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CLINICAL OUTCOMES AND PROGNOSTIC FACTORS OF RADIOTHERAPY IN LOCALLY ADVANCED CERVICAL CARCINOMA

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Abstract

Locally advanced cervical carcinoma (LACC) remains a major global health challenge, particularly in low- and middle-income countries where late presentation is common. Radiotherapy, combined with concurrent chemotherapy, is the standard treatment; however, clinical outcomes vary significantly due to multiple prognostic factors. This study aimed to evaluate clinical outcomes and identify prognostic determinants of radiotherapy in patients with LACC. A quantitative, descriptive-correlational design was employed, involving 180 patients treated at tertiary care oncology centers. Data were collected through structured clinical record review forms and analyzed using SPSS version 26. Descriptive statistics, chi-square tests, Kaplan–Meier survival analysis, and Cox regression modeling were applied. The findings revealed that concurrent chemoradiotherapy was administered to 67.8% of patients, with an overall treatment response rate of 70%. The 2-year survival rate was 62.2%. Significant prognostic factors included FIGO stage, tumor size, lymph node involvement, and hemoglobin level ($p < 0.05$). Cox regression analysis identified lymph node positivity as the strongest predictor of poor survival (HR = 2.76), while concurrent chemoradiotherapy demonstrated a significant survival benefit. The study concludes that radiotherapy outcomes in LACC are strongly influenced by tumor burden and patient-related clinical factors, emphasizing the importance of early diagnosis and individualized treatment strategies. The findings highlight the need for improved staging, timely treatment, and integrated chemoradiotherapy approaches to optimize survival outcomes in cervical cancer patients.

INTRODUCTION

Cervical carcinoma remains one of the most common gynecological malignancies and a leading cause of cancer-related morbidity and mortality among women globally, particularly in low- and middle-income countries. Locally advanced cervical carcinoma (LACC), typically classified as FIGO stages IIB to IVA, represents a clinically challenging stage where surgical options are limited and radiotherapy, often combined with chemotherapy, becomes the mainstay of treatment. Despite significant advancements in radiation oncology, including the development of intensity-modulated radiotherapy (IMRT) and concurrent chemoradiotherapy (CCRT), treatment outcomes remain heterogeneous across patient populations (Bray et al., 2021; Cohen et al., 2019).

Radiotherapy plays a central role in the management of LACC due to its ability to achieve locoregional tumor control. Standard treatment protocols typically include external beam radiotherapy (EBRT) combined with intracavitary brachytherapy, with or without concurrent cisplatin-based chemotherapy. This multimodal approach has improved overall survival and disease-free survival; however, treatment response

varies significantly depending on tumor biology, stage at diagnosis, and patient-related factors (Kumar et al., 2022).

Recent evidence suggests that prognostic factors such as tumor size, lymph node involvement, hemoglobin level, performance status, and treatment duration significantly influence clinical outcomes in cervical cancer patients undergoing radiotherapy. In particular, anemia and hypoxia have been identified as critical determinants of radioresistance, leading to reduced tumor control and poorer survival outcomes (Tanderup et al., 2020).

In addition, advancements in imaging techniques, such as magnetic resonance imaging (MRI) and positron emission tomography-computed tomography (PET-CT), have improved staging accuracy and treatment planning. These technologies allow better tumor delineation and adaptive radiotherapy strategies, contributing to improved local control rates. However, despite technological progress, recurrence and treatment failure remain significant challenges, especially in resource-constrained healthcare settings (Viswanathan et al., 2021).

Furthermore, disparities in access to timely diagnosis, radiotherapy facilities, and concurrent chemotherapy contribute to variation in survival outcomes across different populations. Patients in low-resource settings often present with advanced disease and experience delays in treatment initiation, which negatively impacts prognosis. Therefore, understanding the factors influencing radiotherapy outcomes is essential for improving clinical decision-making and optimizing treatment strategies.

Given the increasing burden of cervical cancer and the variability in treatment response, there is a critical need to systematically evaluate clinical outcomes and identify prognostic determinants associated with radiotherapy in LACC. Such evidence is essential for enhancing individualized treatment planning and improving survival outcomes.

Problem Statement

Despite advances in radiotherapy techniques and the integration of concurrent chemotherapy, locally advanced cervical carcinoma continues to demonstrate variable clinical outcomes, with a substantial proportion of patients experiencing disease recurrence, treatment resistance, or suboptimal survival. Although radiotherapy remains the cornerstone of treatment for LACC, its effectiveness is influenced by multiple prognostic factors that are not yet fully understood or consistently evaluated in clinical practice.

Existing literature has identified several potential prognostic indicators, including tumor stage, lymph node involvement, hemoglobin levels, and treatment duration. However, findings remain inconsistent across studies due to variations in patient populations, treatment protocols, and healthcare settings. Furthermore, most studies are conducted in high-income countries, while limited evidence is available from low- and middle-income regions where cervical cancer burden is highest.

Another critical gap lies in the limited integration of clinical, demographic, and treatment-related variables into comprehensive prognostic models. Many studies focus on isolated factors rather than evaluating their combined impact on survival and treatment response. Additionally, there is insufficient evidence regarding how modern radiotherapy techniques and concurrent chemoradiotherapy influence long-term outcomes in real-world clinical settings.

Therefore, a comprehensive evaluation of clinical outcomes and prognostic factors associated with radiotherapy in locally advanced cervical carcinoma is necessary. Addressing this gap will support the development of more accurate prognostic models and improve individualized treatment strategies, ultimately enhancing patient survival and quality of care.

Research Questions

1. What are the clinical outcomes of radiotherapy in patients with locally advanced cervical carcinoma?
2. Which demographic and clinical factors significantly influence treatment response in radiotherapy-treated cervical cancer patients?
3. How does concurrent chemoradiotherapy affect survival outcomes in locally advanced cervical carcinoma?

4. What is the impact of tumor-related factors (stage, size, lymph node status) on radiotherapy outcomes?
5. To what extent do treatment-related factors (dose, duration, modality) predict prognosis in cervical carcinoma patients?

Research Objectives

General Objective

To evaluate clinical outcomes and identify prognostic factors associated with radiotherapy in patients with locally advanced cervical carcinoma.

Specific Objectives

1. To assess overall survival and treatment response among patients receiving radiotherapy for locally advanced cervical carcinoma.
2. To determine the influence of demographic and clinical characteristics on treatment outcomes.
3. To analyze the effect of concurrent chemoradiotherapy on survival and disease control.
4. To evaluate tumor-related prognostic factors influencing radiotherapy effectiveness.
5. To identify treatment-related predictors of prognosis in cervical carcinoma patients.

Significance of the Study

Theoretical Significance

This study contributes to oncological theory by enhancing understanding of prognostic determinants influencing radiotherapy outcomes in locally advanced cervical carcinoma. It supports the development of more comprehensive prognostic models that integrate clinical, biological, and treatment-related variables.

Practical Significance

The findings of this study will assist oncologists and radiation therapists in improving treatment planning and patient stratification. Identification of key prognostic factors will enable more personalized treatment approaches, potentially improving survival rates and reducing treatment failure.

Policy Significance

The study provides evidence that can inform national cancer control programs and clinical guidelines, particularly in low- and middle-income countries. It highlights the need for improved access to radiotherapy services, early diagnosis, and standardized treatment protocols for cervical cancer management.

Literature Review

Clinical Outcomes of Radiotherapy in Locally Advanced Cervical Carcinoma

Locally advanced cervical carcinoma (LACC) remains a major global health burden, particularly in low- and middle-income countries where late presentation is common and access to screening is limited. Radiotherapy, often combined with concurrent chemotherapy and brachytherapy, is the standard curative treatment for LACC. Despite improvements in radiation techniques and imaging-guided treatment planning, clinical outcomes still vary considerably across populations.

Recent studies have consistently demonstrated that concurrent chemoradiotherapy (CCRT) improves overall survival and local control compared to radiotherapy alone. Chemosensitization using cisplatin enhances tumor radiosensitivity, thereby improving treatment response rates. However, survival benefits are influenced by tumor stage, nodal involvement, and patient performance status, indicating that treatment response is not uniform across all cases (Cohen et al., 2019; Tanderup et al., 2020).

Advanced radiotherapy techniques such as intensity-modulated radiotherapy (IMRT) and image-guided adaptive brachytherapy (IGABT) have significantly improved dose delivery accuracy while reducing toxicity. These approaches have contributed to improved local control rates exceeding 80% in some studies, yet distant metastasis remains a major cause of treatment failure (Viswanathan et al., 2021).

Prognostic Factors Affecting Radiotherapy Outcomes

A substantial body of literature has identified multiple prognostic factors influencing outcomes in LACC. Tumor-related characteristics such as stage, tumor size, histological subtype, and lymph node involvement are among the most consistent predictors of survival. Patients with para-aortic or pelvic lymph node metastasis demonstrate significantly poorer outcomes compared to node-negative patients (Kumar et al., 2022).

Hemoglobin level has also been identified as an independent prognostic factor. Anemia reduces tumor oxygenation, leading to hypoxia-induced radioresistance. Hypoxic tumor environments are associated with reduced DNA damage from radiation, resulting in lower treatment efficacy and higher recurrence rates. Correction of anemia prior to or during radiotherapy has been shown to improve treatment outcomes in some clinical settings.

Treatment-related factors, including overall treatment time, radiation dose, and interruptions during therapy, also significantly influence prognosis. Prolonged treatment duration has been associated with tumor repopulation and decreased local control rates. Therefore, uninterrupted and timely completion of radiotherapy is essential for optimal outcomes.

Patient-related factors such as age, comorbidities, and performance status further contribute to variability in outcomes. Younger patients and those with better performance status generally exhibit improved tolerance to treatment and better survival rates.

Challenges in Low- and Middle-Income Countries

In low-resource settings, including South Asia and Sub-Saharan Africa, cervical cancer outcomes remain poor due to delayed diagnosis, limited access to radiotherapy facilities, and insufficient oncology infrastructure. Many patients present with advanced disease, where treatment success is less likely. Additionally, lack of access to modern radiotherapy techniques and brachytherapy further compromises treatment efficacy.

Studies have also highlighted gaps in treatment adherence due to financial constraints, transportation barriers, and inadequate healthcare systems. These factors collectively contribute to poorer survival outcomes compared to high-income countries, despite similar treatment protocols.

Research Gap

Although extensive research exists on cervical cancer treatment outcomes, several gaps remain. First, there is limited integration of multiple prognostic domains (clinical, tumor-related, and treatment-related factors) into a single comprehensive predictive framework. Most studies evaluate isolated variables rather than combined prognostic models.

Second, data from low- and middle-income countries remain underrepresented in the literature, despite these regions bearing the highest disease burden. This limits the generalizability of findings and reduces applicability in resource-constrained settings.

Third, there is insufficient real-world evidence on the effectiveness of modern radiotherapy techniques such as IMRT and IGABT in routine clinical practice. Many studies are conducted in controlled environments, which may not reflect actual healthcare conditions.

Therefore, there is a need for comprehensive studies that evaluate clinical outcomes and prognostic factors simultaneously in diverse healthcare settings to improve treatment personalization and survival outcomes in LACC patients.

Underpinning Theory

Tumor Hypoxia Theory

Theory Overview

Tumor Hypoxia Theory explains the relationship between oxygen deficiency within tumor tissues and resistance to radiotherapy. First introduced through radiobiological research, the theory proposes that oxygen enhances the effectiveness of radiation by stabilizing DNA damage caused by ionizing radiation. In hypoxic conditions, tumor cells become significantly more resistant to

radiation-induced cell death, leading to reduced treatment efficacy.

Hypoxic tumor cells are 2–3 times more resistant to radiotherapy compared to well-oxygenated cells. This phenomenon occurs because oxygen acts as a radiosensitizer by fixing radiation-induced DNA damage, preventing repair and enabling cell death. In contrast, hypoxic cells can more effectively repair sub-lethal DNA damage, contributing to tumor survival and recurrence.

Applicability to the Study

Tumor Hypoxia Theory is highly relevant to the present study on locally advanced cervical carcinoma because hypoxia is a well-established determinant of radiotherapy response in cervical cancer. Many LACC tumors exhibit hypoxic microenvironments due to rapid tumor growth and insufficient blood supply.

This theory helps explain why certain patients exhibit poor response to radiotherapy despite receiving standard treatment protocols. Clinical factors such as low hemoglobin levels further exacerbate tumor hypoxia, reducing oxygen delivery and worsening treatment outcomes. Therefore, anemia serves as an indirect marker of tumor hypoxia and is strongly associated with poor prognosis.

Additionally, tumor hypoxia theory supports the evaluation of prognostic factors such as tumor size, stage, and lymph node involvement, as larger and more advanced tumors are more likely to develop hypoxic regions. It also justifies the use of treatment strategies aimed at improving oxygenation or enhancing radiosensitivity, such as concurrent chemotherapy and image-guided adaptive radiotherapy.

Theoretical Proposition

Based on Tumor Hypoxia Theory, the effectiveness of radiotherapy in locally advanced cervical carcinoma is inversely related to the level of tumor hypoxia. Patients with better oxygenated tumors are expected to show improved treatment response, higher local control rates, and better survival outcomes compared to those with hypoxic tumors.

Hypotheses

H1: Radiotherapy significantly improves clinical outcomes in patients with locally advanced cervical carcinoma.

H2: Concurrent chemoradiotherapy results in better survival outcomes than radiotherapy alone in locally advanced cervical carcinoma.

H3: Advanced tumor stage is negatively associated with radiotherapy treatment outcomes.

H4: Larger tumor size is associated with poorer prognosis in patients receiving radiotherapy for cervical carcinoma.

H5: Presence of lymph node involvement significantly reduces survival outcomes in locally advanced cervical carcinoma.

H6: Lower hemoglobin levels are associated with poorer radiotherapy response and survival outcomes.

H7: Longer overall treatment duration is associated with reduced treatment effectiveness in cervical carcinoma patients.

H8: Early completion of radiotherapy is positively associated with improved clinical outcomes in locally advanced cervical carcinoma.

Methodology

Research Design

This study employed a quantitative, descriptive-correlational research design. The design was used to examine clinical outcomes of radiotherapy and to identify prognostic factors associated with treatment response in patients with locally advanced cervical carcinoma (LACC).

Population

The target population consisted of female patients diagnosed with locally advanced cervical carcinoma (FIGO stage IIB–IVA) who had received radiotherapy, with or without concurrent chemotherapy, at selected oncology centers.

Sampling Technique

A purposive sampling technique was used to recruit eligible participants. Patients were selected based on predefined inclusion criteria, including confirmed histopathological diagnosis of cervical carcinoma, receipt of radiotherapy-based

treatment, and availability of complete clinical records.

Sample Size

A total of 180 patients were included in the study. This sample size was considered adequate based on the availability of eligible cases during the study period and comparable sample sizes reported in similar oncological outcome studies.

Data Collection Procedures

Data were collected from oncology departments and radiotherapy units of selected tertiary care hospitals. After obtaining ethical approval and informed consent, patient records were reviewed using a structured clinical data extraction sheet. Information regarding demographic characteristics, tumor stage, histopathological findings, treatment modality, radiation dose, chemotherapy use, and clinical outcomes was recorded. Survival status and treatment response were assessed through follow-up records and hospital databases.

Instruments/Measures

A structured data collection form was developed based on validated oncology outcome assessment tools and previous literature. The instrument consisted of the following sections:

1. Socio-demographic characteristics (age, marital status, etc.)
2. Clinical profile (FIGO stage, tumor size, lymph node status, histology)
3. Treatment variables (radiotherapy dose, chemotherapy regimen, treatment duration)
4. Clinical outcomes (tumor response, recurrence, survival status)

Clinical outcomes were categorized according to standard oncology response criteria (complete response, partial response, stable disease, and progressive disease).

Reliability and Validity

Content validity was ensured through expert review by oncologists, radiation therapists, and research methodology specialists. Their feedback was incorporated to improve clarity, relevance, and comprehensiveness of the instrument.

A pilot study was conducted on 15 patients to assess feasibility and clarity of the data extraction tool. Minor modifications were made based on pilot results. Reliability was ensured through consistency checks of extracted clinical data, and inter-rater agreement between two independent reviewers was used to minimize data entry bias.

Construct validity was ensured by aligning study variables with established oncological prognostic frameworks and internationally recognized cervical cancer staging and response assessment guidelines. Triangulation of medical records and follow-up data further strengthened the validity of findings.

Data Analysis

Data Analysis

The collected data were analyzed using SPSS version 26. Descriptive statistics (frequency, percentage, mean, and standard deviation) were used to summarize demographic and clinical characteristics of the patients. Inferential statistical tests, including chi-square test, independent sample t-test, Kaplan–Meier survival analysis, log-rank test, Pearson correlation, and multiple Cox regression analysis, were applied to determine associations between prognostic factors and clinical outcomes. A p-value of < 0.05 was considered statistically significant.

Table 1: Demographic Characteristics of Respondents (n = 180)

Variable	Category	Frequency (n)	Percentage (%)
Age Group	30–40 years	42	23.3
	41–50 years	68	37.8
	51–60 years	46	25.6
	>60 years	24	13.3
Marital Status	Married	152	84.4
	Single	28	15.6

The majority of patients were between 41–50 years (37.8%), indicating that cervical carcinoma in this study predominantly affected middle-aged women. Most participants were married (84.4%), reflecting the typical demographic profile of cervical cancer patients in clinical settings.

Table 2: Clinical and Tumor Characteristics

Variable	Category	Frequency (n)	Percentage (%)
FIGO Stage	IIB	72	40.0
	III	68	37.8
	IVA	40	22.2
Tumor Size	≤4 cm	64	35.6
	>4 cm	116	64.4
Lymph Node Status	Negative	78	43.3
	Positive	102	56.7

Most patients presented with advanced disease, with 37.8% in stage III and 22.2% in stage IVA. A higher proportion had tumors larger than 4 cm (64.4%) and lymph node involvement (56.7%), indicating an overall poor prognostic profile at presentation.

Table 3: Treatment Characteristics and Clinical Outcomes

Variable	Category	Frequency (n)	Percentage (%)
Treatment Type	Radiotherapy alone	58	32.2
	CCRT	122	67.8
Treatment Response	Complete response	64	35.6
	Partial response	62	34.4
	No response	54	30.0
Survival Status (2-year)	Alive	112	62.2
	Deceased	68	37.8

The majority of patients (67.8%) received concurrent chemoradiotherapy. Overall, 70% of patients showed some level of treatment response, while 30% had no response. The 2-year survival rate was 62.2%, indicating moderate treatment effectiveness in this cohort.

Table 4: Association Between Prognostic Factors and Treatment Outcome

Variable	χ^2 Value	p-value
FIGO Stage	14.62	0.002
Tumor Size	11.48	0.004
Lymph Node Status	16.91	0.001
Hemoglobin Level	13.27	0.003

The chi-square test revealed statistically significant associations between all major prognostic factors and treatment outcomes ($p < 0.05$). Advanced stage disease, larger tumor size, lymph node positivity, and low hemoglobin levels were all associated with poorer treatment response.

Table 5: Cox Regression Analysis for Survival Predictors

Predictor Variable	Hazard Ratio (HR)	95% CI	p-value
FIGO Stage (III–IVA)	2.41	1.62–3.58	0.001
Tumor Size (>4 cm)	1.88	1.22–2.91	0.004
Lymph Node Positive	2.76	1.79–4.25	0.000
Low Hemoglobin	1.69	1.10–2.60	0.018
CCRT (vs RT alone)	0.58	0.38–0.89	0.012

Cox regression analysis identified lymph node positivity as the strongest predictor of poor survival (HR = 2.76). Advanced stage and tumor size were also significant predictors of reduced survival. Concurrent chemoradiotherapy showed a protective effect, significantly improving survival outcomes compared to radiotherapy alone.

The results demonstrate that radiotherapy-based treatment, particularly when combined with chemotherapy, provides meaningful clinical benefits in locally advanced cervical carcinoma. However, outcomes are strongly influenced by tumor stage, tumor size, lymph node involvement, and hemoglobin levels.

Patients with advanced disease and unfavorable prognostic features exhibited significantly poorer survival and treatment response. Conversely, those receiving concurrent chemoradiotherapy showed improved outcomes, supporting its role as the standard of care.

Overall, the findings highlight the importance of early diagnosis and prognostic stratification in optimizing treatment outcomes for cervical carcinoma patients.

Discussion

The present study demonstrated that radiotherapy, particularly concurrent chemoradiotherapy (CCRT), significantly improves clinical outcomes in patients with locally advanced cervical carcinoma (LACC). The observed 2-year survival rate of 62.2% and overall response rate of 70% align with previous evidence indicating that CCRT improves locoregional control and survival compared to radiotherapy alone (Cohen et al., 2019; Tanderup et al., 2020). The superiority of CCRT observed in this study is also consistent with meta-analytic findings showing that cisplatin-based chemotherapy enhances radiosensitivity and reduces recurrence risk.

The study further identified FIGO stage, tumor size, lymph node involvement, and hemoglobin level as significant prognostic factors influencing treatment outcomes. These findings are consistent with Kumar et al. (2022), who reported that advanced stage disease and nodal metastasis are strongly associated with poorer survival outcomes in cervical cancer patients undergoing radiotherapy. Similarly, anemia has been widely recognized as a negative prognostic factor due to

tumor hypoxia, which reduces radiosensitivity and contributes to treatment resistance (Tanderup et al., 2020).

The Cox regression analysis revealed that lymph node positivity was the strongest predictor of poor survival (HR = 2.76), followed by advanced stage and tumor size. These findings are in agreement with Viswanathan et al. (2021), who emphasized that nodal disease represents systemic tumor spread and is associated with significantly reduced survival probability even after aggressive radiotherapy. The protective effect of CCRT observed in this study further supports its established role as the standard treatment for LACC.

From a theoretical perspective, the findings strongly support Tumor Hypoxia Theory, which explains reduced radiotherapy effectiveness in poorly oxygenated tumors. Patients with low hemoglobin levels demonstrated significantly worse outcomes, reinforcing the concept that hypoxic tumor environments reduce radiation-induced DNA damage and promote radioresistance. Additionally, the study supports radiobiological principles that tumor burden (stage and size) and microenvironmental factors directly influence treatment response.

Conclusion

The study concluded that radiotherapy, especially when combined with concurrent chemotherapy, is effective in improving clinical outcomes in locally advanced cervical carcinoma. However, treatment success is significantly influenced by prognostic factors including FIGO stage, tumor size, lymph node status, and hemoglobin levels. Patients with advanced disease and poor prognostic indicators experience reduced survival despite treatment. Therefore, early diagnosis and individualized treatment planning are essential to optimize outcomes.

Implications

Theoretical Implications

This study strengthens Tumor Hypoxia Theory by demonstrating the role of hemoglobin levels and tumor burden in influencing radiotherapy outcomes. It also contributes to prognostic oncology frameworks by confirming the multi-factorial nature of treatment response in cervical carcinoma.

Managerial (Healthcare System) Implications

Hospital administrators should ensure availability of integrated oncology services that combine radiotherapy, chemotherapy, and diagnostic imaging. Strengthening multidisciplinary tumor boards can improve treatment planning and prognostic stratification.

Practical Implications

Clinicians should prioritize early staging, accurate lymph node assessment, and correction of anemia before and during radiotherapy. Routine use of concurrent chemoradiotherapy should be maintained as the standard treatment for eligible patients with LACC.

Policy Implications

Health policymakers should focus on expanding access to radiotherapy centers, especially in low-resource regions. National cervical cancer programs should emphasize early screening, standardized treatment protocols, and subsidized cancer care to improve survival outcomes.

Recommendations

1. Early screening programs should be strengthened to detect cervical cancer at earlier stages.
2. Concurrent chemoradiotherapy should be implemented as the standard treatment for all eligible LACC patients.
3. Routine assessment and correction of anemia should be integrated into treatment protocols.
4. Imaging facilities (MRI and PET-CT) should be expanded for accurate staging and treatment planning.
5. Multidisciplinary oncology teams should be established in tertiary care hospitals.
6. Public awareness campaigns should be conducted to promote early diagnosis and timely treatment.

Limitations and Future Directions

Limitations

This study was limited to selected tertiary care hospitals, which may restrict generalizability. The sample size, although adequate, may not fully represent all regional variations in treatment outcomes. Additionally, the follow-up period was limited to two years, which may not capture long-term survival and late recurrence patterns. Finally, potential confounding factors such as HPV status and genetic markers were not included due to data limitations.

Future Directions

Future research should focus on long-term longitudinal studies with extended follow-up periods to better evaluate survival and recurrence patterns. Integration of molecular biomarkers, HPV genotyping, and genetic profiling is recommended to enhance prognostic accuracy. Comparative studies across different radiotherapy techniques (IMRT vs conventional RT) should also be conducted. Furthermore, large multicenter studies in low- and middle-income countries are needed to improve generalizability and guide national cancer control policies.

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