COMPARATIVE OUTCOMES OF RADIATION TREATMENT MODALITIES FOR PROSTATE CANCER IN A RESOURCE-LIMITED SETTING

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ABSTRACT

Background: Prostate cancer remains a major malignancy in sub-Saharan Africa, where access to advanced radiotherapy is limited.

Objective: This study compares biochemical recurrence-free survival (bRFS) and toxicity outcomes among prostate cancer patients who received external beam radiotherapy (EBRT) alone, high-dose-rate brachytherapy (HDRBT) monotherapy, or combined EBRT+HDRBT at West Africa's first Prostate HDR brachytherapy centre.

Methods: This retrospective cohort study included 109 prostate cancer patients treated at University College Hospital, Ibadan, Nigeria, from January 2020 to December 2023. Patients were grouped by modality: EBRT alone (n=67), HDRBT monotherapy (n=24), and EBRT+HDR BT (n=18). Biochemical recurrence was defined per Phoenix criteria (nadir PSA+2ng/mL). Toxicity was graded using the Common Terminology Criteria for Adverse Events v5.0. Kaplan-Meier analysis estimated bRFS, with log-rank test for comparisons and multivariable Cox regression for predictors. Logistic regression assessed toxicity predictors. $p < 0.05$ was denoted as significant.

Results: Median follow-up was 21 months (range:6-42 months). Kaplan-Meier estimated bRFS at 30 months was 41.7%, 56.5% and 84.4% for HDRBT, EBRT and EBRT+HDRBT, respectively (p=0.075). Multivariable Cox analysis identified the Gleason score as the only significant predictor (HR=1.34, 95% CI:1.07-1.69; p=0.012). EBRT+BT had better biochemical control compared to EBRT. (HR=0.30, 95% CI:0.09-1.06; p=0.061). ≥Grade 2 toxicity was lower in BT (4.2%) compared to EBRT (35.8%) and EBRT+HDRBT (27.8%; p<0.001), with HDRBT associated with reduced odds (AOR=0.069, 95% CI:0.008-0.609; p=0.016).

Conclusion: In this LMIC cohort, combined EBRT+HDRBT showed a non-significant trend toward improved bRFS compared to EBRT alone, and significantly better outcomes than BT monotherapy. HDRBT monotherapy offered the best tolerability.

Keywords: Prostate Cancer; External Beam Radiotherapy; High-Dose-Rate Brachytherapy; Toxicity; Biochemical Recurrence-Free Survival

INTRODUCTION

Prostate cancer is a major contributor to global cancer morbidity and mortality, ranking as the leading malignancy among men in sub-Saharan Africa.[1] Despite its high burden, access to definitive treatments, including radiotherapy, remains limited in most low- and middle-income countries (LMICs), where infrastructural deficits, limited technical expertise, and cost constraints are common.[2]

External beam radiotherapy (EBRT) remains the main approach for curative treatment in localised and locally advanced prostate cancer.[3] However, traditional EBRT courses typically span 25–30 fractions over 5-6 weeks, imposing significant travel, time, and financial burdens on patients.[4,5] Advances in radiotherapy, particularly high-dose-rate (HDR) brachytherapy, have demonstrated superior dose conformity, biological effectiveness, and convenience, especially when combined as a boost with EBRT.[5,6] HDR brachytherapy offers distinct advantages for LMICs by enabling shorter treatment durations, reducing equipment needs, and allowing higher patient throughput, which is beneficial where radiotherapy resources are limited.

Several studies from high-income countries have shown that HDR brachytherapy, whether used alone or with EBRT, leads to better biochemical control and comparable or better survival outcomes compared to EBRT alone.[7-9] Prostate HDR brachytherapy and EBRT have also been demonstrated to have manageable toxicities. Acute and late genitourinary and gastrointestinal toxicities from these treatment options were mostly grade one and two.[10] Nonetheless, evidence from LMICs remains limited, and local data are essential to confirm these benefits within different healthcare settings. In Nigeria, the establishment of the first HDR prostate brachytherapy centre at the University College Hospital (UCH), Ibadan, presents an opportunity to assess the outcomes of EBRT alone, HDR-BT monotherapy, and combined EBRT+HDR-BT in a real-world, resource-constrained environment.

This study aimed to compare (1) bRFS and (2) the toxicity among patients treated with EBRT.
alone, HDR-BT monotherapy, and combined EBRT+HDR-BT, and (3) identify clinical predictors of biochemical relapse and toxicity.

MATERIALS AND METHODS

A retrospective cohort study was conducted, including all prostate cancer patients treated between January 2020 and December 2023 at UCH Ibadan. Patients with prior pelvic radiotherapy and those with incomplete records were excluded. Patients were grouped by treatment modality: EBRT alone, HDR brachytherapy monotherapy, and combined EBRT+HDRBT. Data collected from patients' records using a form included demographics (age), tumour characteristics (PSA, Gleason score, TNM stage), treatment details (modality, dose, androgen deprivation therapy [ADT]), and outcomes (biochemical recurrence and toxicity). The primary endpoints were biochemical relapse-free survival (bRFS). Biochemical recurrence was defined according to the Phoenix criteria (nadir + 2 ng/mL). Secondary endpoints included ≥Grade 2 toxicity (genitourinary/gastrointestinal combined). Toxicity was graded using the Common

Terminology Criteria for Adverse Events (CTCAE) v5.0.

This study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from study participants, and the study was approved by the Joint Ethical Committee of the University of Ibadan and University College Hospital Ibadan (IRB number UI/EC/23/0775).

Description of Treatment Modalities: All patients received definitive or combined modality radiotherapy for histologically confirmed adenocarcinoma of the prostate at the Department of Radiation Oncology, University College Hospital (UCH), Ibadan—West Africa's first centre to implement high-dose-rate (HDR) brachytherapy for prostate cancer. Allocation to treatment modality was determined by disease risk group, prostate volume, physician discretion, and patient preference, taking into account logistical and financial factors common in a resource-limited setting.

1. **External Beam Radiotherapy (EBRT) Alone:** Patients in the EBRT-only group received external beam radiotherapy using a Cobalt-60 teletherapy unit, after 2D radiotherapy treatment planning or a Linear accelerator using the 3D conformal radiotherapy technique. Treatment was administered with a total dose (Biologic effective dose) of 66–74 Gy. Although image guidance was not routinely available, patient setup was verified daily through laser alignment and field marks.

2. **High-Dose-Rate (HDR) Brachytherapy Monotherapy:** HDR brachytherapy was performed using a Cobalt-60 (^{60}Co) remote afterloading system. Under spinal anaesthesia, transperineal needles were inserted under transrectal ultrasound (TRUS) guidance using a perineal template. CT-based planning was conducted immediately after implantation. The prostate gland served as the clinical target volume (CTV) with a 3–5 mm margin, excluding the rectum and bladder. Dose optimisation and dwell time adjustment were performed to achieve a D90 of at least 100% of the prescribed dose while maintaining dose constraints for the rectum and bladder. Patients typically received two fractions of 9–13.5 Gy each (total dose 18–27 Gy) delivered 24 hours apart. Selected low-risk patients received a single fraction of 15 Gy. The entire procedure was performed on a short-stay basis, reflecting the efficiency and suitability of HDR brachytherapy for low-resource settings.

3. **Combined EBRT + HDR Brachytherapy:** In the combined-modality group, patients received pelvic EBRT followed by HDR brachytherapy boost. EBRT was delivered at a dose of 45–50 Gy in 1.8–2 Gy fractions, targeting the prostate and pelvic lymphatics, followed by HDR boost of one or two fractions of 9–10.5 Gy to the prostate. HDR brachytherapy used the same Cobalt-60 system and planning process as in monotherapy. The interval between completing EBRT and the HDR boost was typically 1–2 weeks to ensure treatment continuity and optimal biological dose escalation.

4. **Androgen Deprivation Therapy (ADT):** ADT was administered according to disease risk and physician discretion. Patients received either luteinizing hormone-releasing hormone (LHRH) agonists or bilateral orchidectomy for medical or surgical castration, respectively. The ADT duration ranged from 6 months (intermediate-risk) to 24–36 months (high risk), in line with institutional and international practice recommendations.

Quality Assurance: All EBRT and HDR plans underwent independent review by a radiation oncologist and medical physicist, who were not part of the managing team, before treatment delivery. For HDR brachytherapy, pre-treatment verification of catheter geometry, source calibration, and dwell times was routinely performed. EBRT plans underwent independent dose verification to ensure accuracy and reproducibility of delivered doses.

Statistical analysis plan: Descriptive statistics were presented using frequencies, percentages, medians, and interquartile ranges (IQRs) or ranges in tables. The chi-square test was used to compare proportions between treatment modalities. In contrast, the Kruskal-Wallis test was employed to assess differences in the average age and PSA levels across treatment groups. Survival outcomes were estimated with the Kaplan-Meier method, and log-rank tests were used for comparisons (Bonferroni-corrected for pairwise comparisons: alpha = 0.017). The Cox proportional hazards model and logistic regression identified predictors of bRFS and toxicity, respectively, while adjusting for age, TNM stage, Gleason score, PSA, and ADT. Post-hoc power analysis for bRFS was performed using G*Power (event rate = 40%, alpha = 0.05, groups = 3). Statistical analyses were conducted using SPSS version 25, with significance set at $p < 0.05$.

RESULTS

Patient Characteristics

A total of 109 patients were included in the analysis, comprising 67 (61.5%) who received external beam radiotherapy (EBRT) alone, 24 (22.0%) treated with brachytherapy (BT) monotherapy, and 18 (16.5%) who received combined EBRT and BT (EBRT+HDR-BT). The median age of participants who received EBRT alone, BT monotherapy, and combined EBRT and BT were 66 years (IQR: 62; 70 years), 71 years (IQR: 63; 73 years), and 66 years (IQR: 59; 73.5 years), respectively $p = 0.556$). Median pre-treatment PSA levels were also comparable across groups ($p = 0.563$) [Table 1].

The distribution of Gleason scores was similar between treatment modalities ($p = 0.620$). Overall, 29 (43.3%) patients had a Gleason score of 7, while 12 (17.9%), 7 (10.4%), 10 (14.9%), and 9 (13.4%) had Gleason scores ≤6, 8, 9, and 10, respectively. ADT was administered to 70.1% of EBRT patients but to only 16.7% of those in the BT and EBRT+BT groups ($p < 0.001$). Most patients in the BT (62.5%) and EBRT+BT (66.7%) groups had early-stage (Stage 1/2) disease, whereas the EBRT group had higher proportions of Stage 3 (23.9%) and Stage 4 (35.8%) cases ($p < 0.001$) [Table 1].

Survival Outcomes

During follow-up, 44 (40.4%) biochemical recurrence events were recorded (22.2% for

EBRT+BT, 37.5% for BT alone and 46.3% for EBRT alone) [Table 2].

The Kaplan–Meier estimated bRFS at 30 months was 84.4% in the EBRT+BT group, 56.5% in the EBRT only arm and 41.7% among patients receiving BT alone. The mean estimated bRFS time was longest in the EBRT+BT group (36.4 ± 2.4 months), compared with EBRT alone (29.6 ± 1.7 months) and BT monotherapy (21.2 ± 2.1 months) (p = 0.075). Pairwise comparisons showed that EBRT+BT achieved significantly better bRFS compared with BT monotherapy (p = 0.012), and a non-significant trend toward improvement compared with EBRT alone (p = 0.162). No significant difference was observed between the EBRT and BT groups (p = 0.172) [Figure 1].

Table 1: Baseline Characteristics for Study Participants

Variable	EBRT+HDR-BT Median (IQR)/ Frequency (%)	HDR-BT Median (IQR)/ Frequency (%)	EBRT Median (IQR)/ Frequency (%)	p-value
Age (Years)	66.0 (62.0; 70.0)	71.0 (63.0; 73.0)	66.0 (59.0; 73.5)	0.556
IPSA (ng/mL)	26.0 (16.0; 56.8)	8.6 (23.1; 38.3)	23.3 (13.6; 35.7)	0.563
Duration of Follow-up	24.0 (15.0; 36.0)	12.0 (6.0; 21.0)	23.3 (14.0; 34.7)	<0.001
Gleason Score				
≤6	5 (27.8)	6 (25.0)	12 (17.9)	
7	8 (44.4)	10 (41.7)	29 (43.3)	
8	1 (5.6)	4 (16.7)	7 (10.4)	0.620
9	4 (22.2)	3 (12.5)	10 (14.9)	
10	0 (0.0)	1 (4.2)	9 (13.4)	
ADT				
NO	15 (83.3)	20 (83.3)	20 (29.9)	
YES	3 (16.7)	4 (16.7)	47 (70.1)	<0.001
TNM_STAGE				
Stage 1&2	12 (66.7)	15 (62.5)	43 (64.2)	
Stage 3	5 (27.8)	6 (25.0)	0 (0.0)	
Stage 4A	1 (5.6)	1 (4.2)	16 (23.9)	<0.001
Stage 4B	0 (0.0)	2 (8.3)	8 (11.9)	

IPSA: Initial Prostate Specific Antigen. ADT: Androgen Deprivation Therapy.
EBRT: external beam radiotherapy, HDR-BT: high-dose-rate brachytherapy, EBRT+HDR-BT: combined external beam radiotherapy and high-dose-rate brachytherapy

In the multivariable Cox proportional hazards model, the Gleason score was the sole independent predictor of biochemical recurrence–free survival. Each one-unit increase in Gleason score was linked to a 34.4% higher hazard of recurrence (HR = 1.34; 95% CI: 1.07–1.69; p = 0.012).

Age (HR = 1.02; 95% CI: 0.98–1.06; p = 0.340), TNM stage (HR = 1.06; 95% CI: 0.78–1.44; p = 0.719), and baseline PSA level (HR = 0.99; 95% CI: 0.98–1.01; p = 0.640) were not significant predictors. Post-hoc power analysis for the primary bRFS comparison across three treatment arms was 62%. Patients in the combined EBRT+HDR-BT group showed a lower hazard of recurrence compared to the EBRT group (HR = 0.30; 95% CI: 0.09–1.06; p = 0.061). There was no statistically significant difference in

the HR between BT monotherapy and EBRT (HR = 1.33; 95% CI: 0.56–3.18; p = 0.519). Use of ADT showed no statistically significant impact on recurrence (HR = 0.65; 95% CI: 0.29–1.47; p = 0.298) [Table 3]. Post-hoc power analysis for the primary bRFS comparison across three treatment arms was 62%.

Toxicity

Treatment-related side effects were significantly less frequent among BT patients (8.4%) compared to 83.6% in the EBRT group and 38.9% in the combined group (p<0.001) [Table 2]. There were no grade 4 and 5 toxicities.

Multivariable logistic regression identified age and treatment modality as significant determinants of treatment-related toxicity, p<0.05. The odds of treatment-related toxicity increased by 11% with each additional year (AOR = 1.112; 95% CI: 1.042–1.186, p=0.001). Patients who received BT monotherapy had 93% lower odds of treatment-related toxicity compared to those treated with EBRT alone (AOR = 0.069; 95% CI: 0.008–0.609; p=0.016), while there was no significant difference in the odds of treatment-related toxicity between patients who had EBRT alone and those who received EBRT+BT (AOR = 0.954; 95% CI: 0.243–3.747, p=0.946). Neither TNM stage (p = 0.394), baseline PSA (p = 0.945), nor Gleason score (p = 0.423) was a significant predictor of toxicity [Table 4].

Table 2: Treatment Outcome of Study Participants

Variable	EBRT+HDR-BT Frequency (%)	HDR-BT Frequency (%)	EBRT Frequency (%)	p-value
BRFS Outcome				
No Reoccurrence	14 (77.8)	15 (62.5)	36 (53.7)	
Reoccurrence	4 (22.2)	9 (37.5)	31 (46.3)	0.173
Side Effect				
0	11 (61.1)	22 (91.6)	11 (16.4)	
1	2 (11.1)	1 (4.2)	32 (47.8)	<0.001
≥ 2	5 (27.8)	1 (4.2)	24 (35.8)	

BRFS: biochemical recurrence-free survival, EBRT: external beam radiotherapy, HDR-BT: high-dose-rate brachytherapy, EBRT+HDR-BT: combined external beam radiotherapy and high-dose-rate brachytherapy

Table 3: Multivariate Analysis of the Relationship between Variables and Biochemical Recurrence–Free Survival

Variables	HR	95.0% CI for HR		p-value
		Lower	Upper	
Age	1.020	0.980	1.062	0.340
TNM_STAGE	1.058	0.777	1.442	0.719
Gleason score	1.344	1.067	1.693	0.012
IPSA	0.997	0.984	1.010	0.640
ADT				
No	Ref			
Yes	0.648	0.286	01.466	0.298
Treatment Modality				
EBRT	Ref			
EBRT+HDR-BT	0.302	0.086	1.057	0.061
HDR-BT	1.331	0.557	3.181	0.519

IPSA: Initial Prostate Specific Antigen, ADT: Androgen Deprivation Therapy, EBRT: external beam radiotherapy, HDR-BT: high-dose-rate brachytherapy, EBRT+HDR-BT: combined external beam radiotherapy and high-dose-rate brachytherapy

Table 4: Multivariate Analysis of Association between Variables and Treatment-Related Toxicity ≥ grade 2

Variables	AOR	95% CI for AOR		p-value
		Lower	Upper	
Age	1.112	1.042	1.186	0.001
TNM_STAGE_Q	1.227	0.766	1.966	0.394
Gleason Score	0.849	0.569	1.267	0.423
IPSAA	1.001	0.984	1.017	0.945
ADT				
No	Ref			
Yes	1.297	0.431	3.907	0.643
Treatment Modality				
EBRT	Ref			
EBRT+HDR-BT	0.954	0.243	3.907	0.946
HDR-BT	0.069	0.008	0.609	0.016

IPSA: Initial Prostate Specific Antigen, ADT: Androgen Deprivation Therapy, EBRT: external beam radiotherapy, HDR-BT: high-dose-rate brachytherapy, EBRT+HDR-BT: combined external beam radiotherapy and high-dose-rate brachytherapy

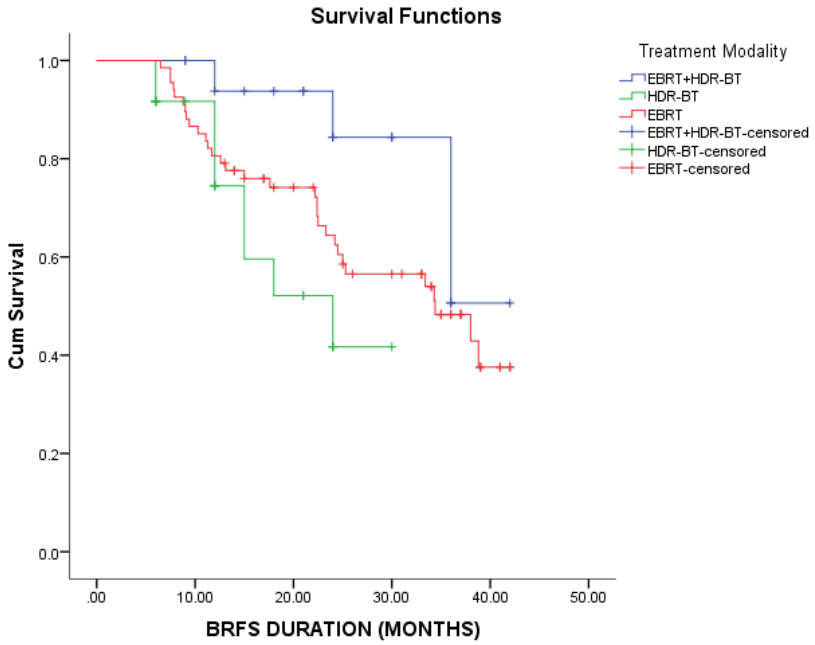

Figure 1: Kaplan–Meier Estimate of Biochemical Recurrence Free Survival (BRFS) based on Radiation Treatment Options

DISCUSSION

This study compared the effectiveness of external beam radiotherapy (EBRT), EBRT combined with high-dose-rate brachytherapy (EBRT+HDR-BT), and HDR brachytherapy (HDR-BT) monotherapy in localised prostate cancer, evaluating biochemical recurrence-free survival (bRFS) and treatment-related toxicity. Over a median follow-up of 21 months, EBRT+HDR-BT showed a non-significant trend toward improved bRFS relative to EBRT alone, while demonstrating a significant advantage over HDR-BT monotherapy. Several systematic reviews and meta-analyses have reported superior biochemical control with combined external beam radiation therapy (EBRT) and high-dose rate brachytherapy (HDR-BT) regimens compared to EBRT alone. Slevin et al., in a systematic review assessing the benefits and harms of EBRT+HDRBT, included seventy-three studies and found that EBRT+HDR-BT is associated with better biochemical control than EBRT alone.[11] Likewise, Kee et al. conducted a systematic review confirming that there was a significant benefit in the 5-year biochemical progression-free survival in favour of EBRT+HDR-BT versus EBRT, with a 51% pooled relative reduction in the hazard of biochemical recurrence.[12] Furthermore, several landmark clinical trials and large-scale retrospective studies have also demonstrated superior biochemical control with combined EBRT+HDR-BT compared to EBRT alone, especially among intermediate- and high-risk patients.[13,14] Hoskin et al. reported in a randomised phase III trial that adding an HDR brachytherapy boost to EBRT significantly improved biochemical relapse-free survival, with a 31% relative reduction in the risk of biochemical or clinical failure.[15]

Similarly, Oshikane et al. retrospectively compared the efficacy and safety of HDR-BT boost versus EBRT alone for high-risk prostate cancer, reporting that the 5-year biochemical recurrence-free survival rate was notably higher in the HDR-BT group.[16] In contrast, Smolska-Ciszewska et al., in a study with a median follow-up of 6 years among 229 patients treated for localised T1-T2N0M0 prostate cancer, found that biochemical recurrences were significantly more frequent in EBRT+HDR-BT compared to EBRT alone, with EBRT alone showing a significantly better 5-year bRFS even after controlling for other variables.[17] This variation may be due to differences in study design. Additionally, the absence of a statistically significant hazard ratio in the present study may relate to its modest event rate and comparatively short follow-up since the benefits of HDR-BT boost often emerge more clearly after 5–10 years.[18] Therefore, while the early results in this current study are consistent with the positive trend, longer follow-up is needed to determine whether the hazard reduction in our cohort will achieve statistical and clinical significance over time.

Evidence suggests that for low- to intermediate-risk prostate cancer, HDR-BT monotherapy can achieve comparable long-term biochemical control to the combination of EBRT and HDR-BT, but for high-risk patients, the combined approach often shows superior efficacy. Willen et al reported no statistically significant difference in freedom from biochemical failure between HDR-BT monotherapy and EBRT+HDR-BT among patients with unfavourable intermediate-risk disease.[19] Conversely, the present study found significantly better bRFS with EBRT+HDR-BT than HDR monotherapy, likely reflecting differences in study population characteristics, such as risk stratification or the use of androgen deprivation therapy. Furthermore, the comparison between HDR-BT monotherapy and EBRT in this study revealed no statistically significant difference in biochemical outcomes. This aligns with several recent studies that suggest HDR brachytherapy offers comparable biochemical control outcomes to EBRT alone in selected low- and favourable-intermediate-risk patients but may be less effective for higher-risk disease unless combined with EBRT.[20,21] Yoshioka et al. demonstrated that HDR-BT monotherapy achieved a 5-year biochemical relapse-free survival rate of approximately 90% in low-risk patients and 80% in intermediate-risk patients, comparable to the rates achieved with EBRT.[22] However, in contrast, Goy et al. found a significantly higher proportion of 10-year Freedom from biochemical failure for brachytherapy compared to external radiation among patients with intermediate risk.[23] This difference may be a result of variation in study design; for instance, in the study by Goy et al., the cohort that had brachytherapy was significantly younger than those who had EBRT. In contrast, the current study found no significant difference between the groups. In addition, evidence suggests that HDR-BT monotherapy is most appropriate for patients with smaller prostate volumes, lower PSA, and limited extracapsular extension,[24.25] of which these criteria may not have been uniformly met in this current study population, potentially explaining the absence of a significant advantage relative to EBRT.

Regarding toxicity, this study found no significant difference in ≥Grade 2 toxicity between EBRT+HDR-BT and EBRT alone,

whereas HDR-BT monotherapy demonstrated significantly lower toxicity than both EBRT-based approaches. These findings align with evidence suggesting that HDR-BT monotherapy, when properly planned and executed, can achieve high conformality and steep dose fall-off, thereby minimising radiation exposure to surrounding organs at risk.[20,23] Morton et al. reported that HDR-BT monotherapy achieved excellent biochemical control with <5% late Grade 2 urinary or rectal toxicity.[20] Similarly, Goy et al. observed that HDR-BT monotherapy was associated with significantly lower rates of rectal late toxicities.[23] The study reported that grades 1 and 2 rectal toxicities occurred in 6.5% of brachytherapy patients vs. 15.2% of EBRT, although grade 3 and 4 rectal toxicities were not significantly different.[23]

Furthermore, results from some recent studies have shown that the addition of HDR-BT boost to EBRT does not significantly increase moderate or severe toxicity when modern planning and image-guided techniques are employed.[11,12] Hoskin et al. reported that late Grade ≥ 2 rectal and urinary toxicities were comparable between EBRT alone and EBRT+HDR-BT arms, despite higher biologically effective doses delivered in the combination group.[15] Similarly, Tamihardja et al. found no significant rise in ≥ Grade 2 late genitourinary or gastrointestinal events following HDR-BT boost, attributing this to precise dose conformity and improved organ-at-risk sparing with the current protocols.[26] Morton et al., in a study to determine the short- and medium-term effects of a single high-dose-rate brachytherapy fraction of 15Gy and hypofractionated external beam radiation therapy for prostate cancer, also noted that with refined treatment planning and optimised fractionation, the HDR-BT boost can safely intensify the tumour dose without compromising the patient's quality of life.[27] Therefore, our findings reinforce the view that modern HDR-BT boost regimens can enhance local control potential without a significant increase in clinically relevant toxicity compared to EBRT alone, particularly when applied within a contemporary image-guided radiotherapy framework and experienced institutional settings. Overall, the results of this current study support the growing consensus that HDR-BT monotherapy offers a favourable toxicity profile. In contrast, EBRT+HDR-BT achieves enhanced biochemical control with acceptable tolerability, highlighting the importance of individualised treatment planning that balances tumour risk and normal tissue preservation.

Study Limitations

While the present analysis offers valuable early evidence, several limitations should be acknowledged. The retrospective design and limited sample size reduce statistical power (62% post-hoc) and increase the likelihood of a Type II error, particularly in subgroup analyses. The shorter median follow-up may also underestimate both late toxicity and long-term biochemical recurrence rates. Also, separating grade 2 and grade 3 toxicity would have provided a better toxicity profile. Furthermore, androgen deprivation therapy (ADT) status was not uniformly documented, which may confound outcome comparisons, as ADT is known to enhance local control in conjunction with radiotherapy in intermediate- and high-risk disease. Despite these limitations, the hazard estimates align directionally with high-quality randomised data, suggesting the findings are biologically

plausible and clinically meaningful within the study's constraints.

Another consideration is that patient characteristics and risk stratification have a significant influence on comparative outcomes. Most previous randomised studies included predominantly intermediate- and high-risk patients, whereas the present cohort comprised a broader spectrum of risk categories, which may have altered the observable treatment effect. Furthermore, the median follow-up period of approximately 2 years in this current cohort is considerably shorter than the 5–15 years typically required to observe meaningful biochemical failure differences, as prostate cancer recurrences often occur late. Therefore, while the directionality of our HRs supports the established efficacy hierarchy, statistical confirmation will likely require continued surveillance and expanded sample size. An additional strength of the current study lies in its relevance to low- and middle-income country (LMIC) contexts, where HDR brachytherapy offers a cost-effective means of achieving biologically potent dose escalation with minimal infrastructure compared to full EBRT dose escalation. Reports from similar LMIC settings have shown HDR-BT to be logistically feasible, well tolerated, and associated with acceptable toxicity when delivered by trained teams.[26]

Our findings provide further support for incorporating HDR-BT as part of integrated radiotherapy strategies to optimise resource utilisation and patient outcomes. Nevertheless, logistical challenges, including equipment availability, patient throughput, and brachytherapy expertise, remain significant limiting factors for the widespread implementation of this approach across LMIC centres.[28]

CONCLUSION

This study contributes to the growing evidence that combination EBRT+HDR-BT improves biochemical control compared with EBRT alone and is at least equivalent or superior to HDR-BT monotherapy in localised prostate cancer. Although the difference did not reach conventional significance thresholds, the observed hazard reduction and favourable toxicity profile suggest a potential therapeutic advantage that warrants confirmation through longer follow-up and larger, multi-institutional, prospective studies. The study underscores the feasibility of HDR, based on dose escalation in resource-limited settings, offering an efficacious and tolerable option for optimising prostate radiotherapy outcomes.

DECLARATIONS

Conflict of interest: The authors have no conflicts of interest to declare.

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Data availability: The data supporting the findings of this study are available from the

corresponding author upon reasonable request.

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