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# Long-term Outcomes of Radical Prostatectomy versus Radiation Therapy for High- and Very High-Risk Localized Prostate Cancer: An IPTW Analysis from a Multi-center Asian Database

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## Abstract

**Background:** While oncological outcomes of radical prostatectomy (RP) and radiation therapy (RT) for localized prostate cancer are well-evaluated, data focusing on Asian populations remain limited. This study aimed to compare the outcomes of RP versus RT in Asian patients with NCCN high-risk and very high-risk localized prostate cancer.

**Methods:** We retrospectively analyzed 1,641 patients with high-risk or very high-risk disease treated between January 2005 and September 2021 from the Chang Gung Research Database (CGRD). Inverse probability of treatment weighting (IPTW) was applied to adjust for baseline confounders—including age, prostate-specific antigen, clinical T stage, and Charlson Comorbidity Index—effectively minimizing significant selection bias, particularly regarding age. Overall survival (OS) and cancer-specific survival (CSS) were evaluated.

**Results:** In the high-risk cohort, RP demonstrated superior OS and CSS compared to RT before and after IPTW adjustment (post-IPTW 10-year OS:  $p=0.038$ , CSS:  $p=0.015$ ; 12-year OS:  $p=0.021$ , CSS:  $p=0.013$ ). Similarly, for very high-risk patients, 10- and 12-year OS and CSS were significantly better following RP both before and after weighting (all post-IPTW  $p < 0.001$ ). Furthermore, across both risk strata, patients undergoing RT required subsequent androgen deprivation therapy more frequently, indicating poorer long-term PSA control.

**Conclusions:** This real-world study demonstrates that RP offers robust, statistically significant OS and CSS benefits over RT for Asian patients with high-risk and very high-risk localized prostate cancer. Validated through rigorous IPTW adjustment, these findings provide valuable clinical evidence to support personalized treatment decision-making in this specific population.

**Keywords:** Localized Prostate Cancer, Radical Prostatectomy, Radiation Therapy, In-verse probability of treatment weighting

## 1. Introduction

The prostate cancer incidence rate among men continued to increase in recent years.[1,2] Thus, more and more studies were published to discuss the oncological out-come for prostate cancer regardless of treatment choice[3]. Among these, localized prostate cancer has been widely investigated worldwide, with numerous studies evaluating whether radical prostatectomy (RP) or radiation therapy (RT) combined with androgen deprivation therapy (ADT) represents the optimal treatment strategy for patients with high-risk and very high-risk disease. Current National Comprehensive Cancer Network (NCCN) guidelines recommend both RP and RT combined with long-term ADT (12–36 months) as standard first-line treatment options for these patients. This aligns with the recent consensus in Taiwan, which emphasizes a multidisciplinary approach for high-risk and locally advanced disease.[4]

Despite the availability of randomized controlled trials, retrospective cohort studies, and systematic reviews comparing these two treatment strategies, the optimal approach remains controversial.[5] This uncertainty is largely attributable to heterogeneity in study populations, treatment protocols, and follow-up durations, as well as the inherent selection bias present in non-randomized studies. In addition, most existing evidence has been derived from Western populations, while data focusing on Asian patients remain relatively limited.

To address this gap, we conducted a large-scale, multi-institution retrospective study using the Chang Gung Research Database (CGRD) to compare oncological outcomes between RP and RT in Taiwanese patients with high-risk and very high-risk localized prostate cancer. IPTW was applied to mitigate treatment selection bias and balance baseline covariates between groups.

## 2. Materials and Methods

### 2-1. Study Population

Data were obtained from the Taiwan Cancer Registry Database within the Chang Gung Memorial Hospital system, integrated into the Chang Gung Research Database (CGRD). A total of 9,690 patients diagnosed with prostate cancer (ICD-10 code C61) between January 2005 and September 2021 were initially identified.

Patients were excluded if they had metastatic disease at diagnosis, missing essential clinical data (including initial prostate-specific antigen [PSA] level or clinical T stage), did not receive either RP or RT as definitive local treatment, or initiated treatment more than 365 days after diagnosis. Based on the NCCN risk classification, 612 patients were categorized as high-risk and 1,029 as very high-risk and were included in the final analysis. (Fig. 1)

The primary endpoints were overall survival (OS) and cancer-specific survival (CSS) at 10 years for both high-risk and very high-risk cohorts. Secondary endpoints included the use and duration of post-treatment systemic therapies, including ADT, novel hormonal agents (NHA), and docetaxel.

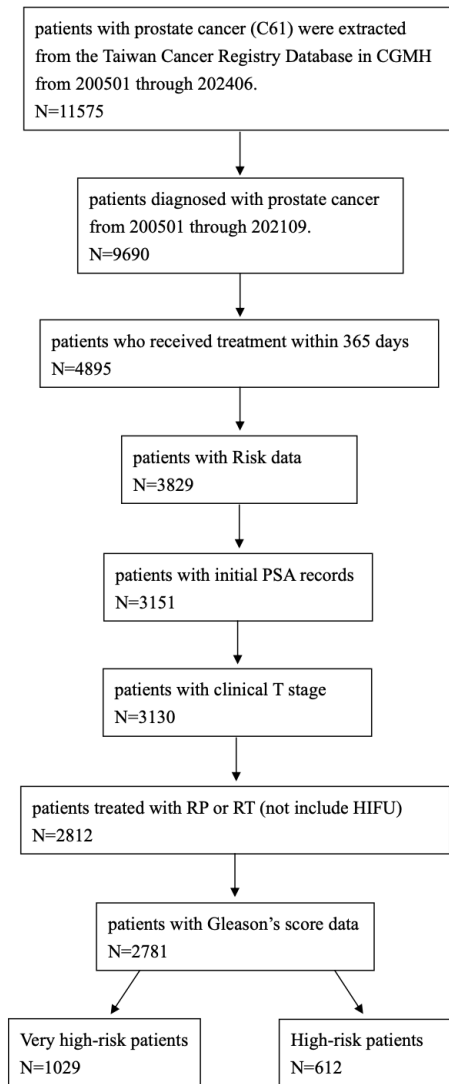


**Figure 1.** Patient selection flow chart

## 2-2. Statistical Analysis

Baseline characteristics of patients receiving RP and RT were summarized in Table 1, including age, follow-up duration, initial PSA level, Charlson Comorbidity Index (CCI), clinical T and N stages, Gleason score, and major comorbidities such as hypertension, coronary artery disease, and diabetes mellitus. Continuous variables were presented as means with standardized differences (SD), while categorical variables were reported as proportions.

Meaningful baseline imbalances were observed in age, initial PSA level, CCI score, and clinical T stage ( $T > 2$ ), each demonstrating standardized differences greater than 0.1. Although coronary artery disease also showed imbalance between groups, it was incorporated into the CCI score and therefore was not included as a separate variable in the inverse probability of IPTW model.[6,7]

IPTW was applied to create a weighted pseudo-population in which baseline covariates were balanced between treatment groups. Propensity scores were estimated using logistic regression based

on age, PSA level, clinical T stage, and CCI score. Covariate balance before and after IPTW was assessed using standardized mean differences.

Kaplan-Meier survival curves and log-rank tests were used to compare OS and CSS between RP and RT groups in both the original and IPTW-adjusted cohorts. All tests were two-sided, and statistical significance was defined as  $p < 0.05$ . Analyses were performed using SAS Enterprise Guide.

### 3. Results

#### 3-1. Clinical Characteristics

A total of 612 patients in the high-risk group and 1,029 patients in the very high-risk group were included. Overall, patients undergoing RP were younger, had lower initial PSA levels, and lower CCI scores compared with those receiving RT, regardless of risk category.

In the high-risk cohort, patients treated with RP tended to have higher Gleason scores, while no substantial difference in clinical T stage distribution was observed between RP and RT groups. In contrast, within the very high-risk cohort, a higher proportion of patients in the RT group had clinical T stage greater than T2, whereas Gleason score distribution was comparable between treatment modalities.(Table 1A and 1B)

| Variables              | Study population before IPTW (n =612) |               |                         | After IPTW match |               |                         |
|------------------------|---------------------------------------|---------------|-------------------------|------------------|---------------|-------------------------|
|                        | RP (N=357)                            | RT (N= 255)   | Standardized difference | RP               | RT            | Standardized difference |
| Age (mean± SD)*        | 66.68 ±6.87                           | 72.77 ±6.99   | 0.879                   | 68.95 ±7.11      | 68.14 ±9.21   | 0.098                   |
| Follow up (mean± SD)   | 77.17 ±42.16                          | 88.37 ±45.43  | 0.256                   | 74.64 ±41.57     | 89.81 ±45.08  | 0.350                   |
| PSA (mean± SD)*        | 20.52 ±20.27                          | 27.80 ±25.19  | 0.318                   | 24.29 ±28.27     | 24.61 ±22.78  | 0.012                   |
| CCI scores (mean± SD)* | 4.61 ±2.79                            | 5.77 ±3.28    | 0.380                   | 5.10 ±3.11       | 5.40 ±3.10    | 0.097                   |
| T stage >2*            | 141.0 (39.5)                          | 94.0 (36.9)   | 0.054                   | 229.7 (37.9)     | 238.7 (37.7)  | 0.004                   |
| N stage =1             | 1(0.28)                               | 253.0 (100.0) | <0.001                  | 604.6 (100.0)    | 627.0 (100.0) | <0.001                  |
| Gleason scores (%)     |                                       |               | 0.274                   |                  |               | 0.098                   |
| <7                     | 83.0 (23.2)                           | 85.0 (33.3)   |                         | 152.4 (25.2)     | 177.4 (28.0)  |                         |
| =7                     | 196.0 (54.9)                          | 135.0 (52.9)  |                         | 348.0 (57.5)     | 332.6 (52.6)  |                         |
| >7                     | 78.0 (21.8)                           | 35.0 (13.7)   |                         | 105.3 (17.4)     | 122.7 (19.4)  |                         |
| HTN (%)                | 212.0 (59.4)                          | 162.0 (63.5)  | 0.085                   | 386.4 (63.8)     | 362.9 (57.4)  | 0.132                   |
| CAD (%)                | 73.0 (20.4)                           | 68.0 (26.7)   | 0.147                   | 134.7 (22.2)     | 151.3 (23.9)  | 0.040                   |
| DM (%)                 | 111.0 (31.1)                          | 90.0 (35.3)   | 0.089                   | 215.2 (35.5)     | 199.7 (31.6)  | 0.084                   |

**Table 1A.** Pre-treatment clinical characteristics of high-risk patients before and after inverse probability of treatment weighting (IPTW)

| Variables              | Study population before IPTW (n =1029) |               |                         | After IPTW match |               |                         |
|------------------------|----------------------------------------|---------------|-------------------------|------------------|---------------|-------------------------|
|                        | RP (N=476)                             | RT (N= 553)   | Standardized difference | RP               | RT            | Standardized difference |
| Age (mean± SD)*        | 66.74 ±6.58                            | 72.45 ±7.26   | 0.824                   | 69.20 ±6.71      | 69.42 ±8.30   | 0.029                   |
| Follow up (mean± SD)   | 74.55 ±40.60                           | 80.08 ±42.56  | 0.133                   | 71.79 ±39.26     | 82.98 ±43.58  | 0.270                   |
| PSA (mean± SD)*        | 27.67 ±29.24                           | 56.85 ±225.05 | 0.182                   | 35.83 ±41.36     | 44.08 ±166.10 | 0.068                   |
| CCI scores (mean± SD)* | 4.82 ±3.02                             | 5.81 ±3.72    | 0.292                   | 5.27 ±3.22       | 5.33 ±3.53    | 0.016                   |
| T stage >2*            | 348.0 (73.1)                           | 459.0 (83.0)  | 0.241                   | 791.1 (78.9)     | 843.2 (81.4)  | 0.063                   |
| N stage =1             | 0.0 (0.0)                              | 2.0 (0.4)     | 0.086                   | 0.0 (0.0)        | 3.5 (0.3)     | 0.082                   |
| Gleason scores (%)     |                                        |               | 0.065                   |                  |               | 0.042                   |
| <7                     | 51.0 (10.7)                            | 51.0 ( 9.2)   |                         | 102.5 (10.2)     | 97.6 (9.4)    |                         |
| =7                     | 121.0 (25.4)                           | 153.0 (27.7)  |                         | 260.9 (26.0)     | 286.5 (27.7)  |                         |
| >7                     | 304.0 (63.9)                           | 349.0 (63.1)  |                         | 639.2 (63.8)     | 651.5 (62.9)  |                         |
| HTN (%)                | 291.0 (61.1)                           | 345.0 (62.4)  | 0.026                   | 643.3 (64.2)     | 625.2 (60.4)  | 0.078                   |
| CAD (%)                | 89.0 (18.7)                            | 129.0 (23.3)  | 0.114                   | 208.6 (20.8)     | 215.5 (20.8)  | <0.001                  |
| DM (%)                 | 173.0 (36.3)                           | 186.0 (33.6)  | 0.057                   | 387.0 (38.6)     | 331.4 (32.0)  | 0.138                   |

IPTW: inverse probability of treatment weighting

\* observations endpoint with IPTW-adjusted

**Table 1B.** Pre-treatment clinical characteristics of very-high-risk patients before and after inverse probability of treatment weighting (IPTW)

### 3-2. IPTW Adjustment

Before IPTW adjustment, age exhibited the greatest imbalance in both high-risk and very high-risk cohorts, with standardized mean differences ranging from approximately 0.8 to 0.9. Initial PSA level, CCI score, and clinical T stage ( $T > 2$ ) also demonstrated meaningful imbalance ( $SMD > 0.1$ ).

After IPTW adjustment, all included covariates achieved adequate balance, with standardized mean differences below 0.1, indicating negligible residual imbalance. The distributions of covariates before and after IPTW adjustment for both risk groups are illustrated in Figure 2A, 2B, 3A, and 3B.

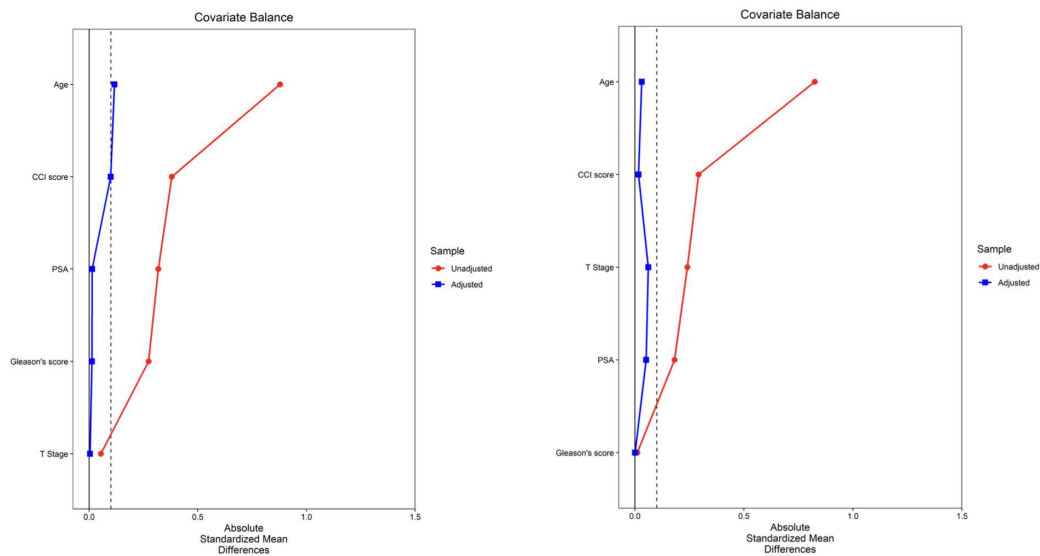


**Figure 2A.** Standardized mean difference (SMD) of RP vs. RT in high-risk patients before and after IPTW

**Figure 2B.** Standardized mean difference (SMD) of RP vs. RT in very-high-risk patients before and after IPTW

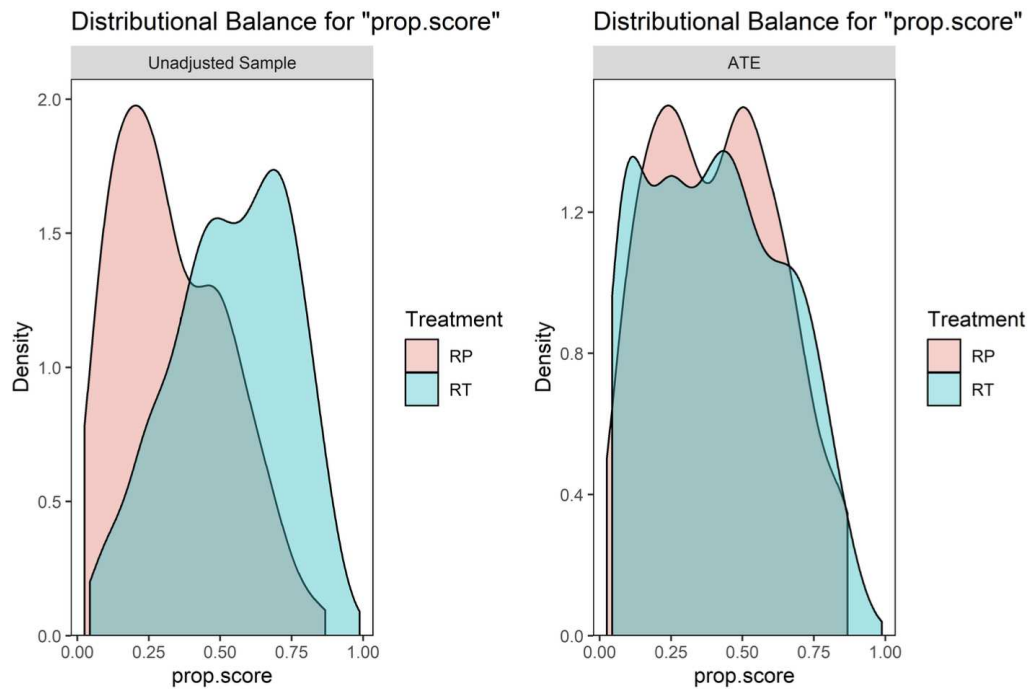


**Figure 3A.** Visualization of distribution of covariates before and after IPTW in high-risk patients

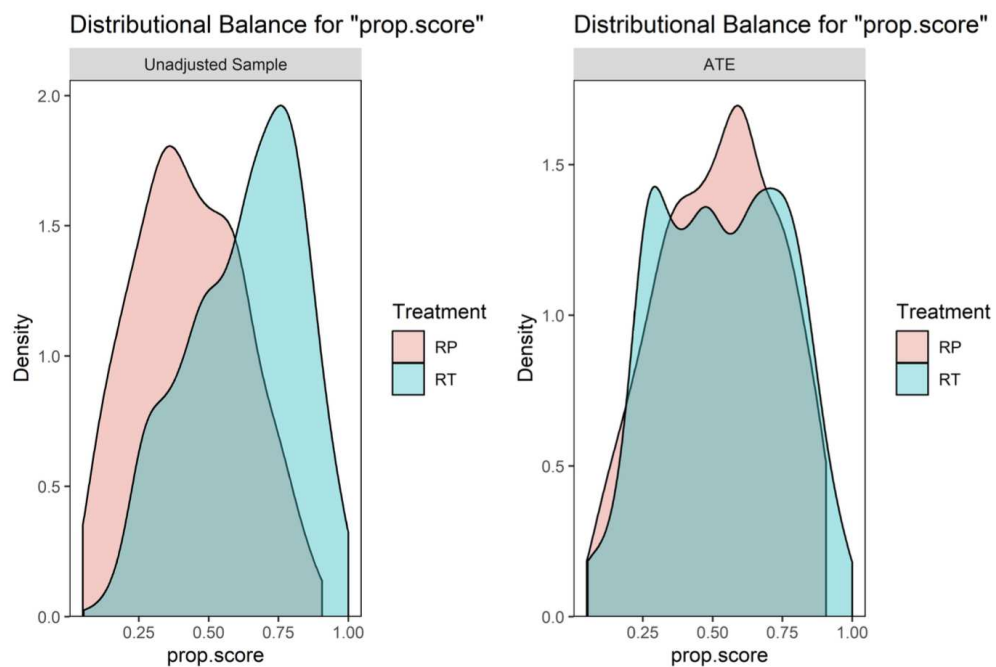


**Figure 3B.** Visualization of distribution of covariates before and after IPTW in very-high-risk patients

### 3-3. Survival Analysis in the High-Risk Group

In the high-risk cohort, unadjusted Kaplan–Meier analysis demonstrated significantly better OS and

CSS in patients treated with RP compared with RT (log-rank test,  $p < 0.001$  for both out-comes). (Fig 4A)

After IPTW adjustment, RP remained associated with superior cancer-specific survival and overall survival at 10 and 12 years(p-value of each result: OS10yr:0.038, CSS10yr:0.015 ; OS12yr:0.021, CSS12yr:0.013)

Additionally, patients receiving RT were more likely to require subsequent ADT, suggesting less favorable biochemical control following initial treatment.(Table 2A)

Table 2A. Clinical characteristics of high-risk patients before and after inverse probability of treatment weighting (IPTW)

| Variables                     | Study population before IPTW (n =612) |              |                         | After IPTW match |              |                         |
|-------------------------------|---------------------------------------|--------------|-------------------------|------------------|--------------|-------------------------|
|                               | RP (N=357)                            | RT (N= 255)  | Standardized difference | RP               | RT           | Standardized difference |
| Post-ADT (%)                  | 111.0 (31.1)                          | 201.0 (78.8) | 1.093                   | 177.9 (29.4)     | 504.0 (79.7) | 1.170                   |
| ADT duration (mean± SD)       | 34.77 ±36.76                          | 26.19 ±30.14 | 0.256                   | 35.33 ±37.80     | 24.93 ±30.57 | 0.302                   |
| Post-NHA (%)                  | 3.0 (0.8)                             | 4.0 (1.6)    | 0.067                   | 5.6 (0.9)        | 10.8 (1.7)   | 0.068                   |
| NHA duration (mean± SD)       | 18.32 ±4.16                           | 3.18 ±3.64   | 3.873                   | 18.74 ±3.60      | 2.82 ±3.18   | 4.687                   |
| Post-Docetaxel (%)            | 4.0 (1.1)                             | 5.0 (2.0)    | 0.068                   | 6.0 (1.0)        | 10.4 (1.6)   | 0.057                   |
| Docetaxel duration (mean± SD) | 11.62 ±11.20                          | 5.57 ±4.01   | 0.719                   | 14.46 ±12.39     | 5.71 ±3.27   | 0.966                   |
| Death (%)                     | 31.0 (8.7)                            | 73.0 (28.6)  | 0.530                   | 65.8 (10.9)      | 138.4 (21.9) | 0.301                   |
| Cancer death (%)              | 11.0 (3.1)                            | 32.0 (12.5)  | 0.358                   | 24.3 (4.0)       | 69.9 (11.1)  | 0.269                   |

IPTW: inverse probability of treatment weighting

\* observations endpoint with IPTW-adjusted

**Table 2A.** Post-treatment clinical characteristics of high-risk patients before and after inverse probability of treatment weighting (IPTW)

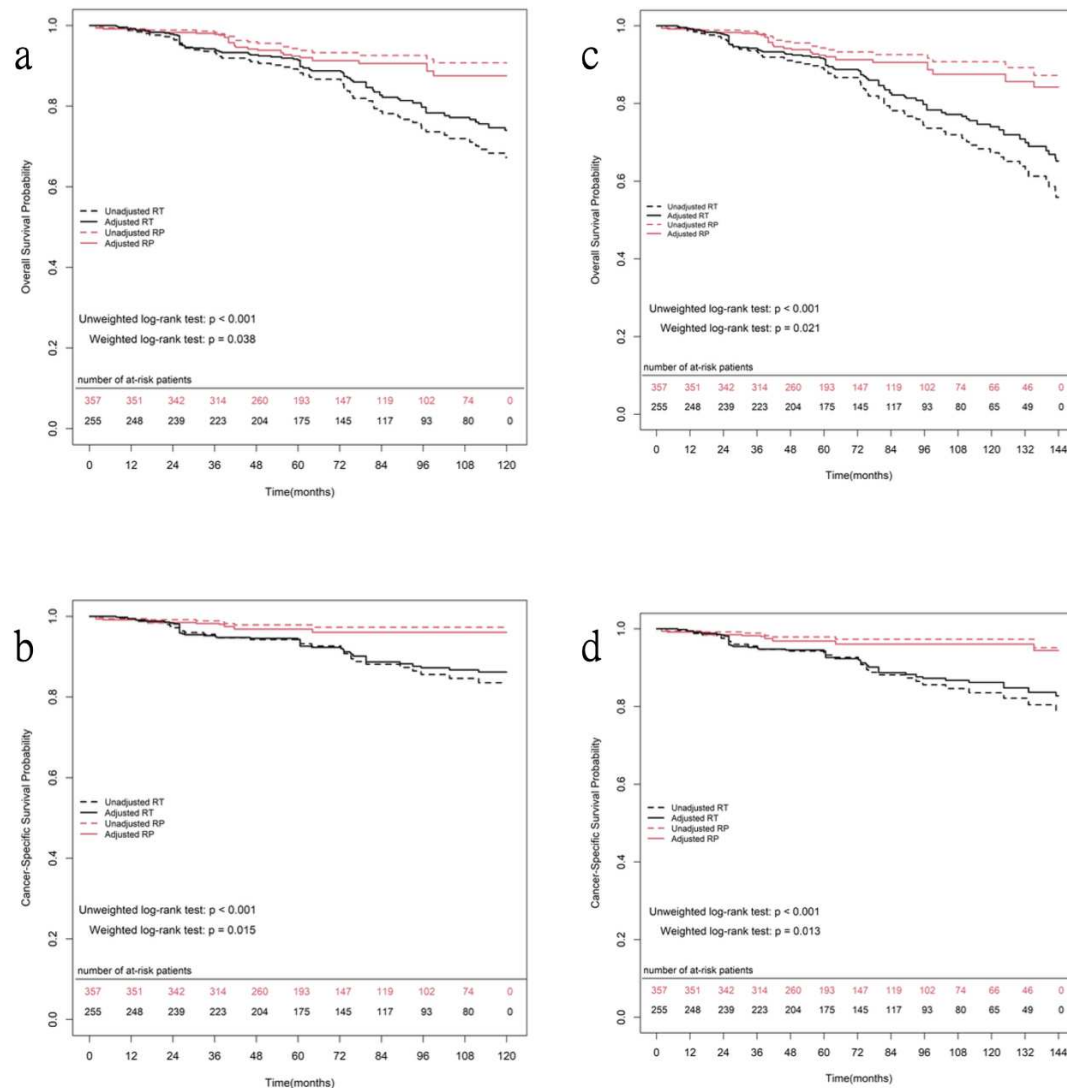


**Figure 4A.** Survival analysis of high-risk patients before and after IPTW(a: 10-year overall survival, b: 10-year cancer-specific survival, c: 12-year overall survival, d: 12-year cancer-specific survival)

### 3-4. Survival Analysis in the Very High-Risk Group

In the very high-risk cohort, both OS and CSS at 10 and 12 years were significantly superior in patients undergoing RP compared with those receiving RT, both before and after IPTW adjustment ( $p < 0.001$ ). (Fig 4B)

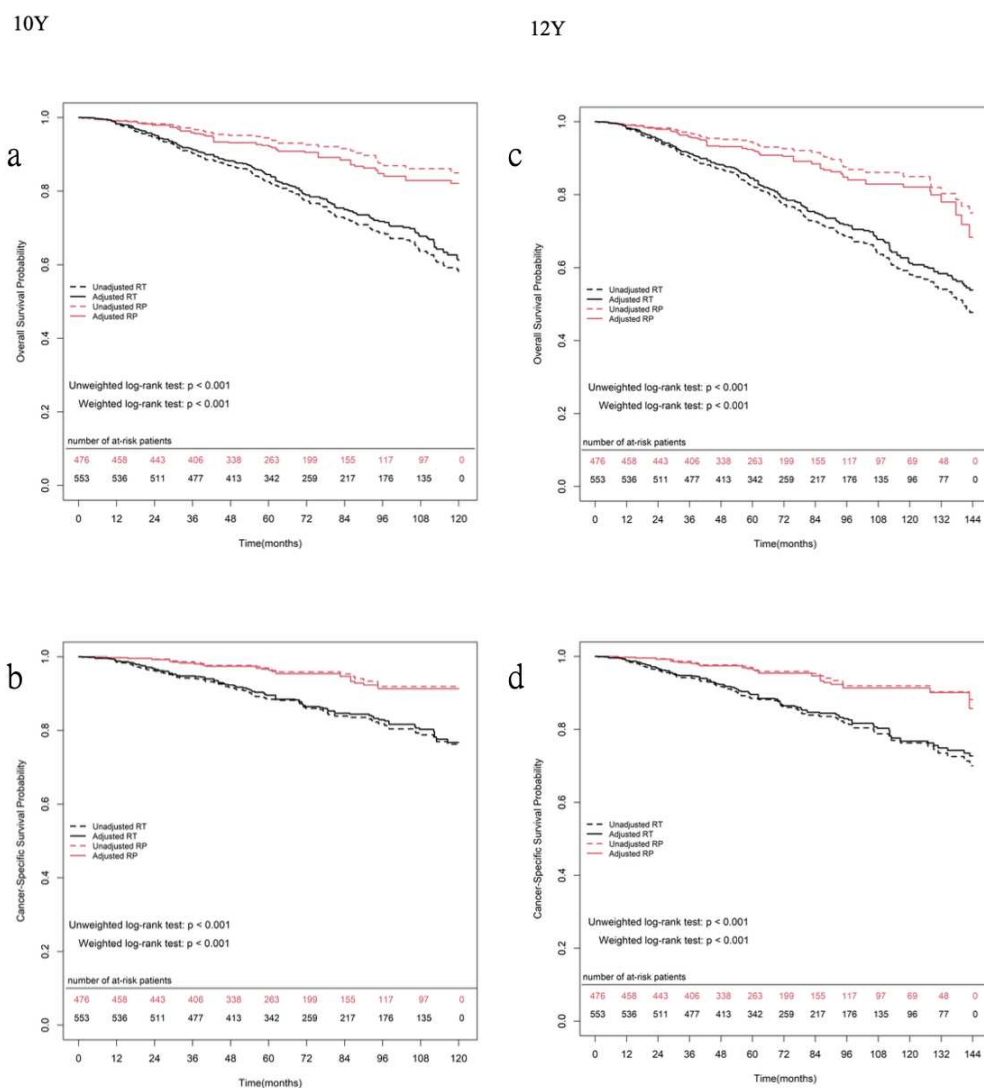
These findings remained robust after adjustment for baseline differences, indicating a consistent survival advantage associated with RP in patients with very high-risk localized prostate cancer. Similar to the high-risk group, post-treatment systemic therapy, particularly ADT, was more frequently required in the RT group.(Table 2B)

Table 2B. Clinical characteristics of very-high-risk patients before and after inverse probability of treatment weighting (IPTW)

| Variables                     | Study population before IPTW (n =1029) |              |                         | After IPTW match |              |                         |
|-------------------------------|----------------------------------------|--------------|-------------------------|------------------|--------------|-------------------------|
|                               | RP (N=476)                             | RT (N= 553)  | Standardized difference | RP               | RT           | Standardized difference |
| Post-ADT (%)                  | 254.0 (53.4)                           | 417.0 (75.4) | 0.473                   | 573.4 (57.2)     | 787.5 (76.0) | 0.408                   |
| ADT duration (mean± SD)       | 38.48 ±35.44                           | 35.88 ±31.96 | 0.077                   | 39.03 ±35.56     | 37.47 ±34.72 | 0.044                   |
| Post-NHA (%)                  | 15.0 (3.2)                             | 17.0 (3.1)   | 0.004                   | 28.6 (2.9)       | 35.1 (3.4)   | 0.031                   |
| NHA duration (mean± SD)       | 15.61 ±12.46                           | 10.43 ±12.55 | 0.414                   | 12.68 ±11.81     | 11.75 ±14.81 | 0.069                   |
| Post-Docetaxel (%)            | 10.0 (2.1)                             | 21.0 (3.8)   | 0.100                   | 17.5 (1.7)       | 48.2 (4.7)   | 0.166                   |
| Docetaxel duration (mean± SD) | 9.55 ±7.08                             | 5.44 ±5.35   | 0.654                   | 9.59 ±7.16       | 4.93 ±4.89   | 0.760                   |
| Death (%)                     | 49.0 (10.3)                            | 179.0 (32.4) | 0.560                   | 124.6 (12.4)     | 304.7 (29.4) | 0.427                   |
| Cancer death (%)              | 25.0 (5.3)                             | 93.0 (16.8)  | 0.376                   | 55.6 (5.5)       | 167.9 (16.2) | 0.348                   |

IPTW: inverse probability of treatment weighting

\* observations endpoint with IPTW-adjusted

**Table 2B.** Post-treatment clinical characteristics of very-high-risk patients before and after inverse probability of treatment weighting (IPTW)**Figure 4B.** Survival analysis of very-high-risk patients before and after IPTW(a: 10-year overall survival, b: 10-year cancer-specific survival, c: 12-year overall survival, d: 12-year cancer-specific survival)

## 4. Discussion

In this retrospective multicenter analysis using IPTW adjustment, we observed that radical prostatectomy was associated with favorable cancer-specific survival in both high-risk and very high-risk groups and improved overall survival, most notably among patients with very high-risk localized prostate cancer.

Several large population-based studies have reported a potential survival advantage associated with radical prostatectomy, particularly among patients with very high-risk or locally advanced disease.[8] Studies based on the SEER database have reported lower cancer-specific mortality following radical prostatectomy compared with external beam radiotherapy in very high-risk patients, while no statistically significant difference was consistently observed in patients with high-risk disease. [9,10] Comparable observations have been described in studies focusing on locally advanced prostate cancer, in which radical prostatectomy as part of multimodal treatment strategy has been associated with improved overall and cancer-specific survival compared with radiation-based approaches alone. [11,12,13]

In contrast, several studies have reported no statistically significant difference in long-term oncological outcomes between radical prostatectomy and radiation combined with androgen deprivation therapy, particularly among patients with high-risk disease. [14,15,16,17] Single-institution and multicenter retrospective studies using propensity score matching method have reported comparable overall survival and cancer-specific survival between treatment modalities when RT was delivered with adequate dose escalation and long-term ADT.[18] Furthermore, robust data from the Phase III randomized controlled ProtecT trial demonstrated no statistically significant difference in outcomes between RP and RT+ADT. However, the trial primarily enrolled patients with low- and intermediate-risk localized prostate cancer, comprising only 5% high-risk patients and excluding those with very high-risk disease.[5] These observations are consistent with the current NCCN guideline recommendations that both RP and RT+ADT represent acceptable first-line options for high-risk localized prostate cancer.

Furthermore, intensified radiation therapy (EBRT plus a brachytherapy boost and long-term ADT) has demonstrated improved cancer-specific survival (CSS) compared to RP, particularly in very high-risk disease. However, these studies consistently report no significant difference in overall survival (OS) between the two modalities.[13,19,20] Beyond comparable overall survival, the clinical application of this intensified strategy requires careful consideration of its associated toxicities. As noted in the literature, this approach carries increased risks of severe genitourinary complications, alongside the technical demands of brachytherapy and the cardiovascular burdens of prolonged ADT. Consequently, for appropriately selected and surgically fit patients, radical prostatectomy offers a valuable alternative that avoids these specific combined toxicities. It remains a practical option that

provides excellent initial oncological control while preserving the feasibility of subsequent multimodal treatments.

Importantly, a recent systematic review published in 2023 highlighted the lack of high-level evidence to definitively establish the superiority of either RP or RT+ADT for high-risk localized prostate cancer. The authors emphasized that most available studies are retrospective, prone to residual confounding, and highly heterogeneous with regard to patient selection, radiation techniques, ADT duration, and outcome definitions. Consequently, although some studies suggest a potential oncological advantage for RP—particularly in very high-risk disease—others demonstrate no significant difference, underscoring the ongoing uncertainty in this field. [16,20]

Across the limited but growing Asian literatures, differences in reported outcomes between radical prostatectomy and radiation-based approaches may partly reflect variations in study design, included risk spectra, and follow-up duration. A single-institution Japanese study using propensity score matching reported no significant difference in overall survival between RP and radiation therapy among patients with localized prostate cancer but included patients across all-risk categories. [18] Similarly, a Korean population-based study also enrolled relatively heterogeneous population and demonstrated comparable cancer-specific and overall survival between RP and RT combined with long-term ADT in high-risk localized prostate cancer after adjustment for baseline characteristics, suggesting that both treatment approaches can achieve acceptable oncological outcomes when appropriately selected. [21] In contrast, the Taiwanese registry-based study by Wu et al., focusing on younger patients with unfavorable intermediate-risk disease, suggested that surgery may confer advantages in earlier-stage disease among Asian patients. [22]

Compared with these prior reports, our study is distinctive in that it focuses specifically on high-risk and very high-risk localized prostate cancer and provides a longer follow-up window, which may allow further assessment of long-term oncological and overall survival differences after definitive local therapy. Importantly, given the retrospective nature of our analysis, our findings should be interpreted as associations rather than causal effects, and residual confounding cannot be fully excluded despite IPTW adjustment. Nevertheless, one plausible explanation for the observed survival signal favoring radical prostatectomy is that our cohort represents patients deemed surgically fit through multidisciplinary evaluation, and surgery may serve as an initial step within a multi-modal treatment pathway. In contemporary practice, patients who undergo radical prostatectomy can be further risk-stratified based on pathological findings and may have access to subsequent adjuvant or salvage therapies when indicated. In addition, as our cohort includes more recently treated patients, the broader availability of post-treatment salvage systemic options in the modern era may have contributed to improved long-term outcomes, potentially amplifying the benefit of initiating treatment with surgery in selected high-risk patients. Taken together, our results suggest that, among appropriately selected and

surgically fit patients with high-risk disease, radical prostatectomy as part of a multimodal strategy may be a reasonable option to consider in shared decision-making.

## **Limitations**

This study has several limitations. First, given its retrospective design, residual con-founding cannot be completely excluded despite the application of IPTW. Second, detailed information regarding radiation dose, technique, and duration of ADT was not uniformly available, which limited our ability to fully adjust for treatment heterogeneity. Third, biochemical recurrence and quality-of-life outcomes were not assessed, restricting the analysis primarily to survival endpoints.

## **5. Conclusions**

In this large Asian cohort of patients with high-risk and very high-risk localized prostate cancer, radical prostatectomy was associated with favorable cancer-specific and overall survival compared with radiation therapy, particularly among the patients with very high-risk disease. The consistency of these findings after IPTW adjustment suggests that the observed survival benefits are less influenced by selection bias. These results add to the growing Asian real-world evidence and may help inform shared decision-making for patients with high-risk localized prostate cancer.

### **Author Contributions:**

Conceptualization, Chih-Wei Chu and Hao-Lun Luo ; methodology, Hao-Lun Luo ; software, Hao-Lun Luo ; validation, Chih-Wei Chu and Hao-Lun Luo ; formal analysis, Jia-Yun Liu and Hao-Lun Luo ; investigation, Hao-Lun Luo ; resources, Hui Ying Liu, Yin Lun Chang, Yi Yang Liu, Hung-Jen Wang, Yen-Ta Chen, Yuan-Tso Cheng, Chih-Hsiung Kang, Wei-Quen Tee, Tsung-Yu Yu, I-Wen Lee, Hao-Lun Luo ; data curation, Hao-Lun Luo ; writing—original draft preparation, Chih-Wei Chu ; writing—review and editing, Hao-Lun Luo ; visualization, Hao-Lun Luo ; super-vision, Hao-Lun Luo ; project administration, Hao-Lun Luo ; funding acquisition, Hao-Lun Luo. All authors have read and agreed to the published version of the manuscript.

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**Institutional Review Board Statement:** The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Chang Gung Medical Foundation (IRB number: 202501592B0)

**Informed Consent Statement:** Patient consent was waived due to the retrospective nature of this study using de-identified electronic health records from the Chang Gung Research Database, which poses minimal risk to the subjects.

**Data Availability Statement:** The data presented in this study are available on request from the

corresponding author due to strict privacy and ethical restrictions. The data are not publicly available as they contain sensitive electronic health records managed by the Chang Gung Medical Foundation.

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#### **Abbreviations**

The following abbreviations are used in this manuscript:

RP radical prostatectomy

RT radiation therapy

CGRD Chang Gung Research Database

IPTW inverse probability of treatment weighting

PSA prostate-specific antigen

CCI Charlson Comorbidity Index

OS overall survival

CSS cancer-specific survival

ADT androgen deprivation therapy

NCCN guideline National Comprehensive Cancer Network guideline

NHA novel hormonal agents

SD standardized differences

SMD Standardized mean difference

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