Full Title: Impact of prostate position-based image-guidance in intensity-modulated radiation therapy for localized prostate cancer

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Short Running Title: IGRT for prostate cancer

Abstract

Background/Purpose:

The long-term clinical impact of prostate position-based image-guided radiotherapy (IGRT) for localized prostate cancer remains unclear.

Materials and Methods:

We retrospectively compared clinical outcomes following intensity-modulated radiation therapy (IMRT) with cone-beam computed tomography-based prostate position-based IGRT (P-IGRT) or without P-IGRT (non-P-IGRT). From June 2011, we applied P-IGRT in IMRT for intermediate-risk (IR) prostate cancer (PCa) (D'Amico risk classification) (76 Gy in 38 fractions, with smaller margins). Clinical outcomes of patients who received P-IGRT between June 2011 and June 2019 were retrospectively compared with those of patients with IR PCa who received IMRT without P-IGRT between October 2002 and May 2011 in our institution (74 Gy in 37 fractions).

Results:

A total of 222 consecutive patients were analyzed: 114 in the P-IGRT cohort and 108 in the non-P-IGRT cohort. The median follow-up period after IMRT was 7.1 years for the P-IGRT cohort and 10.8 years for the non-P-IGRT cohort. The biochemical failure-free rate was significantly better in the P-IGRT cohort (94.9% for the P-IGRT cohort versus

82.7% for the non-P-IGRT cohort at 10 years, p = 0.041). The rate of rectal bleeding which need intervention including use of suppositories was significantly lower in the P-IGRT cohort (p < 0.001).

Conclusions:

The use of P-IGRT with higher doses and smaller margins was correlated with significantly better biochemical control, and a lower incidence of rectal bleeding in IMRT for intermediate-risk prostate cancer. The enhanced accuracy using P-IGRT has the potential to independently improve disease control and reduce late rectal bleeding.

Key words:

prostate cancer, image-guided radiotherapy, intensity-modulated radiation therapy, biochemical tumor control, late toxicity

Abbreviations:

IMRT, intensity-modulated radiation therapy; PCa, prostate cancer; IGRT, image-guided radiotherapy; EBRT, external-beam radiotherapy; P-IGRT, prostate position-based image-guided radiotherapy; CBCT, cone-beam computed tomography; IR, intermediate-risk; ADT, androgen-deprivation therapy; CRPC, castration-resistant prostate cancer; CTV, clinical target volume; PTV, planning target volume; VMAT, volumetric-modulated arc therapy; DWA, Dynamic WaveArc; PSA, prostate-specific antigen; BF, biochemical failure; GI, gastrointestinal; GU, genitourinary; UVA, univariate analysis; IQR, interquartile range; HR, hazard ratio; CI, confidence interval

Introduction

High-dose intensity-modulated radiation therapy (IMRT) is one of the standard treatments for non-metastatic prostate cancer (PCa) [1]. Image-guided radiotherapy (IGRT) is a critical technique to correct geographic errors in the target position during the treatment course, such as patient set-up error, using imaging modalities, which enhances the accuracy of dose delivery to the prostate and helps facilitate high-precision IMRT [2,3]. The method of IGRT in external-beam radiotherapy (EBRT) for PCa can be categorized into two types according to the target of image-guidance: the pelvic bony structure, and prostate. Owing to recent technical advances in EBRT, the latter method, prostate position-based IGRT (P-IGRT), using techniques such as cone-beam computed tomography (CBCT), implanted fiducial markers, ultrasound, or magnetic resonance imaging (MRI), is mainly used in daily clinical practice [2].

However, large day-to-day movements of the prostate due to bladder and rectal filling during the treatment course have been reported [4]. Hence, there is a risk of a decrease in the actual dose delivered to the prostate due to positioning error of the prostate caused by such movements. As P-IGRT can correct this type of positioning error and increase the actual dose delivered to the prostate, it has the theoretical potential to improve tumor control. However, most previous reports that evaluated the benefit of P-IGRT were

based on medium-term clinical data (median follow-up typically < 5 years), which are considered insufficient for assessing its impact on tumor control [5-13]. To our knowledge, only one retrospective study reported comparative data with a median follow-up duration of more than 7 years [14]. Due to the lack of high-level evidence based on long-term follow-up data, the clinical impact of P-IGRT on tumor control remains unclear.

Thus, the purpose of the current study was to evaluate the long-term clinical impact of P-IGRT in IMRT for localized PCa, by comparing the clinical outcomes from two cohorts with similar backgrounds treated with or without P-IGRT.

Materials and Methods

This study followed the tenets of the Helsinki Declaration, with approval from the institutional ethical review board (approval number: R1048-1). Written informed consent to the current study was not obtained due to the retrospective nature of the study. Instead, that was obtained in the form of opt-out on our web site. Those who rejected were excluded.

Study design and patients

In our institution, P-IGRT using CBCT was initiated from June 2011 as routine clinical practice in IMRT for intermediate-risk (IR) PCa. Prior to that, patient set-up error correction in IMRT was performed based on the pelvic bony structure, using on-line or off-line radiographs (non-P-IGRT). In this study, we performed a retrospective comparison of clinical outcomes of patients with IR PCa who received IMRT with P-IGRT (after June 2011; P-IGRT cohort) versus without P-IGRT (before May 2011; non-P-IGRT cohort).

The medical records of patients with prostate adenocarcinoma categorized into IR according to the D'Amico classification [15], consecutively treated with IMRT between October 2002 and June 2019 at our institution, were retrospectively reviewed

using our institutional PCa database. Atypical cases receiving long-term neoadjuvant androgen-deprivation therapy (ADT) (> 1 year), or cases developing castration-resistant PCa (CRPC) during neoadjuvant ADT were excluded.

Intensity-modulated radiation therapy (IMRT) methods

The details of IMRT procedures were described previously [10,16]. The clinical target volume (CTV) consisted of the prostate and base of the seminal vesicles in both cohorts. The margin for the planning target volume (PTV) added to CTV to account for set-up uncertainties and organ motion was 9 mm (except for 6 mm in the rectal direction and 9–10 mm in the cranio-caudal direction) in the non-P-IGRT cohort, while it was reduced to 6 mm (except for 5 mm in the rectal direction and 7.5 mm in the cranio-caudal direction) in the P-IGRT cohort.

Regarding IMRT delivery, static beam IMRT was employed in the non-P-IGRT cohort, while static beam IMRT, volumetric-modulated arc therapy (VMAT), or volumetric-modulated Dynamic WaveArc (DWA) therapy [17] was employed in the P-IGRT cohort. Prescribed doses were 74 Gy in 37 fractions in the non-P-IGRT cohort, and increased to 76 Gy in 38 fractions in the P-IGRT cohort. In both cohorts, the total dose was reduced by 4 Gy in patients with risk factors for rectal bleeding, such as receiving

anticoagulant/antiplatelet therapy, and severe diabetes mellitus (glycosylated hemoglobin ≥ 8.0%), as well as in patients with an advanced age (≥80 years) in order to avoid any further aggravation of the risk of rectal bleeding.

Patients were instructed to void the bladder and rectum approximately 1–1.5 hours before treatment, according to their individual urinary conditions. Patients were treated in a prone position before January 2016, and in a supine position thereafter.

Image-guidance method

Details of image-guidance methods were described previously [10,18]. In the non-P-IGRT cohort, daily on-line or off-line set-up error corrections were performed based on orthogonal radiographs of the pelvic bone in all treatment sessions. In the P-IGRT cohort, daily on-line set-up error corrections were conducted based on direct visualization of the prostate using CBCT (manual soft-tissue registration for prostate alignment) in all treatment sessions. No intraprostatic implanted fiducial marker or rectal spacer system was used in any patient in either cohort.

Androgen-deprivation therapy

The same ADT protocol for IR PCa of our institution was consistent during the

study period, for both the P-IGRT and non-P-IGRT cohorts. Details of the protocol were previously reported [16,18]. In brief, short-term neoadjuvant ADT basically consisted of 6 months of combined androgen blockade. However, there were some variations regarding the duration and contents, because a number of patients were introduced to our hospital after ADT had been initiated, and patients with liver dysfunction or special requests were administered a luteinizing hormone-releasing hormone analogue only. No adjuvant ADT was applied.

Patient follow-up

Patients were seen every 1–3 months during the first 2 years and every 3–6 months thereafter. Prostate-specific antigen (PSA) levels were examined at every visit, and no additional radiographic studies were conducted unless there were an increase in PSA levels or symptoms suspected of indicating clinical failure.

Statistical analyses

Chi-square analysis for categorical variables and the Mann-Whitney U test for continuous variables were used to compare the characteristics of patients and treatment

of the two cohorts.

The timing of occurrence of each event was calculated from the date of IMRT initiation. Biochemical failure (BF) was evaluated based on the Phoenix definition (nadir plus 2.0 ng/mL) [19]. The Kaplan-Meier method was used to estimate the BF-free rate, in which death from other causes without a BF event was censored at the last visit. To evaluate the clinical impact of using P-IGRT on BF, univariate analysis (UVA) and multivariable analysis (MVA) were conducted using the Cox proportional hazard model, in which the following covariates were included: IGRT method (P-IGRT versus non-P-IGRT), and favorable versus unfavorable IR (according to the National Comprehensive Cancer Network [NCCN] risk classification version 2022.4 [1])

Late gastrointestinal (GI) and genitourinary (GU) toxicities were re-evaluated based on the Common Terminology Criteria for Adverse Events version 5.0. The time to development of the worst-grade toxicity was documented for late toxicities. For GI toxicities, the use of suppositories was not counted as grade 2 toxicities because these medications were often prescribed for rectal bleeding which is equivalent to grade 1 bleeding. For GU toxicities, only urinary retention and hematuria were assessed, because increased urinary frequency, incontinence, and urgency occur as typical consequences of aging. Toxicities that appeared during the IMRT course and continued for more than three

months were categorized as late toxicities, and the event date was recorded at the end of the IMRT course. The cumulative incidence method was used to calculate the rate of ≥ grade 2 late GI or GU toxicities, in which death without those events was accounted for as a competing risk, and UVA was conducted using the Fine and Gray's regression model. In addition, we also compared the rate of patients with rectal bleeding who needed interventions including the use of suppositories using Chi-square analysis.

All statistical analyses were carried out using EZR version 1.61, which is a graphical user interface for R version 4.1.2 (The R Foundation for Statistical Computing, Vienna, Austria) [20]. A p-value < 0.05 was regarded as significant.

Results:

Patient characteristics

A total of 254 patients met the eligibility criteria. Among them, hypo-fractionated IMRT were applied in 31 patients, and radiation dose was reduced to 66 Gy due to severe concomitant illnesses in one patient. Therefore, these patients were excluded, and the remaining 222 patients were included in the analysis: 114 patients in the P-IGRT cohort, and 108 patients in the non-P-IGRT cohort.

The median age was 71 years old (interquartile range [IQR]: 67–75) in the P-IGRT cohort and 70 years old (IQR: 65–75) in the non-P-IGRT cohort at IMRT initiation ($p = 0.267$). Although the initial PSA level was lower in the P-IGRT cohort (median: 7.3 versus 10.2 ng/mL, respectively, $p < 0.001$) and there was a significant difference in the distribution of the clinical T stage ($p = 0.04$), no significant differences were observed in the distribution of risk classes between the two cohorts, according to the NCCN risk classification version 2022.4 ($p = 0.33$) [1]. Specifically, 37.7% ($n = 43$) and 62.3% ($n=71$) in the P-IGRT cohort, and 30.6% ($n = 33$) and 69.4% ($n = 75$) in the non-P-IGRT were categorized into favorable and unfavorable IR, respectively. Details of patient characteristics are shown in Table 1.

The median follow-up periods were 9.1 years (IQR: 6.0–11.0) for all patients, 7.1 years (IQR: 5.0–9.1) for the P-IGRT cohort, and 10.8 years (IQR: 9.2–13.0) for the non-P-IGRT cohort. The follow-up period after IMRT was significantly shorter in the P-IGRT cohort ($p < 0.001$).

Treatment

The median prescribed dose was 76 Gy (IQR: 72–76) in 38 fractions in the P-IGRT cohort, and 74 Gy (IQR:70–74) in 37 fractions in the non-P-IGRT cohort ($p < 0.001$).

The median duration of neoadjuvant ADT was 7.1 months (IQR: 6.4–7.8) for the P-IGRT cohort, and 6.7 months (IQR: 5.5–8.0) for the non-P-IGRT cohort. No significant difference was observed in the duration of neoadjuvant ADT between the two cohorts ($p = 0.064$).

The details of treatments are shown in Table 1.

Oncological outcomes and late toxicities

During follow-up, 5.3% (n = 6) of the P-IGRT cohort and 11.1% (n = 12) of the non-P-IGRT cohort died, but no mortality was due to PCa.

During follow-up, 3.5% (n = 4) of the P-IGRT cohort and 16.7% (n = 18) of the non-P-IGRT cohort developed recurrence. The BF-free rate was significantly better in the P-IGRT compared with non-P-IGRT cohort (hazard ratio [HR]: 3.31, 95% confidence interval [CI]: 1.10–9.97, p = 0.034) (Fig.1). Specifically, the 5- and 10-year BF rates were 98.0% (95% CI: 92.1–99.5) and 94.9% (95% CI: 86.6–98.1) in the P-IGRT cohort, and 91.3% (95% CI: 83.9–95.4) and 82.7% (95% CI: 73.2–89.1) in the non-P-IGRT cohort, respectively. In MVA, the use of P-IGRT was identified as an independent predictive factor for improved biochemical control (HR: 3.17, 95% CI: 1.05–9.58, p = 0.041). Details of the results of UVA and MVA are shown in Table 2.

Regarding the cumulative incidence of ≥ grade 2 late GI toxicities, although the rate of cumulative incidence was lower in the P-IGRT cohort, the difference was not statistically significant (HR: 3.08, 95% CI:0.63–15.04, p = 0.16) (Fig.2A). Specifically, the 5- and 10-year cumulative incidence rates of ≥ grade 2 late GI toxicities were both 1.8% (95% CI: 0.3–5.7) in the P-IGRT cohort, and 4.7% (95% CI: 1.7–9.9) and 5.7% (95% CI: 2.3–11.2) in the non-P-IGRT cohort, respectively. The rate of patients with rectal bleeding who needed interventions including use of suppositories were significantly lower in the P-IGRT cohort: 6.1% (n = 7) in the P-IGRT cohort versus 25.0% (n = 27) in the non-P-IGRT cohort (p < 0.001).

Regarding the cumulative incidence of ≥ grade 2 late GU toxicities, no significant difference was observed between the P-IGRT cohort and the non-P-IGRT cohort (HR: 1.32, 95% CI: 0.68–2.55, p = 0.41) (Fig.2B). Specifically, the 5- and 10-year cumulative incidence rates of ≥ grade 2 late GU toxicities were 10.0% (95% CI: 5.3–16.5) and 17.8% (95% CI: 9.5–28.1) in the P-IGRT cohort, and 17.7% (95% CI: 11.1–25.5) and 20.9% (95% CI: 13.7–29.1) in the non-P-IGRT cohort, respectively.

Discussion

In the current study, we retrospectively evaluated the clinical impact of prostate position-based image-guidance in IMRT on an IR PCa population, in whom the contents of local treatment are considered to directly reflect the results of disease control. As a result of comparison between P-IGRT and non-P-IGRT cohorts, the use of prostate-based image-guidance was correlated with significantly better biochemical control, and a lower incidence of rectal bleeding. To the best of our knowledge, the current study involved the longest reported follow-up period among published investigations regarding comparison of the IGRT method in definitive EBRT for localized PCa (median: 9.1 years).

As modalities of P-IGRT, indirect visualization of the prostate position using orthogonal radiographs with implanted fiducial makers, and direct visualization of the prostate using CBCT, ultrasound, or MRI are currently available [21]. In the current study, on-line set-up error corrections using CBCT were performed in all treatment sessions in the P-IGRT cohort. In our institution, after applying P-IGRT, we increased the prescribed dose by 2 Gy (from 74 to 76 Gy) and decreased the PTV margin by 3 mm universally except posteriorly and 1 mm posteriorly. Biochemical tumor control was significantly better in the P-IGRT compared with non-P-IGRT cohort (HR: 3.17, 95% CI: 1.05–9.58, $p = 0.041$). Our results are consistent with the findings of a phase 3 trial by de Crevoisier

et al., which compared clinical outcomes of daily versus weekly IGRT among non-metastatic PCa patients [5]. In that trial, P-IGRT using CBCT, ultrasound, or orthogonal radiographs with implanted fiducial markers was employed as an IGRT modality. As a result of comparison, the BF-free interval was significantly longer in the daily IGRT group (HR: 0.45; 95% CI: 0.25–0.80, p = 0.007). Specifically, BF incidence rates at 5 years were 9% (95% CI: 5–15) in the daily IGRT group and 21% (95% CI: 15–29) in the weekly IGRT group. Similarly, according to a retrospective study comparing P-IGRT using implanted fiducial markers and non-IGRT (without fiducial markers) by Zelefsky *et al.*, the use of P-IGRT was correlated with significantly better BF-free survival in a high-risk population (97 versus 77.7% at 3 years, respectively, p = 0.05), although no significant differences were observed among low-risk and IR populations [6]. All these findings taken together point toward the importance of accurate prostate targeting, which leads to an increase in the actual dose delivered to the prostate. Therefore, P-IGRT has the potential to independently improve tumor control.

Excellent tumor control achieved via the combination of brachytherapy and EBRT has been reported [22,23]. According to the ASCENDE-RT phase 3 trial by Morris *et al.*, which compared the clinical outcomes of the combination of pelvic irradiation (46 Gy in 23 fractions) and low-dose-rate prostate brachytherapy (minimal peripheral dose of

115 Gy) with dose-escalated EBRT (pelvic irradiation followed by EBRT boost to the prostate: total 78 Gy in 39 fractions), BF-free survival was significantly lower in the EBRT arm (HR: 2.04; 95% CI: 1.25–3.33, p = 0.004) [22]. In the EBRT arm, as the use of IGRT was not mandatory in that trial, the actual dose delivered to the prostate may have been lower than that prescribed. This could be one possible explanation for decreased tumor control in the EBRT arm. In their subgroup analysis of IR PCa populations, the BF-free survival rate of the brachytherapy arm was approximately 95% at 5 years. In our P-IGRT cohort, the BF-free rate was 98.0% at 5 years, which was similar to that of their brachytherapy arm, even though we applied ADT with a shorter duration (median: 7.1 months in our P-IGRT cohort versus 1 year in the ASCENDE-RT trial) and prescribed a lower dose to the prostate (median: 76 Gy in our P-IGRT cohort versus 78 Gy in the EBRT arm of the ASCENDE-RT trial). Similarly, according to a Japanese phase 2 study of moderate hypofractionated IMRT (70 Gy in 28 fractions) with P-IGRT techniques by Nihei *et al.*, in which 60% of the enrolled patients had IR PCa, the BF-free survival rate was 90.4% at 5 years [24]. Therefore, these results suggest that modern IMRT with P-IGRT can achieve tumor control similar to brachytherapy.

In the current study, although difference in the rate of ≥ grade 2 late GI toxicities was not statistically significant (p = 0.16), the patients treated with P-IGRT developed

rectal bleeding needing interventions including the use of suppositories far less frequently ($p < 0.001$). Our results were similar to those observed in previous studies [5,8]. In the previously mentioned phase 3 trial, which compared clinical outcomes of daily versus weekly IGRT, ≥ grade 1 late rectal toxicity rates were significantly lower in the daily IGRT group (37% in the daily IGRT group versus 46% in the weekly IGRT group at 5 years, HR: 0.71; 95% CI: 0.53–0.96, $p = 0.027$), although no significant difference was observed regarding ≥ grade 2 late rectal bleeding ($p = 0.261$) [5]. Similarly, in a retrospective analysis of 554 PCa patients treated with or without fiducial marker-based IGRT by Kok *et al.*, rates of moderate/severe late GI toxicities were significantly higher in the group treated without fiducial marker-based IGRT, despite the fact that the prescribed dose for this group was lower than the dose for the group treated with fiducial marker-based IGRT (74 versus 78 Gy, respectively, HR: 3.66; 95% CI: 1.63–8.23, $p = 0.003$) [8]. Therefore, P-IGRT has a marked effect to reduce late GI toxicities in IMRT for localized PCa.

The current study had several limitations, including its retrospective nature and analysis involving only a single institution. The prescribed dose was slightly different between P-IGRT and non-P-IGRT cohorts (median: 76 versus 74 Gy, respectively) because we increased the prescribed dose after the introduction of P-IGRT in IMRT for

localized PCa, as described above. Therefore, our findings regarding the clinical impact of prostate-based image-guidance are not conclusive but merely hypothetical. However, we believe that our findings serve as base-line data that support the merit of P-IGRT in IMRT for localized PCa due to the lack of high-level evidence based on long-term follow-up data.

In conclusion, the current study revealed that the use of P-IGRT with higher doses and smaller margins was correlated with significantly better biochemical control, and a lower incidence of rectal bleeding. The enhanced accuracy using P-IGRT has the potential to independently improve tumor control and late rectal bleeding. Further investigations are warranted to confirm our findings.

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Disclosure Statement:

RA, HI, II, KN, TO, SA, TG, KM, TS, and YK report no conflicts of interest related to the subject matter of this study. TK reported receiving honoraria for lectures from Astellas Pharma, Janssen Pharma, and Bayel Pharma. TM reported receiving funds for research or education and honoraria for lectures from Varian, Hitachi, and BrainLab; and consulting fees from Varian.

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Figure legends:

Figure 1. Kaplan-Meier curves of biochemical failure-free rate after intensity-modulated radiation therapy stratified by the image-guidance method.

Abbreviations: BF, biochemical failure; P-IGRT, prostate position-based image-guided radiotherapy; HR, hazard ratio; CI, confidence interval.

Figure 2. Cumulative incidence curves of ≥ grade 2 late gastrointestinal toxicities (A) or genitourinary toxicities (B) after intensity-modulated radiation therapy stratified by the image-guidance method.

Abbreviations: GI, gastrointestinal; GU, genitourinary; P-IGRT, prostate position-based image-guided radiotherapy; HR, hazard ratio; CI, confidence interval.

This document has been checked by a professional medical editor, who is a native speaker of English.

Tables:

Table 1. Patient and treatment characteristics (P-IGRT vs. non-P-IGRT cohort).

	Group	
	P-IGRT	Non-P-IGRT
No. of patients	114	108
Age at IMRT		
Median (IQR)	71 (67–75)	70 (65–75)
Follow-up (years)		
Median (IQR)	7.1 (5.0–9.1)	10.8 (9.2–13.0)
Clinical T stage, n (%)		
T1c	37 (32.4)	41 (38.0)
T2a	67 (58.8)	43 (39.8)
T2b	10 (8.8)	24 (22.2)
Combined GS, n (%)		
3+3	9 (7.9)	16 (14.8)
3+4	56 (49.1)	53 (49.1)
4+3	49 (43.0)	39 (36.1)
Initial PSA (ng/mL)		
Median (IQR)	7.3 (5.6–10.3)	10.2 (6.5–13.6)
NCCN risk classification ver. 2022, n (%)		
Favorable intermediate-risk	43 (37.7)	33 (30.6)

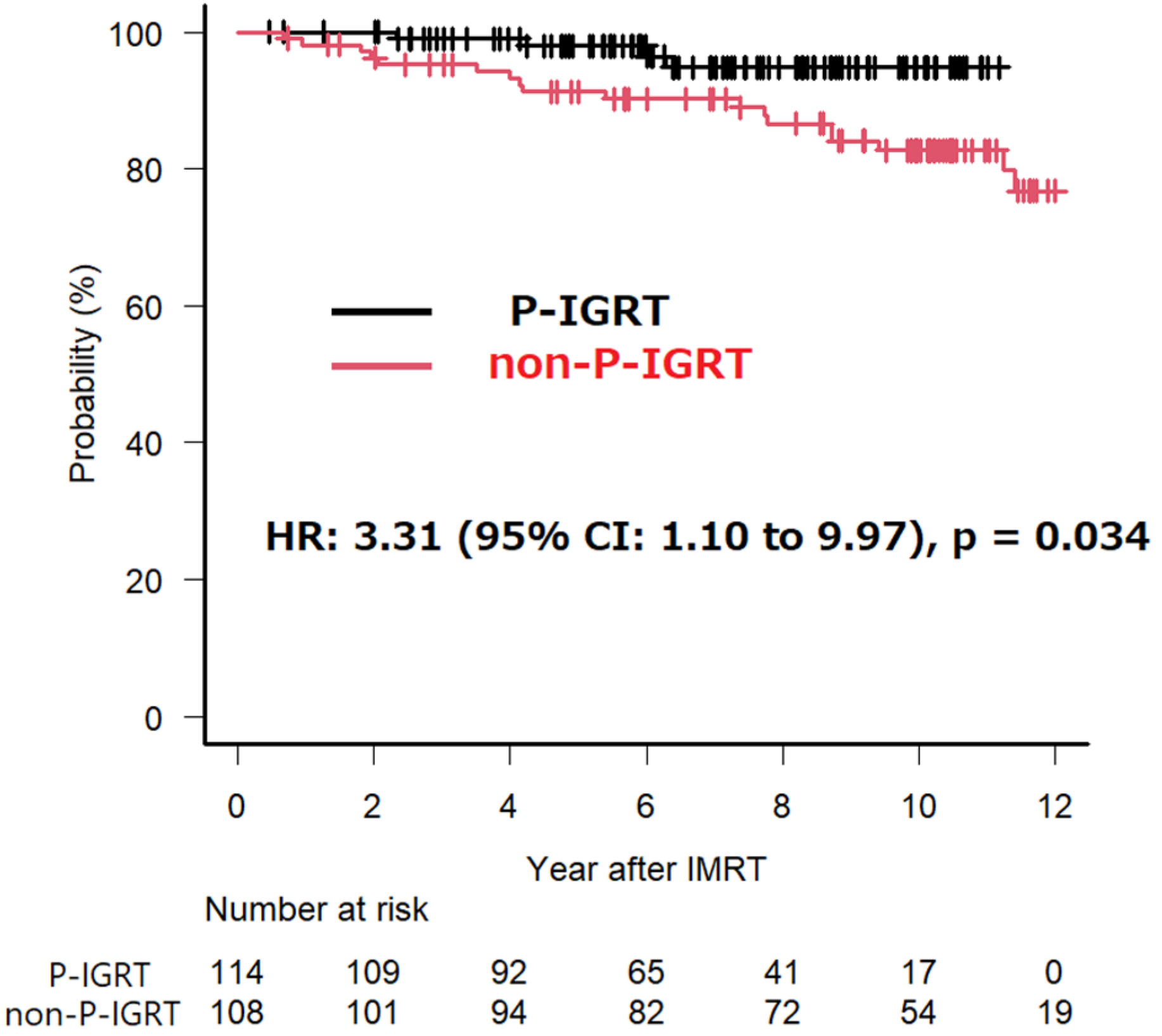
Unfavorable intermediate-risk	71 (62.3)	75 (69.4)
Duration of neoadjuvant ADT (months)		
Median (IQR)	7.1 (6.4–7.8)	6.7 (5.5–8.0)
IMRT dose, n (%)		
70 Gy	1 (0.9)	29 (26.9)
72 Gy	37 (32.5)	0 (0.0)
74 Gy	0 (0.0)	74 (68.5)
76 Gy	76 (66.7)	0 (0.0)
78 Gy	0 (0.0)	5 (4.6)

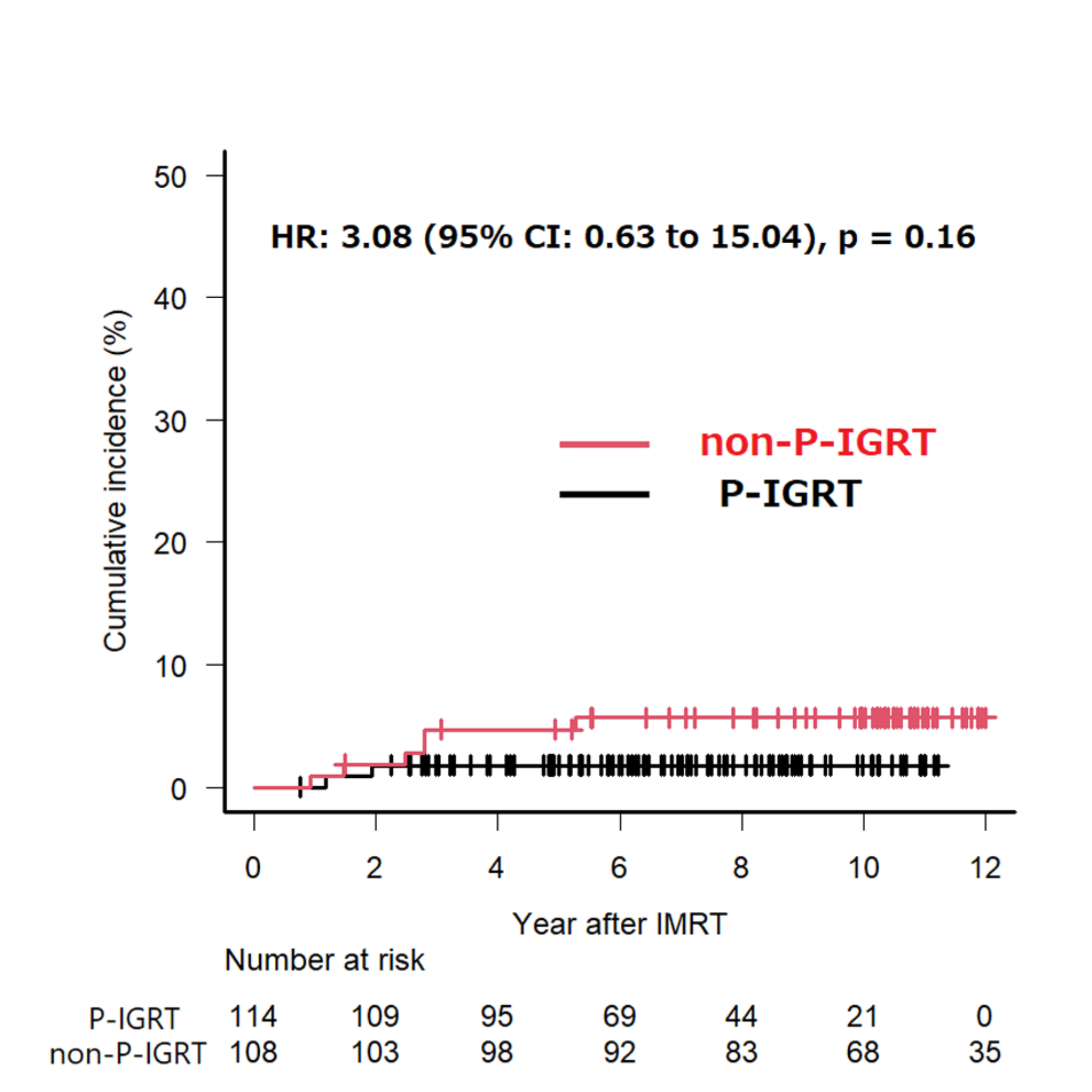
Abbreviations: P-IGRT, prostate position-based image-guided radiotherapy; IMRT, intensity-modulated radiation therapy; IQR, interquartile range; GS, Gleason score; PSA, prostate-specific antigen; NCCN, National Comprehensive Cancer Network; ADT, androgen-deprivation therapy.

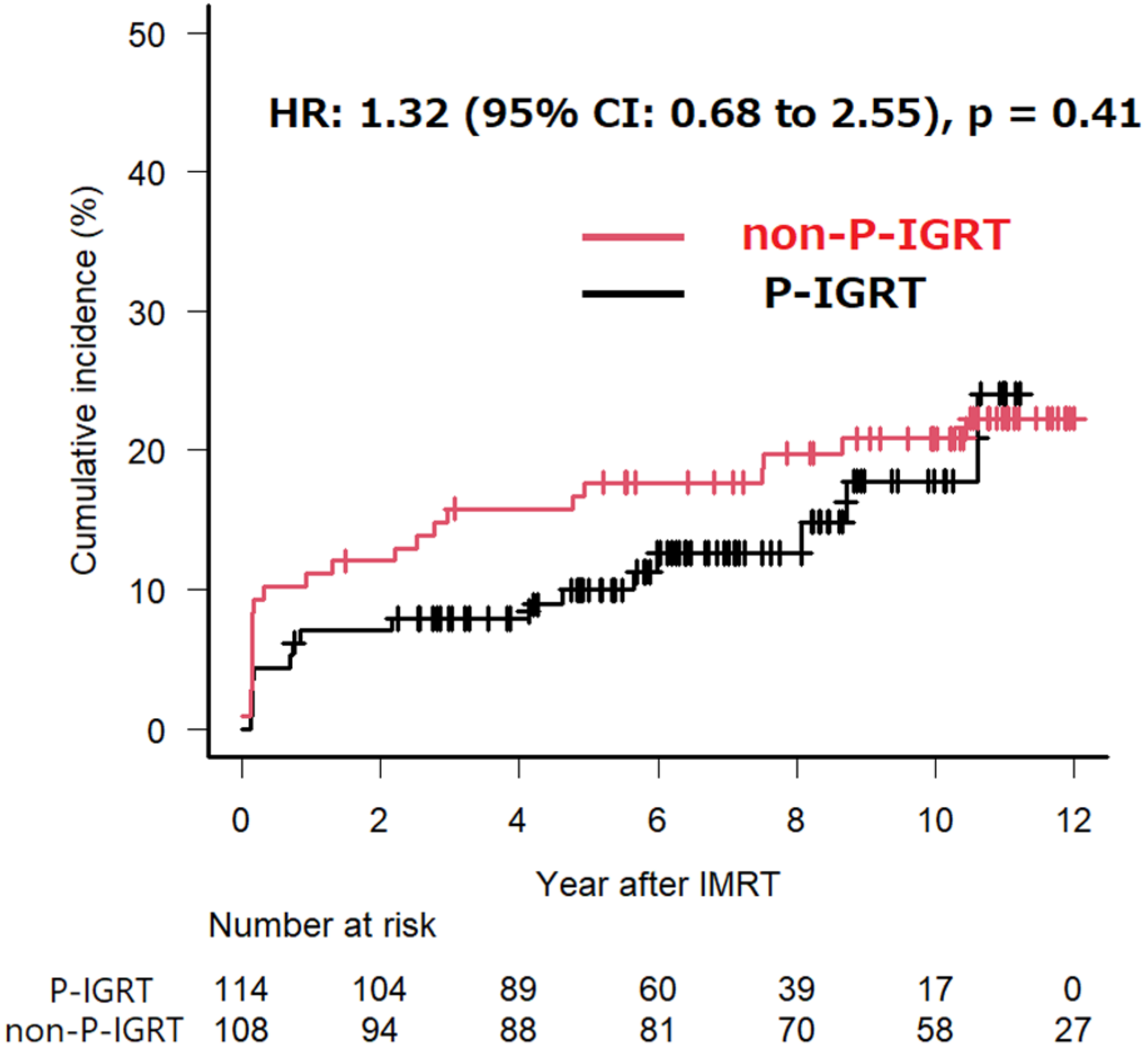
Table 2. Univariate and multivariable analyses of predictive factors for biochemical failure.

Factor	Univariate			Multivariable		
	HR	95% CI	*p*	HR	95% CI	*p*
P-IGRT vs. non-P-IGRT	3.31	1.10–9.97	0.034	3.17	1.05–0.58	0.041
unfavorable IR vs. favorable IR	1.83	0.68–4.97	0.23	1.68	0.62–4.56	0.31

Abbreviations: HR, hazard ratio; 95% CI, 95% confidence interval; P-IGRT, prostate position-based image-guided radiotherapy; IR, intermediate-risk (according to the National Comprehensive Cancer network risk classification version 2022.4).


100
80
60
40
20
0
Probability (%)
P-IGRT
non-P-IGRT
HR: 3.31 (95% CI: 1.10 to 9.97), p = 0.034
0
2
4
6
8
10
12
Year after IMRT
Number at risk
P-IGRT 114 109 92 65 41 17 0
non-P-IGRT 108 101 94 82 72 54 19


HR: 3.08 (95% CI: 0.63 to 15.04), p = 0.16
non-P-IGRT
P-IGRT
Cumulative incidence (%)
50
40
30
20
10
0
0
2
4
6
8
10
12
Year after IMRT
Number at risk
P-IGRT 114 109 95 69 44 21 0
non-P-IGRT 108 103 98 92 83 68 35


HR: 1.32 (95% CI: 0.68 to 2.55), p = 0.41
non-P-IGRT
P-IGRT
Cumulative incidence (%)
50
40
30
20
10
0
0
2
4
6
8
10
12
Year after IMRT
Number at risk
P-IGRT 114 104 89 60 39 17 0
non-P-IGRT 108 94 88 81 70 58 27