Original Article

# Comparative outcomes between adjuvant and salvage radiotherapy in prostate cancer after minimally invasive radical prostatectomy

*Naphon Sriwachirawat, Apirak Santi-ngamkun, Julin Opanuraks, Kavirach Tantiwongse, Supoj Ratchanon, Kamol Panumatrassamee*

Division of Urology, Department of Surgery, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Bangkok, Thailand

**Keywords:**
Prostate cancer, adjuvant, salvage, radiotherapy, radical prostatectomy

## Abstract

**Objective:** Radical prostatectomy (RP) is the standard treatment in clinically localized prostate cancer. However, the timing of postoperative radiotherapy (RT) in patients with adverse pathologic features or PSA persistence remains controversial. The objective of this study is to compare the survival outcomes and treatment complications between adjuvant radiotherapy (aRT) and salvage radiotherapy (sRT) in patients after minimally invasive RP.

**Materials and Methods:** This retrospective study reviewed the clinical data in patients who underwent minimally invasive RP in our institution between January 2012 and April 2021. The patients were divided into three groups: no RT, aRT, and sRT. Patient demographic data, pathological reports, RTOG/EORTC toxicity scores, functional outcomes, and survival outcomes were compared between aRT and sRT groups.

**Results:** A total of 487 patients were included in the study. One-hundred and thirty-three patients (27.3%) received postoperative RT. The pathological stage and positive margin rate were significantly higher in the aRT group. Five-year ADT-free survival (78.8% vs 80%, p = 0.68), 5-year metastasis-free survival (80.2% vs 92.2%, p = 0.38), and 5-year overall survival (97.1% vs 100%, p = 0.68) were no different between groups. There were no significant differences in continence, potency, genitourinary or gastrointestinal toxicities between groups.

**Conclusions:** Timing of postoperative RT does not affect survival. Functional outcomes and radiation toxicity were comparable between patients undergoing aRT and sRT.

**Insight Urol 2024;45(1):1-9. doi: 10.52786/isu.a.79**

**Corresponding author:** Kamol Panumatrassamee

**Address:** Division of Urology, Department of Surgery, King Chulalongkorn Memorial Hospital, Bangkok 10330, Thailand

**E-mail:** kamol.pa@chula.ac.th

**Manuscript received:** April 25, 2023 **Revision received:** March 5, 2024

**Accepted after revision:** April 12, 2024

## Introduction

Prostate cancer is the fifth most common malignancy in men in Thailand.[1] Radical prostatectomy (RP) is the standard treatment for clinically localized prostate cancer in a patient with a long-life expectancy. However, biochemical recurrence (BCR) occurred in 20-40% of patients after RP within 10 years.[2] BCR is an independent risk factor for the development of metastasis, prostate cancer-specific mortality, and overall mortality.[2]

Postoperative radiation therapy (RT) has an important role in reducing recurrence and increasing survival.[3-5] There are 2 major types of postoperative RT. Adjuvant RT (aRT) which is started after the patient's recovery, aiming to reduce the disease recurrence in patients at a high-risk of recurrence based on the adverse pathological features. Salvage RT (sRT) which is administered after the detection of BCR, aims to treat recurrent disease. Oncological benefits from the treatment should be balanced with the adverse effects of the treatment.

Currently, based on large randomized controlled trial studies, the role of aRT was found to be limited.[6-8] aRT did not demonstrate superior outcomes over sRT in terms of disease progression, and also increases the risk of genitourinary toxicity (GU) including urethral stricture, incontinence, and hematuria.[6-8]

This study aimed to investigate and compare the treatment outcomes between aRT and sRT including disease control rates and radiation-related complications in prostate cancer patients after minimally invasive (laparoscopic and robot-assisted) RP.

## Materials and Methods

### Study populations

After approval of the study protocol from the institutional review board and the ethics committee (Protocol Number: 659/64), all medical records of the patients who underwent minimally invasive RP in our institution between January 2012 and April 2021 were retrospectively reviewed. The patients were divided into three groups: those who did not receive postoperative RT, those who received aRT, and those who received sRT.

Patients in the aRT group received RT at the prostatic fossa (55.2-70.2 Gy in 30-39 fractions) after they recovered from surgery without having BCR. Patients in the sRT group received an RT dose of 66-79.2 Gy in 33-39 fractions when they had BCR which was defined as an increase in the serum PSA level of more than 0.2 ng/ml twice after surgery. The decision regarding treatment is based on surgeon and patient preference after consideration of the pathological results and disease staging.

### Surgical techniques

The surgical techniques have been described previously.[9] Briefly, all the procedures were performed by the conventional transperitoneal approach with 5-trocar insertion. Robot-assisted RP was performed by the da Vinci Si Surgical System (Intuitive Surgical, Sunnyvale, CA, USA). Pelvic lymphadenectomy was performed using the standard template in the patients who had a high risk of metastasis following the nomogram. Neurovascular bundles were preserved in the selected patient. Urethro-vesical anastomosis was performed with the continuous suture by two V-loc 3/0 sutures.

The patients were followed up at 1, 3, 6, and 12 months after surgery and then subsequently every 6 months. Serum PSA, continence, and potency status were recorded.

### Outcome measurement and statistical analyses

Demographic data, pathological reports, and functional outcomes after surgery from all patients were analyzed. These parameters were also compared between the aRT and the sRT group. Pathological staging was classified following the 2017 American Joint Committee on Cancer AJCC Staging 8th edition.[10] Continence was defined as no pad used or use of a protective pad. Potency was defined as being able to have an erection sufficient for sexual intercourse with or without using a phosphodiesterase type 5 inhibitor.

The primary outcomes of this study were the oncological results among the patients who received postoperative RT. Androgen deprivation therapy (ADT)-free survival, metastasis-free survival, and overall survival were compared between the aRT group and sRT group. ADT-free survival was defined as a patient who did not receive ADT after complete adjuvant or salvage treatment which included patients who received ADT in combination with RT.

The secondary outcome was to compare the adverse effects of radiation therapy between aRT and sRT groups. The genitourinary (GU) and gastrointestinal (GI) tract toxicity grades were allocated in accordance with the guidelines published by the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC)[11] throughout the follow-up period.

This study also compared the results from a subgroup of patients with "high-risk features" defined as patients with pTstage 3-4 or Gleason grade group 4-5 or positive surgical margin status.

Statistical analysis was carried out using STATA version 17 (StataCorp, College Station, Texas, USA). Categorial variables were compared using the chi-square or Fisher exact test and presented as number and percentage. Continuous variables were compared using the Wilcoxon rank sum test and presented as median and interquartile range (IQR).

Survival was analyzed using the Kaplan-Meier method. Survival in the study group was compared using the log-rank test, with the significance level set at 5%. Results are presented as survival at various time points with their associated 95% confidence interval (CI).

## Results

A total of 501 patients with clinically localized prostate cancer underwent minimally invasive RP in our institution during the study period. Eight patients were excluded due to incomplete medical records and six patients with variant histology were also excluded from the study. Among the remaining patients, 354 patients did not receive postoperative RT, 63 patients received aRT, and 70 patients received sRT (Figure 1).

Demographic data of all patients are presented in Table 1. The median age was 67 years. The median preoperative PSA was 10.1 ng/ml. Most of the patients were at pT2 stage (54.7%) and had a Gleason score of 7 (67.5%). The positive surgical margin rate was 41.1%. The median follow-up duration was 3.7 years.

### Comparisons of aRT and sRT group

In the group of patients who received postoperative RT, comparative outcomes between the aRT and sRT group are shown in Table 2. Patients in the aRT group had significantly higher pathological staging and positive surgical margin rate ($p = 0.03$, and $p < 0.001$ respectively). The median time after surgery to RT was 5 months in

**Table 1.** Patient characteristics of total populations at baseline (N=487)

| Variables | |
|---|---|
| **Age (years), median (IQR)** | 67 (62-71) |
| BMI (kg/m$^2$), median (IQR) | 24.1 (22.3-26.4) |
| Preoperative PSA (ng/dl), median (IQR) | 10.1 (7.1-15.3) |
| Pathological T stage, n (%) | |
| pT2 | 266 (54.7) |
| pT3a | 152 (31.3) |
| pT3b | 65 (13.4) |
| pT4 | 3 (0.6) |
| Gleason score, n (%) | |
| 6 | 87 (17.9) |
| 7 | 328 (67.5) |
| 8-10 | 71 (14.6) |
| Follow-up duration (years), median (IQR) | 3.7 (2-5.6) |
| Positive margin rate, n (%) | 200 (41.1) |

IQR = interquartile range, PSA = prostate specific antigen

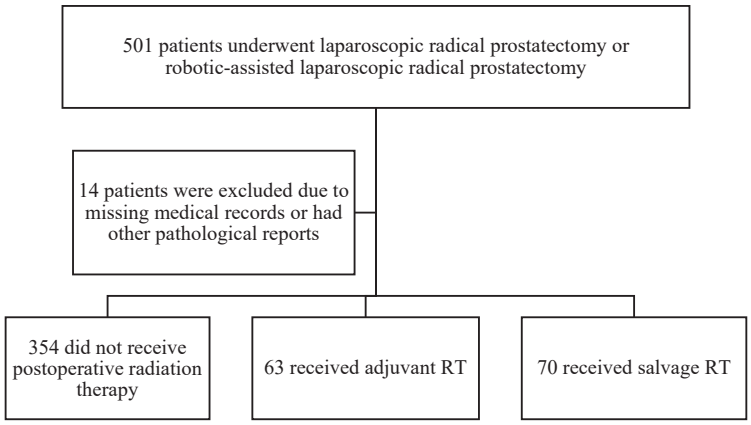



**Figure 1.** Trial population

**Table 2.** Baseline patient characteristics of postoperative RT populations (n=133)

| | Adjuvant RT (n=63) | Salvage RT (n=70) | P-value |
|---|---|---|---|
| **Age (years), median (IQR)** | 68 (62-71) | 66 (62-70) | 0.39 |
| BMI (kg/m$^2$), median (IQR) | 24.2 (22.3-26.6) | 25.3 (23.5-26.9) | 0.14 |
| Preoperative PSA (ng/dl), median (IQR) | 14.6 (7.8-20.7) | 10.8 (7.6-17) | 0.21 |
| Pathological T stage, n (%) | | | 0.03 |
| pT2 | 20 (31.8) | 35 (50) | |
| pT3a | 23 (36.5) | 25 (35.7) | |
| pT3b | 20 (31.8) | 10 (14.3) | |
| pT4 | 0 | 0 | |
| Gleason score, n (%) | | | 0.13 |
| 6 | 3 (4.8) | 9 (12.9) | |
| 7 | 40 (63.5) | 47 (67.1) | |
| 8-10 | 20 (31.8) | 14 (20) | |
| Time to postoperative radiation (months), median (IQR) | 5 (3-6) | 21 (12-34) | - |
| Length of follow-up (years), median (IQR) | 4.6 (3.2-6.3) | 5 (3.4-7.1) | 0.78 |
| Combined ADT, n (%) | 21 (33.3) | 23 (32.9) | 0.95 |
| Positive margin rate, n (%) | 54 (85.7) | 35 (50) | <0.001 |
| Continence, n (%) | | | |
| Months 1 | 0/43 (0) | 9/63 (14.3) | 0.01 |
| Months 3 | 9/44 (20.5) | 17/58 (29.3) | 0.31 |
| Months 6 | 21/47 (44.7) | 31/59 (52.5) | 0.42 |
| Months 12 | 25/45 (55.6) | 45/60 (75) | 0.04 |
| Potency, n (%) | | | |
| Months 1 | 0/6 (0) | 3/43 (7) | 0.50 |
| Months 3 | 1/9 (11.1) | 5/42 (11.9) | 0.95 |
| Months 6 | 1/7 (14.3) | 7/39 (18) | 0.81 |
| Months 12 | 1/5 (20) | 7/33 (21.2) | 0.95 |

IQR = interquartile range, BMI = body mass index, PSA = prostate specific antigen, RT = radiation therapy, ADT = androgen deprivation therapy

the aRT group and 21 months in the sRT group. The median (IQR) PSA level at the time of sRT was 0.28 (0.21-0.49) ng/dl.

One-third of patients in both groups received ADT in combination with RT (33.3% in the aRT group and 32.9% in the sRT group). The duration of additional ADT was between 6 months to 2-3 years in all patients. Continuous ADT was required if the disease couldn't be controlled during the treatment. Continence rates were significantly better in the sRT group at 1, and 12 months after surgery (p = 0.01, and p = 0.04 respectively). Potency was no different between groups. Median follow-up was 4.6 years in the aRT group and 5 years in the sRT group.

There were 9 deaths (1.85%) in the total population during the follow-up period. Eight patients were from the non-postoperative RT group (4 patients from pneumonia, 1 patient from prostate cancer, 1 patient from pancreatic cancer, 1 patient from leukemia, and 1 patient from COVID-19). Only one patient from the aRT group died from prostate cancer. None of the patients in the sRT group died during the study.

The Kaplan-Meier curves of the survival studies are shown in Figure 2. There were no significant differences in the survival rates between groups. Five-year ADT-free survival was 78.8% (95% CI 62.2-88.7) in the aRT group and 80% (95% CI 68-88.7) in the sRT group (p = 0.68). Five-year metastasis-free survival was 80.2% (95% CI 63.2-89.9) in the aRT group and 92.2% (95% CI 82.4-96.7) in the sRT group (p = 0.38). However, 10-year metastasis-free survival was significantly better in the sRT group (p = 0.01). Five-year overall survival was 97.1% (CI 83.6-97.3) in the adjuvant RT group and 100% in the salvage RT group (p = 0.68).

Toxicities from postoperative RT were compared between groups and presented in Table

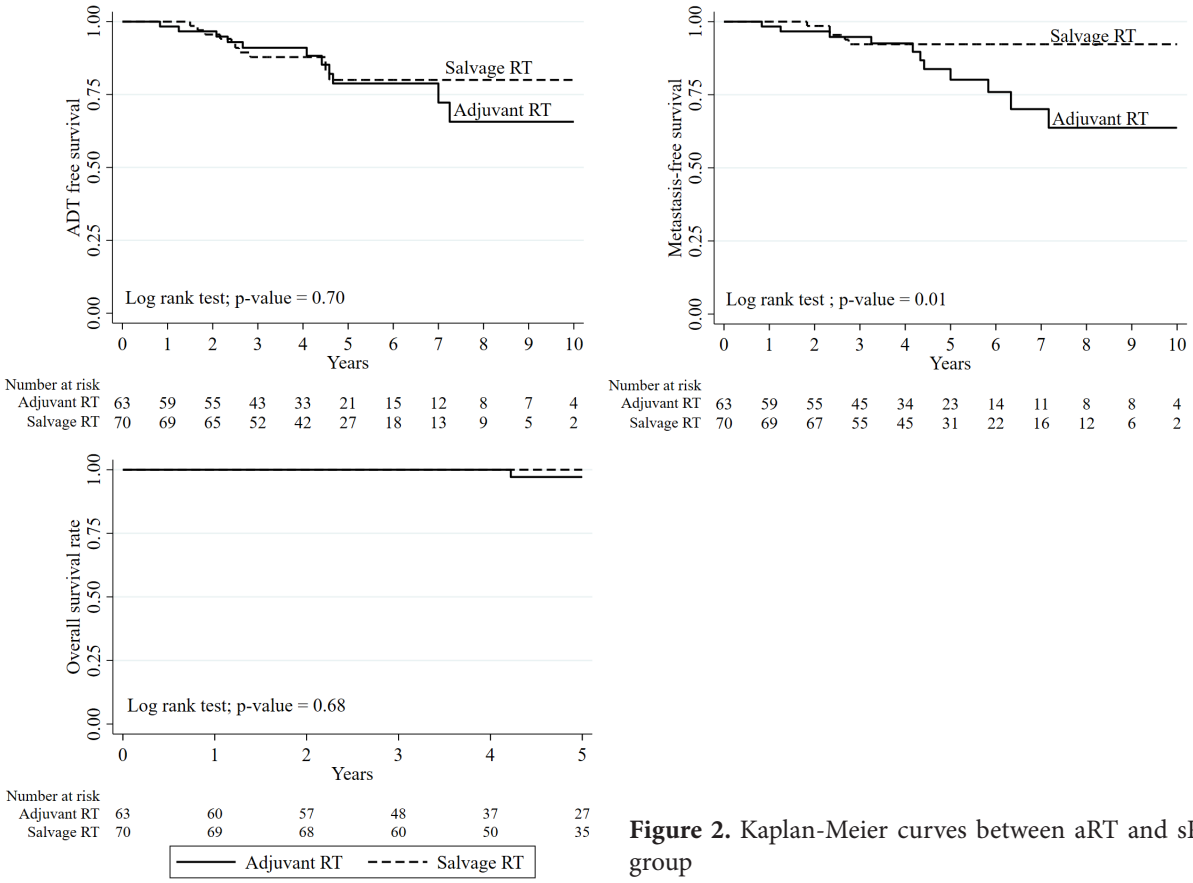



**Figure 2.** Kaplan-Meier curves between aRT and sRT group

**Table 3.** Radiation toxicity

| RTOG/EORTC toxicity score | Adjuvant RT (n=63) | Salvage RT (n=70) | P-value |
|---|---|---|---|
| **Acute radiation morbidity, n (%)** | | | |
| Genitourinary organ | | | 0.56 |
| Grade 1 | 14 (22.2) | 15 (21.4) | |
| Grade 2 | 1 (1.6) | 0 (0) | |
| Gastrointestinal organ | | | 0.62 |
| Grade 1 | 1 (1.6) | 2 (2.9) | |
| **Late radiation morbidity, n (%)** | | | |
| Genitourinary organ | | | 0.49 |
| Grade 1 | 5 (7.9) | 2 (2.9) | |
| Grade 2 | 5 (7.9) | 6 (8.6) | |
| Grade 3 | 0 | 1 (1.4) | |
| Gastrointestinal organ | | | 0.17 |
| Grade 1 | 0 | 5 (8.8) | |
| Grade 2 | 2 (3.2) | 1 (1.4) | |
| Grade 3 | 1 (1.6) | 1 (1.4) | |

RTOG = Radiation Therapy Oncology Group, EORTC = European Organization for Research and Treatment of Cancer, RT = radiation therapy

3. Incidence of early and late GU and GI tract toxicities were not significantly different between groups. Approximately 20% of patients in each group experienced acute GU tract toxicities, the majority being grade 1. There were 3 late grade 3 toxicities that occurred in this study. Two patients experienced severe bladder telangiectasia with intractable gross hematuria treated with bladder fulguration and hyperbaric oxygen therapy. One patient had rectal mucosa necrosis that required endoscopic treatment.

### Subgroup analysis of high-risk patients

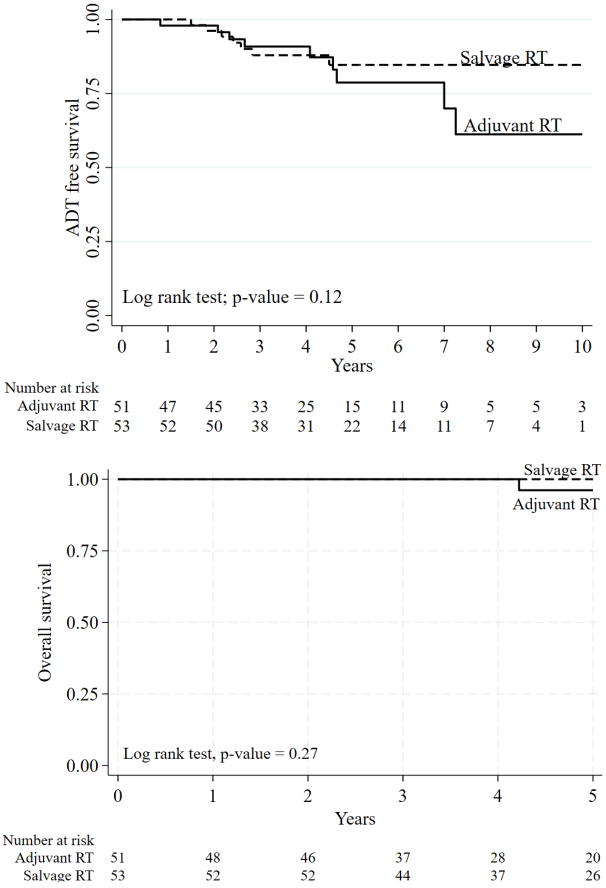
There were 51 high-risk patients in the aRT group and 53 high-risk patients in the sRT group. The continence rate was significantly better in the sRT group at 1 month after surgery (0% vs 14.6%, p = 0.02). There were no significant differences in radiation toxicities between groups in both GU toxicity and GI toxicity.

Survival rates among these 2 subgroups were not significantly different. Five-year ADT-free survival was 78.8% (95% CI 62.2-88.7) in the aRT group and 84.7% (95% CI 70-92.5) in the sRT group (p = 0.75). Five-year metastasis-free survival was 79.1% (95% CI 58-90.4) in the aRT group and 91.9% (95% CI 79.7-96.9) in the sRT group (p = 0.94). Five-year overall survival was 96.5% (CI 75.7-99.5) in the aRT group and 100% in the sRT group (p = 0.27). The Kaplan-Meier curves of the survival studies from the high-risk patient are shown in Figure 3.

## Discussion

The optimum time for post-radical prostatectomy radiation therapy is controversial. Early aRT may improve biochemical progression; however, sRT can avoid unnecessary treatment with a low rate of radiation-related toxicity. There remains an ongoing debate among medical professionals regarding which of these two approaches is the most effective for treating prostate cancer after RP. The choices have mainly relied on the local protocols and the preferences of the patient and their physicians.

Previously, The American Urological Association and the American Society for Radiation Oncology (AUA/ASTRO), and the European Association of Urology (EAU) Guidelines suggest that patients who are at high risk of recurrence (pT3-T4, positive surgical margin) should be offered aRT.[12-14] aRT at the surgical bed in patients with adverse pathologic features has been shown to increase biochemical progression-free survival[4,5] and may also increase overall survival or prevent metastasis compared to observation.[5] However, not all these patients will experience the survival benefits from aRT, and some patients will have toxicity from radiation therapy. This is likely since the tissues surrounding the prostate bed have not yet fully healed after surgery. Therefore, aRT is associated with a higher risk of urinary toxicities such as urinary incontinence and urethral stricture.[6,7]



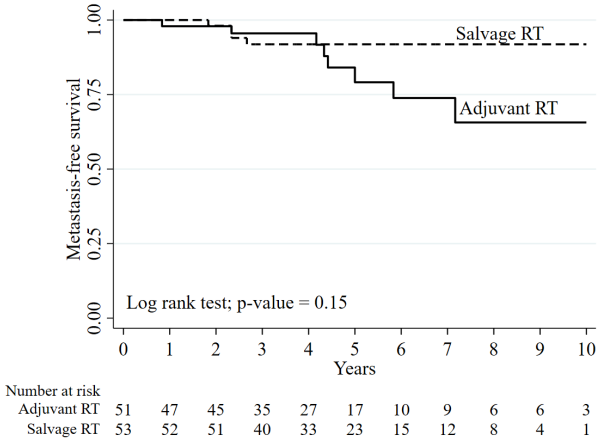




**Figure 3.** Kaplan-Meier curves between aRT and sRT in high-risk patients subgroup

Several studies have compared the outcomes of aRT and sRT after RP in patients with clinically localized and locally advanced prostate cancer. The results of immediate aRT within 6 months after surgery were compared with sRT that was administered when the patient had biochemical progression. The results from 3 large randomized controlled trial studies showed no statistically significant difference in the survival outcomes. This has led to a decrease in the popularity of aRT.[15]

The results from the RADICALS-RT trial[7] did not support the routine use of aRT. Five-year biochemical progression-free survival was 85% in the aRT group and 88% in the sRT group (HR 1.1; 95% CI 0.81-1.49, p = 0.56). The freedom from the non-protocol ADT at 5 years was 93% in the aRT group and 92% in the sRT group (HR 0.88; 95%CI 0.58-1.33, p = 0.53). Moreover, early and late RTOG toxicities were significantly higher in the aRT group in both GU and GI tracts. The RAVES trial[6], which is a non-inferiority trial, supported using the sRT with the comparable biochemical control with aRT, and 50% of patients in the sRT group may avoid radiation therapy. Five-year freedom of biochemical progression was 86% in the aRT group compared with 87% in the sRT group (stratified HR 1·12, 95% CI 0·65-1·90; p = 0·15). The GETUG-AFU 17 trial[8] found aRT with 6-month ADT has no benefit for 5-year event-free survival (92% vs 90%, HR 0·81, 95% CI 0·48–1·36; log-rank p = 0·42) and 5-year overall survival (96% vs 99%, HR 1.6, 95%CI 0.71-3.6, p = 0.25) over sRT with 6-month ADT.

Vale et al. reported a meta-analysis incorporating data from these 3 RCTs with a total of 2,151 patients. There was no evidence of an advantage in event-free survival with aRT compared to early sRT (HR 0.95; 95% CI 0.75–1.21, p = 0.7).[16]

In a study in Thai patients, Woranisarakul et al.[17] compared the results between aRT and sRT in 151 prostate cancer patients with adverse pathological features after radical prostatectomy. There were no statistically significant differences in 5-year BCR-free survival (78.7% vs 69.1%, p = 0.11) and 5-year metastasis-free survival (100% vs 90.6%, p = 0.05) between groups. The incidences of grade 3 to 4 late gastrointestinal and genitourinary toxicities were 5.8% and 10.8% respectively. In our study, we found that the survival rates between the two treatment groups (both the total population and the subgroup of the high-risk patients) were not significantly different. These findings are consistent with the results from all the previous studies. However, the metastasis-free survival curve showed a separation starting after 5 years of follow-up, resulting in better outcomes in the sRT group compared with the aRT group at 10 years (p = 0.01). This could be due to the high proportion of locally advanced disease and positive surgical margin patients in the aRT group which has a greater chance of being resistant to treatment and causing disease progression. Furthermore, there was no difference in both acute and late radiation toxicities. However, the continence rate was better in the sRT group only in some periods.

The combination of ADT with sRT is an important factor in survival outcomes and is still undergoing debate. The RGOT 9601 study[18] showed the benefit of adding daily 150 mg of bicalutamide for 24 months to sRT in comparison with sRT-only in recurrent prostate cancer. The 12-year overall survival rate was significantly better in the combination group, especially in the subgroup of patients with PSA > 1.5 ng/ml (HR 0.45, 95%CI 0.25-0.81, p = 0.007). The incidences of 12-year metastasis prostate cancer and prostate cancer-related death were also significantly lower in the combination group. More recently, the results from GETUG-AFU 16[19] supported the benefit of short-term ADT by using 6 months of goserelin combined with sRT over sRT alone. 10-year progression-free survival (HR 0.54, 95%CI 0.43-0.68, p < 0.0001) and metastasis-free survival (HR 0.73, 95%CI 0.54-0.98, p = 0.03) were significantly better in the combination group.

In contrast, the results from Thai patients showed a combination of ADT with aRT in high-risk prostate cancer patients after radical prostatectomy couldn't improve 10-year metastasis-free survival (p = 0.78). However, combined treatment resulted in an improving trend in improving BCR-free survival over aRT alone (HR 0.4, 95%CI 0.16-1.03, p = 0.05).[20]

Spratt et al.[21] presented a decision framework for the use of hormonal therapy combined with sRT in recurrent prostate cancer based on the pre-sRT PSA, margin status, and ISUP grade. The patient with a high risk of progression may benefit from combined long-term (2 years) ADT. For the patient at a low risk of progression, combined short-term (6 months) ADT may be sufficient.

In the patients with low-risk profiles, combined ADT may not be helpful.

The limitation of this study is its retrospective nature with a selection bias which limits the reliability of the data. Patients in the aRT group had a higher pT stage and higher positive margin rates. There is no standard rationale for combining ADT with RT. This relies on the individual decision made mutually by the surgeon and patient, the duration of ADT varying which is influenced by the evolution of treatment over time.

## Conclusions

The timing of postoperative RT after radical prostatectomy does not affect survival outcomes. Functional outcomes and radiation toxicities were comparable between aRT and sRT. Our findings support the use of early sRT over aRT in patients with adverse pathological features.

## Conflicts of Interest

The authors declare no conflicts of interest.

## References


1. Database of Cancer Patients Unit, National Cancer Institute, Department of Medical Services, Ministry of Public Health. Top 10 Most Common Cancer in Males. In: Sangariyawanich E, Pitakngarnkul S, Buasom R, editors. Hospital-Based Cancer Registry 2021. Bangkok: Medical Digital Division, National Cancer Institute; 2022. p. 1.
2. den Broeck TV, van den Bergh RCN, Arfi N, Gross T, Moris L, Briers E, et al. Prognostic value of biochemical recurrence following treatment with curative intent for prostate cancer: a systematic review. Eur Urol 2019;75:967-87.
3. Bolla M, van Poppel H, Collette L, van Cangh P, Vekemans K, Da Pozzo L, et al. Postoperative radiotherapy after radical prostatectomy: a randomised controlled trial (EORTC trial 22911). Lancet 2005; 366:572-8.
4. Bolla M, van Poppel H, Tombal B, Vekemans K, Da Pozzo L, de Reijke TM, et al. Postoperative radiotherapy after radical prostatectomy for high-risk prostate cancer: long-term results of a randomised controlled trial (EORTC trial 22911). Lancet 2012; 380:2018-27.
5. Thompson IM, Tangen CM, Paradelo J, Lucia MS, Miller G, Troyer D, et al. Adjuvant radiotherapy for pathological T3N0M0 prostate cancer significantly reduces risk of metastases and improves survival: long-term followup of a randomized clinical trial. J Urol 2009;181:956-62.
6. Kneebone A, Fraser-Browne C, Duchesne GM, Fisher R, Frydenberg M, Herschtal A, 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;21:1331-40.
7. Parker CC, Clarke NW, Cook AD, Kynaston HG, Petersen PM, Catton C, et al. Timing of radiotherapy after radical prostatectomy (RADICALS-RT): a randomised, controlled phase 3 trial. Lancet 2020; 396:1413-21.
8. Sargos P, Chabaud S, Latorzeff I, Magné N, Benyoucef A, Supiot S, et al. Adjuvant radiotherapy versus early salvage radiotherapy plus short-term androgen deprivation therapy in men with localised prostate cancer after radical prostatectomy (GETUG-AFU 17): a randomised, phase 3 trial. Lancet Oncol 2020;21:1341-52.
9. Siripalangkanont J, Panumatrassamee K. Comparison of treatment outcomes between laparoscopic and robot-assisted laparoscopic radical prostatectomy in clinically localized prostate cancer, a single-surgeon experience. J Med Assoc Thai 2020; 103:1300-8.
10. Gospodarowicz MK, Wittekind C, Brierley JD, editors. TNM classification of malignant tumours. 8th ed. New York: Wiley-Blackwell; 2016.
11. 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 1995;31:1341-6.
12. Thompson IM, Valicenti RK, Albertsen P, Davis BJ, Goldenberg SL, Hahn C, et al. Adjuvant and salvage radiotherapy after prostatectomy: AUA/ASTRO Guideline. J Urol 2013;190:441-9.
13. Pisansky TM, Thompson IM, Valicenti RK, D'Amico AV, Selvarajah S. Adjuvant and salvage radiation therapy after prostatectomy: ASTRO/AUA Guideline Amendment, Executive Summary 2018. Pract Radiat Oncol 2019;9:208-13.
14. Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M, et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, diagnosis, and local treatment with curative intent. Eur Urol 2017;71:618-29.
15. Sineshaw HM, Gray PJ, Efstathiou JA, Jemal A. Declining use of radiotherapy for adverse features after radical prostatectomy: results from the National Cancer Data Base. Eur Urol 2015;68:768-74.
16. Vale CL, Fisher D, Kneebone A, Parker C, Pearse M, Richaud P, et al. 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;396:1422-31.
17. Woranisarakul V, Leewansangtong S, Dankulchai P, Apiwarodom N, Srinualnad S, Taweemonkongsap T, et al. Oncological outcomes of radiotherapy after radical prostatectomy in Thai patients with prostate cancer. J Med Assoc Thai 2017;100:S179-S85.
18. Shipley WU, Seiferheld W, Lukka HR, Major PP, Heney NM, Grignon DJ, et al. Radiation with or without antiandrogen therapy in recurrent prostate cancer. N Engl J Med 2017;376:417-28.
19. Carrie C, Magne N, Burban-Provost P, Sargos P, Latorzeff I, Lagrange JL, et al. Short-term androgen deprivation therapy combined with radiotherapy as salvage treatment after radical prostatectomy for prostate cancer (GETUG-AFU 16): a 112-month follow-up of a phase 3, randomised trial. Lancet Oncol 2019;20:1740-9.
20. Kiatbamrungpunt C, Nualyong C, Srinualnad S, Leewansangtong S, Taweemonkongsap T, Chaiyaprasithi B, et al. Long term outcomes between adjuvant radiotherapy and combined radiotherapy with hormonal treatment after radical prostatectomy in high risk prostate cancer. Insight Urol 2021;42:7-12.
21. Spratt DE, Dess RT, Zumsteg ZS, Lin DW, Tran PT, Morgan TM, et al. A systematic review and framework for the use of hormone therapy with salvage radiation therapy for recurrent prostate cancer. Eur Urol 2018;73:156-65.