

Complete androgen blockade vs. medical castration alone as adjuvant androgen deprivation therapy for prostate cancer patients following radical prostatectomy: a retrospective cohort study

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Abstract

Background: Till date, the optimal treatment strategy for delivering adjuvant androgen deprivation therapy (ADT) in localized and locally advanced prostate cancer (PCa), as a lower stage in PCa progression compared with metastatic PCa, is still unclear. This study compares the efficacy of castration alone with complete androgen blockade (CAB) as adjuvant ADT in patients with localized and locally advanced PCa undergoing radical prostatectomy (RP).

Methods: Patients diagnosed with PCa, without lymph node or distant metastasis, who received RP in West China Hospital between January 2009 and April 2019, were enrolled in this study. We performed survival, multivariable Cox proportional hazard regression, and subgroup analyses.

Results: A total of 262 patients were enrolled, including 107 patients who received castration alone and 155 patients who received CAB. The survival analysis revealed that there was no significant difference between the two groups (hazard ratios [HR]=1.07, 95% confidence intervals [95% CI]=0.60–1.90, $P=0.8195$). Moreover, the multivariable Cox model provided similarly negative results before and after adjustment for potential covariant. Similarly, there was no significant difference in the clinical recurrence between the two groups in both non-adjusted and adjusted models. Furthermore, our subgroup analysis showed that CAB achieved better biochemical recurrence (BCR) outcomes than medical castration alone as adjuvant ADT for locally advanced PCa (P for interaction=0.0247, HR=0.37, 95% CI=0.14–1.00, $P=0.0497$).

Conclusion: Combined androgen blockade achieved better BCR outcomes compared with medical castration alone as adjuvant ADT for locally advanced PCa without lymph node metastasis.

Keywords: Prostatic neoplasms; Androgens; Therapy; Recurrence; Androgen deprivation therapy; Complete androgen blockade

Introduction

In the United States, prostate cancer (PCa) was the most common type of cancer in men in 2020, accounting for >20% of the population. In addition, it has been estimated that in 2020, PCa was responsible for the second highest number of cancer-related deaths in men.^[1] In the meantime, increasing aging-adjusted incidence rates of PCa in Asia have also been observed.^[2] Globally, the social and economic burden from PCa is increasing, even though novel screening and treatment strategies are being employed.^[3] Until recently, radical prostatectomy (RP) was the gold standard treatment for localized PCa.^[4] Furthermore, biochemical recurrence (BCR) was a prognostic indicator of PCa after RP. BCR was defined

as two consecutive rising post-operative prostate-specific-antigen (PSA) values of >0.2 ng/mL.^[5] Approximately 15% to 30% of patients with localized PCa experience BCR after RP.^[6] The purpose of post-operative hormonal therapy is to treat residual lesions, positive lymph nodes, and micrometastases at the surgical margin to improve prognosis. In Siddiqui *et al*'s study,^[7] it was confirmed that adjuvant androgen deprivation therapy (ADT) improves local and systemic control after RP for pT3b PCa. There are two methods to conduct ADT: by either suppressing the secretion of testicular androgens or inhibiting the action of circulating androgens at the level of their receptor. Complete androgen blockade (CAB) combines these two methods. Compared with castration alone, CAB targets the receptor and can block the functions of

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androgens from other sources, including adrenal androgens.^[8]

For advanced PCa, a large meta-analysis based on hormonal therapy found that CAB has improved 5-year survival rates compared with androgen suppression alone.^[9] In addition, a retrospective study evaluating the efficacy of CAB and castration alone in advanced PCa recommended CAB in patients with metastatic PCa, while stating that castration alone might be adequate in non-metastatic PCa.^[10] However, the optimal treatment strategy for adjuvant ADT in localized and locally advanced PCa, as a lower stage in PCa progression compared with metastatic PCa, is still unclear.

Although PSA public screening in China has been generalized in aging men in recent years, patients with locally advanced PCa still account for a considerable proportion of the total population,^[11] especially in southwest China. Since low-risk PCa prognosis is optimistic, it is particularly important to focus on novel strategies to treat high-risk PCa. Moreover, in consideration of the genomic particularity of the Chinese population,^[12] we infer that it is necessary to use the Chinese population as an external validation. Hence, the study aimed to compare the efficacy of castration alone with CAB as an adjuvant therapy in patients with localized and locally advanced PCa undergoing RP in western China.

Methods

Study population

Given the retrospective nature of the study, requirement for informed consent was waived by the Institutional Review Board of West China Hospital (Sichuan University, Chengdu, China). This retrospective cohort study was approved by the Institutional Ethics Review Board of West China Hospital of Sichuan University (No. 2017–324). We identified patients with PCa who had undergone RP between January 2009 and April 2019 at the West China Hospital.

West China Hospital is a national center for the diagnosis and treatment of critical diseases in western China. It caters to the requirements of 83 million people in Sichuan and 267 million in 11 other provinces, autonomous regions, and municipalities. This large population ensures the representativeness of the research population utilized in the present study.

A total of 1298 patients were included. As a study based on a large tertiary hospital, some patients in this study were also enrolled in the national PCa cohort. Then, each participant was screened according to our study's inclusion and exclusion criteria. The inclusion criteria were as follows: pathological diagnosis of PCa, undergoing RP treatment in our hospital settings, lymph node and distant metastasis free, receiving medical castration alone or CAB within 6 months post-operatively irrespective of PSA, and complete follow-up data. The exclusion criteria were failure to follow the treatment, BCR within 6

months, and receipt of other adjuvant therapies, including adjuvant radiation therapy and chemotherapy. Based on adjuvant ADT regimen, patients were divided into two cohort populations: the medical castration-alone cohort and CAB cohort. Patients who received only luteinizing hormone-releasing hormone agonist (LHRHa) (goserelin, leupror-elin, and triptorelin) were defined as medical castration alone, whereas patients who received LHRHa plus non-steroidal anti-androgens (flutamide and bicalutamide) were defined as CAB.

Data collection and study outcomes

Each patient was assigned a unique code after checking by registration number, name and date of birth, or other similar information. Baseline demographics, clinicopathological characteristics, and various treatments of patients were obtained from their respective medical records. This information included patients' age, body mass index (BMI), clinical and pathological T stage, Gleason score (GS), positive surgical margins, PSA level, neoadjuvant therapy, and BCR and clinical recurrence outcomes. GS was evaluated on the basis of the 2014 International Society of Urological Pathology (ISUP) grading system.^[13] Given that the overall survival rate of PCa is relatively high, with a lower rate of clinical recurrence, BCR was chosen as the main endpoint. BCR was defined as two consecutive rising post-operative PSA values that were > 0.2 ng/mL.^[5] The European Association of Urology (EAU) risk group classification for BCR and ISUP grade was defined according to the EAU guideline,^[4] and related factors and outcomes were obtained from the hospital medical history system and regular follow-ups. Clinical recurrence was defined as radiographic evidence (including bone scintigraphy, positron emission tomography scans, computed tomography scans, and magnetic resonance imaging) for PCa with or without the presence of symptoms.^[14] All clinical data were retrieved from medical records and were collected separately by two researchers. Inconsistent data were adjusted by two researchers and resolved by agreement. The critical information, especially for pathological characteristics, was obtained from the pathology report. These measures ensured the accuracy and homogeneity of the information. Finally, patients' information and clinical outcomes were integrated into Empower DataWeb data collection system (X&Y Solutions, Boston, MA, USA). The patients were followed up at a 3-month interval with an outpatient visit or by contact with the patient's family members. The classification of the patient's ADT types was comprehensively judged according to the outpatient prescription information and follow-up content. The status of the events was updated on the Empower DataWeb each time. The last follow-up time was October 2019 and the loss to follow-up rate was 18.97%.

Statistical analysis

Baseline characteristics were assessed to determine potentially significant differences between our study's populations. Two independent sample t, Kruskal-Wallis, Pearson's chi-square, and Fisher's exact tests were performed for both continuous and categorical variables, as

appropriate. Kruskal-Wallis H-tests were used for non-normal distributions. Continuous variables were presented as mean ± standard deviation. For neoadjuvant therapy duration and BCR time and clinical recurrence time (in months), medians and interquartile ranges were reported. Categorical variables were shown as frequencies and their proportions. The BCR times of the two groups were compared using Kaplan-Meier curves and the log-rank test. Hazard ratios (HR) and their 95% confidence intervals (95% CI) were calculated using the multivariable Cox proportional hazard models. The following covariates were adjusted: age, BMI, PSA level, pathological T stage, pathological GS, surgical margin status, and preoperative neoadjuvant therapy. To compare the effectiveness of CAB and chemical castration alone in different groups of patients, subgroup analyses were performed using multivariate regression analysis for BCR. Tests for interactions were also used in the subgroup analyses for the identification of special populations. Each stratification factor was adjusted for all factors and preoperative neoadjuvant therapy except the stratification factor itself and the EAU risk group classification. All analyses were performed with the statistical software packages R (<http://www.R-project.org>, The R Foundation) and EmpowerStats (<http://www.empowerstats.com>, X&Y Solutions, Inc., Boston, MA, USA).

Results

Baseline characteristics of the study population

A total of 262 patients, including 107 patients who received castration alone and 155 patients who received CAB after RP, were enrolled in this study [Figure 1], and the patients' baseline characteristics are presented in Table 1. Patients in both groups had a similar age, BMI, pathological GS, D'Amico's classification, EAU risk group classification, and clinical recurrence proportions. Furthermore, advanced pathological T stage, greater frequencies of surgical margin status, and higher pre-operative

PSA levels were observed in the CAB group. The castration-alone group more commonly received neoadjuvant therapy (30.84% vs. 18.06%, $P=0.016$), but there was no significant difference in neoadjuvant therapy duration compared with the CAB group ($P=0.190$).

Survival analyses

There was no significant difference in the BCR proportion between the two groups. Moreover, a longer BCR time was found in the CAB group than in the castration-alone group (36.36 ± 25.26 vs. 29.29 ± 21.30 months, $P=0.019$), and our survival analyses revealed that there was no significant difference between the two groups [$P=0.820$, Figure 2]. Table 2 presents several multivariable Cox proportional hazard models. To compare the efficacy of CAB and castration alone, a non-adjusted model was performed, and no significant difference between the two groups was noted (HR=1.07, 95% CI=0.60–1.90, $P=0.8195$). Considering the influence of confounding effects, important clinicopathological factors were included in the adjusted models, but still no statistically significant difference between the two groups was found (HR=1.18, 95% CI=0.61–2.27, $P=0.6288$, adjusted model I). Furthermore, similar results were observed after adjusting all covariates (HR=1.19, 95% CI=0.45–3.13, $P=0.4700$, adjusted model II). Given that each model reached the same conclusion before and after adjustments, we confirmed that there was no statistically significant difference in BCR between the castration-alone and the CAB groups. Similarly, there was no significant difference in the clinical recurrence between the two groups in both non-adjusted and adjusted models [Table 2].

Subgroup analyses

Table 3 shows the results of the subgroup analysis. After adjusting for covariates, locally advanced PCa based on D'Amico's classification was observed with significant interaction in the test (P for interaction=0.0247, CAB vs. castration, HR=0.37, 95% CI=0.14–1.00, $P=0.0497$). The difference was found in the Kaplan-Meier survival curves of the subgroup of locally advanced PCa [$P=0.093$, Figure 3], and the difference between the two curves demonstrated a tendency to be significant, a finding that could be explained by the greater proportion of other high-risk factors in the CAB group. Factors, including preoperative PSA level, pathological T stage, pathological GS, surgical margin status, and receiving neoadjuvant therapy or not, might not have interacted with patients who underwent castration alone or CAB, and they had no significant effect on the treatments. These results suggest that CAB achieved better BCR outcomes compared with medical castration alone as adjuvant ADT for locally advanced PCa. However, it may be sufficient for patients with localized PCa to undergo medical castration alone.

Discussion

In this study, we aimed to compare the efficacy of medical castration alone with CAB as adjuvant therapy in patients undergoing RP. The survival analysis revealed that there was no significant difference between the two groups.

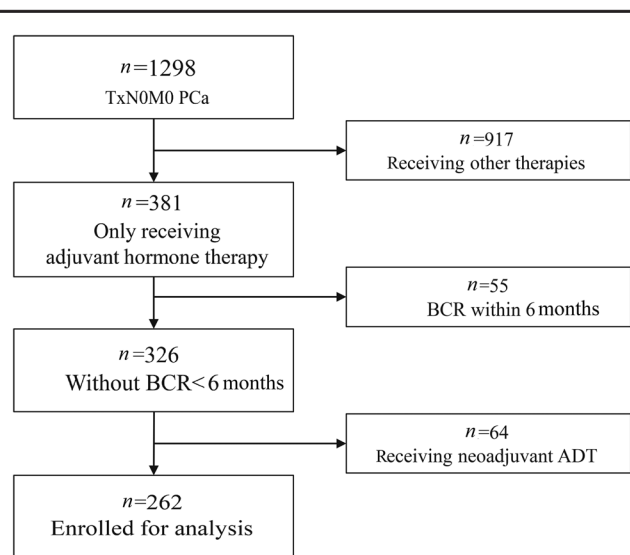


Figure 1: The flow chart of screening the study population. ADT: Androgen deprivation therapy; BCR: Biochemical recurrence; PCa: Prostate cancer.

Table 1: Baseline demographic and clinicopathological characteristics of patients with prostate cancer who had undergone radical prostatectomy.

Patients' characteristics	Castration (n = 107)	CAB (n = 155)	Statistics	P
Mean age (years), mean ± SD	68.4 ± 6.9	68.9 ± 6.8	-0.61 [§]	0.541
BMI (kg/m ²)	23.38 ± 2.67	24.00 ± 2.94	-1.43 [§]	0.155
Pre-operative cT stage, n (%)			4.59 [†]	0.332
cT1	5 (4.7)	4 (2.6)		
cT2	74 (69.2)	97 (62.6)		
cT3	20 (18.7)	31 (20.0)		
cT4	2 (1.9)	9 (5.8)		
Unknown	6 (5.6)	14 (9.0)	13.28 [†]	
pT stage (N=240), n (%)				0.001
pT2	28 (29.8)	22 (15.1)		
pT3	62 (66.0)	100 (68.5)		
pT4	4 (4.3)	24 (16.4)	0.42 [†]	
pGS (N=246), n (%)				0.810
≤6	1 (1.0)	1 (0.7)		
7	49 (50.5)	70 (47.0)		
≥8	47 (48.5)	78 (52.4)	5.36 [†]	
ISUP grade (N=246), n				0.252
1	1	1		
2	18	21		
3	31	49		
4	17	15		
5	30	63		
Positive surgical margins, n (%)			12.51 [†]	<0.001
No	74 (69.2)	73 (47.1)		
Yes	33 (30.8)	82 (52.9)		
Pre-operative PSA (ng/mL)	22.52 (11.75–43.08)	26.81 (15.04–58.76)	4.07 [‡]	0.044
PSA-DT (1 year, N=95), n (%)				0.335
No	9 (28.1)	24 (38.1)		
Yes	23 (71.9)	39 (61.9)	5.79 [†]	
Neoadjuvant therapy, n (%)				0.016
No	74 (69.2)	127 (81.9)		
Yes	33 (30.8)	28 (18.1)		
Neoadjuvant therapy time (months), median (IQR)	3.47 (1.10–6.43)	2.67 (1.37–4.10)	1.72 [‡]	0.190
D'Amico's classification, n (%)			6.18 [†]	0.103
Low	3 (2.8)	1 (0.7)		
Intermediate	7 (6.5)	4 (2.6)		
High	86 (80.4)	140 (90.3)		
Unknown	11 (10.3)	10 (6.5)		
EAU risk group classification, n (%)			1.91 [†]	0.384
Localized	74 (69.2)	105 (67.7)		
Locally advanced	22 (20.6)	40 (25.8)		
Unknown	11 (10.3)	10 (6.5)		
BCR, n (%)			1.04 [†]	0.308
No	89 (83.2)	121 (78.1)		
Yes	18 (16.8)	34 (21.9)		
BCR time (months)				
Mean ± SD	29.29 ± 21.30	36.36 ± 25.26	-2.37 [§]	0.019
Median (IQR)	25.02 (13.27–37.27)	31.23 (16.67–48.05)	5.20 [‡]	0.023
Clinical recurrence, n				0.090
No	104	148		
Yes	3	7		
Clinical recurrence time (months)				
Mean ± SD	34.57 ± 25.51	42.50 ± 26.64	-2.41 [§]	0.017
Median (IQR)	27.95 (15.16–47.13)	37.71 (21.80–57.85)	7.25 [‡]	0.007

* *t* values. † χ^2 values. ‡ Chi-square from Kruskal-Wallis tests. BCR: Biochemical recurrence; BMI: Body mass index; CAB: Complete androgen blockade; EAU: European Association of Urology; IQR: Interquartile range; ISUP; International Society of Urological Pathology; pGS: pGleason score; PSA: Prostate-specific antigen; PSA-DT: Prostate-specific antigen doubling time; SD: Standard deviation. For pT stage, pGS, ISUP grade and PSA-DT, the unknown cases were not including in analysis.

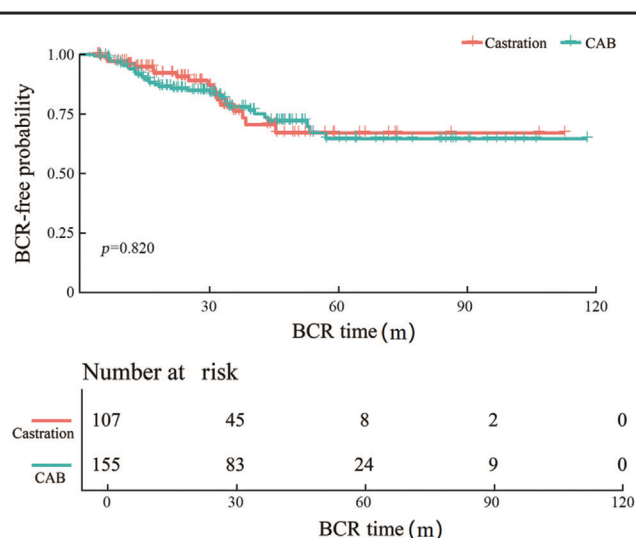


Figure 2: The Kaplan-Meier curves and the log-rank test of BCR time between castration alone group and CAB group in all PCa. BCR: Biochemical recurrence; CAB: Complete androgen blockade; PCa: Prostate cancer.

Table 2: Multivariable Cox proportional hazard model of biochemical and clinical recurrence.

CAB vs. castration	Samples	HR (95% CI)	P
BCR			
Non-adjusted model	262	1.07 (0.60, 1.90)	0.8195
Adjusted model I	223	1.18 (0.61, 2.27)	0.6288
Adjusted model II	145	1.19 (0.45, 3.13)	0.7244
Clinical recurrence			
Non-adjusted model	262	1.29 (0.33, 5.00)	0.7113
Adjusted model I	223	0.89 (0.16, 5.15)	0.9010
Adjusted model II	145	0.91 (0.08, 10.64)	0.9374

Non-adjusted model adjust for: None. Adjusted model I adjusted for: PSA, pT stage, pGS, surgical margins status, neoadjuvant therapy. Adjusted model II adjusted for: Age, BMI, PSA, pT stage, pGS, surgical margins status, neoadjuvant therapy. BCR: Biochemical recurrence; BMI: Body mass index; CAB: Complete androgen blockade; CI: Confidence interval; HR: Hazard ratio; pGS: pGleason score; PSA: Prostate-specific antigen.

Moreover, after adjusting for the potential covariant, the multivariable Cox model provided us with similar results. Furthermore, the subgroup analysis showed that ADT types had different outcomes in locally advanced PCa. These results indicate that medical castration alone may not be inferior to CAB as an adjuvant therapy in patients with localized PCa. However, it should be mentioned that CAB achieved a lower BCR rate compared with castration alone as an adjuvant ADT for locally advanced PCa without lymph node metastasis.

Previous studies have shown that ADT is an effective treatment method for PCa.^[7,15] A recent meta-analysis suggested that adjuvant ADT improved progression- and metastasis-free survival compared with neoadjuvant ADT in patients with localized PCa with prostate-directed radio-therapy.^[16] In fact, this study highlighted the sequencing of ADT in PCa treatment modalities. Although

adjuvant ADT has drawn considerable attention in recent years, there is still limited evidence in terms of selecting monotherapy or CAB in localized and locally advanced PCa. Previous studies have mainly focused on patients with advanced PCa. For metastatic PCa, a large randomized controlled trial (RCT) in distant metastases PCa found that flutamide was not associated with enhanced benefit after surgical castration.^[17] Moreover, a meta-analysis on advanced PCa found that CAB had a statistically significant limited higher rate of 5-year overall survival (0–5%) compared with castration alone.^[18] However, studies have underlined the increased risk of adverse effects compared with the overall quality of life from CAB. In recent years, the appropriate quality of life has been widely valued in PCa. Compared with monotherapy, CAB has presented several disadvantages, including the development of adverse events^[19] and increased cardiovascular risk.^[20] Consequently, there is an urgent need to balance disease control and quality of life by appropriately selecting either CAB or monotherapy. In contrast, cyproterone acetate trials could confirm potential benefits for CAB schemes.^[9] Another long-term follow-up study focusing on locally advanced or metastatic PCa found that the combination of CAB with the bicalutamide group provided significant overall survival advantages compared with monotherapy.^[21] Compared with this study, our study population was partly similar, and both studies investigated locally advanced PCas. However, the authors of that study used ADT as the initiation treatment rather than the adjuvant treatment. In China, a previous retrospective study found that the overall survival findings of CAB were similar to those of castration alone in patients with advanced PCa, but CAB could improve progression-free survival times.^[10] When it comes to adjuvant hormone therapy, Ye *et al*^[22] performed in China recruited 189 patients with high-risk localized and locally advanced PCa. The CAB group demonstrated the least recurrence rates; however, the difference among groups was non-significant.^[22] In addition, there were some differences between the present study and that of Ye *et al*. First, Ye *et al* enrolled N1M0 PCa. Positive lymph node metastasis might urge doctors to choose more aggressive treatments and minimize differences among groups. Second, the LHRHa group had a lower sample size as only 13 patients received LHRHa. Chang *et al*^[23] compared CAB with bicalutamide alone in 209 patients with high-risk localized PCa. The CAB group exhibited longer BCR-free survival rates compared with the bicalutamide group.^[23] In western populations, the evidence for choosing CAB or monotherapy after RP in localized PCa is limited. However, Nanda *et al*^[24] found that CAB as adjuvant treatment proved to be superior to monotherapy in localized PCa patients undergoing brachytherapy. Altogether, these findings demonstrate that the selection of an optimal strategy for adjuvant ADT after RP remains unclear. Thus, a multicenter prospective controlled study is necessary to further investigate this issue.

In our study, CAB achieved better outcomes compared with medical castration alone as adjuvant ADT for locally advanced PCa without lymph node metastasis. In brief, our study included a large sample size in China and provided novel evidence for selecting adjuvant ADT.

Table 3: The subgroup analysis for interaction between two therapies and potential covariates.

CAB vs. castration	Sample size	HR (95% CI)	P value	P for interactions
pT stage				0.0549
pT2	50	0.00 (0.00, Inf)	0.9988	
pT3	162	1.57 (0.74, 3.31)	0.2365	
pT4	28	0.41 (0.06, 2.81)	0.3613	
Pre-operative PSA				0.5664
<10 ng/mL	41	6.36 (0.40, 101.96)	0.1913	
10–20 ng/mL	61	1.40 (0.34, 5.79)	0.6381	
>20 ng/mL	144	0.91 (0.39, 2.14)	0.8289	
pGS				0.9236
≤6	2	–	–	
7	119	0.78 (0.27, 2.30)	0.6534	
≥8	125	1.35 (0.58, 3.15)	0.4850	
Positive surgical margins				0.8810
No	147	0.96 (0.37, 2.50)	0.9406	
Yes	115	1.28 (0.46, 3.56)	0.6348	
Neoadjuvant therapy				0.2610
No	201	0.95 (0.46, 1.98)	0.8925	
Yes	61	3.14 (0.35, 28.37)	0.3091	
EAU risk group classification			0.0247	
Localized	179	1.76 (0.78, 4.02)	0.1757	
Locally advanced	62	0.37 (0.14, 1.00)	0.0497	

CAB vs. castration, the comparison of BCR between CAB cohort and castration alone cohort. BCR: Biochemical recurrence; CAB: Complete androgen blockade; CI: Confidence interval; EAU: European Association of Urology; HR: Hazard ratio; pGS: pGleason score; PSA: Prostate-specific antigen; -: Not applicable.

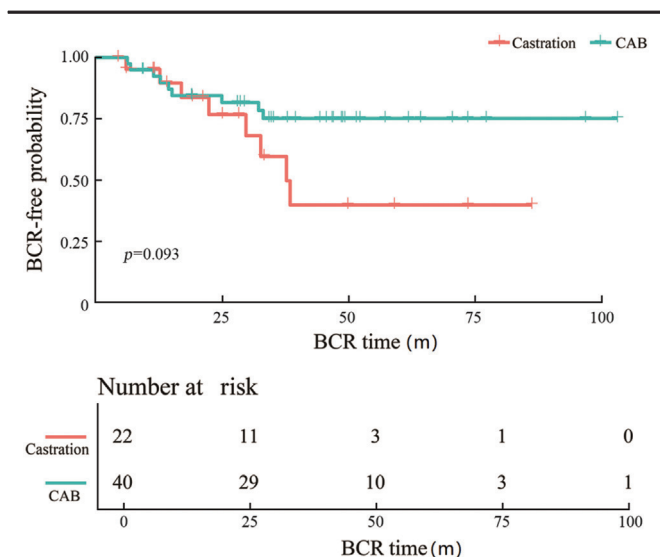


Figure 3: The Kaplan-Meier curves and the log-rank test of BCR time between castration alone group and CAB group in locally advanced. BCR: Biochemical recurrence; CAB: Complete androgen blockade; PCa: Prostate cancer.

Compared with previous studies, our study found locally advanced PCa as a special population via subgroup analysis, and this population may benefit from CAB compared with castration alone. However, current literature provides limited comparative evidence between the two methods. In China, a significant proportion of patients with PCa are diagnosed with elevating PSA levels, without any other obvious symptoms. A study performed in Shanghai retrospectively analyzed their PCa samples

and found that 37.4% of Chinese patients had CAPRA-S high-risk disease compared with 6.5% of patients in the United States.^[11] In recent years, although PSA public screening has been generalized in aging men, PCa awareness in the Chinese society remains limited. Patients with locally advanced PCa still account for a considerable proportion of the total population. Furthermore, the rates of localized PCa may become even greater following early screening. Therefore, this study provides solid evidence in terms of selecting the appropriate treatment.

There are two methods for castration alone: medical and surgical castration. A population-based study found that surgical castration was used less frequently and was not associated with differences in survival rates compared with medical castration.^[25] Besides, a study that aimed to analyze testosterone levels in ADT found that triptorelin was deemed to be superior to subcapsular orchiectomy.^[26] However, medical castration has an increased risk of facilitating several adverse effects, including fractures and cardiovascular disease, compared with orchiectomy.^[27] In recent years, novel and more effective drugs have been manufactured, which have in turn provided more alternative treatment options. The TITAN trial (NCT02489318) revealed that the addition of apalutamide to ADT was an effective and safe option to patients with metastatic, castration-sensitive PCa.^[28] Moreover, the ENZAMET trial (NCT02446405) indicated that enzalutamide was associated with better prognosis compared with standard care.^[29] These novel CAB options had better effects than the traditional scheme, and thus the combination of these drugs warrants further studies.

Nonetheless, this study has several strengths. First, subgroup analyses were conducted to identify special populations and thus provide more precise and accurate findings and conclusions. Second, we provided novel evidence in terms of selecting adjuvant ADT based on the experience gained from a high-volume institution in China.

Based on recent data, clinical practice may become more precise. However, our study also has several limitations. First, our analysis was limited because of its retrospective nature. Therefore, selection bias was inevitable. These data provided supportive evidence for selecting CAB or castration alone, and thus further RCTs are needed to prospectively compare and elucidate the efficacy of both methods. Second, although our analysis included 262 patients, our sample size was also limited. Third, our findings are limited by the fact that ADT strategies are mainly based on traditional castration drugs, and hence our conclusions cannot be further generalized. Further studies can focus on new combinations of effective drugs. Fourth, the primary clinical outcome was BCR, which is a relatively short-term and alternative outcome compared with clinical recurrence; thus, a practical long-term survival outcome should be estimated to provide more evidence.

In conclusion, on the basis of the retrospective experiences gained from a high-volume institution in China, combined androgen blockade achieved better BCR outcomes compared with medical castration alone as an adjuvant ADT for locally advanced PCa without lymph node metastasis. Besides, further prospective cohort studies or RCTs are needed to verify this conclusion.

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Conflicts of interest

None.

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