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Original Research Article

Magnitude of the Bladder and Rectal Toxicities in the Patients of Locally Advanced CA Cervix Who Have Received Concurrent Chemoradiotherapy Followed by Cobalt Based Brachytherapy and Quality of Life of the Patients Who Have Completed the Treatment with Chemoradiotherapy Followed by Brachytherapy

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Conflict of interest: Nil

Abstract:

Introduction: Cervical cancer remains a significant cause of morbidity and mortality among women globally, particularly in developing countries. Concurrent chemoradiotherapy (CCRT) followed by brachytherapy is the standard of care for locally advanced cervical cancer (FIGO stages IIB–IIIB). While this combined modality improves survival, it is associated with treatment-related toxicities, particularly involving the bladder and rectum, which can significantly affect patients' quality of life (QoL). Assessment of both acute and late genitourinary (GU) and gastrointestinal (GI) toxicities is essential to optimize patient management and supportive care.

Methods: The study was a prospective observational study conducted at the Department of Radiotherapy, Burdwan Medical College and Hospital, Burdwan, from 1st February 2021 to 31st January 2022. The study population included 60 patients attending the radiotherapy outpatient department with biopsy-proven squamous cell carcinoma of the cervix in locally advanced stages (FIGO Stage IB2–IVA) who received concurrent chemoradiotherapy followed by intracavitary brachytherapy. The study variables assessed were bowel toxicities, bladder toxicities, grading of bladder toxicity, functional scale, symptom scale, and global health scale to evaluate both treatment-related adverse effects and quality of life outcomes.

Results: Before treatment, bowel and bladder toxicities were minimal. Following concurrent chemoradiotherapy and brachytherapy, mild bowel issues such as diarrhea (up to 14.5%), rectal discharge (15.8%), and intermittent bleeding (3.6%) peaked at 3 months but improved by 6 and 9 months, with severe complications like obstruction and fistula being rare (1.9%). Bladder toxicities, including mild cystitis, urinary frequency, urgency, and dysuria, followed a similar pattern, with most patients exhibiting grade 0 toxicity and severe events uncommon. Quality of life progressively improved over time, with functional scores increasing from 65.44 ± 12.98 to 81.09 ± 7.94, symptom scores decreasing from 35.05 ± 11.96 to 21.36 ± 8.77, and global health status rising from 48.35 ± 5.98 to 75.67 ± 12.79.

Conclusions: Concurrent chemoradiotherapy followed by cobalt-based brachytherapy in locally advanced cervical cancer is effective but associated with measurable bladder and rectal toxicities, mostly mild to moderate in severity. While overall quality of life recovers post-treatment, persistent GU and GI symptoms can negatively impact patient well-being. Continuous monitoring, early management of toxicities, and supportive interventions are crucial to maintain QoL in survivors of cervical cancer.

Keywords: Locally advanced cervical cancer, concurrent chemoradiotherapy, cobalt brachytherapy, bladder toxicity, rectal toxicity, quality of life, RTOG, EORTC.

Introduction

Cervical cancer remains a significant global health concern, ranking as the fourth most common cancer among women worldwide. In 2020, approximately 604,000 new cases and 342,000 deaths were attributed to cervical cancer [1]. In India, where cervical cancer incidence is notably high, the standard treatment for locally advanced cervical cancer (LACC) involves concurrent chemoradiotherapy (CCRT) followed by brachytherapy [2]. This multimodal approach aims to enhance local control and overall survival [3]. The integration of chemotherapy with radiotherapy has been established as an effective treatment for LACC; however, this combination can lead to various toxicities, particularly affecting the bladder and rectum due to their proximity to the cervix [4]. Acute toxicities commonly observed include urinary tract infections, diarrhea, and gastrointestinal disorders, while long-term complications may encompass rectal bleeding, bowel complications requiring surgery, stenosis, or recto-vaginal fistula [5]. Brachytherapy, a form of internal radiation therapy, is employed to deliver high doses of radiation directly to the tumor site. While it offers the advantage of precise targeting, it also poses risks to adjacent organs. Studies have indicated that rectal toxicity is a significant concern, with potential outcomes including rectal bleeding and bowel complications [6], and similarly, bladder-related toxicities such as urinary retention and incontinence have been reported [7]. The assessment of quality of life (QoL) in patients undergoing treatment for LACC is crucial, as the therapeutic interventions can profoundly impact physical, emotional, and social well-being [8]. Research indicates that patients who received chemoradiotherapy as part of their treatment had a better overall QoL compared to those who received either radiotherapy or chemotherapy alone [9]; however, despite these improvements, challenges persist. Factors influencing QoL outcomes include the severity of treatment-related toxicities, psychological distress, and the ability to resume daily activities post-treatment [10]. Addressing these factors is essential to enhance the overall well-being of patients and to inform strategies for supportive care.

Materials and Methods

Study Design: Prospective observational study.

Place of study: Department of Radiotherapy, Burdwan Medical College and Hospital, Burdwan.

Period of study: 1st February 2021 to 31st January 2022.

Study Population: Patients attending Radiotherapy outpatient department with biopsy proven squamous cell carcinoma of cervix in locally advanced stages.

Study Variables

- Bowel Toxicities
- Bladder Toxicities
- Grading of Bladder Toxicity
- Functional Scale
- Symptoms
- Global Health Scales

Sample Size

60 Patients with [FIGO Stage IB2-IVA] received concurrent chemoradiotherapy followed by intracavitary brachytherapy.

Inclusion Criteria

- Patients with histopathologically proven carcinomas of cervix , in advanced stage, based on TNM staging.
- Female patients aged between 18 years to 70 years.
- No previous chemotherapy or radiotherapy for carcinoma of cervix.
- Adequate performance status (ECOG 0 to 2).
- Provision of informed consent.
- Adequate life expectancy.
- Histological, Renal, and Hepatic function within normal limits.

Exclusion Criteria

- Distant metastasis or recurrent cervical cancer
- Pregnancy or lactation
- Severe comorbidities contraindicating chemotherapy or radiotherapy
- Known hypersensitivity to cisplatin or paclitaxel
- Previous malignancy within 5 years (except non-melanoma skin cancer)

Statistical Analysis

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. Z-test (Standard Normal Deviate) was used to test the significant difference of proportions. Once a t value is determined, a p-value can be found using a table of values from Student's t-distribution. If the calculated p-value is below the threshold chosen for statistical significance (usually the 0.10, the

0.05, or 0.01 level), then the null hypothesis is rejected in favor of the alternative hypothesis. P-value ≤ 0.05 was considered for statistically significant.

Result

Table 1: Incidence and Severity of Bowel Toxicities in Patients Following Concurrent Chemoradiotherapy and Brachytherapy

Incidence and Severity of Bowel Toxicities		Frequency	Percent
Bowel toxicity Diarrhea (Before treatment)	**No**	55	100.00%
Bowel toxicity Diarrhea 3 months after follow-up	Mild	8	14.50%
	Moderate	1	1.80%
	No	46	83.60%
Bowel Diarrhea 6 months after follow-up	Mild	8	14.80%
	Moderate	4	7.50%
	No	42	77.80%
Bowel Diarrhea 9 months after follow-up	Mild	5	9.40%
	Moderate	3	5.70%
	No	37	69.80%
	Normal	8	15.10%
Bowel Movements 3 months after follow-up	Less than 5	6	10.90%
	More than 5	1	1.80%
	No	6	10.90%
	Normal	42	76.40%
Bowel Movements 6 months after follow-up	Less than 5	2	3.70%
	More than 5	4	7.40%
	Normal	48	88.90%
Bowel Movements 9 months after follow-up	Less than 5	3	5.60%
	More than 5	2	3.70%
	No	1	1.90%
	Normal	48	88.90%
Bowel toxicity Rectal Discharge (Before treatment)	Mild	2	3.60%
	No	53	96.40%
Bowel Rectal Discharge 3 months after follow-up	Excessive	1	1.80%
	Mild	9	15.80%
	Moderate	1	1.80%
	No	46	80.70%
Bowel Rectal Discharge 6 months after follow-up	Excessive	3	5.60%
	Mild	9	16.70%
	Moderate	1	1.90%
	No	41	75.90%
Bowel Rectal Discharge 9 months after follow-up	Excessive	6	11.20%
	Mild	7	13.00%
	Mod-severe	1	1.90%
	No	40	74.10%
Bowel Rectal Bleeding 3 months after follow-up	Intermittent	2	3.60%
	Mild	1	1.80%
	No	52	94.50%
Bowel Rectal Bleeding 6 months after follow-up	Intermittent	2	3.70%
	Mild	4	7.40%
	No	48	88.90%
Bowel Rectal Bleeding 9 months after follow-up	Intermittent	5	9.30%
	Mild	5	9.30%
	No	44	81.50%
Bowel Obstruction 6 months after follow-up	No	53	98.10%
	Yes	1	1.90%
Bowel Obstruction 9 months after follow-up	No	53	98.10%
	Present	1	1.90%
Bowel Fistula Formation 9 months after follow-up	No	52	98.10%
	Yes	1	1.90%

Table 2: Grading of Bowel Toxicity During Follow-Up

Bowel Toxicity Grade 3 months after follow-up	Absent	3	5.00%
	Death	2	3.30%
	G0	42	70.00%
	G1	10	16.70%
	G2	3	5.00%
Bowel Toxicity Grade 6 months after follow-up	Absent	3	5.10%
	Death	1	1.70%
	G0	36	61.00%
	G1	12	20.30%
	G2	6	10.20%
	G3	1	1.70%
Bowel Toxicity Grade 9 months after follow-up	Absent	3	5.20%
	G0	38	65.50%
	G1	7	12.10%
	G2	8	13.80%
	G3	1	1.70%
	G4	1	1.70%

Table 3: Incidence and Severity of Bladder Toxicities Following Concurrent Chemoradiotherapy and Brachytherapy

		Frequency	Percent
Cystitis Before treatment	Mild	1	1.90%
	No	51	96.20%
	Yes	1	1.90%
Cystitis 3 months after follow-up	Mild	5	9.40%
	Moderate	1	1.90%
	No	46	86.80%
	Yes	1	1.90%
Cystitis 6 months after follow-up	Mild	10	18.90%
	Moderate	2	3.80%
	No	41	77.40%
Cystitis 9 months after follow-up	Mild	7	13.20%
	No	46	86.80%
Frequency of urination Before treatment	Mild	1	1.90%
	No	50	94.30%
	Yes	2	3.80%
Frequency of urination 3 months after follow-up	Mild	6	11.30%
	Moderate	1	1.90%
	No	46	86.80%
Frequency of urination 6 months after follow-up	Mild	7	13.20%
	Moderate	1	1.90%
	No	43	81.10%
	Normal	2	3.80%
Frequency of urination 9 months after follow-up	Mild	7	13.20%
	Moderate	1	1.90%
	No	44	83.00%
	Severe	1	1.90%
Urgency of urination Before treatment	No	52	98.10%
	sometimes	1	1.90%
Urgency of urination 3 months after follow-up	Mild	5	9.40%
	Moderate	1	1.90%
	No	46	86.80%
	sometimes	1	1.90%
Urgency of urination 6 months after follow-up	Mild	3	5.70%
	Moderate	1	1.90%
	No	48	90.60%
	Yes	1	1.90%

Urgency of urination 9 months after follow-up	Mild	7	13.20%
	Moderate	1	1.90%
	No	44	83.00%
	Yes	1	1.90%
Dysuria Before treatment	No	53	100.00%
Dysuria 3 months after follow-up	Mild	5	9.40%
	No	48	90.60%
Dysuria 6 months after follow-up	Mild	4	7.50%
	Moderate	1	1.90%
	No	48	90.60%
Dysuria 9 months after follow-up	Mild	3	5.70%
	No	49	92.50%
	Severe	1	1.90%
Nocturia Before treatment	No	53	100.00%
Nocturia 3 months after follow-up	No	53	100.00%
Nocturia 6 months after follow-up	Mild	1	1.90%
	No	52	98.10%
Incontinence 3 months after follow-up	Mild	1	1.90%
	No	52	98.10%
Incontinence 6 months after follow-up	Mild	3	5.70%
	No	50	94.30%
Hematuria 3 months after follow-up	Mild	4	7.50%
	No	49	92.50%
Hematuria 6 months after follow-up	Intermittent	1	1.90%
	Mild	2	3.80%
	Minor	3	5.70%
	No	47	88.70%
Hematuria 9 months after follow-up	Frequent	1	1.90%
	Mild	3	5.70%
	No	49	92.50%

Table 4: Grading of Bladder Toxicity During Follow-Up

Grade of Bladder Toxicity, 3 months after follow-up	Absent	3	5.10%
	Death	1	1.70%
	G0	39	66.10%
	G1	13	22.00%
	G2	2	3.40%
	G3	1	1.70%
Grade of Bladder Toxicity, 6 months after follow-up	Absent	3	5.10%
	Death	1	1.70%
	G0	38	64.40%
	G1	14	23.70%
	G2	3	5.10%
Grades of Bladder Toxicity, 9 months after follow-up	Absent	3	5.20%
	G0	40	69.00%
	G1	13	22.40%
	G2	1	1.70%
	G3	1	1.70%

Table 5: Quality of Life Assessment Using Functional, Symptom, and Global Health Scales

	Number of patients	Mean score	SD
Functional scale before treatment(Baseline)	55	65.4364	12.9797
Functional scale 3 months after follow-up	55	71.2364	9.2576
Functional scale 6 months after follow-up	55	75.8	7.1554
Functional scale 9 months after follow-up	55	81.0909	7.9426
Symptom scale score before treatment(Baseline)	55	35.0545	11.9574
Symptom scale 3 months after follow-up	55	29.8545	9.9804
Symptom scale 6 months after follow-up	55	26.1636	8.5781

Symptom scale 9 months after follow-up	55	21.3636	8.7652
Global health status score Before treatment(Baseline)	55	48.3455	5.9821
Global health status 3 months after follow-up	55	58.4727	7.2721
Global health status 6 months after follow-up	55	66.4909	10.263
Global health status 9 months after follow-up	55	75.6727	12.7948

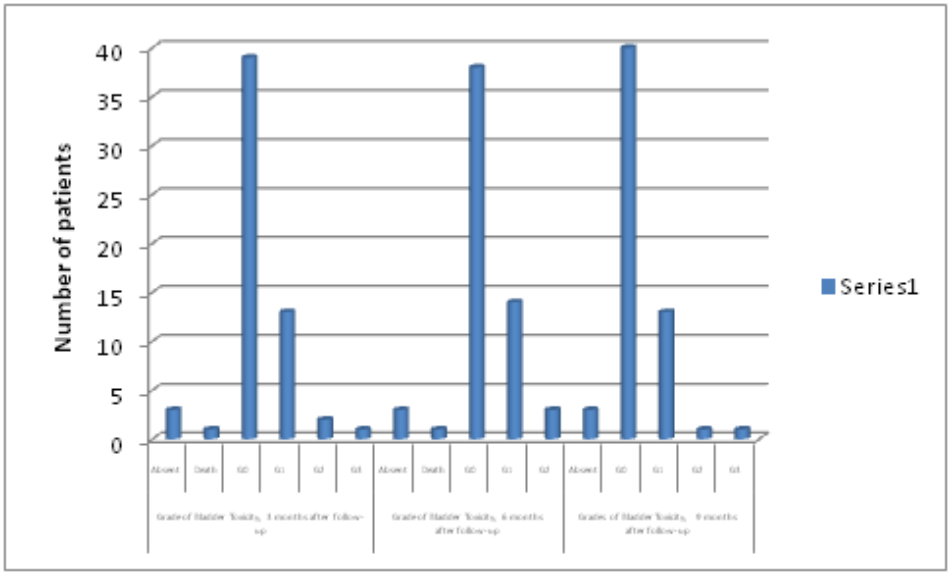

Figure 1: Grade of Bladder Toxicity at 3, 6, and 9 Months After Follow-Up

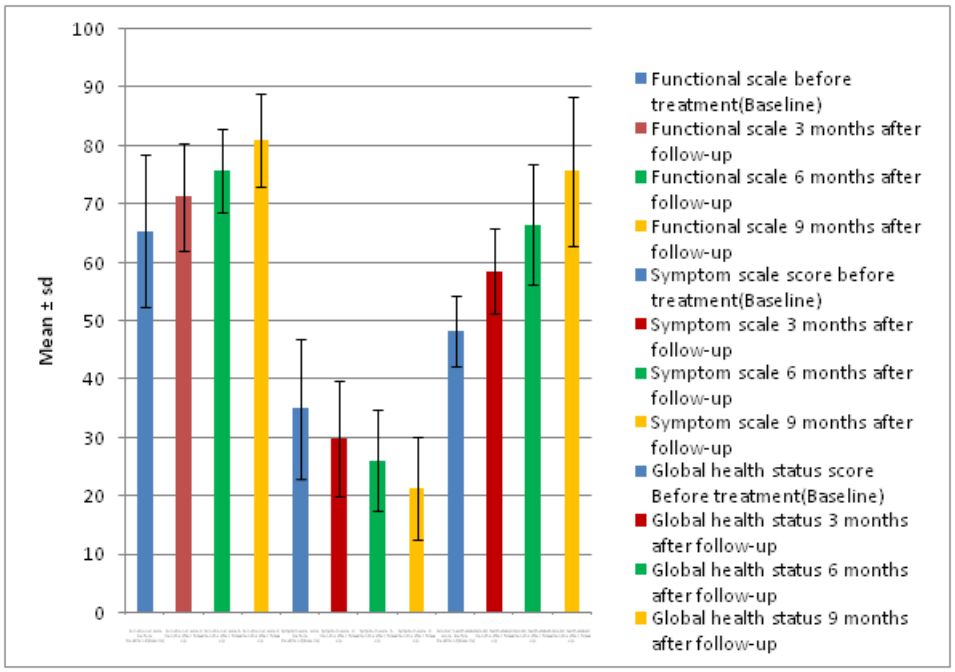

Figure 2: Quality of Life Assessment Using Functional, Symptom, and Global Health Scales

Before treatment, bowel toxicities were minimal, with no diarrhea and only 3.6% reporting mild rectal discharge. At 3 months post-treatment, mild diarrhea occurred in 14.5% and mild rectal discharge in 15.8% of patients; intermittent rectal bleeding was seen in 3.6%. By 6 months, diarrhea and bowel movement abnormalities decreased, with most patients (88.9%) reporting normal bowel patterns.

Rectal discharge and bleeding remained low, and bowel obstruction was rare (1.9%). At 9 months, the majority of patients maintained normal bowel function, with only small percentages experiencing mild-to-moderate diarrhea, rectal discharge, or bleeding. Bowel obstruction and fistula formation were each observed in 1.9% of patients, indicating overall improvement in bowel-related toxicities over time.

At 3 months post-treatment, the majority of patients had grade 0 (70%) bowel toxicity, while 16.7% had grade 1 and 5% had grade 2 toxicity; 5% were absent, and 3.3% of patients had died. At 6 months, grade 0 toxicity was observed in 61% of patients, grade 1 in 20.3%, grade 2 in 10.2%, and grade 3 in 1.7%; 5.1% were absent, and 1.7% had died. By 9 months, 65.5% of patients had grade 0 toxicity, 12.1% grade 1, 13.8% grade 2, 1.7% grade 3, and 1.7% grade 4; 5.2% were absent.

Before treatment, bladder toxicities were minimal, with mild cystitis in 1.9% of patients and mild frequency of urination in 1.9%, while dysuria and nocturia were absent (0%). At 3 months post-treatment, mild cystitis was observed in 9.4% and moderate cystitis in 1.9% of patients. Mild frequency of urination occurred in 11.3%, moderate in 1.9%, mild urgency in 9.4%, and moderate urgency in 1.9%. Mild dysuria was reported in 9.4%, incontinence in 1.9%, and hematuria in 7.5%; nocturia remained absent (0%). At 6 months, mild cystitis increased to 18.9%, moderate cystitis in 3.8%, mild frequency of urination in 13.2%, moderate in 1.9%, mild urgency in 5.7%, dysuria in 7.5%, incontinence in 5.7%, and hematuria in 11.4%; nocturia was minimal (1.9%). By 9 months, mild cystitis persisted in 13.2%, mild frequency and urgency in 13.2% and 13.2%, dysuria in 5.7%, severe dysuria in 1.9%, and hematuria in 5.7%; nocturia and incontinence were rare.

At 3 months post-treatment, most patients had grade 0 bladder toxicity (66.1%), while 22% had grade 1, 3.4% had grade 2, and 1.7% had grade 3; 5.1% were absent, and 1.7% of patients had died. At 6 months, grade 0 toxicity was observed in 64.4% of patients, grade 1 in 23.7%, and grade 2 in 5.1%; 5.1% were absent, and 1.7% had died. By 9 months, 69% of patients had grade 0 toxicity, 22.4% grade 1, 1.7% grade 2, and 1.7% grade 3; 5.2% were absent.

The functional scale scores improved progressively over time, with a mean of 65.44 ± 12.98 at baseline, increasing to 71.24 ± 9.26 at 3 months, 75.8 ± 7.16 at 6 months, and 81.09 ± 7.94 at 9 months. Symptom scale scores decreased, indicating symptom improvement, from 35.05 ± 11.96 at baseline to 29.85 ± 9.98 at 3 months, 26.16 ± 8.58 at 6 months, and 21.36 ± 8.77 at 9 months. Global health status scores also improved from 48.35 ± 5.98 at baseline to 58.47 ± 7.27 at 3 months, 66.49 ± 10.26 at 6 months, and 75.67 ± 12.79 at 9 months.

Discussion

The present study evaluated the magnitude of bowel and bladder toxicities and their impact on quality of life in patients with locally advanced cervical cancer (LACC) treated with concurrent chemoradiotherapy (CCRT) followed by cobalt-based brachytherapy. Cervical cancer remains a major cause of morbidity and mortality worldwide, particularly in low- and middle-income countries, with LACC often presenting at advanced stages and requiring multimodal treatment [1]. While CCRT combined with brachytherapy significantly improves local control and overall survival [2,3], it is associated with gastrointestinal and genitourinary toxicities that may compromise patients' functional status and quality of life [4]. In this study, bowel toxicities were minimal before treatment, with no diarrhea and only 3.6% of patients reporting mild rectal discharge. Post-treatment follow-up showed a transient increase in bowel-related adverse effects: at 3 months, mild diarrhea and rectal discharge were noted in 14.5% and 15.8% of patients, respectively, with intermittent rectal bleeding in 3.6%. By 6 months, the incidence of diarrhea and bowel movement abnormalities decreased, with 88.9% of patients reporting normal bowel patterns. Rectal discharge and bleeding remained low, and bowel obstruction was rare (1.9%). At 9 months, most patients maintained normal bowel function, although mild-to-moderate diarrhea, rectal discharge, or bleeding persisted in a small proportion, and bowel obstruction and fistula formation were observed in 1.9% of patients [5,6]. Grading of bowel toxicity revealed that the majority of patients had grade 0 toxicity at all follow-up intervals, with only a small fraction experiencing grade 2–4 toxicities or death, demonstrating that severe bowel complications were uncommon [7]. Similarly, bladder toxicities were minimal before treatment, with only 1.9% of patients reporting mild cystitis or urinary frequency, and no patients reporting dysuria or nocturia. At 3 months post-treatment, mild cystitis was observed in 9.4% and moderate cystitis in 1.9% of patients. Mild frequency and urgency of urination were seen in 9–11% of patients, with moderate cases being rare. Mild dysuria, incontinence, and hematuria were observed in small percentages, while nocturia remained absent. By 6 months, mild cystitis increased to 18.9%, mild frequency and urgency of urination were noted in 13.2% and 5.7% of patients, respectively, and mild dysuria, incontinence, and hematuria were slightly higher, although severe complications remained uncommon.

At 9 months, most bladder functions returned toward normal, with only a small proportion experiencing mild cystitis, frequency, urgency, dysuria, or hematuria, and severe events were rare [8]. Grading of bladder toxicity similarly demonstrated that the majority of patients had grade 0 toxicity throughout follow-up, with grade 1–3 toxicities occurring in a minority, and death in 1.7% at early follow-up intervals [9]. The gradual improvement in both bowel and bladder function is consistent with previous studies showing that acute

treatment-related toxicities peak early and often resolve or decrease over time with appropriate management. The present findings also highlight the importance of monitoring and managing genitourinary and gastrointestinal symptoms to prevent long-term complications that can significantly impact quality of life.

Quality of life assessment in this study demonstrated a consistent improvement across functional, symptom, and global health scales. Functional scores increased from 65.44 ± 12.98 at baseline to 81.09 ± 7.94 at 9 months, indicating enhanced physical, emotional, and social functioning. Symptom scale scores decreased from 35.05 ± 11.96 at baseline to 21.36 ± 8.77 at 9 months, reflecting a reduction in treatment-related symptoms. Global health status also improved progressively from 48.35 ± 5.98 at baseline to 75.67 ± 12.79 at 9 months, suggesting an overall enhancement in patient well-being and satisfaction with life post-treatment [10].

These findings corroborate prior reports that effective management of acute and late toxicities, along with supportive care, contributes to improved quality of life in LACC patients undergoing CCRT and brachytherapy.

Conclusion

This study demonstrates that neoadjuvant chemotherapy with weekly cisplatin and paclitaxel followed by standard chemoradiation is a feasible and effective treatment strategy for patients with locally advanced cervical cancer. The regimen achieved a high overall response rate with significant tumor size reduction, manageable toxicity, and encouraging short-term survival outcomes. Patients who responded well to neoadjuvant chemotherapy showed significantly improved progression-free and overall survival, underscoring the importance of tumor response as a prognostic indicator. The integration of neoadjuvant chemotherapy into the multimodal treatment of locally advanced disease, further large-scale randomized trials with longer follow-up are needed to confirm the long-term benefits and optimize treatment protocols. Ultimately, this approach holds promise to improve outcomes and quality of life for women facing this challenging diagnosis.

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