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Research Article

Mortality Predictors and Survival Analysis in Cervical Cancer Patients Treated with Brachytherapy: A Retrospective Study at RMCH

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Abstract

Cervical cancer remains a significant health burden, particularly in low- and middle-income countries, where over 85% of cases occur. Bangladesh exhibits crude incidence and mortality rates of 10.2 and 6.1 per 100,000, respectively, highlighting the impact of cervical cancer. This retrospective study, conducted at Rajshahi Medical College Hospital, assessed 141 cervical cancer patients treated with brachytherapy between December 2016 and December 2020. The primary objective was to examine survival outcomes and associated mortality factors in relation to the stage of cervical cancer at diagnosis. The study revealed that 59 patients (42%) were alive at the time of analysis, of which 88% had achieved disease-free survival. Conversely, 35 patients (25%) were deceased, with advanced-stage disease being predominant among them. Renal failure was identified as the leading cause of death (37%). Results suggest that early-stage cervical cancer correlates with improved survival outcomes, underscoring the necessity of early detection and prompt treatment. Despite the curative potential of brachytherapy when combined with external beam radiotherapy and cisplatin-based chemotherapy, global disparities in access to brachytherapy hinder effective cervical cancer management, particularly in low-resource settings. Enhanced screening programs, vaccination efforts, and broader access to advanced treatment modalities, including brachytherapy, are critical in reducing cervical cancer-related mortality in low- and middle-income countries.

Keywords

Cervical Cancer, Brachytherapy, Survival Outcomes, Low- and Middle-Income Countries, Renal Failure, Radiotherapy, HPV

1. Introduction

Cervical cancer is the fourth most common gynecological malignancy worldwide, with over 85% of cases occurring in low- and middle-income countries such as those in Sub-Saharan Africa and Southeast Asia [1]. According to the

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GLOBOCAN 2020 database, the crude incidence and mortality rates for cervical cancer in Bangladesh are 10.2 and 6.1 per 100,000, respectively [2, 3]. The primary cause of cervical cancer is the sexually transmitted Human Papilloma Virus (HPV). In 2018, approximately 570,000 cases of cervical cancer were detected globally, making it the fourth most common cancer type, with an estimated 311,000 related fatalities [4]. The majority of these deaths—about 88%—occurred in low- and middle-income countries, with the highest incidence rates observed in Western, Eastern, and Southern Africa [5].

External beam radiation therapy (EBRT) combined with cisplatin-based chemotherapy is a curative treatment for locally advanced cervical cancer that is followed with brachytherapy. It has been discovered that brachytherapy improves clinical results, including overall survival, when added to the current paradigm for treating cervical cancer [6]. Therefore, brachytherapy is advised as a crucial component of curative treatment in national and international guidelines for the treatment of cervical cancer [7, 8].

A comprehensive approach, including prevention through effective screening and vaccination, early detection, and treatment, can significantly reduce the high mortality rate of cervical cancer. The standard treatment for cervical cancer involves radiotherapy, which includes both external beam radiotherapy and intracavitary brachytherapy [9, 10]. Brachytherapy, in particular, is crucial for improving overall survival and clinical outcomes, making it an essential component of the therapeutic paradigm for cervical cancer. However, there are significant disparities in the availability of brachytherapy at both national and global levels, leading to its underutilization worldwide [11].

A total of 141 cervical cancer patients underwent brachytherapy in the Department of Radiotherapy at Rajshahi Medical College & Hospital from December 2016 to December 2020. Consequently, a facility-based retrospective study was conducted to assess the survival status and associated factors of death among these patients. The primary aim of this study was to explore the relationship between survival and mortality status with the stage of the disease in cervical cancer patients who received brachytherapy at Rajshahi Medical College Hospital during this period. Additionally, the study aimed to identify the predominant causes of death among these cervical cancer patients.

2. Manuscript Formatting

2.1. Figures

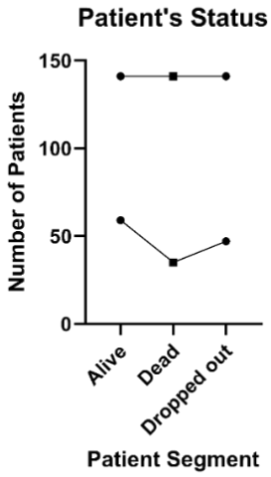

Figure 1. *Number of participants with segment.*

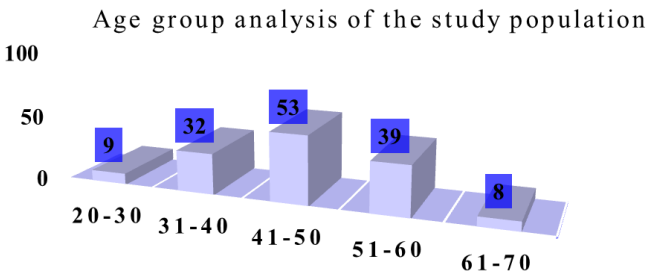

Figure 2. *Age group analysis of the study population.*

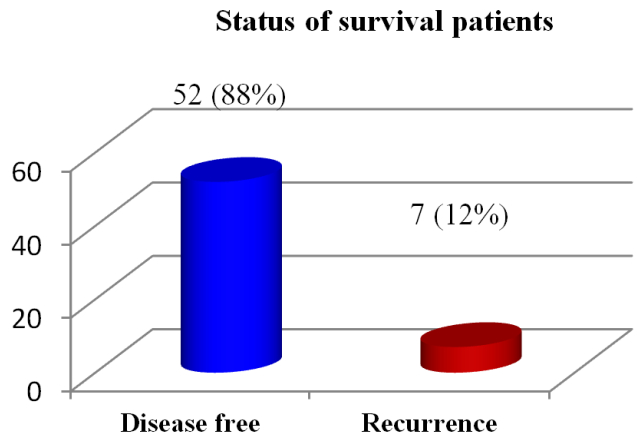

Figure 3. *Status of survival patients.*

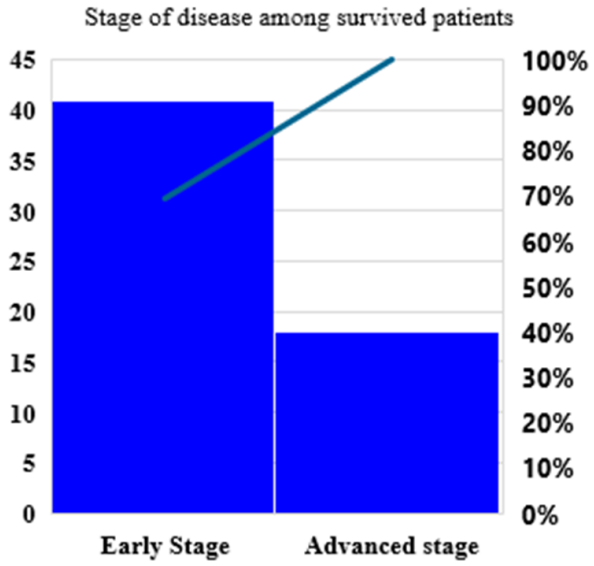

Figure 4. Stage of disease among survived patients.

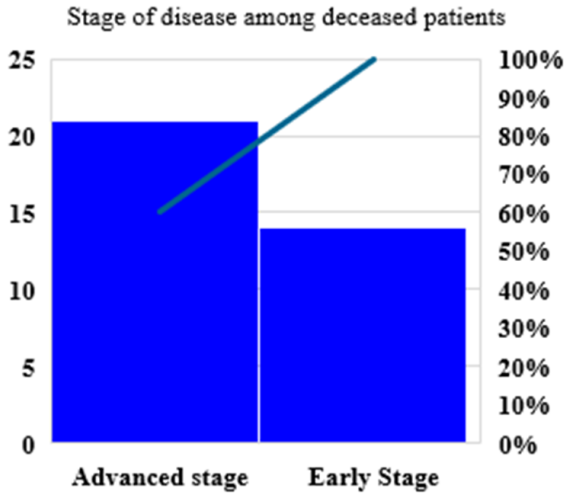

Figure 5. Stage of disease among deceased patients.

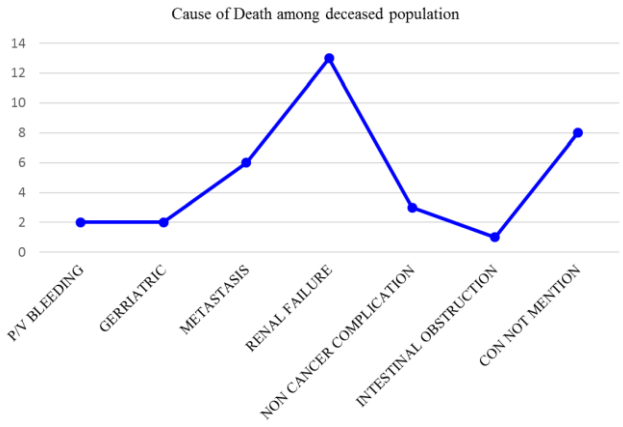

Figure 6. Cause of Death among deceased population.

2.2. Tables

Table 1. Distribution of patients according to staging.

	Early stage	Advanced stage	P-value
Survived patient	41	18	
Deceased	14	21	0.009626
Total	55	39	

Table 2. Cause of Death Analysis Across Centers.

Cause of Death	RMCH (%)	Global Study A (%)	Global Study B (%)
Renal Failure	37%	30%	35%
Metastatic Complications	17%	25%	20%
Geriatric	6%	10%	8%
P/V Bleeding	6%	8%	5%
Intestinal Obstruction	3%	5%	3%
Non-Cancer Related Issues	9%	12%	15%
Unspecified	23%	10%	14%

Table 3. Comparative Survival Analysis by Treatment Modality.

Treatment Modality	Disease-Free Survival (%)	Overall Survival (%)	Recurrence Rate (%)
Intracavitary Brachytherapy	88%	75%	12%
Interstitial Brachytherapy	92%	80%	8%
Combined Modality	95%	82%	5%

3. Materials and Methods

A retrospective study was conducted in the Department of Radiotherapy at Rajshahi Medical College Hospital, involving 141 cervical cancer patients who underwent brachytherapy treatment from December 2016 to December 2020. All early-stage patients received surgery followed by external beam radiotherapy (EBRT) and intracavitary radiotherapy (ICRT) with 7 Gy in 2 fractions, while all advanced-stage patients were treated with concurrent chemoradiation and

ICRT with 7 Gy in 3 fractions. Data was collected using standard data collection sheets, and participants were interviewed via telephone at least four years after completing treatment. In cases of death, the patient's husband or relatives were contacted. The last interview was conducted in March 2024.

3.1. Techniques

Brachytherapy (BT) can be characterized by the duration of irradiation, the positioning of radionuclides, and the dose rate. There are two types based on irradiation duration: permanent brachytherapy, where radioactive seeds (radionuclides) remain inside the body, and temporary brachytherapy, where isotopes are inserted into or near a tumor and then removed [12]. Based on radionuclide positioning, BT is divided into interstitial brachytherapy, where radioactive sources are placed inside the tumor, and contact brachytherapy (plesiobrachytherapy), where sources are positioned close to the tumor [13]. Contact brachytherapy includes four subtypes: intracavitary, intraluminal, endovascular, and surface brachytherapy. According to the dose rate defined by the ICRU, BT is categorized as low-dose-rate (LDR) with 0.4-2.0 Gy/h, pulsed-dose-rate (PDR) with 0.5-1.0 Gy/h, medium-dose-rate (MDR) with 2-12 Gy/h, high-dose-rate (HDR) with >12 Gy/h, and ultra LDR (permanent implants) with 0.01-0.3 Gy/h [14].

Low-dose-rate (LDR) remote afterloading systems provide radiation protection but lack the flexibility in designing alternative isodose volumes compared to higher dose rate sources, which offer adjustable stepping positions and dwell times. Consequently, LDR systems are not widely used in many countries. Conversely, high-dose-rate (HDR) afterloading employs a single 192Ir source moved by computer to various dwell positions, allowing for highly flexible isodose volume selection [15]. This method can deliver large doses within minutes and requires well-shielded bunkers similar to those used for linear accelerators. Despite the radiobiological disadvantage of high-dose rates (1-3 Gy/min), which increase the ratio of late tissue effects, this issue can be mitigated through careful catheter placement and ensuring patient immobility during the brief exposure periods [16].

Pulsed-dose-rate (PDR) treatment is a recent brachytherapy modality that integrates the physical advantages of high-dose-rate (HDR) technology—such as isodose optimization, planning flexibility, and radiation safety—with the radiobiological benefits of low-dose-rate (LDR) brachytherapy, including repair advantages. PDR utilizes a single stepping 192Ir source with an activity of 15-37 GBq (0.5-1 Ci), producing treatment dose rates of up to about 3 Gy per hour, typically pulsed every hour for 24 pulses per day. The source, enclosed in a 2.5 mm long capsule with a diameter of 1.1 mm, moves through all the implanted catheters during each pulse. Each pulse lasts on average 10 minutes per hour, potentially increasing to 30 minutes after three months due to source decay. PDR brachytherapy employs a stronger radiation source than LDR, delivering short exposures of 10 to 30 minutes each hour, resulting in approximately the same total dose over the same overall time [17]. The high-activity source's trajectory through the implanted catheter is precisely programmed by a dedicated computer and executed by a remote source projector, allowing for optimized isodoses through dwell time modulation based on the source's path within the implanted volume. This approach individualizes dose distributions while minimizing radiation exposure to medical staff. The PDR source strength is 10 to 20 times lower than that used in HDR brachytherapy, requiring less stringent shielding—typically less than two additional half-value layers in an ordinary brachytherapy room [18, 19].

3.2. Patient Preparation for Brachytherapy

3.2.1. Previous Night

Patients undergoing brachytherapy are generally advised to follow specific dietary and fasting instructions to optimize treatment outcomes and reduce the risk of complications. On the evening prior to the procedure, patients are typically recommended to consume a soft or liquid diet, which aids digestion and minimizes bowel content during the treatment process. In addition, fasting (NPO, or "nothing by mouth") is required from 10:00 PM onwards to ensure that the stomach is empty, which helps to reduce the risk of aspiration during anesthesia. To further prepare the bowel, patients are often prescribed Tab. Ultra Carbon (2+2+2), which is a medication used to reduce intestinal gas and promote bowel clearance, ensuring a clearer treatment field during the procedure [20].

3.2.2. Morning on the Day of Treatment

On the morning of the brachytherapy procedure, patients undergo several preparatory steps to ensure optimal conditions for treatment. A Fleet Enema is administered rectally to clear the bowel, providing a clearer view of the treatment area and minimizing the risk of interference from bowel contents. Additionally, 1000 ml of normal saline (N/S) is infused intravenously at a slow rate to maintain proper hydration and fluid balance throughout the procedure [21]. This is particularly important as patients may be fasting and could be at risk of dehydration. Finally, to reduce the risk of infection during the procedure, the genital area is thoroughly cleaned and shaved.

3.3. Instrumentation

Brachytherapy is a pivotal technique for the management of cervical cancer, combining precision and efficacy in localized radiation delivery. At Rajshahi Medical College Hospital (RMCH), spinal or saddle anesthesia is routinely administered to ensure patient comfort. The procedure begins with meticulous preparation, including a perianal wash, sterile draping,

and catheterization using a urinary catheter filled with radiopaque dye to aid imaging. Cervical dilation with dilators allows the insertion of brachytherapy applicators, such as the central tandem and lateral ovoids, followed by vaginal packing to stabilize their position. Simulation is conducted using 2D imaging with a Rico-Box, acquiring anterior-posterior (A-P) and lateral X-ray views to confirm applicator placement. Planning follows the Manchester system, emphasizing dose calculation at critical anatomical points, particularly Point A (2 cm superior and lateral to the cervical os) for uterine artery-targeted therapy, and Point B (3 cm lateral to Point A) for pelvic lymph nodes. Critical organ dose limits are maintained through monitoring of the rectal probe and bladder catheter balloon to safeguard against excessive radiation exposure [22].

Dose delivery employs a remote afterloading system using high-dose-rate (HDR) Cobalt-60 (Co-60), ensuring precise radiation targeting with minimized healthcare staff exposure. Verification confirms that 100% of the prescribed dose reaches Point A, while Point B receives a reduced dose of 20-25% to protect adjacent tissues. Additionally, bladder and rectal doses are carefully restricted to 80% of the prescribed amount to prevent toxicity. This methodology underscores RMCH's commitment to balancing effective treatment with organ preservation and safety. The Manchester system remains a cornerstone for brachytherapy planning, demonstrating robustness in dose optimization. This approach aligns with established guidelines, as highlighted in prior studies, to maximize therapeutic outcomes while minimizing side effects [23].

4. Results

A total of 141 participants were enrolled. Among them, 59 individuals (42%) were recorded as alive at the time of analysis, while 35 participants (25%) had deceased. Additionally, 47 participants (33%) were classified as dropped out from the study, Figure 1. Depicts this scenario.

As per figure 2, The age of the patients in the study was between 20-70 years and majority 53 (38%) patients belongs to 41-50 years age group. As per figure 3, Among the total 59 patients who were alive at the time of assessment, 52 patients (88%) were reported to have achieved disease-free survival, while 7 patients (12%) experienced disease recurrence.

As per figure 4, Among the patients who survived, 41 individuals (69%) were in early-stage, whereas 18 individuals (31%) were in advanced stage disease. As per figure 5, Total 35(25%) patients were found dead during investigations of this study, among them 21(60%) patients were in advanced stage, 14(40%) patient were in early stage at presentation. As per table 1, Among deceased patients, cause of death were Renal failure 13(37%), Metastatic complications 6(17%), Geriatric 2(6%), P/V Bleeding 2(6%), Intestinal obstruction 1(3%), Non-Cancer Related Problem 3(9%) and Cause not specified 8(23%) patients.

5. Discussion

In developed nations, the adoption of the Papanicolaou smear has significantly reduced cervical cancer rates by enabling early detection and preventing cervical intraepithelial neoplasia (CIN) from progressing to invasive disease [24, 25]. However, in many low- and middle-income countries (LMICs), such screening techniques are less accessible, leading to a disproportionate impact of cervical cancer. Mortality from cervical disease remains high in regions like Central and South America, East Africa, South and Southeast Asia, and the Western Pacific due to limited screening, low HPV vaccination rates, and co-infections like HIV, which predispose individuals to persistent HPV infections [26, 27].

Brachytherapy plays a crucial role in cervical cancer care, particularly in LMICs where 60% of cases present with locally advanced disease. Challenges to implementing brachytherapy programs include geographic and economic barriers, inadequate funding, poor infrastructure, inconsistent referral processes, and a shortage of trained professionals [28]. A study by Zubizarreta et al. estimated that approximately 295,000 cervical cancer patients in LMICs would require brachytherapy, but the availability of HDR afterloaders is sparse and uneven. In sub-Saharan Africa, for example, brachytherapy is available in only 20 out of 52 nations, with the capacity to treat an estimated 24,300 patients annually, despite the incidence of cervical cancer being 119,314 in 2018. This stark disparity highlights the urgent need for improved access to brachytherapy in these regions [29, 30].

In the Asia-Pacific region, there are 450 radiation centers, primarily in India and China, but few offer brachytherapy. In India, most brachytherapy units are in the south, with a deficit in 14 northern states requiring 127 additional units for adequate cervical cancer treatment. Thailand has one HDR brachytherapy unit treating 1,000 cases annually. Effective brachytherapy delivery necessitates trained professionals and imaging, with MRI being the gold standard. However, 3D imaging and MRI are limited in availability and cost in LMICs [31]. Efforts to address these gaps include international collaborations like the International Cancer Expert Corps (ICEC) and the American Brachytherapy Society (ABS) supporting training in Tanzania, and the nonprofit Rayos Contra Cancer offering HDR brachytherapy courses [32]. The Elekta BrachyAcademy has also trained over 1,000 participants through workshops in India and Thailand since 2013. Expanding training opportunities is crucial for improving cervical cancer care in LMICs [33, 34].

The Directory of Radiotherapy Centers (DIRAC) reports 3,318 brachytherapy units worldwide, with a concentration in high-income regions, resulting in limited access for rural patients .31 Despite national and international guidelines highlighting brachytherapy as vital for locally advanced cervical cancer, its use in the U.S. declined from 83% in 1988 to 58% in 2009. Financial factors, including a fee-for-service model and insufficient Medicare reimbursements, contribute

to this decline. Although the new Radiation Oncology Alternative Payment Model (RO Model) proposed bundled payments, concerns about inadequate reimbursement for brachytherapy led to its exclusion from the 2022 final rule. Conversely, in Europe, brachytherapy has a robust history and widespread use, supported by the GEC-ESTRO group [35, 36]. 34 A 2010 survey showed 60% of European centers offered brachytherapy, with increased use of CT-guided planning. In Australia and New Zealand, CT and MRI guidance utilization for brachytherapy has tripled since 2005 [37].

Brachytherapy is a specialized skill requiring substantial training, but opportunities have declined. In the U.S., the number of interstitial brachytherapy procedures performed per resident dropped by 25%, with only 54% feeling confident to start a brachytherapy practice post-residency .36, 37 French and Canadian trainees report insufficient training and formal objectives. To address this, the U.S. Accreditation Council for Graduate Medical Education (ACGME) increased the required number of implants during residency, though the experience may still be inadequate [34, 38]. The Canadian Royal College established a formal brachytherapy curriculum and fellowship program, including the University of Toronto's fellowship, which has trained 42 brachytherapists since 2014 [39]. Expanding training and support for brachytherapy is crucial to improving cervical cancer care globally.

The results of this study indicate that renal failure was the leading cause of death among the deceased patients (37%), followed by metastatic complications (17%), geriatric issues, P/V bleeding, and others. This presents an opportunity to discuss the specific clinical reasons why renal failure and other causes were predominant, particularly in the context of advanced-stage cervical cancer.

Renal failure as a primary cause of death is a well-documented complication in advanced cervical cancer patients. Tumor infiltration into the urinary tract, including the ureters, can cause obstructive uropathy, leading to hydronephrosis and eventual renal failure. Studies have shown that up to 10-15% of advanced cervical cancer patients experience urological complications, particularly obstructive uropathy, which contributes significantly to morbidity and mortality.

A study by Wu et al. (2021) discusses that patients with advanced-stage cervical cancer are at high risk for obstructive uropathy, which often progresses to renal failure if left untreated or if treatment is delayed [40]. Radiotherapy and brachytherapy can exacerbate these complications by causing scarring and further obstruction in the pelvic region, particularly in patients with pre-existing renal impairment. This suggests that closer monitoring and proactive management of renal function should be an integral part of the treatment regimen for advanced-stage patients [41].

Metastatic complications are the second most common cause of death in cohort. Cervical cancer can metastasize to distant organs such as the lungs, liver, and bones. When metastasis occurs, it often signals a poor prognosis and complicates treatment strategies, making palliative care the primary focus.

According to a study by Siegel et al. (2022), metastatic cervical cancer represents a critical juncture where curative treatment options are limited, and the focus shifts to managing symptoms and maintaining quality of life [42]. Patients with metastases to the liver and lungs, in particular, experience rapid clinical decline due to organ failure. Early identification of metastatic spread through regular imaging may allow for more timely interventions that can extend survival, though such measures are often unavailable in low-resource settings [37].

These results clearly demonstrate that early-stage cervical cancer patients have significantly better survival outcomes. This highlights the critical importance of early detection through effective screening programs such as the Papanicolaou (Pap) smear or HPV testing. Increasing access to these screening methods in low-resource settings can dramatically reduce cervical cancer mortality by catching the disease at a treatable stage.

Research by Arbyn et al. (2020) shows that widespread use of HPV vaccination and early screening has reduced cervical cancer incidence in high-income countries by up to 70%. In contrast, low- and middle-income countries (LMICs) face significant barriers to implementing these programs due to economic, geographic, and sociocultural challenges. Expanding HPV vaccination coverage and integrating it with accessible screening programs could drastically reduce advanced-stage presentations and associated mortality [7].

The underutilization of brachytherapy in LMICs, despite its proven effectiveness, remains a significant barrier to improved outcomes for advanced-stage cervical cancer patients. This study suggests that many patients who died did not receive adequate brachytherapy due to limitations in infrastructure and trained personnel.

Viswanathan et al. (2020) report that brachytherapy, when used alongside external beam radiation and chemotherapy, improves local control and overall survival, particularly in advanced-stage patients. However, access to brachytherapy remains uneven, and in many LMICs, facilities lack the equipment or trained staff to offer this treatment modality. Expanding international collaborations, training initiatives, and funding for infrastructure development are critical to addressing this gap. The Elekta Brachy Academy, for example, has trained hundreds of professionals in India and Southeast Asia, demonstrating the potential for scaling up this lifesaving treatment [21].

Given the high incidence of renal failure as a cause of death, it would be beneficial to implement routine monitoring of renal function in advanced-stage cervical cancer patients. Early intervention with nephrostomy or stent placement can alleviate obstructive uropathy and prevent renal failure, thereby improving survival outcomes.

A study by Mishra et al. (2019) found that patients who underwent early nephrostomy placement for obstructive

uropathy due to advanced cervical cancer had improved survival rates compared to those who did not receive timely intervention. This suggests that routine renal function screening should be integrated into the management protocols for cervical cancer patients, particularly in advanced stages [42, 43].

This study underscores the critical need for enhanced prevention strategies, early detection, and equitable access to advanced treatment modalities like brachytherapy to reduce the burden of cervical cancer in low- and middle-income countries. While the results emphasize that early-stage cervical cancer patients have better survival outcomes, the high mortality rate among advanced-stage patients highlights the urgent need for improved treatment protocols, particularly in managing complications like renal failure and metastatic spread. Strengthening healthcare infrastructure and training programs in LMICs can bridge the gap in treatment accessibility, ultimately improving survival outcomes for cervical cancer patients worldwide.

6. Conclusions

This study demonstrates a clear correlation between the stage of cervical cancer at diagnosis and patient survival outcomes, with the majority of survivors presenting with early-stage disease and the majority of deceased patients presenting with advanced-stage disease. Notably, renal failure emerged as the leading cause of death among the deceased cohort. These findings underscore the critical importance of early detection and prompt treatment in reducing cervical cancer-related mortality. Therefore, enhanced focus on prevention strategies, routine screening programs, and timely therapeutic interventions is paramount. Addressing these areas will likely improve survival rates and reduce the burden of cervical cancer, emphasizing the need for more comprehensive public health initiatives aimed at prevention and early diagnosis.

Abbreviations

HPV	Human Papillomavirus
EBRT	External Beam Radiation Therapy
GLOBOCAN	Global Cancer Incidence, Mortality and Prevalence Database
RMCH	Rajshahi Medical College & Hospital
RT	Radiotherapy
BT	Brachytherapy

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Author Contributions

Khatun Julekha: Conceptualization, Datacuration, FormalAnalysis, Investigation, Methodology, Visualization, Writing–originaldraft

Karim Md. Abdul: FormalAnalysis, Methodology, Software, Writing–review&editing

Jahan Shahrin: Datacuration, Resources, Validation,

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Biswas Saikat: FormalAnalysis, Resources, Writing–originaldraft

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Data Availability Statement

The data is available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

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Biography

Khatun Julekha is a distinguished oncologist with over 6 years of experience specializing in the treatment and management of cancer. She is currently affiliated with the department of Radiotherapy Rajshahi Medical College Hospital. Specializing in the medical management of cancer through chemotherapy, targeted therapy, immunotherapy, and hormonal therapy, she has made significant contributions to the care and well-being of patients dealing with cancer. Dr. Julekha Khatun earned her medical degree MBBS from Rajshahi Medical College Hospital followed by FCPS in Radiotherapy from Bangladesh College of Physician & Surgeon (BCPS) in January 2019. She had training on brachytherapy in 2015 from India

Research Fields

Khatun Julekha: Brachytherapy, Combination Therapies, Clinical Oncology.

Karim Md. Abdul: Radiotherapy, Immunotherapy, Geriatric Oncology.

Jahan Shahrin: Chemotherapy Optimization, Palliative Care & Management.

Chowdhury Jannatul Mawa: Non-Communicable disease, Patient Safety and Quality Improvement.

Biswas Saikat: Connective tissue disease, Drug-drug/protein interaction, Infectious disease, Genetic disease.