Review Article

Combination approach using neoadjuvant therapy with radical prostatectomy for improving oncological outcomes of high-risk prostate cancer: a narrative review

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Background and Objective: Prostate cancer (PCa) is the most common cancer in men. High-risk PCa is associated with an increased risk of PCa-related death. The combined use of androgen deprivation therapy (ADT) is essential to improve oncological outcomes in patients with high-risk PCa, and relatively long-term ADT administration is preferred when radiotherapy is performed. Meanwhile, whether neoadjuvant therapy for radical prostatectomy (RP) improves oncological outcomes remains controversial. This study aimed to review the oncological outcomes of RP in high-risk PCa and emphasize the significance of neoadjuvant therapy including neoadjuvant hormonal therapy (NHT) and neoadjuvant chemohormonal therapy (NCHT) followed by RP for managing high-risk PCa.

Methods: We searched for articles published in the PubMed and Scopus databases from January 1, 2005 to March 30, 2023 using the medical subject headings (MeSH) terms: prostate cancer, prostatectomy, radiation therapy, neoadjuvant therapy, and treatment outcome.

Key Content and Findings: The study on NHT before RP for high-risk PCa found that NHT was associated with reduced adverse pathological features, such as pT3, positive surgical margins (PSM), and lymph node involvement. However, despite shorter operative times and improved surgical outcomes, NHT did not significantly enhance biochemical recurrence (BCR) or other oncological outcomes. The combination therapy using ADT and androgen receptor signaling inhibitors (ARSI) showed varying results. Another investigation explored NCHT with taxane-based agents, indicating acceptable treatment benefits and improved BCR-free survival rates in high-risk PCa patients, demonstrating potential feasibility for this approach. Ongoing trials, like the PROTEUS trial, aim to further evaluate the therapeutic efficacy of neoadjuvant therapy in high-risk PCa.

Conclusions: NHT for high-risk PCa does not contribute to improved oncological outcome and should not be administered easily for downstaging or PSM reduction. NHT in combination with ARSI has the potential advantage of improving the oncological outcome of high-risk PCa compared to RP alone, but the results are currently unsatisfactory, and the development of individualized treatment strategies using several different therapeutic approaches is needed.

Keywords: Prostate cancer (PCa); surgery; radiotherapy (RT); neoadjuvant therapy; treatment outcome

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Introduction

Prostate cancer (PCa) progresses relatively slowly, and according to several guidelines, approximately 85% of patients with PCa are diagnosed with low- or intermediate-risk disease (1-3). Consequently, the prognosis for PCa without metastases is recognized as having relatively better oncological outcomes, including better overall survival (OS), PCa-specific mortality (PCSM), metastatic-free survival (MFS), and biochemical recurrence-free survival (BRFS) (1-3). However, approximately 15% of patients are diagnosed with high-risk PCa, which has biological features different from those of the above-mentioned cohorts (3). High-risk PCa is one of the most heterogeneous oncologically specific diseases and demonstrates clinical heterogeneity across a wide range of clinical variants (4). In addition to frequent locoregional invasion, these cancers often have micrometastases at the time of diagnosis and are associated with an increased risk of lymph node or distant metastases and PCSM (4,5). Therefore, over the last few decades, various therapeutic regimens, such as local and systemic therapies, to control high-risk PCa, have been combined or sequentially administered (5).

The European Urological Association guidelines recommend that RP with extended pelvic lymph node dissection (ePLND) should be performed in selected patients with high-risk PCa who have a life expectancy of >10 years; however, the precise classification of selected patients with high-risk PCa remains unclear (2). RP has been suggested to have potential benefits in improving oncologic outcomes, such as prolonged OS and decreased PCSM, with second-line therapy after biochemical recurrence (BCR) (6,7). By contrast, patients with high-risk PCa are recommended to receive 76–78 Gy of external beam radiotherapy (EBRT) and/or brachytherapy (BT) boost in conjunction with 2–3 years of long-term ADT (2). Several studies in the past decade on radiotherapy (RT) have revealed that approximately half of the patients with high-risk PCa who received ADT plus EBRT developed BCR, and approximately 40% died of PCa (8,9). Therefore, multidisciplinary treatment combining other therapies in addition to RT may be necessary to further improve the oncological outcomes of patients with high-risk PCa (10). However, no completed, ongoing, or planned trials have compared RP with RT in patients with high-risk PCa (11). Unfortunately, level 1 evidence comparing mainstream therapies that define the gold standard of management for high-risk PCa remains inconclusive (10).

Currently, no consensus on the treatment that should be combined with RP has been established. This narrative-review aimed to confirm the oncologic outcomes of RP for high-risk PCa and further investigate the utility and importance of combination therapy with neoadjuvant therapy and RP in improving oncologic outcomes. We present this article in accordance with the Narrative Review reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-2394/rc).

Methods

For this narrative review, we searched the literature through March 2023 using the online database PubMed and Scopus. Eligible references included peer-reviewed English-language articles published between January 1, 2005, and March 20, 2023, and contained the following medical subject headings (MeSH) terms: prostate cancer, prostatectomy, radiotherapy, neoadjuvant therapy and free text: high-risk prostate cancer, chemohormonal therapy. We excluded meeting abstracts, case reports, studies with insufficient data and duplicate records. Two authors (K.N., T.K.) participated in screening of the literature, data extraction and quality assessment of the articles. Screening and data extraction were performed independently by two authors (K.N. and T.K.). The search strategy is summarized in *Table 1*.

Efficacy of combined ADT in RT for high-risk PCa

Before examining the therapeutic efficacy of RP, we reviewed the outcomes of RT plus ADT in patients with high-risk PCa.

In this open-label, multicenter, phase III, randomized, controlled trial, patients with PCa in clinical stages T1–T3b were stratified by PCa risk and received either 4 months of ADT with a minimum dose of 76 Gy of three-dimensional conformal RT (short-term ADT group) or

Table 1 The search strategy summary

Items	Specification
Date of search	Mar 20, 2023
Databases and other sources searched	PubMed and Scopus
Search terms used	MeSH terms: prostate cancer, prostatectomy, radiotherapy, neoadjuvant therapy and free text: high-risk prostate cancer, chemohormonal therapy
Timeframe	From Jan 1, 2005 to Mar 20, 2023
Inclusion and exclusion criteria	Inclusion criteria: only papers written in English were eligible for inclusion
	Exclusion criteria: meeting abstracts, case reports, studies with insufficient data and duplicate records were excluded
Selection process	Screening and data extraction were performed independently by 2 authors (K.N. and T.K.)

MeSH, medical subject headings.

the same treatment followed by 24 months of adjuvant ADT (long-term ADT group) (12). The 5-year BRFS was significantly better in patients who received long-term ADT than in those who received short-term ADT [90% *vs.* 81%; hazard ratio (HR), 1.88; P=0.01] (12). Patients in the long-term ADT group also had a significantly better 5-year OS (95% *vs.* 86%; HR, 2.48; P=0.009) and 5-year MFS (94% *vs.* 83%; HR, 2.31; P=0.01) than those in the short-term ADT group (12). Subgroup analyses according to PCa risk categories were performed for BRFS, OS, and MFS in the long-term ADT group (12). The 5-year BRFS benefits tended to be higher in the high-risk group than in the intermediate-risk group (12). A benefit in OS prolongation was observed in the high-risk group (HR, 3.43; P=0.015) but was not statistically significant in the intermediate-risk group (HR, 1.67; P=0.318) (12). Furthermore, the benefit of MFS was greater in patients with high-risk PCa than in those with intermediate-risk PCa (HR, 2.27; P=0.041) (12). In the randomized, controlled TROG 03.04 RADAR trial, 1,051 patients with PCa who had clinical stage T2b–T4 or cT2a with Gleason grade (GG) ≥4 and prostate-specific antigen (PSA) >10 ng/mL were randomized to receive ADT for 6 months and 24 months, respectively (13). Compared to 6 months of ADT, 18 months of ADT reduced distant metastases independent of radiation dose (13).

In a multicenter phase III study with a median follow-up of 7.3 years, 263 patients with clinical T3–4 PCa were enrolled and randomized to receive ADT alone or ADT + EBRT (14). Both groups received ADT for 3 years, and patients in the ADT + EBRT group received 46 Gy to the entire pelvis and an additional 20–26 Gy to the prostate (14). The 8-year BRFS was 48% in the ADT + EBRT group and 7% in the ADT group [HR, 0.27, 95% confidence interval (CI): 0.17–0.39; P<0.001], which was significantly higher in the ADT + EBRT group (14). Although the risk of death from PCa was significantly lower in the ADT + EBRT group (sub-HR, 0.48; 95% CI: 0.25–0.91; P=0.02), the 8-year OS rate was not significantly different between the both groups (14). Despite significantly lower local recurrence in the ADT + EBRT group (P=0.01), the MFS was comparable between the two groups (14). In a meta-analysis of BT, 5,602 patients with high-risk PCa were identified in 11 studies, and oncologic outcomes with or without ADT were evaluated (15). ADT was used in 40–91% of patients, and the median duration of ADT ranged from 3 to 12 months (15). In this analysis, an improvement in BRFS was observed with long-term ADT administration, and the overall benefit was approximately 6–16% (15).

These results suggest that the combined use of ADT is essential to improve oncological outcomes in patients with high-risk PCa, and relatively long-term ADT administration is preferred when RT is performed. Therefore, in this mini-review, we discuss the differences in the therapeutic effects of RT and RP, assuming that RT is treated with ADT combination therapy.

Comparison of treatment efficacy between RP alone and RT + ADT for high-risk PCa

The standard therapeutic modalities for locally advanced PCa include RP plus ePLND or RT plus ADT; however, the optimal therapy remains controversial (16). Locally advanced PCa was defined as clinical T3–4N0–1M0 for further discussion (17).

Table 2 Comparison of prostate cancer-related specific mortality between radical prostatectomy and external beam radiation therapy

Authors [year] (reference)	Enrolled patients	Treatment methods (number)		Age (years), median [IQR]		PSA (ng/mL), median [IQR]		PCSM (%)	HR
		RP	EBRT	RP	EBRT	RP	EBRT		
Sooriakumaran *et al.* [2014] (7)	34,515	21,533	12,982	62 [58–66]	66 [62–70]	7.0 [5.0–11.0]	10.9 [6.8–20.0]	15-year PCSM: RP, 1.4; EBRT, 4.9	0.54
Ciezki *et al.* [2017] (10)	2,557	1,308	734	62 [43–79]	68.5 [40–86]	NA		10-year PCSM: RP, 6.8; EBRT, 11.2	0.002
Bandini *et al.* [2018] (19)	5,500	2,507	2,993	61.9 [52–67]	68 [62–73]	7.1 [4.9–11.4]	10.9 [6.3–24.7]	10-year PCSM: RP, 8.1; EBRT, 15.8	0.62
Chierigo *et al.* [2022] (20)	24,407	9,823	14,594	64 [59–68]	71 [65–76]	8 [6–20]	13 [7–27]	5-year PCSM: RP, 3.5; EBRT, 6.0	0.58

IQR, interquartile range; PSA, prostate-specific antigen; PCSM, prostate cancer-specific mortality; HR, hazard ratio; RP, radical prostatectomy; EBRT, external beam radiation therapy; NA, not applicable.

A comparison of clinical outcomes by propensity score-matched analysis between RP and RT + ADT for high-risk PCa revealed that RP had a significantly higher risk of BCR than RT + ADT (P<0.001) (12). RT + ADT was significantly correlated with a reduced risk of BCR compared to RP (HR, 0.16; 95% CI: 0.07–0.37; P<0.001) (12). Kaplan-Meier analysis revealed no statistically significant differences in local recurrence-free survival, MFS, or OS, and differences in clinical covariates and treatment modalities did not predict oncological outcomes (12). A retrospective study that enrolled 4,041 patients undergoing RP classified as having high-risk or very high-risk PCa by the National Comprehensive Cancer Network stratification between 1992 and 2016, 1,835 patients were evaluated for final analysis demonstrated that 50.6% of patients experienced BCR, with a median time from RP to BCR of 10.8 months for very-high-risk PCa and 14.3 months for high-risk PCa (P=0.002) (11). The 5- and 8-year BRFS rates were 47.8% [interquartile range (IQR), 45.3–50.4 months] and 39.6% (IQR, 36.8–42.7 months) for the entire cohort (11). At the last follow-up, 234 patients (12.8%) experienced distant metastases, and 107 (6%) died of PCa (11). The 5- and 8-year MFS rates ranged from 81.8% (IQR, 77.6–86.1%) to 71.5% (IQR, 64.1–79.7%) for very-high-risk PCa, compared with 91.2% (IQR, 89.6–92.9%) and 86.1% (IQR, 83.8–88.6%) for high-risk PCa, respectively (P<0.001) (11). The 5- and 8-year OS rates were 85.7% (IQR, 82–89.6%) and 76.1% (IQR, 69.1–83.8%) for very-high-risk PCa and 91.5% (IQR, 89.8–93.2%) and 83.7% (IQR, 91–86.5%) for high-risk PCa (11). Based on these studies, RT may be the preferred treatment modality for high-risk PCa more often than RP because of the higher incidence of BCR in high-risk PCa in RP than in RT. However, a direct comparison of the therapeutic outcomes of RT and RP seems practically difficult because of the different definitions of BCR in both treatment modalities (18).

The four studies comparing the outcomes of RP and EBRT with those of PCSM are listed in *Table 2*. A nationwide population-based cohort study based on the Prostate Cancer Data Base Sweden database enrolled 34,515 patients who received RP or RT as primary treatment for PCa, with a median follow-up of 5.37 years (IQR, 3.00–7.81 years) (7). In patients with non-metastatic PCa, the PCSM rates were significantly lower, and the PCa mortality rates favored RP over RT (sub-HR, 1.76; 95% CI: 1.49–2.08; P<0.001), whereas no clear difference in treatment effect was observed in those with metastatic PCa (7). The subgroup analysis revealed a clearer benefit of surgery in younger, fitter men with intermediate- and high-risk diseases (7). The Cleveland Clinic reported the results of a retrospective study that evaluated BRFS and PCSM in 2,557 patients with high-risk PCa who received EBRT with or without ADT, BT with or without ADT, and RP with or without salvage RT (10). The 5- and 10-year BRFS rates were 74% and 53%, respectively, in the EBRT group; 74% and 52%, respectively, in the BT group; and 65% and 47%, respectively, in the RP group (10). The BCR rate of patients treated with RP was higher than that of their counterparts (10). The 5- and 10-year PCSM rates were 5.3% and 11.2% in the EBRT group; 3.2% and 3.6% in the BT group; and 2.8% and 6.8% in the RP group, respectively (10). EBRT had the highest proportion of PCMS compared to the other two treatments, contrary to the results for BRFS (10). Among 5,550 patients with PCa

having clinical T3N0–1 in the Surveillance Epidemiology and End Results (SEER) database, the 10-year PCSM and other causes of death rates were significantly higher after EBRT (15.8% and 28.2%) than after RP (8.1% and 10.4%) (all P<0.0001) (19). In multivariate cumulative incidence plots and competing risk regression models, RP demonstrated a lower PCSM than EBRT (HR, 0.62) (19). Using the SEER database, 24,407 patients with high-risk PCa were identified and divided into two groups according to the Jons Hopkins University classification. The high-risk group (presence of at least one of the following criteria: clinical T3a, GG 4/5, or PSA >20 ng/mL) and the very-high-risk group (presence of at least one of the following criteria: cT3b–cT4 and/or primary Gleason pattern 5 and/or 2–3 HR features and/or ≥5 positive biopsy cores with GG 4/5) (20). In the entire cohort, the 5-year PCSM rate was 3.5% for RP and 6.0% for EBRT, with a multivariate HR of 0.68 (95% CI: 0.54–0.86, P<0.001) in favor of RP (20). Although the 5-year PCSM rate was 3.5% for RP and 6.0% for EBRT (multivariate HR, 0.58; 95% CI: 0.44–0.77; P<0.001), which favored RP in patients with very high-risk PCa, no significant difference was noted between RP and EBRT in patients with high-risk PCa (HR, 0.7; 95% CI: 0.39–1.25; P=0.2) (20).

Thus, when considering PCSM as the main endpoint, RP may reduce the risk of death from PCa compared with EBRT in patients with high-risk PCa. However, the definition of BCR differs between RP and RT.

Utility of neoadjuvant hormone therapy prior to RP for high-risk PCa

The administration of neoadjuvant ADT before RP was associated with reduced pT3, proportion of positive surgical margins (PSM), and incidence of lymph node involvement compared to RP alone (2). Sun *et al.* (21) retrospectively analyzed the clinical data of 385 patients with high-risk PCa who underwent RP, including 168 who received NHT followed by RP, and 217 who underwent RP alone. Although patients who received neoadjuvant ADT had shorter operative times, decreased blood loss volume, lower PSM rates, and higher rates of GG downstaging after RP (P<0.05), no statistically significant improvements in BCR, BRFS, or perioperative complications were observed between the patient groups (21). In the entire cohort, initial PSA, biopsy GG, clinical T stage, and NHT use were significantly correlated with PSM (P<0.05); however, NHT did not improve BCR (21). Therefore, NHT for high-risk PCa should not be easily performed for downstaging or PSM reduction because it does not contribute to improved oncological outcomes. Furthermore, the European Association of Urology noted that evidence for neoadjuvant ADT is weak, limiting its recommendation for preoperative NHT for PCa (2).

Currently, neoadjuvant combination therapy using ADT and androgen receptor signaling inhibitors (ARSI) is increasingly being performed; however, reports on its oncological outcomes are scarce (*Table 3*). These studies used minimal residual disease (MRD) for pathological evaluation and defined residual tumors as those <5 mm (22). Taplin *et al.* (22) have reported that 6 months of ADT + ARSI therapy did not decrease pathological complete response (pCR) rate (10%), and the yield to treatment pathological T3 (ypT3) rate was relatively high (48%), even though patients who received 6-month ADT + abiraterone (AA) therapy had a better pathological response rate than those who received 3-month ADT + AA therapy (3.6%) after 3 months of ADT alone. In a randomized, open-label, non-comparative study comparing enzalutamide (ENZ) monotherapy with 6-month neoadjuvant ENZ + dutasteride (DUT) + ADT therapy, the pathologic response rate was only 17%, pCR rates were low (4.3%), and the ypT3 rates were relatively high (61%), although the ENZ + DUT + ADT group achieved better outcomes (23). In a phase II trial comparing the pathological effects of ADT + ENZ and ADT + ENZ + AA, patients with PCa who had either GG >3, PSA >20 ng/mL, or clinical T3 were enrolled (24). The pCR or MRD rate was 30% in the ADT + ENZ + AA group and 16% in the ADT + ENZ group, and ypT3 was approximately 50% in both groups, and the differences were not significant. However, the therapeutic effect was limited in the two regimens (24). A pooled analysis of three clinical trials of NHT using ARSI followed by RP enrolled 117 patients with PCa, including 78.6% in the high-risk group, with the primary endpoint being time to BCR (25). A total of 21.4% of the patients exhibited MRD, including 9.4% with pCR after NHT (25). Overall, 25 patients (21.4%) had MRD, and 11 (9.4%) had pCR (25). At the end of the follow-up period, 49 patients (41.9%) developed BCR, and the 3-year BRFS rate was 59.1% (25).

In a phase II single-arm study (NEAR trial) with the primary endpoint of postoperative pCR rate, 30 patients with intermediate- or high-risk PCa according to the D'Amico classification were treated with apalutamide (APA) 240 mg once daily for 12 weeks, followed by RP (26). Although the median reduction rate of PCa volume in

Table 3 Overview of pathological outcomes at radical prostatectomy

Authors [year] (reference)	Treatment methods	Enrolled patients (N)	pCR (%)	MRD (%)	LNI (%)	PSM (%)	pT3 (%)
Taplin *et al.* [2014] (22)	AA + ADT	58	3	4	11	19	48
	ADT followed by ADT + AA		1	0	24	10	59
Montgomery *et al.* [2017] (23)	ENZ + DUT + ADT	48	4.3	13	21.7	26.1	61
	ENZ		0	0	16	4	72
McKay *et al.* [2019] (24)	ADT + AA + ENZ	50	10	20	10	18	50
	ADT + ENZ	25	8	8	12	12	56
McKay *et al.* [2021] (25)	AA	34	11.8	2.9	17.6	8.8	52.1
	ENZ	17	29.4	17.6	11.8	11.8	80.6
	AA + ENZ	66	37.9	15.2	9.1	15.2	51.5
Lee *et al.* [2022] (26)	APA	30	0	NE	16	16	48
Devos *et al.* [2023] (27)	ADT + APA	45	51	38	20	18	49
	ADT	44	27	9	16	18	73
Ravi *et al.* [2022] (28)	Neo-RP	112	10	12	11	13	55
	RP alone	259	0	NE	15	26	72

pCR, pathological complete response; MRD, minimal residual disease; LNI, lymph node involvement; PSM, positive surgical margin; pT3, pathological T3 disease; AA, abiraterone; ADT, androgen deprivation therapy; ENZ, enzalutamide; DUT, dutasteride; APA, apalutamide; neo-RP, neoadjuvant androgen receptor signaling inhibitors and radical prostatectomy; RP, radical prostatectomy; NE, not evaluated.

enrolled patients was 41.7% (IQR, 33.3–60%), none of the patients achieved the primary endpoint of pCR (26). Furthermore, they investigated the biochemical response of patients with PSA <0.03 ng/mL at week 24 after the start of APA and no subsequent PSA relapse as a secondary endpoint of this study (26). Although they found no association between PCa tumors with low androgen receptor activity and PAM50 basal status in cases with insufficiently decreased PSA, these molecular phenotypes were not significantly correlated with pathological response (26). The phase II randomized ARNEO trial evaluated the efficacy of 3-month ADT with or without APA prior to RP in 89 patients with clinically non-metastatic high-risk PCa (27). Patients who received ADT + APA therapy exhibited significantly better pathological responses than those who received ADT alone (38% *vs.* 9%; relative risk, 4.2; P=0.002) (27). Ravi *et al.* (28) attempted to compare oncologic outcomes in patients with high-risk PCa between a group that received neoadjuvant therapy with ARSI before RP (neo-RP group) and a group that underwent RP first (RP group). Pathological results showed pCR only in the neo-RP group (13%), and also significantly lower incidence of PSM (13% *vs.* 56%) and pT3–T4 lesions (55% *vs.* 72%) compared to the RP group (P<0.01 and P<0.001, respectively) (28). The 3-year BRFS rate was 59% in the neo-RP group and 15% in those who received the RP group (HR, 0.25; P<0.01). The 3-year MFS rates in the neo-RP and RP-alone groups were 96% and 68%, respectively (HR, 0.26; P<0.01) (28). In addition, the rates of adjuvant (7% *vs.* 24%) and salvage therapy (34% *vs.* 46%) were also lower in the neo-RP group than in the RP group (28).

Although NHT with ARSI has potential benefits in improving oncologic outcomes in high-risk PCa compared with RP alone, the results are currently unsatisfactory. In the ongoing phase III PROTEUS trial (NCT03767244), the therapeutic efficacy of APA in addition to standard ADT in patients with high-risk PCa undergoing RP is currently awaited (28).

Feasibility of neoadjuvant chemohormonal therapy (NCHT) for high-risk PCa

Chemotherapy with taxane-based antitumor agents has also been used to prolong the survival of patients with hormone-sensitive or castration-resistant PCa (CRPC) (29). Several clinical studies have demonstrated that NCHT is well tolerated and has acceptable treatment benefits (30,31). In a retrospective study of 177 patients with very high-risk

locally advanced PCa, the patients were divided into the docetaxel-based NCHT, NHT, and RP-alone groups, and were compared for BRFS (30). BCR occurred in 14%, 47%, and 81% of patients in the NCHT, NHT, and RP-alone groups, respectively, and the median BRFS was 19, 13, and 9 months, respectively (P<0.001) (30). In an open-label, multicenter, phase II study of patients with high-risk PCa, patients were randomized to ADT + AA with or without cabazitaxel (CBZ) prior to RP (30). Although pathological pCR or MRD was observed in 43.2% and 45.5% of patients receiving and not receiving CBZ, respectively, no significant difference between the two groups was observed (29). Patients with pCR or MRD revealed a significant improvement in the 12-month BRFS rate compared to their counterparts (96.0% *vs.* 62.0%, P=0.03) (31).

We currently perform NCHT with gonadotropin-releasing hormone (GnRH) and tegafur-uracil (UFT) for patients with high-risk PCa (32). Multiple studies have reported on the efficacy and safety of UFT-containing regimens for various malignant neoplasms, including lung, breast, and gastric cancers (32). Particularly for CRPC, the usefulness of UFT has been demonstrated with late administration and in combination with other anticancer agents (32). The 1- and 2-year BRFS rates were 95.8% and 92.0%, respectively (32). Grade ≥3 NCHT-related adverse events included liver disorder in seven patients (5.9%), rash with liver disorder in one (0.9%), and anorexia with liver disorder in one (0.9%) (32). Although this regimen requires long-term follow-up, it may be an option for NCHT in patients at a high risk of PCa because of its ease of administration.

Conclusions

High-risk PCa is a highly aggressive and heterogeneous tumor that is often difficult to cure with monotherapy. Therefore, developing individualized treatment strategies using several different therapeutic approaches is necessary. We look forward to the accumulation of cases and results of future prospective clinical trials.

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Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-2394/rc

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