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ORIGINAL RESEARCH

Radiation Therapy for Local or Biochemical Recurrence Following Radical Prostatectomy in Patients with Prostate Cancer

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Introduction and Objectives: To investigate outcomes of patients with biochemical or local recurrence, without distant metastasis, who received radiation therapy targeting the prostate bed at our hospital following radical prostatectomy for prostate cancer.

Methods: Patients suspected of recurrence after radical prostatectomy, indicated by an increase in PSA levels or other factors, were evaluated through imaging tests for local recurrence and distant metastasis. Those who showed no local recurrence received salvage radiotherapy to the prostate bed at a dose of 64.8 Gy. Patients with local recurrence received radiotherapy of 70.8 Gy to the site of local recurrence and 64.8 Gy to the prostate bed.

Results: Among 19 cases of local recurrence following radical prostatectomy, three out of nine patients who did not receive ADT experienced recurrence after local radiation therapy. In contrast, none of the ten patients who received ADT during radiation therapy experienced recurrence following treatment. No significant difference was observed in clinical recurrence-free survival between patients receiving radiation therapy alone and those receiving ADT during radiation therapy. ($p = 0.302$) Fifty-six of the 57 patients without local recurrence were evaluated regarding their PSA doubling time (PSADT). Those with a PSADT of 6 months or more at the time of recurrence following radical prostatectomy tended to show longer clinical recurrence-free survival after local radiation therapy compared with showing PSADT of less than 6 months. ($p=0.06$) Patients with local recurrence who were treated with escalated radiation doses did not show any difference in the incidence of radiotherapy-related gastrointestinal toxicity compared with patients without local recurrence.

Conclusion: Although this study was conducted at a single institution with a small sample size and a limited number of patients, ADT may be beneficial in preventing recurrence following radiation therapy for local recurrence after radical prostatectomy. When considering salvage radiation therapy for patients with biochemical recurrence following radical prostatectomy, PSADT may be useful.

Keywords: prostate cancer, prostatectomy, local recurrence, biochemical recurrence, radiation therapy

Introduction

Radical prostatectomy is a standard treatment for localized prostate cancer.[1,2] A subsequently rising prostate specific antigen (PSA) level occurs in a significant proportion of patients with localized prostate cancer following radical prostatectomy. Patients with biochemical recurrence—some of whom already have metastases—include those whose metastatic sites remain undetectable, as well as those in whom local recurrence cannot be identified through conventional imaging techniques.

Current guidelines recommend local radiation therapy, with or without androgen deprivation therapy (ADT), for patients without metastases who experience biochemical recurrence following radical prostatectomy.[3–5]

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We investigated the clinical conditions and outcomes of patients with biochemical or local recurrence, without distant metastasis, who received radiation therapy targeting the prostate bed at our hospital following radical prostatectomy for prostate cancer. Our results underscore the need for more accurate diagnostic methods to detect PSA recurrence following radical prostatectomy.

Patients and Methods

This study was conducted with institutional review board approval (E2024000201).

Patients

After radical prostatectomy, patients are regularly monitored using PSA tests and other procedures. Here, those with suspected recurrence after radical prostatectomy, indicated by an increase in PSA levels or other factors, were evaluated through imaging tests for local recurrence and distant metastasis. For patients not undergoing androgen deprivation therapy (ADT), imaging was conducted when the PSA level exceeded 0.2 ng/mL. For those receiving ADT, evaluations were carried out on an individual basis. CT, bone scans, and whole-body MRI were utilized to confirm the presence or absence of metastasis. Multiparametric MRI was applied to evaluate local recurrence in the prostate bed. The multiparametric MRI images were interpreted exclusively by Y.I.

PSA Doubling Time (PSADT)

PSADT can be utilized to predict changes in PSA levels over time and as an indicator of biochemical and clinical progression. It was calculated as the natural log of 2 (0.693) divided by the slope of the linear regression of the natural log of PSA levels vs the time of PSA measurement in months. If the PSA level slope was 0 (constant PSA level) or negative (decreasing PSA level after initial increase), PSADT was arbitrarily set to 100.[6]

Radiotherapy

Patients who showed no local recurrence or metastasis, as determined by imaging evaluation, received salvage radiotherapy to the prostate bed at a dose of 64.8 Gy, delivered in 36 fractions. Patients with local recurrence and no distant metastases, as determined by imaging evaluation, received radiotherapy of 70.8 Gy to the site of local recurrence and 64.8 Gy to the prostate bed. One patient with pelvic lymph node recurrence underwent whole pelvic radiation therapy at a dose of 50.4 Gy.

Radiotherapy-Related Gastrointestinal (GI) Toxicities

Radiotherapy-related GI toxicities were retrospectively graded according to Radiation Therapy Oncology Group (RTOG) acute and late toxicity criteria. In both cases, 0 indicates the absence of radiation effects and 5 means the effects were fatal. The severity of reactions was graded from 1 to 4. (Grade 0: No change, 1:Increased frequency or change in quality of bowel habits not requiring medication/rectal discomfort not requiring analgesics, Grade 2: Diarrhea requiring parasympatholytic drugs (eg, Lomotil)/mucous discharge not necessitating sanitary pads/rectal or abdominal pain requiring analgesics, Grade 3: Diarrhea requiring parenteral support/severe mucous or blood discharge necessitating sanitary pads/abdominal distention (flat plate radiograph demonstrates distended bowel loops), Grade 4:Acute or subacute obstruction, fistula or perforation; GI bleeding requiring transfusion; abdominal pain or tenesmus requiring tube decompression or bowel diversion).[7]

Follow-up After Radiation Therapy

Patients are regularly monitored using PSA tests and other procedures following radiation therapy. Patients underwent re-evaluation imaging when their PSA levels exceeded 1 ng/mL during follow-up after radiation therapy. In the present study, patients with suspected recurrence after radiation therapy, indicated by an increase in PSA levels or other factors, were evaluated through imaging tests for local recurrence and distant metastasis. Any suspicion of recurrence following radiotherapy was evaluated on an individual basis. If no recurrence was detected on imaging, PSADT and other factors were considered before initiating ADT, with shared decision-making involving the patients.

Statistical Analysis

The PSA recurrence rate after radiation therapy was calculated using the Kaplan-Meier method, and significance was assessed using the Log rank test. Differences were considered significant at a P-value <0.05. Statistical analyses were performed using commercial statistical software (SPSS, version 28.0; IBM Corp, SPSS, Inc., Chicago, IL, USA).

Results

Patient Characteristics

The study included 76 patients who received local radiation therapy following prostatectomy between the opening of our hospital in June 2015 and April 2024. (Table 1) Eleven patients who underwent radical prostatectomy at other hospitals were subsequently referred to our hospital for follow-up observation. The age of patients at the time of radical prostatectomy ranged from 56 to 79 years, with a mean age of 67 years. The time from radical prostatectomy to radiation therapy for all patients ranged from five to 211 months, with a median of 32 months.

The average PSA level at the time of prostate cancer diagnosis was 15.7 ng/mL, ranging from 3.68 to 79.64 ng/mL. In three patients, PSA values at the time of diagnosis were not reported when they were referred to our hospital. The pathological grade group at the time of radical prostatectomy was classified as follows: grade 1, 4 cases; grade 2, 20 cases; grade 3, 11 cases; grade 4, 19 cases; and grade 5, 16 cases. Additionally, there were 6 cases in which the grade group was not reported at the time of referral to our hospital, or the grade group was not evaluated due to the patient undergoing hormone therapy. The pathological stage at radical prostatectomy was: pT2 or lower, 36 cases; pT3a, 31 cases; pT3b, 9 cases; pN0, 75 cases; pN1, 1 case.

Table 1 Patient Characteristics

Grade Group	No.
1	4
2	20
3	11
4	19
5	16
Unknown or Not Rated	6
pT	No.
pT2≦	36
pT3a	31
pT3b	9
pN	
pN0	75
pN1	1
ADT (-) at the time of radical prostatectomy	68
ADT (+) at the time of radical prostatectomy	8
Bilateral orchiectomy	1
Preoperative ADT	5
Postoperative ADT	2

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Sixty-eight patients did not receive ADT at the time of radical prostatectomy. Among the patients observed in this study, eight received ADT perioperatively following radical prostatectomy. One patient underwent bilateral orchiectomy, five patients had been treated with ADT prior to surgery, and two patients began ADT immediately after the procedure.

Biochemical Recurrence Following Radical Prostatectomy

The interval between radical prostatectomy and radiation therapy ranged from 6 to 211 months, with a mean duration of 44 months. Following radical prostatectomy, local recurrence was/was not observed in 19 and 57 patients, respectively.

Thirty-five and 41 patients did not/did receive ADT during radiation therapy, respectively. Among those who received ADT, 28 patients were treated with short-term ADT (LHRH agonist (3-month formulation) administered twice at three-month intervals), and 13 patients received long-term ADT (ADT had exceeded six months).

Patients with Local Recurrence

Local recurrence following radical prostatectomy was observed in 19 patients. (Table 2) Local radiation therapy was not used in combination with ADT in nine patients. It was applied in combination with short- and long-term ADT in three and seven patients, respectively. Three out of nine patients who did not receive ADT experienced recurrence following local radiation therapy. In contrast, none of the ten patients who received ADT during radiation therapy developed recurrence after treatment. No significant difference was observed in clinical recurrence-free survival between patients receiving radiation therapy alone and those receiving ADT during radiation therapy ($p = 0.302$) (Figure 1).

Patients Without Local Recurrence

In those without local recurrence at the time of radiation therapy, 26 and 31 patients did not/did receive ADT during treatment, respectively. Among those who received ADT, 28 and three patients were treated with short- and long-term ADT, respectively. (Table 3) Of these patients with ADT, four experienced recurrence. Of the 26 patients who received local radiotherapy without ADT, 11 showed recurrence. No difference was observed in clinical recurrence-free survival between patients receiving radiation therapy alone and those receiving ADT during radiation therapy ($p=0.221$) (Figure 2).

Fifty-three of the 57 patients without local recurrence were evaluated. In four of them, PSA levels could not be assessed due to ADT. Among patients without local recurrence, 26 with a PSA value that had fallen below the sensitivity threshold of 0.01 exhibited a period from radical prostatectomy to local radiation therapy ranging from 21 to 183 months, with an average of 55 months. (Table 4) Four out of the 26 patients with a PSA value below the threshold experienced recurrence after local radiation therapy. The PSA value at time of recurrence was 0.25 ng/mL

Table 2 Use of ADT During Radiation Therapy in Patients with Local Recurrence

	Patients With Local Recurrence	**Patient Age At Time Of Radical Prostatectomy (years old), (range))**	**Time From Radical Prostatectomy To Confirmation of Recurrence (Months, (Range))**	**Patients With Recurrence After Local Radiation Therapy**
Total	19	66 years old (57 to 79)	44 months (4 to 149)	
ADT (-)	9			3
ADT (+)	10			0
Short term ADT	3			
Long term ADT	7			

Note: Short term ADT: LHRH agonist (3-month formulation) administered twice at three-month intervals.Long term.
Abbreviation: ADT, ADT exceeded six months.

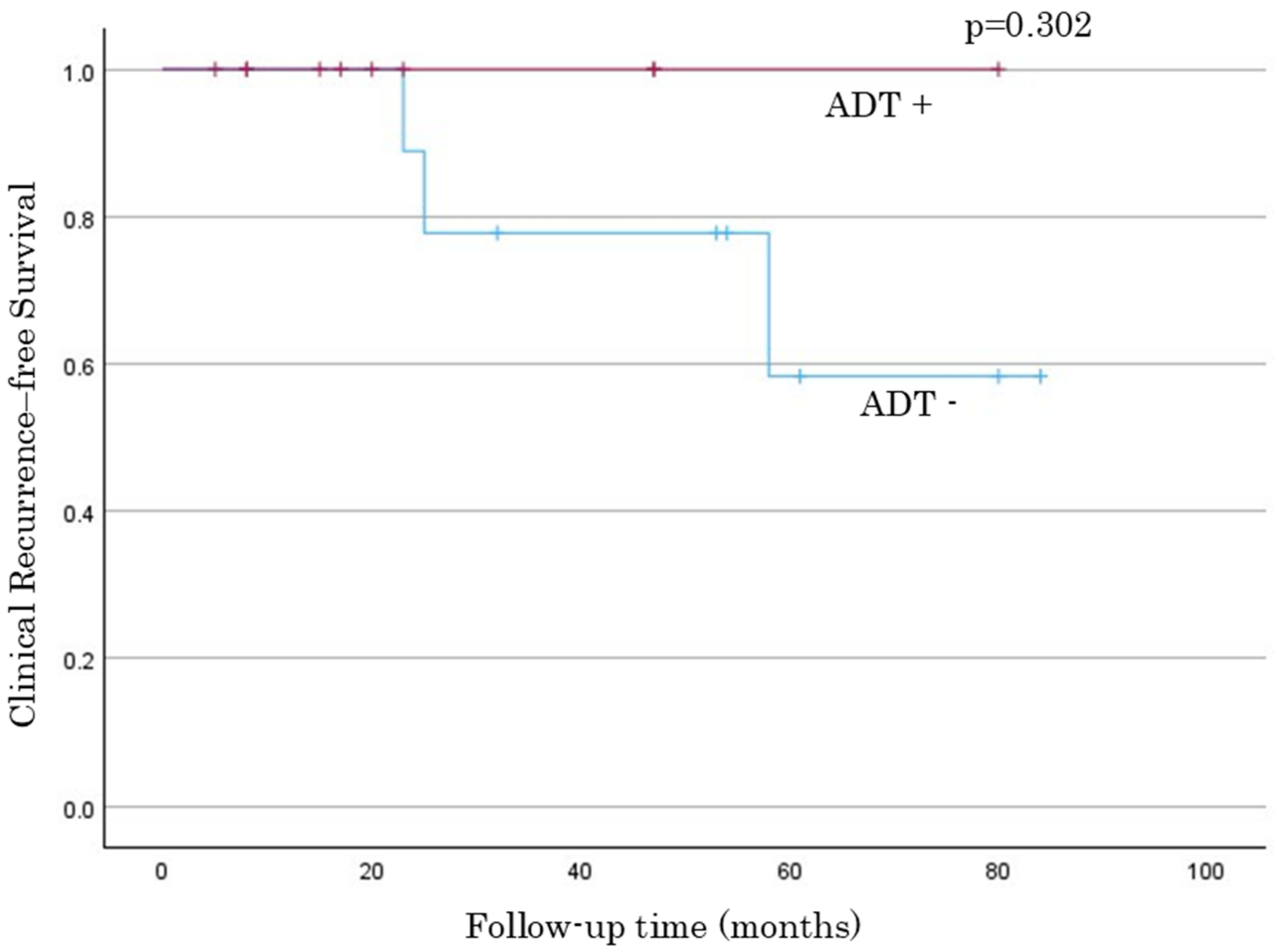

Figure 1 Clinical Recurrence-free Survival After Local Radiation Therapy. Use of ADT During Radiation Therapy for Patients With Local Recurrence.Local recurrence following radical prostatectomy was observed in 19 patients. Local radiation therapy was not used in combination with ADT in nine patients. It was applied in combination with short- and long-term ADT in three and seven patients, respectively. Three out of nine patients who did not receive ADT experienced recurrence following local radiation therapy. In contrast, none of the ten patients who received ADT during radiation therapy developed recurrence after treatment. No difference was observed in clinical recurrence-free survival between patients receiving radiation therapy alone and those receiving ADT during radiation therapy (p=0.302).

(range: 0.2 to 0.46 ng/mL) and PSADT was 8.5 months (range: 2.1 to 14.9 months). In contrast, among the 27 patients whose PSA levels did not fall below the sensitivity threshold of 0.01, the time from radical prostatectomy to local radiation therapy ranged from 7 to 66 months, with a mean duration of 24 months. The PSA value at time of recurrence was 0.55 ng/mL (range: 0.21 to 1.46 ng/mL) and PSADT was 11.0 months (range: 2.8 to 14.9 months). Of these patients, eight showed recurrence. There was no difference in clinical recurrence-free survival after local radiation therapy between patients whose PSA levels declined to less than 0.01 ng/mL following radical prostatectomy and those that did not (p=0.333) (Figure 3).

Fifty-six of the 57 patients without local recurrence were evaluated for PSADT. (Table 5) In one patient, PSADT could not be assessed due to ADT. In the 28 patients with PSADT of 6 months or less, the duration from radical prostatectomy to confirmation of recurrence was 29 months (range: 6 to 83 months), and the PSA level at the time of recurrence was 0.69 ng/mL (range: 0.21 to 6.25 ng/mL). Among these patients, nine experienced recurrence. In the 28 patients with PSADT of 6 months or more, the duration from radical prostatectomy to confirmation of recurrence was 46 months (range: 7 to 183 months), and the PSA level at the time of recurrence was 0.34 ng/mL (range: 0.21 to 1.46 ng/mL). Among these patients, five showed recurrence. Patients with PSADT of 6 months or more at the time of recurrence following radical prostatectomy tended to show longer clinical recurrence-free survival after local radiation therapy compared with those whose PSADT was less than 6 months (p=0.06) (Figure 4).

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Table 3 Use of ADT During Radiation Therapy in Patients Without Local Recurrence

	Patients Without Local Recurrence	Patient Age At Time Of Radical Prostatectomy (Years Old, (Range))	Time From Radical Prostatectomy to Confirmation of Recurrence (Months, (Range))	Patients With Recurrence After Local Radiation Therapy
Total	57	67 years old (56 to 79)	37 months (3 to 183)	15
ADT (-)	26			11
ADT (+)	31			4
Short term ADT	28			
Long term ADT	3			

Note: Short term ADT: LHRH agonist (3-month formulation) administered twice at three-month intervals.Long term.
Abbreviation: ADT, ADT exceeded six months.

Radiotherapy-Related GI Toxicities

Patients who showed no local recurrence or metastasis received salvage radiotherapy to the prostate bed at a dose of 64.8 Gy. Patients with local recurrence and no distant metastases received radiotherapy of 70.8 Gy to the site of local

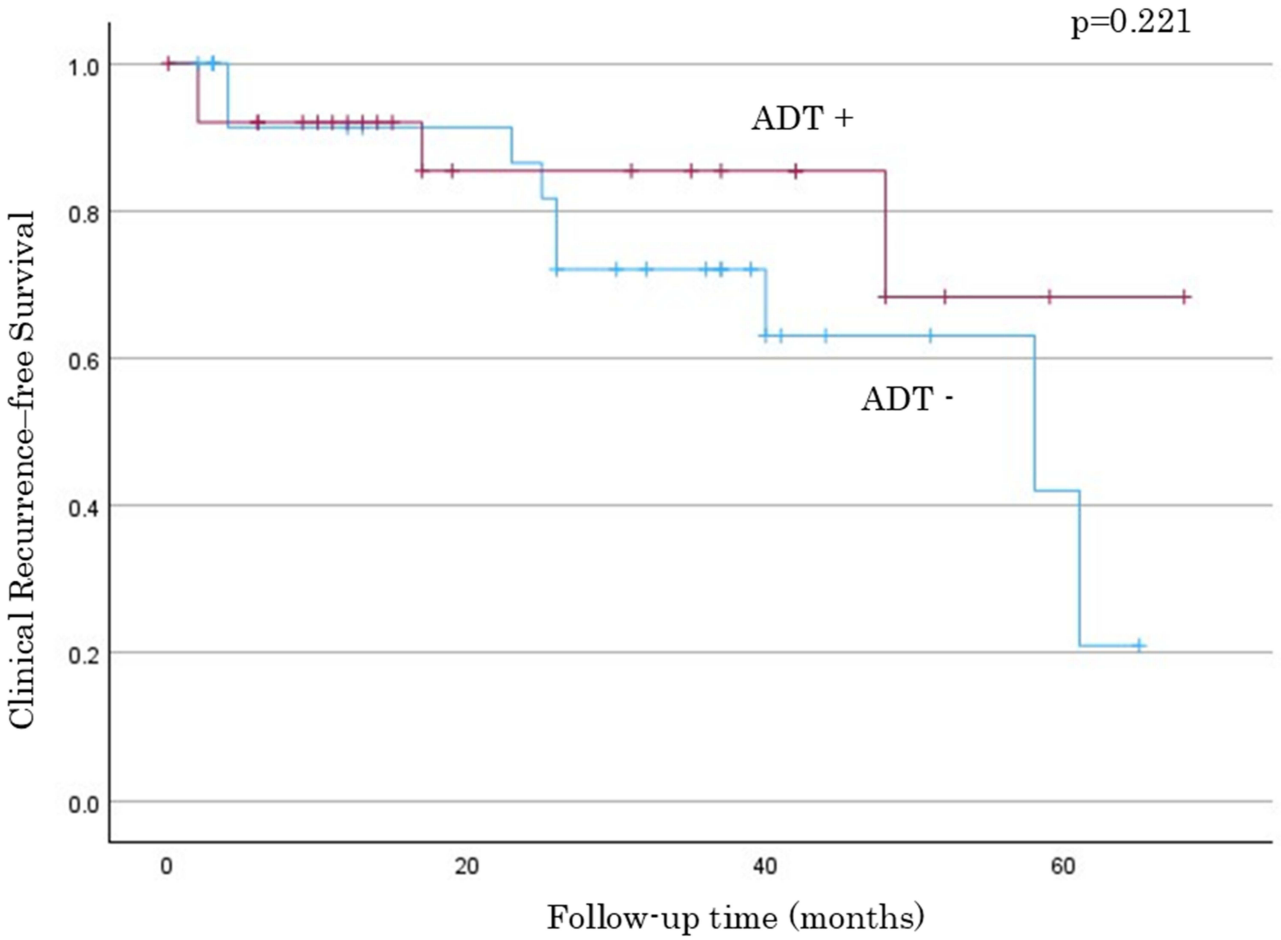

Figure 2 Clinical Recurrence-free Survival After Local Radiation Therapy. Use of ADT During Radiation Therapy for Patients Without Local Recurrence.In patients without local recurrence at the time of radiation therapy, 26 did not receive ADT during treatment, while 31 patients did. Among those who received ADT, 28 were treated with short-term ADT, and three received long-term ADT. Of these patients with ADT, four experienced recurrence. Local radiation therapy without ADT was administered to 26 patients. Of these patients without ADT, 11 showed recurrence. No difference was observed in clinical recurrence-free survival between patients receiving radiation therapy alone and those administered ADT during radiation therapy (p=0.221).

Table 4 PSA Minimum (0.01ng/Ml) in Patients Without Local Recurrence

PSA Minimum (0.01ng/mL)	Patients	Time From Radical Prostatectomy To Confirmation Of Recurrence (Months, (Range))	PSA at Time of Recurrence (ng/mL)	PSADT at Time of Recurrence (Months, (Range))	Patients WITH Recurrence After Local Radiation Therapy
PSA<0.01ng/mL	26	55 (21 to 183)	0.25 (0.2 to 0.46)	8.5 (2.1 to 14.9)	4
PSA≧0.01ng/mL	27	24 (7 to 66)	0.55 (0.21 to 1.46)	11.0 (2.8 to 14.9)	8

Notes: Fifty-three of the 57 patients without local recurrence were evaluated. In four patients, PSA levels could not be assessed due to ADT.

recurrence. In 57 patients without local recurrence, 13 experienced GI toxicities related to radiotherapy (Grade 1 in 12 patients; Grade 2 in one patient). (Table 6) In 19 patients with local recurrence, five developed GI toxicities related to radiotherapy (Grade 1 in four patients; Grade 2 in one patient). Patients with local recurrence who were treated with escalated radiation doses did not experience any difference in the incidence of radiotherapy-related gastrointestinal toxicity compared with patients without local recurrence.

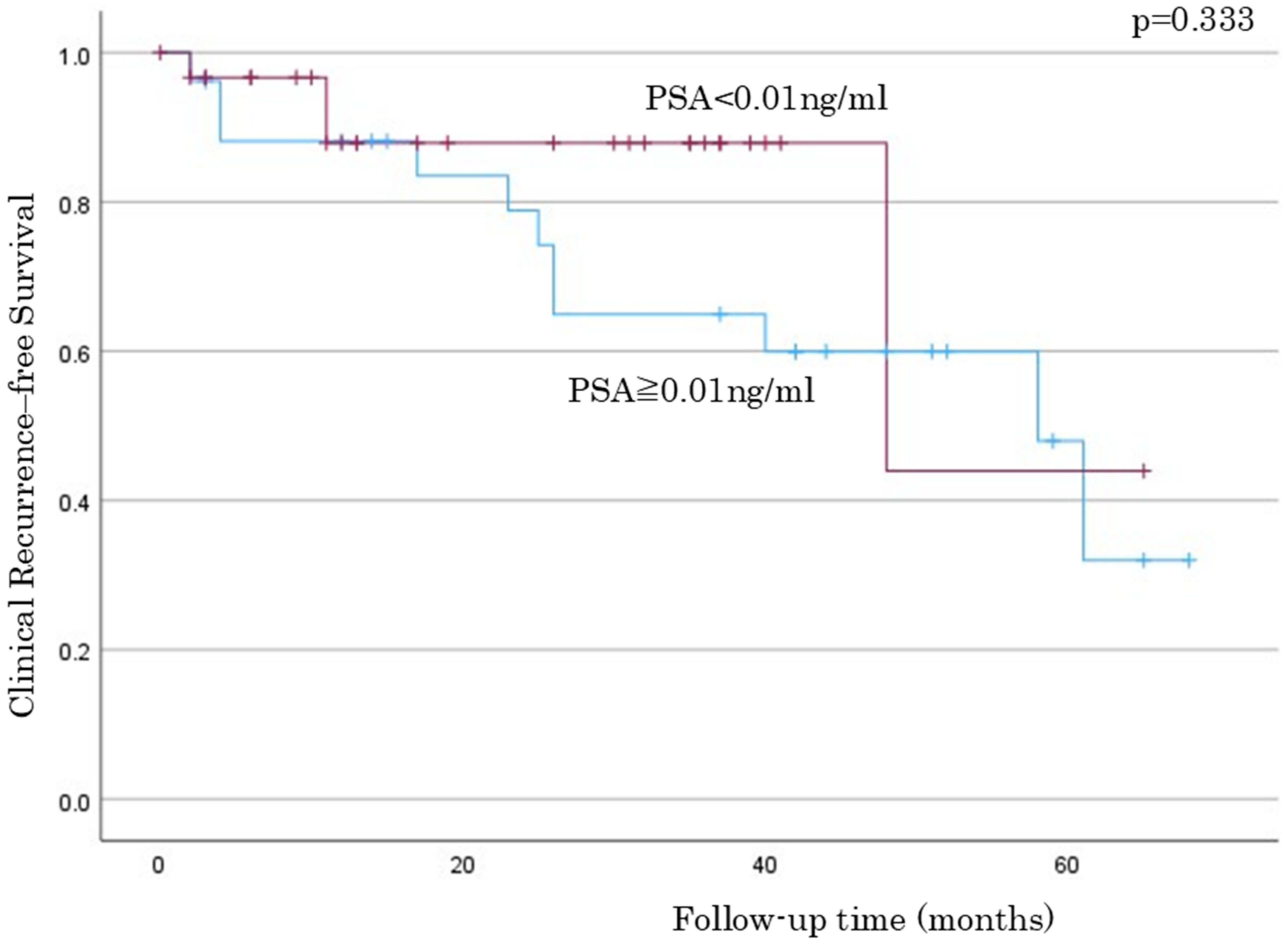

Figure 3 Clinical Recurrence-free Survival After Local Radiation Therapy. PSA Minimum (0.01 ng/mL) in Patients Without Local Recurrence.Four out of 26 patients with a PSA value that had fallen below detection limits experienced recurrence after local radiation therapy. In contrast, among the 27 patients whose PSA levels did not fall below the sensitivity threshold of 0.01, eight showed recurrence. There was no difference in clinical recurrence-free survival after local radiation therapy. (p=0.333).

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Table 5 PSADT at the Time of Recurrence in Patients Without Local Recurrence

PSADT Divided at 6 Months	Patients	Time From Radical Prostatectomy to Confirmation of Recurrence (Months, (Range))	PSA At Time Of Recurrence (ng/mL)	PATIENTS with Recurrence After Local Radiation Therapy
PSADT < 6 months	28	29 (4 to 83)	0.69 (0.21 to 6.25)	9
PSADT ≧ 6 months	28	46 (7 to 183)	0.34 (0.21 to 1.46)	5

Note: Excluding one patient who is undergoing ADT.

Discussion

This study summarizes the clinical course of local radiotherapy in 76 patients who experienced biochemical recurrence following radical prostatectomy and had no distant metastasis. Of the 76 patients who experienced PSA recurrence following radical prostatectomy, 19 (25%) exhibited local recurrence, while 57 patients did not show any signs of local recurrence. Patients received radiation therapy targeting the prostate bed and any local recurrence lesions. However, 18 have since shown signs of recurrence. ADT may be beneficial in preventing recurrence following radiation therapy for local recurrence after radical prostatectomy. PSADT may be a valuable predictor of recurrence following radiation therapy.

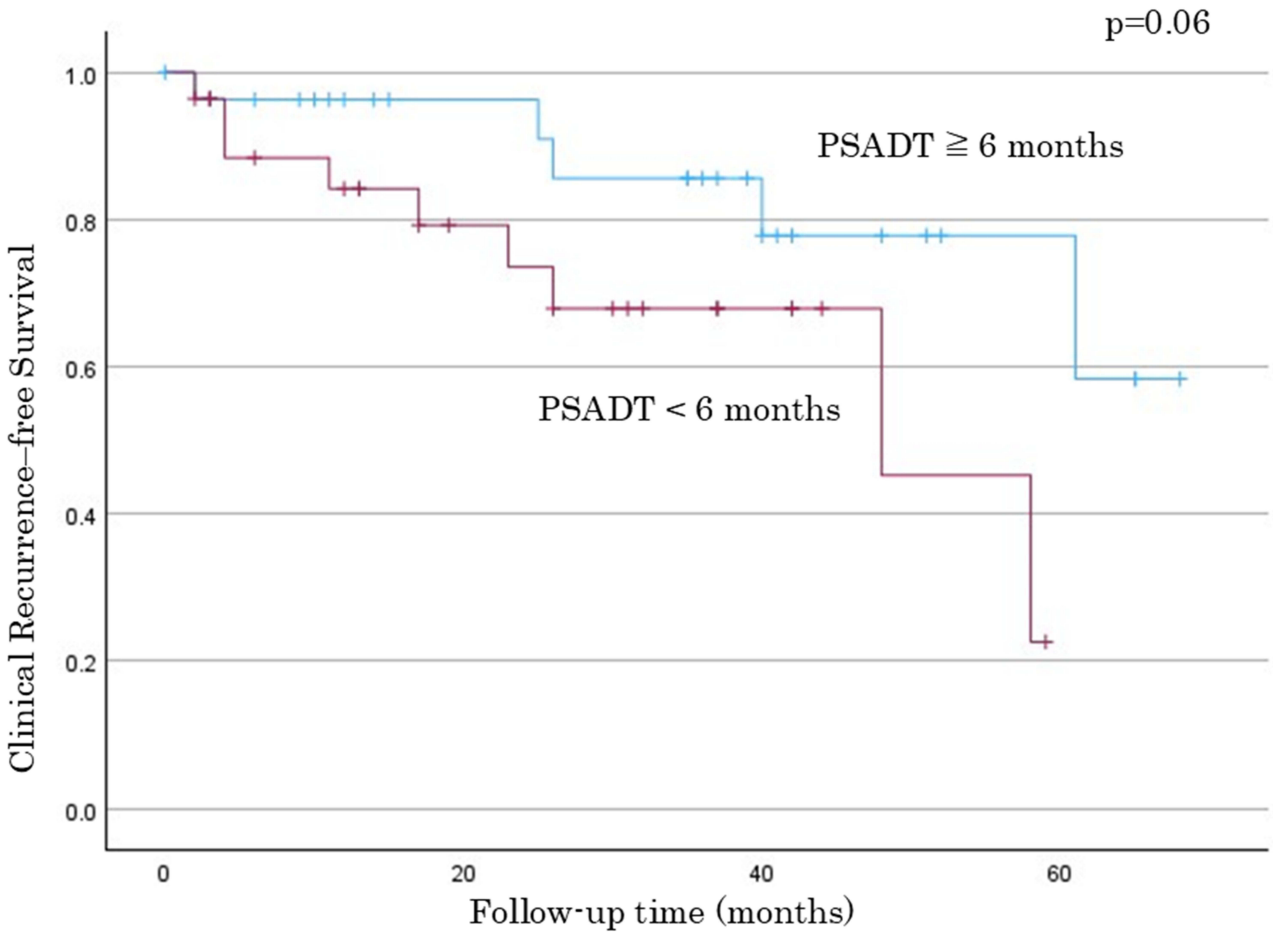

Figure 4 Clinical Recurrence-free Survival After Local Radiation Therapy. PSADT at the Time of Recurrence in Patients Without Local Recurrence.In the 28 patients with PSADT of 6 months or less, nine experienced recurrence. In the 28 patients with PSADT of 6 months or more, five showed recurrence. Patients with PSADT of 6 months or more at the time of recurrence following radical prostatectomy tended to show longer clinical recurrence-free survival after local radiation therapy compared with those whose PSADT was less than 6 months. (p=0.06).

Table 6 Radiotherapy-Related GI Toxicities

Local recurrence	+	–
Patients	19	57
GI toxicities	5	13
Grade 1	4	12
Grade 2	1	1

Radical prostatectomy is widely regarded as the definitive curative treatment for patients with non-metastatic prostate cancer.[5] After radical prostatectomy, PSA levels are monitored regularly. If PSA is detectable following prostatectomy, residual or recurrent prostate cancer should be suspected. If the PSA level exceeds a specific threshold, biochemical recurrence is diagnosed, and imaging examinations are conducted to assess distant metastasis and local recurrence. Biochemical recurrence is commonly defined as a PSA level exceeding 0.2 ng/mL; however, this definition is not based on any official guidelines.[8] In a long-term retrospective study conducted by Raisa S. Pompe et al, among patients who experienced biochemical recurrence after radical prostatectomy and did not receive neoadjuvant or adjuvant therapy, 13.4% developed distant metastases, and 9.5% died from prostate cancer.[9] Felix Preisser et al reported that in patients exhibiting persistent PSA levels, salvage radiotherapy improved both overall and cancer-specific survival.[10] The persistence of PSA and high-risk features often serve as indicators of distant micro-metastatic disease, which cannot be effectively treated with local therapy. Ida Sonni et al suggested that 68Ga-PSMA PET may be a valuable tool for guiding salvage radiation therapy planning directed at the prostate bed in cases of postoperative biochemical persistence or recurrence.[11] A systematic review conducted by the EAU Prostate Cancer Guidelines Panel confirmed that oncological outcomes vary between patients with and without biochemical recurrence.[8] The authors proposed a new EAU biochemical recurrence risk stratification. A low risk of biochemical recurrence is defined by PSADT of greater than 1 year and pathological radical prostatectomy specimen Gleason score below 8 (ISUP grade group less than 4). Conversely, a high risk of biochemical recurrence is defined by PSADT of 1 year or less, or pathological radical prostatectomy specimen Gleason score of 8 to 10 (ISUP grade group 4 to 5).[8] The European Association of Urology grouping for the risk of biochemical recurrence of prostate cancer after radical prostatectomy was valid when applied in a European study cohort. Salvage radiation therapy, especially when administered at a PSA level of less than 0.5 ng/mL, was highly effective in preventing metastatic progression.[12]

PSA is a sensitive and specific biomarker for early disease recurrence; however, it does not indicate the disease location. Data on the performance of conventional imaging techniques, including MRI, CT, and bone scans, in the context of biochemical recurrence of prostate cancer following radical prostatectomy are heterogeneous and show low sensitivity for the detection and localization of biochemical recurrence.[13] The advantages of MRI include its effectiveness in detecting local recurrence and sensitivity to early bone changes, which can help resolve discrepancies between bone scans and CT. Overall, pelvic MRI is regarded as an appropriate imaging modality.[14–16] Whole-body MRI can detect lymph node and bone metastases outside of the pelvis and is also considered an appropriate imaging modality.[17,18] In patients with early biochemical recurrence following radical prostatectomy, detection rates reported for PSMA-PET CT are higher than those of any other imaging modality, particularly for smaller lesions with low PSA levels.[19–22] PSMA-PET has been rapidly adopted worldwide and is recognized as a viable imaging option according to the guidelines set forth by EAU, NCCN, and AUA.[3,4] Although it is evident that PSMA-PET is an outstanding diagnostic tool, this test is currently unavailable in Japan. If it were available, early diagnosis of recurrence and metastasis would be possible.

For patients experiencing biochemical recurrence following radical prostatectomy, the primary curative intervention is radiation therapy. Generally, two main approaches are utilized for the timing of radiation therapy: adjuvant and salvage radiotherapy. However, the results of a meta-analysis indicated no evidence of improved event-free survival with adjuvant radiation therapy compared with early salvage radiation therapy.[23,24] In general, for patients with higher-risk characteristics, the addition of ADT to radiotherapy improves survival rates. ESTRO-ACROP recommendations for the

evidence-based use of ADT in combination with external-beam radiotherapy for prostate cancer conclude that no additional ADT should be recommended for low-risk prostate cancer patients. In contrast, for intermediate- and high-risk patients, a duration of four to six months and two to three years of ADT is recommended, respectively.[25–27] The guidelines from the European Association of Urology, European Society for Radiotherapy and Oncology, and International Society of Geriatric Oncology (EAU-ESTRO-SIOG) emphasize the importance of early salvage radiotherapy. This is defined as radiotherapy initiated for patients who experience biochemical recurrence following radical prostatectomy, specifically when the PSA level is less than 0.5 ng/mL.[25] Felix Preisser et al demonstrated a significant survival benefit in patients with EAU high-risk biochemical recurrence who received early salvage radiotherapy compared with those who were under observation. The findings support the recommendation for early salvage radiotherapy in men with EAU high-risk biochemical recurrence. Conversely, surveillance may be appropriate for patients with low-risk biochemical recurrence.[28] In the cases examined in this study, the interval between radical prostatectomy and radiation therapy was influenced by factors such as the use of ADT in combination with radical prostatectomy. The patient with the longest interval underwent surgical castration at the time of radical prostatectomy, resulting in a prolonged period before PSA recurrence was diagnosed.

Local recurrence following radical prostatectomy was observed in 19 patients. Local radiation therapy was not used in combination with ADT in nine patients. Three of the patients experienced recurrence after local radiation therapy. However, none of the patients who received ADT during radiation treatment developed recurrence after local radiation therapy. No significant difference was observed in clinical recurrence-free survival between patients receiving radiation therapy alone and those receiving ADT during radiation therapy ($p = 0.302$).

Regarding the irradiation method, conventional-dose salvage radiotherapy to the prostate bed is adequate for patients showing early biochemical progression of prostate cancer following radical prostatectomy.[29] The long-term results of the RADICALS-RT trial confirm that adjuvant radiotherapy following radical prostatectomy increases the risk of urinary and bowel morbidity without significantly improving disease control. Therefore, an observation policy with salvage radiotherapy for PSA failure should be considered as the current standard of care after radical prostatectomy.[30] The shorter 20-fraction schedule provides a clear advantage in terms of patient convenience, environmental considerations, and hospital capacity. Severe toxicity is rare following post-prostatectomy prostate bed radiotherapy (RT) with either 52.5 Gy in 20 fractions or 66 Gy in 33 fractions. Only modest differences were observed in toxicity and patient-reported quality of life between these two schedules.[31] In our study, we utilized conventional-dose salvage radiotherapy.[29]

The American Urological Association, in collaboration with the American Society for Radiation Oncology and Society of Urologic Oncology, released the 2024 clinical practice guidelines on salvage therapy for prostate cancer.[3,4] These guidelines offer practical, clear, and evidence-based recommendations for managing recurrence following surgery. Based on these findings, the authors proposed a new EAU biochemical recurrence risk stratification. A low risk of biochemical recurrence is defined by PSADT of greater than 1 year and pathological radical prostatectomy specimen Gleason score below 8 (ISUP grade group <4). Conversely, a high risk of biochemical recurrence is defined by PSADT of 1 year or less, or pathological radical prostatectomy specimen Gleason score of 8 to 10 (ISUP grade group 4–5). Almost all international guidelines emphasize the importance of early salvage radiotherapy, which is defined as radiotherapy initiated for patients with biochemical recurrence following radical prostatectomy when the PSA level is less than 0.5 ng/mL. In this study, those with PSADT of 6 months or more at the time of recurrence following radical prostatectomy tended to show longer clinical recurrence-free survival after local radiation therapy compared with those whose PSADT was less than 6 months ($p=0.06$).

Although there is no universally accepted definition of biochemical recurrence following salvage radiotherapy after radical prostatectomy for prostate cancer, Sung Uk Lee et al reported that a serum PSA level greater than 0.8 ng/mL serves as a reasonable threshold for defining biochemical recurrence after salvage radiotherapy.[32] Furthermore, PSADT of six months or less was significantly predictive of subsequent distant metastasis, and the combined application of both parameters improved the predictive accuracy. At our hospital, we re-evaluate imaging when the PSA level exceeds 1 ng/mL during follow-up after salvage radiotherapy. If no recurrence is detected on imaging, we consider PSADT and other factors before initiating ADT, engaging in shared decision-making with the patients. Therefore, in this study, no fixed definition was employed, and recurrence was assessed based on the clinical status of each patient. Those with PSADT of

6 months or more at the time of recurrence following radical prostatectomy tended to show longer clinical recurrence-free survival after local radiation therapy compared with those whose PSADT was less than 6 months (p=0.06).

This study had various limitations. Although it is evident that PSMA-PET is an outstanding diagnostic tool, this test is currently unavailable in Japan. Therefore, the data in this paper did not include PSMA-PET data. It was conducted at a single institution and included a limited number of patients; therefore, the sample size was not calculated or justified. This was a retrospective study. There were no established standards for diagnostic criteria or the use of ADT with radiation therapy. Thus, the data included institutional bias and non-randomized ADT use. Decisions were made on an individual basis for each patient.

Conclusion

Of the 76 patients who experienced PSA recurrence following radical prostatectomy, 19 (25%) exhibited local recurrence, while 57 patients did not show any signs of local recurrence. Patients received radiation therapy targeting the prostate bed and any local recurrence lesions. However, 18 have since shown signs of recurrence. ADT may be beneficial in preventing recurrence following radiation therapy for local recurrence after radical prostatectomy. When considering salvage radiation therapy for patients with biochemical recurrence following radical prostatectomy, PSADT may be useful. However, even in patients with short PSADT, PSA values alone cannot be used to determine whether the disease is local recurrence or distant metastasis. It is considered that some patients showing recurrence following radiation therapy had distant metastases prior to treatment, highlighting the need for more accurate diagnostic methods, such as PSMA-PET.

Ethical Approval

The present study was approved by the Ethical Committee of the Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital (approval no. E2024000201). The need for written informed consent from subjects and legally authorized representatives of deceased subjects for publication of this study was waived by the Ethical Committee of Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital. This study was conducted in accordance with the Declaration of Helsinki.

Author Contributions

All authors reviewed and edited the manuscript and approved its final version for submission. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Informed Consent

We adopted patient-centered medical and health information management. Informed consent consisted of providing an opt-out option.

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Disclosure

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Abdollah F, Sood A, Sammon JD, et al. Long-term cancer control outcomes in patients with clinically high-risk prostate cancer treated with robot-assisted radical prostatectomy: results from a multi-institutional study of 1100 patients. *Eur Urol*. 2015;68(3):497–505. doi:10.1016/j.eururo.2015.06.020
2. Falagario UG, Abbadi A, Remmers S, et al. Biochemical Recurrence and risk of mortality following radiotherapy or radical prostatectomy. *JAMA Netw Open*. 2023. 6(9):e2332900. doi:10.1001/jamanetworkopen.2023.32900
3. Morgan TM, Boorjian SA, Buyyounouski MK, et al. Salvage therapy for prostate cancer: aua/astro/suo guideline part i: introduction and treatment decision-making at the time of suspected biochemical recurrence after radical prostatectomy. *J Urol*. 2024;211(4):509–517. doi:10.1097/JU.0000000000003892
4. Morgan TM, Boorjian SA, Buyyounouski MK, et al. Salvage therapy for prostate cancer: aua/astro/suo guideline part ii: treatment delivery for non-metastatic biochemical recurrence after primary radical prostatectomy. *J Urol*. 2024;211(4):518–525. doi:10.1097/JU.0000000000003891
5. NCCN clinical practice guidelines in oncology (NCCN Guidelines®), Prostate Cancer Version 1.2025 —. Available from: https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1459. Accessed December 4, 2024.
6. Trock BJ, Han M, Freedland SJ, et al. Prostate cancer-specific survival following salvage radiotherapy vs observation in men with biochemical recurrence after radical prostatectomy. *JAMA*. 2008. 299(23):2760–2769. doi:10.1001/jama.299.23.2760
7. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). *Int J Radiat Oncol Biol Phys*. 31(5):1341–1346.
8. Van den Broeck T, van den Bergh RCN, Arfi N, et al. Prognostic value of biochemical recurrence following treatment with curative intent for prostate cancer: a systematic review. *Eur Urol*. 2019;75(6):967–987. doi:10.1016/j.eururo.2018.10.011
9. Pompe RS, Gild P, Karakiewicz PI, et al. Long-term cancer control outcomes in patients with biochemical recurrence and the impact of time from radical prostatectomy to biochemical recurrence. *Prostate*. 2018;78(9):676–681. doi:10.1002/pros.23511
10. Preisser F, Chun FKH, Pompe RS, et al. persistent prostate-specific antigen after radical prostatectomy and its impact on oncologic outcomes. *Eur Urol*. 2019;76(1):106–114. doi:10.1016/j.eururo.2019.01.048
11. Sonni I, Dal Pra A, DP O, et al. (68)Ga-PSMA PET/CT-based atlas for prostate bed recurrence after radical prostatectomy: clinical implications for salvage radiation therapy contouring guidelines. *J Nucl Med*. 2023;64(6):902–909. doi:10.2967/jnumed.122.265025
12. Tilki D, Preisser F, Graefen M, Huland H, Pompe RS. External Validation of the European association of urology biochemical recurrence risk groups to predict metastasis and mortality after radical prostatectomy in a european cohort. *Eur Urol*. 2019;75(6):896–900. doi:10.1016/j.eururo.2019.03.016
13. Calais J, Cao M, Nickols NG. The Utility of PET/CT in the planning of external radiation therapy for prostate cancer. *J Nucl Med*. 2018;59(4):557–567. doi:10.2967/jnumed.117.196444
14. Panebianco V, Villeirs G, Weinreb JC, et al. prostate magnetic resonance imaging for local recurrence reporting (pi-rr): international consensus - based guidelines on multiparametric magnetic resonance imaging for prostate cancer recurrence after radiation therapy and radical prostatectomy. *Eur Urol Oncol*. 2021;4(6):868–876. doi:10.1016/j.euo.2021.01.003
15. Abreu-Gomez J, Dias AB, Ghai SPI-R-R. The Prostate Imaging for Recurrence Reporting System for MRI Assessment of Local Prostate Cancer Recurrence After Radiation Therapy or Radical Prostatectomy-A Review. *AJR Am J Roentgenol*. 2023;220(6):852–861. doi:10.2214/AJR.22.28665
16. Franco PN, Frade-Santos S, García-Baizán A, et al. An MRI assessment of prostate cancer local recurrence using the PI-RR system: diagnostic accuracy, inter-observer reliability among readers with variable experience, and correlation with PSA values. *Eur Radiol*. 2024;34(3):1790–1803. doi:10.1007/s00330-023-09949-7
17. Van Damme J, Tombal B, Michoux N, et al. Value of Whole-body Magnetic Resonance Imaging Using the MET-RADS-P Criteria for Assessing the Response to Intensified Androgen Deprivation Therapy in Metastatic Hormone-naive and Castration-resistant Prostate Cancer. *Eur Urol Oncol*. 2024;5:S2588–9311. doi:10.1016/j.euo.2024.10.009
18. Vilanova JC, Catalá-Sventzetzky V, Hernández-Mancera J. MRI for detection, staging, and follow-up of prostate cancer: synthesis of the PI-RADS v2.1. *Radiología*. 2023;65(5):431–446. doi:10.1016/j.rxeng.2022.12.005
19. Perera M, Papa N, Roberts M, et al. Gallium-68 prostate-specific membrane antigen positron emission tomography in advanced prostate cancer-updated diagnostic utility, sensitivity, specificity, and distribution of prostate-specific membrane antigen-avid lesions: a systematic review and meta-analysis. *Eur Urol*. 2020;77(4):403–417. doi:10.1016/j.eururo.2019.01.049
20. Mena E, Lindenberg L, Choyke P. The Impact of PSMA PET/CT Imaging in Prostate Cancer Radiation Treatment. *Semin Nucl Med*. 2022;52(2):255–262. doi:10.1053/j.semnuclmed.2021.12.008
21. Terlizzi M, Limkin EJ, Moukasse Y, Blanchard P. Adjuvant or salvage radiation therapy for prostate cancer after prostatectomy: current status, controversies and perspectives. *Cancers*. 2022. 14(7):1688. doi:10.3390/cancers14071688
22. Holzgreve A, Armstrong WR, Clark KJ, et al. PSMA-PET/CT findings in patients with high-risk biochemically recurrent prostate cancer with no metastatic disease by conventional imaging. *JAMA Netw Open*. 2025;8(1):e2452971. doi:10.1001/jamanetworkopen.2024.52971
23. Kneebone A, Fraser-Browne C, Duchesne GM, et al. Adjuvant radiotherapy versus early salvage radiotherapy following radical prostatectomy (TROG 08.03/ANZUP RAVES): a randomised, controlled, Phase 3, non-inferiority trial. *Lancet Oncol*. 2020;21(10):1331–1340. doi:10.1016/S1470-2045(20)30456-3
24. Vale CL, Fisher D, Kneebone A, et al. ARTISTIC Meta-analysis Group. Adjuvant or early salvage radiotherapy for the treatment of localised and locally advanced prostate cancer: a prospectively planned systematic review and meta-analysis of aggregate data. *Lancet*. 2020;396;10260:1422–1431. doi:10.1016/S0140-6736(20)31952-8
25. Tilki D, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-ISUP-SIOG guidelines on prostate cancer. part ii-2024 update: treatment of relapsing and metastatic prostate Cancer. *Eur Urol*. 2024;86(2):164–182. doi:10.1016/j.eururo.2024.04.010
26. Pollack A, Karrison TG, Balogh AG, et al. The addition of androgen deprivation therapy and pelvic lymph node treatment to prostate bed salvage radiotherapy (NRG Oncology/RTOG 0534 SPPORT): an international, multicentre, randomised phase 3 trial. *Lancet*. 399(10338):1886–1901. doi:10.1016/S0140-6736(21)01790-6

27. Schmidt-Hegemann NS, Zamboglou C, Mason M, et al. ESTRO-ACROP recommendations for evidence-based use of androgen deprivation therapy in combination with external-beam radiotherapy in prostate cancer. *Radiother Oncol*. 2023;183:109544. doi:10.1016/j.radonc.2023.109544
28. Preisser F, Abrams-Pompe RS, Stelwagen PJ, et al. EAU-YAU Prostate Cancer Working Group. European association of urology biochemical recurrence risk classification as a decision tool for salvage radiotherapy-a multicenter study. *Eur Urol*. 2024;85(2):164–170. doi:10.1016/j.eururo.2023.05.038
29. Ghadjar P, Hayoz S, Bernhard J, et al. Swiss Group for Clinical Cancer Research (SAKK). Dose-intensified Versus Conventional-dose Salvage Radiotherapy for Biochemically Recurrent Prostate Cancer After Prostatectomy: the SAKK 09/10 Randomized Phase 3 Trial. *Eur Urol*. 2021;80(3):306–315. doi:10.1016/j.eururo.2021.05.033
30. Parker CC, Petersen PM, Cook AD, et al. RADICALS investigators. Timing of radiotherapy (RT) after radical prostatectomy (RP): long-term outcomes in the RADICALS-RT trial (NCT00541047). *Ann Oncol*. 2024;35(7):656–666. doi:10.1016/j.annonc.2024.03.010
31. Petersen PM, Cook AD, Sydes MR, et al. Salvage Radiation therapy after radical prostatectomy: analysis of toxicity by dose-fractionation in the RADICALS-RT trial. *Int J Radiat Oncol Biol Phys*. 117(3):624–629. doi:10.1016/j.ijrobp.2023.04.032
32. Lee SU, Kim JS, Kim YS, et al. Optimal definition of biochemical recurrence in patients who receive salvage radiotherapy following radical prostatectomy for prostate cancer. *Cancer Res Treat*. 2022;54(4):1191–1199. doi:10.4143/crt.2021.985