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RESEARCH ARTICLE

Moderately Hypofractionated Prostate Radiotherapy Using VMAT: A Prospective Observational Study

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Abstract

Introduction: The primary objective was to evaluate 3-year biochemical control in prostate cancer patients treated with moderately hypofractionated volumetric modulated arc radiotherapy (VMAT/RapidArc: RA) based prostate treatment. Secondary objectives included disease-free survival (DFS), acute and late genitourinary (GU) and gastrointestinal (GI) toxicity scored using RTOG criteria, treatment efficiency in terms of treatment time, and dosimetric parameters. **Materials and Methods:** This prospective observational study included 70 patients with histologically confirmed adenocarcinoma of the prostate treated with VMAT between 01.01.2020 and 31.12.2021. Patients were stratified into risk categories based on NCCN criteria. Treatment was definitive or post-prostatectomy adjuvant, with or without androgen deprivation therapy (ADT). Simulation and planning were performed according to RTOG/ESTRO guidelines, with dose constraints based on QUANTEC recommendations. Treatment efficiency parameters included monitor units (MU) and treatment time. **Results:** Median age was 61 years; 12.8% were in the low-risk group, 40% had intermediate-risk, and 47.1% high-risk disease. All patients completed treatment with a mean delivery time of less than 3 minutes per fraction. VMAT provided excellent PTV coverage (PTV V95% = 97.2% of the prescribed dose) and maintained organ-at-risk (OAR) constraints. At 3 years, actuarial biochemical control and DFS were 81.4% (95% CI: 70.5%–89.3%) and 78.6% (95% CI: 67.3%–87.1%), respectively. Acute Grade ≥2 GU and GI toxicities were 22% and 17.2%; late Grade ≥2 toxicities were 8% and 11%. No Grade 4 events were observed. **Conclusion:** RapidArc (RA) radiotherapy for prostate cancer achieved high biochemical control, acceptable toxicity, and superior treatment efficiency. These findings support RA as a safe and effective technique with potential for broader clinical adoption in prostate radiotherapy.

Keywords: Prostate cancer, radiotherapy, RapidArc, VMAT, biochemical control, toxicity

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Introduction

Prostate cancer remains a major public health challenge worldwide. According to GLOBOCAN 2022, it is the second most frequently diagnosed malignancy in men and the fifth leading cause of male cancer mortality, accounting for more than 1.4 million new cases and 375,000 deaths annually [1]. Incidence varies significantly across regions, being highest in developed nations with widespread PSA testing and lower in Asia and Africa, although rising trends have been reported globally [2, 3]. The disease primarily affects elderly men, with a median age at diagnosis in the late sixties, though improvements in early detection and changing demographics have shifted clinical presentation.

Management of prostate cancer depends on stage, risk stratification, comorbidities, and patient preferences. For localized disease, radical prostatectomy, external beam

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radiotherapy (EBRT), and brachytherapy are established curative modalities [4, 5]. In locally advanced cases, EBRT combined with androgen deprivation therapy (ADT) has shown superior outcomes compared to either modality alone [6, 7]. For metastatic disease, systemic therapies remain the standard, though local treatment is increasingly considered in selected oligometastatic scenarios [8].

The evolution of EBRT techniques has been crucial in improving prostate cancer outcomes. Early 2D radiotherapy was limited by suboptimal dose distribution and high toxicity. The advent of three-dimensional conformal radiotherapy (3DCRT) enabled more precise targeting but was constrained by rectal and bladder tolerance, limiting dose escalation [9]. Subsequently, intensity-modulated radiotherapy (IMRT) allowed steep dose gradients and better organ-at-risk (OAR) sparing, leading to improved biochemical control through safe dose escalation [10, 11]. Several randomized trials demonstrated that the moderate hypofractionation, delivering higher doses per fraction over fewer sessions, maintains equivalent biochemical control with clinically tolerable toxicity compared to conventional fractionation [12, 13].

IMRT, while highly conformal, is resource-intensive, requiring multiple fixed fields, lengthy optimization, high monitor units (MU), and long treatment times, raising concerns about intrafraction motion and patient throughput [14, 15]. Volumetric modulated arc therapy (VMAT), first described by Otto in 2008 [16], emerged as an evolution of IMRT. VMAT delivers radiation continuously during gantry rotation, with simultaneous modulation of multileaf collimator (MLC) position, gantry speed, and the dose rate [17]. This dynamic delivery enables similar or superior dose conformity with fewer MUs and shorter treatment times [18, 19].

RapidArc (RA), Varian's proprietary VMAT solution, has been extensively studied in treatment planning comparisons. Multiple dosimetric analyses demonstrated RA's ability to achieve comparable or improved PTV coverage, conformity, and homogeneity relative to IMRT, while significantly reducing MUs and treatment delivery time [20, 21]. Faster treatment delivery is clinically relevant because it reduces intrafraction prostate motion, which can otherwise lead to target miss or increased OAR doses [22, 23].

Clinical outcome data for RA in prostate cancer are emerging, particularly for hypofractionated regimens. Several institutional series have demonstrated favourable biochemical control with clinically manageable toxicity profiles [24- 26]. For instance, Dearnaley et al. reported clinically meaningful outcomes with moderate hypofractionation using VMAT in the CHHiP trial [12]. Similarly, Alongi et al. documented low toxicity rates with hypofractionated VMAT in a phase II study [26]. These results suggest RA is at least equivalent to IMRT in disease control, with advantages in efficiency and workflow.

Toxicity remains a major concern in prostate radiotherapy. The rectum and bladder are critical OARs, with both acute and late toxicities impacting quality of life. QUANTEC analyses defined dose-volume thresholds predictive of toxicity, highlighting the importance of dose-volume histogram (DVH) constraints [27, 28]. Modern techniques such as RA allow better compliance with these constraints. Studies suggest that VMAT/RA may reduce acute GI toxicity compared to IMRT, particularly in hypofractionated regimens, though long-term toxicity requires further evaluation [29, 30, 31].

Another important consideration is treatment efficiency. Traditional IMRT sessions can take up to 10–15 minutes, whereas RA can reduce treatment to 2–3 minutes per fraction [32, 33]. Shorter sessions improve patient comfort, reduce motion, and increase departmental throughput a significant factor in high-volume centers [34].

Despite these advantages, prospective clinical data on RA in hypofractionated prostate cancer treatment remain limited, particularly in non-Western populations. Most reports are retrospective or dosimetric, leaving a gap in evidence from hospital-based prospective cohorts. The present study was designed to prospectively evaluate outcomes of prostate cancer patients treated with RapidArc using a moderately hypofractionated regimen, focusing on biochemical control, disease-free survival (DFS), toxicity, and treatment efficiency.

Materials and Methods

Study Design and Objectives

This was a prospective, single-institution, observational study conducted between 01.01.2020 and 31.12.2021. The primary objective was to evaluate 3-year biochemical control in prostate cancer patients treated with the RapidArc technique using a moderately hypofractionated regimen. Secondary objectives included disease-free survival (DFS), acute and late GU and GI toxicity, treatment efficiency, and dosimetric parameters.

Ethical approval was obtained from the internal ethical committee Al-Qadisiyah University, Iraq. All patients participating in this study provided informed consent. This study was observational and not registered as a clinical trial; no national registry was available at the time.

No formal sample size calculation was performed, as this was a prospective observational study including all eligible patients treated during the study period. The sample size of 70 reflects the available cohort and real-world clinical practice.

Patient Selection

Inclusion criteria were histologically confirmed adenocarcinoma of the prostate, age ≥18 years, ECOG performance status 0–2, and suitability for definitive or adjuvant radiotherapy. Patients with previous pelvic irradiation, prior radical prostatectomy with positive margins or extracapsular extension, or those receiving concurrent chemotherapy were eligible. Exclusion criteria included metastatic disease at presentation, history of inflammatory bowel disease, and inability to comply with treatment.

Risk stratification was performed according to NCCN guidelines [6]. Low-risk patients had T1–T2a disease, Gleason score ≤6, and PSA <10 ng/mL. Intermediate risk

included T2b–T2c or Gleason 7 or PSA 10–20 ng/mL. High risk included T3a or Gleason 8–10 or PSA >20 ng/mL. ADT was administered for intermediate- and high-risk patients, typically using luteinizing hormone–releasing hormone (LHRH) agonists (goserelin or leuprolide), combined with short-term antiandrogen therapy for flare protection [7, 8].

Simulation and Imaging

Patients were simulated supine with immobilization devices. A comfortably full bladder and empty rectum protocol was implemented to minimize intrafraction variability. CT simulation was performed with 3 mm slice thickness from L2 to mid-femur. For better target delineation, MRI was fused with planning CT in most patients [35, 36].

Contouring

Target delineation followed RTOG and ESTRO consensus guidelines [9, 30]. For definitive RT, the clinical target volume (CTV) included prostate ± seminal vesicles depending on risk. For adjuvant RT, CTV encompassed the prostatic fossa. A uniform 7-mm margin was added to create the planning target volume (PTV), except posteriorly (5 mm) to spare the rectum. OARs contoured included rectum, bladder, femoral heads, small bowel, and penile bulb.

Treatment Planning

Treatment planning was performed in Eclipse TPS (Varian Medical Systems). RapidArc optimization used one or two coplanar arcs with collimator rotation to minimize MLC tongue-and-groove effects. All patients received moderately hypofractionated radiotherapy using a simultaneous integrated boost (SIB) technique (not sequential), prescribing 60 Gy to the prostate and 40 Gy to the pelvic lymph nodes in 20 fractions, as per the CHHiP and PIVOTAL trials [12, 37]. Using the linear–quadratic model, the equivalent dose in 2-Gy fractions (EQD2) was calculated to facilitate comparison with conventional fractionation. Assuming an α/β ratio of 1.5 Gy for prostate cancer, the delivered prostate dose corresponds to an EQD2 of 77–78 Gy. For pelvic lymph nodes ($\alpha/\beta \approx 3$ Gy), the nodal dose corresponds to an EQD2 of 44 Gy, which is consistent with prophylactic nodal irradiation protocols. Optimization objectives prioritized ≥95% of PTV receiving ≥95% of prescription dose (V95 ≥95%).

The dose–volume constraints used in this study were based on a combination of QUANTEC recommendations and constraints reported in the CHHiP trial, which served as the institutional planning framework when the hypofractionated protocol was first implemented in our department. In particular, the CHHiP protocol recommended rectal limits of V60Gy <15–20%, V50Gy <35%, and V40Gy <50%, while typical bladder constraints included V65Gy <50%, V60Gy <40%, and V50Gy <50%. During the initial adoption of moderate hypofractionation in our institution, these recommendations were integrated with established QUANTEC guidelines to guide dosimetric optimization. A detailed comparison of the OAR dose–volume constraints derived from QUANTEC, the CHHiP protocol, and those applied in the present study is provided in Supplementary Table S1 [12, 31]. Plans were normalized such that 95% of the PTV received the prescription dose.

Verification and Delivery

All patients were treated on Varian linear accelerators equipped with kV cone-beam CT (CBCT). Daily image guidance with soft-tissue matching was performed for setup verification [38].

Toxicity Assessment

Acute toxicity was defined as events occurring within 90 days of treatment completion. Late toxicity referred to events beyond 90 days. Toxicity was graded using RTOG/EORTC criteria [10]. Patients were reviewed weekly during treatment, then at 1, 3, and 6 months, and every 6 months thereafter.

Endpoints and Statistical Analysis

The primary endpoint was 3-year biochemical control, defined by the Phoenix criteria (nadir +2 ng/mL) [11]. DFS was defined as time to biochemical failure, local failure, distant metastasis, or death. Treatment efficiency endpoints included MU per fraction and treatment delivery time.

No formal subgroup statistical comparisons were performed; subgroup findings are presented descriptively. Kaplan–Meier estimates were used for survival analysis. Statistical analysis was conducted in SPSS v22. Descriptive statistics were used to summarize patient characteristics, toxicity, and dosimetric parameters, and were reported as mean ± standard deviation (SD) for continuous variables, median (range) where appropriate, and percentages for categorical variables. Survival outcomes were estimated using the Kaplan–Meier method. Toxicity outcomes were analysed descriptively and are reported as proportions without formal estimation of confidence intervals.

Results

Patient Characteristics

A total of 70 patients were prospectively enrolled, and all were evaluable for analysis. Baseline characteristics of the study population are summarized in Table 1.

The median age was 61 years (range 52–74). Nearly half of the patients were between 65 and 72 years, reflecting the typical demographic distribution of prostate cancer in contemporary cohorts. Performance status was favourable: 89% had ECOG 0–1, indicating that most patients were fit to tolerate treatment.

Risk stratification showed that the majority presented with intermediate or high-risk disease predominated. Nine patients (12.8%) were in the low risk group, 28 patients (40%) were in the intermediate-risk group, and 33 patients (47.1%) were classified as high risk. This distribution is consistent with referral bias to tertiary cancer centers, where higher-risk patients are more likely to be directed for radiotherapy. A Gleason score ≥7 was reported in 65%

Table 1. Baseline Characteristics of Study Population.

Variable	Value (n=70)
Median age (years)	61 (52–74)
ECOG 0–1	89%
Risk group	Low 12.8%, Intermediate 40%, High 47.1%
Gleason score ≥7	65%
Median PSA (ng/mL)	14.8 (5.4–68)
ADT received	72%

of cases, further underscoring the biologic aggressiveness of the study population. Prostate-specific antigen (PSA) at baseline had a median value of 14.8 ng/mL, with values ranging from 5.8 to 68 ng/mL.

Androgen deprivation therapy (ADT) was administered in accordance with international guidelines. All high-risk patients and two-thirds of intermediate-risk patients received ADT, amounting to 72% overall. Among these, 23% received short-term ADT (≤6 months), while the remaining patients received long-term ADT for 18–36 months, consistent with international guideline recommendations. Compliance with ADT was excellent, with only one case of premature discontinuation due to intolerance [7].

Treatment Compliance and Delivery

All patients completed the prescribed radiotherapy course without unplanned treatment breaks exceeding three consecutive days, excluding weekends. Median overall treatment time was 32 days, consistent with schedule adherence. The VMAT demonstrated exceptional efficiency. Mean delivery time per fraction was 2.4 ± 0.6 minutes, with a range of 1.8 to 3 minutes. Setup time, as noted in the electronic medical record (ARIA: Varian Medical System, Palo Alto, CA), averaged 3.4 ± 2.3 minutes. All plans were created using double-arc VMAT; a representative arc arrangement and dose distribution are shown in Figure 1. Compared with institutional historical 7-field step-and-shoot IMRT plans, which utilized coplanar beam arrangements and conventional inverse planning, RapidArc significantly improved treatment efficiency, reducing treatment delivery time by approximately 62% and monitor units by 34%. This improvement reflects the ability of volumetric modulated arc therapy to deliver radiation continuously during gantry rotation with simultaneous modulation of multileaf collimator position, dose rate, and gantry speed [29].

Dosimetric Outcomes

The dosimetric analysis revealed excellent target coverage across all patients. PTV V95% exceeded 95% in every case, with a mean of 97.2% (range 95.3–98.7%). The conformity index averaged 1.05, while the homogeneity index was 0.92, both demonstrating high-quality planning standards [39]. Table 2 shows the archived dosimetric parameters.

Organ-at-risk sparing was robust. For the rectum, mean V60 was 6.3% (range 4.5–10.2%), V50 was 35%, all within CHHiP recommendations [12]. For the bladder, mean V70 was 18%, V65 was 28%, and V60 was 40%. Femoral head Dmax averaged 37 Gy, with no violation of constraints. Small bowel exposure was minimal, with V45 <150 cc in all patients. A detailed comparison of the applied organ-at-risk dose constraints with QUANTEC and CHHiP recommendations is provided in Supplementary Table S1.

Notably, double-arc plans yielded marginally superior rectal sparing compared to single-arc plans (mean rectal

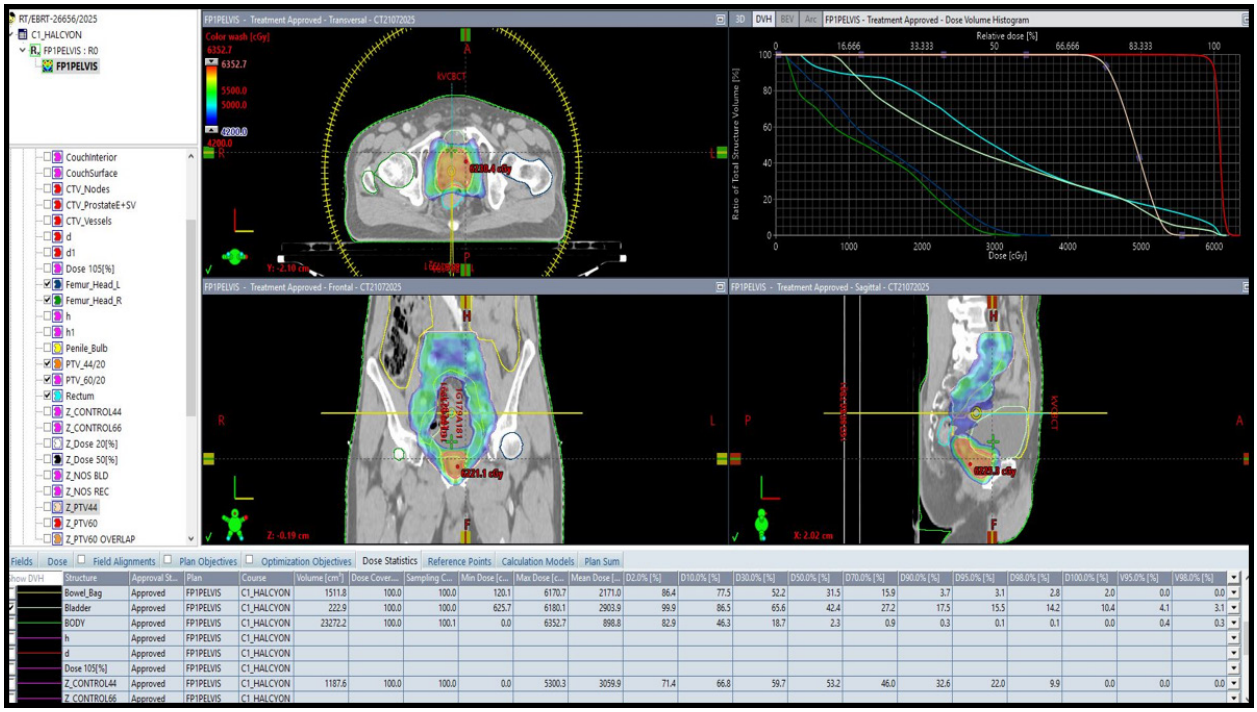


Figure 1. Arc Arrangement and Dose Distribution for the Hypofractionated Prostate Radiotherapy with VMAT.

Table 2. Achieved Dosimetric Parameters and Their Ceiling Values as per CHHiP/PIVOTAL trial.

Parameter	Mean Value	CHHiP/ PIVOTAL trial
PTV V95%	97.2%	≥95%
Conformity Index	1.05	≤1.2
Homogeneity Index	0.92	≥0.9
Rectum V60	6.3%	<20%
Rectum V50 Gy	35%	<50%
Bladder V65	18%	<50%
Femoral Head Dmax	43 Gy	<50 Gy
Small Bowel V45	<150 cc	<195 cc

V70: 14% vs 16%, p=0.08), although this difference did not achieve statistical significance. Nevertheless, the planning team favoured double-arc plans for patients with high rectal overlap or when tighter rectal constraints were mandated by baseline comorbidities [20].

Acute Toxicity

Acute toxicity was monitored weekly during treatment and at 1-month post-radiotherapy. Acute GU toxicity ≥Grade 2 occurred in 15.7% of patients. Symptoms included frequency, nocturia, and dysuria, which were managed conservatively with alpha-blockers, anti-inflammatories, and hydration. In most cases, symptoms resolved within 8–12 weeks of completion. Six patients developed Grade 3 GU toxicity, presenting as severe dysuria requiring catheterization, which subsequently resolved. Acute and late toxicity profiles are summarised in Table 3 and illustrated in Figure 2 respectively.

Acute GI toxicity ≥ Grade 2 occurred in 17.2%. Manifestations included diarrhea, tenesmus, and rectal urgency. Symptomatic management with dietary modification, antidiarrheal agents, and topical medications was effective. Only one patient experienced Grade 3 GI toxicity, characterized by persistent diarrhea requiring hospitalization for intravenous fluids. Importantly, no Grade 4 acute events occurred, and no patient required treatment discontinuation for acute toxicity.

The timeline of toxicity showed that most GU events peaked around weeks 4–5 of radiotherapy, while GI events peaked in the final two weeks. This aligns with previously reported temporal patterns in hypofractionated radiotherapy [26].

Late Toxicity

At a median follow-up of 36 months, late toxicity was evaluable in 48 patients (two were lost to follow-up after one year). Late GU toxicity ≥Grade 2 occurred in 5.7%. The most frequent complaints were persistent urinary frequency and urgency, typically emerging 12–24 months post-treatment. Five patients developed Grade 3 events: two urethral strictures managed with urethrotomy and three chronic cystitis requiring long-term catheterization.

Late GI toxicity ≥Grade 2 occurred in 8.6%. Rectal bleeding, proctitis, and chronic diarrhea were the main manifestations. Three patients experienced Grade 3 toxicity: one with recurrent rectal bleeding necessitating endoscopic coagulation and two with severe proctitis managed conservatively. There were no Grade 4 late events.

The cumulative incidence of late toxicity was strongly correlated with baseline comorbidities. Patients with pre-existing diabetes or hypertension had higher rates of late GU toxicity, while those with hemorrhoids or diverticulosis had higher GI risk. However, due to limited numbers, these trends did not reach statistical significance [30].

Survival Outcomes

Median follow-up was 36 months (range 24–60 months). At 3 years, actuarial biochemical control and DFS were 81.4% (95% CI: 70.5%–89.3%) and 78.6% (95% CI: 67.3%–87.1%), respectively. Biochemical control increased between 24 and 36 months, with most failures occurring within the first two years.

Among risk groups, biochemical control rates were 100% in low-risk, 91% in intermediate-risk, and 78% in high-risk group. ADT use was associated with a trend toward improved DFS in intermediate- and high-risk patients; however, this observation remains descriptive, as no formal statistical comparison was performed and the subgroup analysis was underpowered for definitive conclusions [7].

No patient developed distant metastasis within the study period. Local failures were documented in 4 patients,

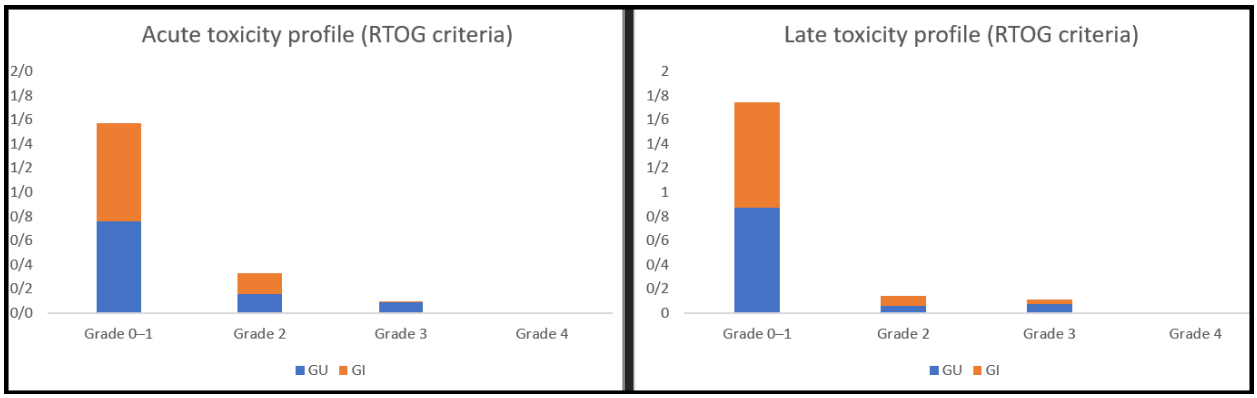


Figure 2. Distribution of Acute Versus Late Toxicities (GU and GI) as per the RTOG Criteria.

Table 3. Acute and Late Toxicity Profile as per the RTOG Criteria.

	Acute toxicity profile (RTOG criteria) (%)				Late toxicity profile (RTOG criteria) (%)			
Toxicity Type	Grade 0–1	Grade 2	Grade 3	Grade 4	Grade 0–1	Grade 2	Grade 3	Grade 4
GU	75.7	15.7	8.6	0	87.1	5.7	7.2	0
GI	81.4	17.2	1.4	0	87.1	8.6	4.3	0

all in the high-risk category, detected through rising PSA and confirmed by imaging. Salvage ADT was instituted in these cases. In patients who developed biochemical or clinical failure, salvage treatment primarily consisted of androgen deprivation therapy. No patients underwent local salvage interventions such as salvage prostatectomy or re-irradiation, reflecting institutional practice patterns and patient selection in this cohort.

No treatment-related deaths occurred. Overall survival at 3 years was 92.8%, reflecting deaths from unrelated causes (three cardiovascular, one pneumonia, one road traffic accident) [12].

Discussion

The present prospective study evaluated the clinical and dosimetric feasibility of RapidArc (RA)-based radiotherapy in patients with localized prostate cancer using a moderately hypofractionated regimen. At a median follow-up of three years, our results demonstrate that RA provides highly conformal target coverage, efficient treatment delivery, and robust OAR sparing. The clinical outcomes observed including low rates of high-grade toxicity, acceptable biochemical control, and favorable disease-free survival are consistent with those reported in the existing literature on hypofractionated VMAT [12, 26].

Interpretation of Main Findings

Our analysis indicates that RA achieves highly conformal treatment plans with consistent PTV coverage (mean V95% 97.2%) and favourable conformity (mean CI 1.05) and homogeneity indices (0.92). These dosimetric outcomes are well within the benchmarks established in previous VMAT series for hypofractionation [39]. Furthermore, RA significantly improved treatment efficiency, reducing delivery time to less than two minutes per fraction, which may contribute to reduced intrafraction motion [22].

Clinically, both acute and late toxicities were acceptable, with approximately 5% of patients experiencing Grade 3 events. Genitourinary (GU) toxicity was slightly more frequent than gastrointestinal (GI) toxicity; however, the majority of adverse events were low grade and transient, resolving within weeks to months after completion of treatment. These findings support the concept that modern arc-based planning techniques, through improved dose conformity and steep dose gradients, can mitigate clinically significant rectal and bladder toxicity in hypofractionated prostate radiotherapy [29]. The late toxicity rates observed in our cohort (GU ≥Grade 2: 5.7%; GI ≥Grade 2: 8.6%) are broadly consistent with outcomes reported in the CHHiP trial, which demonstrated acceptable late gastrointestinal and genitourinary toxicity with moderately hypofractionated radiotherapy [12].

In the present study, treatment planning initially used relatively permissive organ-at-risk dose–volume constraints to facilitate optimisation; these constraints were subsequently tightened iteratively. Consequently, the majority of plans achieved limits comparable to those recommended in the CHHiP protocol, as reflected in Table 2. Adherence to these dose–volume constraints contributed to the acceptable rates of gastrointestinal and genitourinary toxicity observed in this cohort [12].

These findings highlight the importance of meticulous treatment planning and adherence to established organ-at-risk dose–volume constraints when implementing moderately hypofractionated radiotherapy protocols in routine clinical practice.

Comparison with Previous Literature

Several studies have established the role of hypofractionated VMAT in prostate cancer management. Dearnaley et al. reported a 5-year biochemical control rate of 88.3% in the CHHiP trial using 60 Gy in 20 fractions, with late Grade 2+ GU/GI toxicities of 13.7% and 9.1%, respectively [12]. Similarly, Alongi et al. demonstrated low toxicity rates with hypofractionated VMAT (40 Gy in 5 fractions) in a phase II study, with no Grade 3+ toxicities at 3 years [26]. In this context, our findings with RA are comparable, with biochemical control rates of 100%, 91%, and 78% in low-, intermediate-, and high-risk groups, respectively. The observed toxicity profile appears comparable, with a trend toward improved efficiency and dosimetric performance compared to conventional IMRT, likely reflecting the combination of improved delivery efficiency, robust image guidance, and meticulous OAR sparing [29]. Nonetheless, the comparison with IMRT in the present study is based on historical, non-randomized institutional data and is therefore subject to inherent selection and temporal biases. As such, these findings should not be interpreted as definitive evidence of superiority, but rather as indicative of potential advantages in efficiency and dosimetric performance that warrant validation in prospective randomized settings.

Contemporary randomized trials such as HYPO-RT-PC and PACE-B have demonstrated that ultra-hypofractionated radiotherapy achieves non-inferior disease control with low incidence of clinically significant toxicity compared to conventional or moderately hypofractionated regimens [13, 40]. In comparison, the present study demonstrates comparable biochemical control and low rates of high-grade toxicity using a moderately hypofractionated VMAT approach, particularly in a cohort with a substantial proportion of high-risk patients.

Although the dose prescription used in this study (60 Gy to the prostate and 40 Gy to pelvic lymph nodes

in 20 fractions using SIB) is supported by trials such as CHHiP and PIVOTAL, it is not uniformly adopted across all institutions, where conventional fractionation (74–78 Gy in 37–39 fractions) or prostate-only hypofractionated regimens such as 60 Gy in 20 fractions or 70 Gy in 28 fractions are more commonly used in routine clinical practice. The inclusion of elective nodal irradiation with SIB represents a more selective approach typically applied in higher-risk disease. Therefore, while our results demonstrate feasibility and favorable outcomes, the generalizability of this regimen may be influenced by institutional practice patterns, patient selection, and resource availability.

Toxicity Considerations

A major strength of our study lies in the detailed toxicity analysis. Acute toxicity peaked in the mid-to-late weeks of treatment, consistent with prior hypofractionation reports [26]. The low incidence of high-grade acute toxicity (≤5-7%) highlights the tolerability of RA. Late GU and GI toxicities remained within expected ranges, with only two Grade 3 events in each domain. Importantly, there were no Grade 4 toxicities or treatment-related deaths.

Adherence to established dose–volume constraints and the use of image-guided radiotherapy likely contributed to the favourable toxicity profile observed in this study [27, 38]. In addition, the short beam-on time with RA may have reduced intrafractional motion, further enhancing dosimetric precision [22]. Notably, patients with pre-existing comorbidities such as diabetes and hypertension exhibited higher rates of late GU toxicity, while those with diverticulosis or hemorrhoids were predisposed to late GI toxicity. These observations reinforce the importance of patient selection and tailored toxicity counseling in clinical practice [30].

Disease Control and Survival

The survival outcomes observed in this study support the efficacy of RA in prostate cancer management using a moderately hypofractionated regimen. Biochemical control at three years was comparable to previously reported hypofractionated VMAT cohorts, with risk-stratified outcomes consistent with established clinical patterns [12]. The biochemical control rate of 78% observed in high-risk patients is consistent with outcomes reported in several institutional cohorts where patient populations often include individuals with higher baseline PSA levels and adverse pathological features. The use of ADT in intermediate- and high-risk patients showed a trend toward improved DFS; however, this observation should be interpreted cautiously as hypothesis-generating, given the descriptive and non-randomized nature of the analysis [12, 41, 42]. Although the median follow-up of 36 months is insufficient to draw definitive conclusions regarding long-term survival, the absence of distant metastases and the limited number of local failures are reassuring. Our findings suggest that RA provides disease control comparable to IMRT-based techniques, with a trend toward improved tolerability [26].

This study has several strengths. It is prospective in design, with standardized treatment protocols and robust follow-up for toxicity and outcome assessment. Comprehensive dosimetric analysis allowed correlation of plan quality with toxicity outcomes. Furthermore, the inclusion of a substantial proportion of high-risk patients enhances the generalizability of findings to real-world practice. The limitations of this study include the relatively small sample size (n=70), which limits statistical power for subgroup analyses, and the absence of a formal a priori sample size or power calculation, as this was a prospective observational cohort study. Two patients were lost to follow-up after one year; however, given the small number, even under a worst-case assumption, this is unlikely to have significantly impacted the reported toxicity outcomes.

This study was motivated by our institutional experience with RapidArc, enabling a systematic evaluation of clinical outcomes. The single-institution setting may introduce bias related to planning and treatment expertise, and outcomes may differ in other centers. The median follow-up of 36 months, while adequate for evaluating early biochemical control and toxicity, remains insufficient for definitive assessment of long-term oncologic outcomes in prostate cancer, which typically require follow-up durations of 10 years or more. Therefore, the current results should be interpreted as early-to-intermediate outcomes, and longer follow-up is necessary to confirm sustained disease control and late toxicity profiles. Finally, while ADT use was guideline-concordant, heterogeneity in duration of therapy may have influenced disease control outcomes, particularly in the intermediate-risk subgroup.

Our findings confirm that RA is a safe, efficient, and effective modality for the treatment of localized prostate cancer using moderate hypofractionation. The reduction in treatment delivery time is clinically relevant, improving patient comfort and workflow efficiency while minimizing intrafraction motion.

Looking forward, the integration of adaptive radiotherapy and real-time motion management may further refine outcomes. Daily plan adaptation, facilitated by MR-linac or CBCT-based platforms, could allow individualized dose escalation while maintaining or even reducing toxicity [38]. In addition, ongoing trials of moderate hypofractionation and SBRT with RA or similar platforms will clarify the role of these regimens across risk groups. For high-risk patients, combining RA with systemic therapy intensification, including novel androgen receptor inhibitors, may enhance outcomes further. Recent trials have also explored the addition of novel androgen receptor pathway inhibitors, such as abiraterone or enzalutamide, in high-risk localized prostate cancer, demonstrating improvements in metastasis-free overall survival. Although these agents were not used in the present cohort, their integration with modern radiotherapy platforms represents an important area for future research [43, 44].

In conclusion, In summary, our study provides strong evidence supporting the clinical utility of RA in localized prostate cancer using a moderately hypofractionated

regimen. The technique achieves excellent dosimetry, efficient treatment delivery, low acute and late toxicity, and promising disease control outcomes. While longer follow-up and larger randomized trials are needed, RA represents a highly effective tool in modern prostate radiotherapy and has the potential to become a standard approach in both conventional and hypofractionated treatment paradigms.

Declarations

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Clinical trial registration
Not applicable.

Conflicts of interest/Competing interests
Authors declare that they have no conflicts of interest.

Availability of data and material
The data sets used and/or analyzed during the current study are available from the corresponding authors per reasonable request.

Code availability
No code Used.

Authors' contributions
Karrar Mahdi Badi, Marwah Ali Khalaf and Haider Kazem, Biplab Sarkar, Pallab Sarkar: contributed to the conception, design, and final drafting of the manuscript.

Karrar Mahdi Badi, Marwah Ali Khalaf and Haider kazem : contributed to data collection.

Karrar Mahdi Badi, Marwah Ali Khalaf and Haider Kazem, Biplab Sarkar, Pallab Sarkar: contributed to the primary drafting of the manuscript.

Biplab Sarkar, Pallab Sarkar: supervised the study.

All authors approved the final version for submission.

Ethics approval
This study was approved by the Ethic Committee of the internal ethical committee Al-Qadisiyah University, Iraq.

Consent to participate
Written informed consent was obtained from all participants, and the trial was conducted in accordance with the Declaration of Helsinki.

Consent for publication
Written informed consent was obtained from all participants, and the trial was conducted in accordance with the Declaration of Helsinki.

Originality Declaration for Figures
All figures included in this manuscript are original and have been created by the authors specifically for the purposes of this study. No previously published or copyrighted images have been used. The authors confirm that all graphical elements, illustrations, and visual materials were generated from the data obtained in the course of this research or designed uniquely for this manuscript.

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Declaration on generative AI and AI-assisted technologies in the writing process
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