Interpretation of Survival Results: Similar Results

The median overall survival (OS) in the present study, 4.7 months, is in accordance with results found in similar low and middle income country (LMIC) settings where WBRT is the bedrock of care. Studies in India such as Jakhar et al. and Sammaddar et al. have reported the median OS as 4-7 months (18, 20). More recently, reports from Nigeria by Adegboyega et al., and from Indonesia by Andriani et al. reported median survivals of 6.0 and 6.9 months respectively (21, 22). Our estimate is at the lower end of this regional spectrum, a finding that is most likely due to the disease burden in our cohort, with 58.6% presenting with ≥ 4 brain metastases in general, 85.7% with extracranial metastases and only 10.0% in the favorable Recursive Partitioning Analysis (RPA) Class I (19). Such a profile indicates late stages of the patient presentation and is consistent with meta analytic results by O'Leary et al., which emphasized diagnostic delay and advanced disease as hallmarks of neurooncological consideration in Africa (23). The reported 6 month and 12 month survival rates of 38% and 14% respectively correspond with the anticipated drop from the unpublished preliminary TASH data which was 55% for 3 months and 17% at 6

months (Dr. Semira). Although both datasets do not immediately correlate because of differences in timeline, they both highlight the poor prognosis associated with brain metastases in this setting and the importance of earlier diagnosis and intervention.

6.2. Performance Status and The Paramount Importance of This Study

Our study's most telling finding was the striking finding that the Karnofsky Performance Status (KPS) had the overwhelming prognostic significance. Patients with $KPS \geq 70$ had a median overall survival (OS) of 6.4 months, nearly three times the time period that of patients with $KPS < 70$ (2.4 months). In a multivariable analysis, $KPS \geq 70$ was found to result in a 90% reduction in the hazard of death ($HR=0.10$), thus showing it a robust independent prognostic predictor of survival. This is also robust to global literature. Performance status is a bedrock of established prognostic metrics such as the Recursive Partitioning Analysis (RPA) proposed by Gaspar et al. and the Graded Prognostic Assessment (GPA) introduced by Sperduto et al. (7, 13, 19). Its primacy has been repeatedly replicated in LMIC neuro-oncology studies, including that of Jakhar et al. which came from India and the new results in Adegboyega et al. from Nigeria (20, 22). Our results support that, in a resource-poor environment and resource/resource shortage due to lack of advanced imaging and molecular profiling, such a simple clinical assessment of performance status is still a valuable and available tool for stratifying risk, counselling patients and conducting clinical decisions.

6.3. The Detrimental Impact of Treatment Delay

An independent finding specific to our operational setting is a novel and important finding: there is also strong independent association between delays in initiating WBRT and higher mortality. Patients who began WBRT more than 4 weeks in time after BM diagnosis also had a seven times greater risk of death ($HR=7.08$) relative to those who began treatment within 2 weeks. Even 2–4 weeks later then the mortality hazard was twice that ($HR=2.02$). This in turn implies that the extent to which palliative radiation reaches a patient in cases of severe disease, such as brain metastases, is a key effect. Delays may result due to the logistical obstacles common to low-resource settings (inadequate machine time, patient transport, referral bottleneck, or bureaucratic red tape) as emphasized in the meta-analysis conducted by O'Leary and colleagues on CNS metastases in Africa (23). This finding has direct health system implications: optimizing referral pathways, scheduling appointments of BM patients, and ensuring stability of radiotherapy machines are significant, low-cost interventions with the potential to demonstrate quantitatively improved survival outcomes.

6.4. Prognostic Indices and Tumor-Specific Survival Patterns

RPA class and GPA score, on the other hand, were significantly associated with survival in univariable analysis; their significance was lost in the multivariable estimate. This was probably

because their major dimension—performance status—was measured individually, and this does not detract from the worth of these validated indices (7, 13, 19). The predominance of breast cancer (45.7%) as BM's main source in the current group accords with the spread across Africa: >40% of central nervous system metastases originate from breast cancer (23). The increasing tendency towards superior survival within breast cancer patients and poorer survival in small-cell lung cancer (SCLC) and melanoma is also in line with established tumor biology and in agreement with the diagnosis-specific GPA structure, as described by Sperduto et al. (13). However, the loss of importance for histology in the multivariable analysis suggests that the aggressive biology of certain tumors is often expressed clinically as poorer performance status, and this serves as the most proximate predictor of survival.

6.5. Outcome Disparity: Comparison to High-Income Country Benchmarks.

The survival implications from our study are in strong contrast to the recent benchmarks from high-income countries (HICs), highlighting a deep global inequity in neuro-oncological care. This paradigm of management in HICs progressed from a standardised and one-size-fits-all WBRT protocol to a personalized, multimodal approach. This transition has been endorsed by Level I evidence from randomized trials, which includes the RTOG 9508 trial (Andrews et al.) and the JROSG 99-1 trial conducted by Aoyama et al., demonstrating that stereotactic radiosurgery (SRS) is a standard with superior cognitive preservation and equal or improved survival in patients with limited metastases (15, 16). In addition, the phase III NRG Oncology CC001 trial conducted by Brown et al. introduced hippocampal-avoidance WBRT (HA-WBRT) with memantine as a new cognitive-preserving standard in patients who needed whole brain irradiation (11). At the same time, targeting as well as immunotherapy in this way have, as discussed by Achrol et al., increased median survival of a great number of patients beyond 12 months (14). In our setting, the sole dependence on orthodox WBRT, absence of SRS, and the absence of regular molecular profiling result in a therapeutic differential which is mirrored in our observed survival difference. This comparison highlights that survival is not purely a result of tumor biology but is deeply dependent on the resource- and ability-richness of the healthcare system.

6.6. Clinical Practice and Health System Implications

We have substantiated that WBRT is associated with a significant survival benefit where advanced alternatives are limited. The benefit of risk-adapted fractionation which is a longer course (30 Gy/10 fractions) for a majority of RPA Class I patients in which there are no larger interventions, is a reflection of a cautious use of evidence available in face of resource limitations. To improve results, a variety of solutions are required:

1. Early Diagnosis: Increasing the community and professional understanding of cancer patients' symptoms in the neurological domain, and also providing access to neuroimaging, according to O'Leary et al. (23).
2. Health System Reform: Measures to close the treatment initiation delays described in this study.
3. Strategic Investment: It is essential to invest strategically, as gaining SRS capability is a long-term goal, but at this time several intermediate steps would help avoid neurocognitive toxicity by testing HA-WBRT techniques as a solution (11), thereby addressing the feasibility.
4. Integration of Palliative Care: Given the poor survival of patients with low KPS, the early integration of palliative care alongside radiotherapy is essential to optimize quality of life.

6.7. Limitations

However, this study has limitations due to the retrospective, single center design of this study. The size of the sample – though adequate for the current study – restricts subgroup study investigation methods. Information on systemic medications, specific systemic treatments, specific neurocognitive outcomes and cause of death were not consistently available, potentially confounding the analysis of patient survival. Due to lack of testing, the GPA scores could not incorporate molecular subtypes making it less precise. Finally, results from a national referral hospital may not be completely generalizable to regional centers in Ethiopia.

6.8. Conclusion

Finally, this study provides a key baseline to elucidate the management of brain metastases with WBRT at TASH, Ethiopia. The median survival was 4.7 months, significantly affected by patient performance status and substantially worsened with delay in treatment initiation by a patient. While WBRT is still an important palliative tool, these findings emphasize the significant demand for earlier diagnosis, faster care pathways and health system strengthening in order to help maximize survival and quality of life for cancer patients with brain metastases in resource-limited settings. This data set establishes the groundwork of prospective studies, clinical quality improvement initiatives and promotion of improved neurooncology resources in Ethiopia..

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8. ANNEXES

Annex 1 : STANDARDIZED DATA COLLECTION TOOL

Section A: Patient Identification & Follow-up

- Phone number: _____; _____
- Patient Record Number: _____
- Source of Data: (1) EMR (2) Paper Chart (3) Radiotherapy Log (4) Other _____
- Vital Status: (1) Alive (2) Deceased
- Date of Death: ____ (DD/MM/YYYY)
- Last Date of Follow-up: ____ (DD/MM/YYYY) (Date of last clinic note)
- PII Handling Confirmed – Phone number and personal identifiers stored separately and excluded from analysis dataset

Section B : Demographic & Clinical Characteristics

- Age at WBRT Start (Years): _____
- Sex: (1) Male (2) Female
- ECOG Performance Status at WBRT Start: (0) 0 (1) 1 (2) 2 (3) 3 (4) 4
- Calculated KPS Score (from Annex 3): _____ (0–100)
- On Corticosteroids at Baseline? (1) Yes (2) No

Section C: Disease Characteristics

- Primary Cancer Type:
(1) Lung NSCLC (2) Lung SCLC (3) Breast (4) Colorectal (5) Renal (6) Melanoma
(7) Other: _____
- Date of Primary Cancer Diagnosis: ____ (DD/MM/YYYY)
- Date of Brain Metastasis Diagnosis (Imaging): ____ (DD/MM/YYYY)
- Number of Brain Metastases: _____
- Imaging Modality Used for BM Assessment:
(1) MRI with contrast (2) CT with contrast (3) Clinical/Presumed (4) Other _____
- Extracranial Metastases Present? (1) Yes (2) No

- Primary Tumor Control Status at WBRT Start:
(1) Controlled/Stable (2) Progressive (3) Unknown
- Prior Neurosurgery for BM: (1) Yes (2) No → If Yes, Type: (1) Resection (2) Biopsy
Date: _____
- Prior Cranial RT or SRS: (1) Yes (2) No → If Yes, specify type & date:

Section D: Treatment Characteristics

- WBRT Start Date: ____ (DD/MM/YYYY)
- WBRT Total Dose (Gy): _____ Gy
- Number of Fractions: _____
- WBRT Completed as Planned? (1) Yes (2) No → If No, reason: _____
- Receiving Systemic Therapy during WBRT? (1) Yes (2) No

If Yes, Specify Agent(s): _____
Start Date: _____ End Date (if applicable): _____

Section E: Calculated Time Intervals (to be calculated after data entry)

- Interval from Primary Dx to BM Dx (Months): _____
- Interval from BM Dx to WBRT Start (Days): _____ / (Months): _____

Section F: Prognostic Scores Calculation (based on data above)

- RPA Class: (1) I (2) II (3) III
- GPA Score: _____ (0.0 – 4.0)

Notes/Comments:

ANNEX 2: Karnofsky Performance Status (KPS) Scale

Purpose: To standardize the assessment of a patient's functional status, which is critical for determining both RPA class and GPA score.

Score	Description
100	Normal, no complaints; no evidence of disease.
90	Able to carry on normal activity; minor signs or symptoms of disease.
80	Normal activity with effort; some signs or symptoms of disease.
70	Cares for self; unable to carry on normal activity or do active work. (Key distinction)
60	Requires occasional assistance but is able to care for most of their needs.
50	Requires considerable assistance and frequent medical care.
40	Disabled; requires special care and assistance.
30	Severely disabled; hospitalization is indicated, although death not imminent.
20	Very sick; hospitalization necessary; active supportive treatment necessary.
10	Moribund; fatal processes progressing rapidly.
0	Dead

How to Use: The score should be based on the clinician's documented assessment in the record closest to the WBRT start date. If not explicitly documented, the data collector must infer it from clinical notes (e.g., "patient bedbound" \approx KPS 30-40; "patient walks with assistance" \approx KPS 50-60; "fully independent" \approx KPS 90-100). This inferred score must be based on clear evidence in the record.

ANNEX 3: ECOG to KPS Conversion Table

Purpose: To standardize the conversion from the Eastern Cooperative Oncology Group (ECOG) performance status, routinely used at TASH, to the Karnofsky Performance Status (KPS) score required for calculating RPA class and GPA score.

ECOG Performance Status	Karnofsky Performance Status (KPS)	Description
0	90-100%	Fully active, able to carry on all pre-disease performance without restriction.
1	70-80%	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature.
2	50-60%	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.
3	30-40%	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours.
4	10-20%	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.
5	0%	Dead.

How to Use:

1. Identify the ECOG performance status documented in the patient's record closest to the WBRT start date.
2. Use the table above to convert the ECOG score to the corresponding KPS range.

ANNEX 4: Recursive Partitioning Analysis (RPA) Classification Criteria

Purpose: To assign a standard prognostic class based on age, Karnofsky Performance Status (KPS), and status of systemic disease.

Classification Criteria:

RPA Class	Criteria
Class I	All of the following: <ul style="list-style-type: none">• Age < 65 years• Karnofsky Performance Status (KPS) ≥ 70• Controlled primary tumor• No extracranial metastases
Class II	All patients not qualifying for Class I or Class III. <ul style="list-style-type: none">• This is the most common, heterogeneous group.
Class III	<ul style="list-style-type: none">• Karnofsky Performance Status (KPS) < 70

Notes for Data Collectors:

- **Controlled primary tumor** is defined as the primary tumor being treated and in complete remission or stable disease.
- If any of the criteria for Class I are not met *and* the KPS is ≥ 70 , the patient is classified as **Class II**.
- The key determinant for **Class III** is low functional status (KPS < 70), regardless of other factors.

ANNEX 5: Graded Prognostic Assessment (GPA) Index

Purpose: To calculate a general prognostic score from 0.0 to 4.0 based on four key factors. This is the original, non-diagnosis-specific index and will be used for all cancer types where a diagnosis-specific GPA is not available or applicable.

Scoring System:

Prognostic Factor	Criteria	Score
Age	> 60 years	0
	50 – 59	0.5
	< 50 years	1.0
Karnofsky Performance Status (KPS)	< 70	0
	70–80	0.5
	90–100	1.0
Number of Brain Metastases	> 3	0
	2–3	0.5
	1	1.0
Extracranial Metastases	Present	0
	Absent	1.0

How to Calculate the GPA Score:

1. For each of the four factors (Age, KPS, Number of Brain Mets, Extracranial Mets), assign the corresponding score (0, 0.5, or 1.0) based on the patient's status at the time of WBRT.
2. Sum the scores from all four factors.
3. The total score will be a number between **0.0 and 4.0**.