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Original Research

Reduced cancer-specific survival of low prostate-specific antigen in high-grade prostate cancer: A population-based retrospective cohort study

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ABSTRACT

Objective: The aim of this study was to evaluate the survival outcomes of different prostate-specific antigens (PSA) levels in men with high-grade prostate cancer.

Materials and methods: From 2004 to 2015 in the Surveillance, Epidemiology, and End Results database, men diagnosed with clinically localized prostate cancer and a Gleason score (GS) 8–10 were identified. Patients were divided into the PSA levels < 4.0 ng/ml, 4.0–10.0 ng/ml, 10.1–20.0 ng/ml, and > 20.0 ng/ml groups. Multivariable Cox regressions and Kaplan–Meier analysis were adopted to analyze the prostate cancer-specific survival (PCSS).

Results: 59,336 men with a median age of 70 (63–76) years with a GS 8–10 were included. The PCSS of patients with a PSA < 4.0 ng/ml was significantly worse than that of patients with a PSA 4.0–10.0 ng/ml [hazard ratio (HR): 1.43 (1.28–1.58)], but was better than that of patients with a PSA 10.1–20.0 ng/ml [HR: 1.18 (1.06–1.31)]. After stratifying patients by GS, the differences between patients with a PSA < 4.0 ng/ml and a PSA 4.0–10.0 ng/ml were only significant in those with a GS 9 and 10 [GS 9 HR: 1.49 (1.28–1.72); GS 10 HR: 1.42 (1.12–1.8)], but not in those with a GS 8 [HR: 1.04 (0.95–1.14)]. Moreover, the PCSS of patients with a PSA < 4.0 ng/ml and a PSA 10.0–20.0 ng/ml were similar in patients with GS 9 and 10 diseases [GS 9: HR: 1.06 (0.91–1.23); GS 10: HR: 1.13 (0.89–1.44)].

Conclusions: Patients with a PSA < 4.0 ng/ml had poorer PCSS than patients with a PSA 4.0–10.0 ng/ml. Similar PCSS was found in patients whose PSA levels were 10.1–20.0 ng/ml in patients with GS 9–10 prostate cancer.

1. Introduction

Prostate cancer is the most common malignant tumor in the male urogenital system, accounting for about 15% of all malignancies in the world, seriously threatening the lives and health of male patients [1,2]. In 2019, it is estimated that there are more than 174,650 newly diagnosed cases and 31,620 deaths in the United States [3]. Gleason score (GS), prostate-specific antigen (PSA) and tumor-node-metastasis (TNM) classification are the most frequently used prognostic factors of prostate cancer. The GS system has been shown to have a strong prognosis for overall survival and prostate cancer-specific survival (PCSS) in patients with localized prostate cancer [4], but may not be significant in metastatic diseases [5,6]. High-grade prostate cancer (GS grade group 4–5 disease) has established high-risk features and is associated with poor prognosis. Serum PSA is the best initial assessment for prostate cancer detection. PSA 4.0–10.0 ng/ml is considered as the diagnostic gray zone. Within this level, the cancer detection rate is about 16%–39%, and the high-grade cancer rate varies from 4.1% to 25% [7,8].

The PSA levels reflect the burden of tumor cells and are closely related to the prognosis of prostate cancer. In general, prostate cancer with higher levels of pretreated serum PSA is more aggressive and has a higher risk of cancer-specific mortality for patients. However, some previous studies have reported that patients with lower PSA levels have worse survival outcomes in high-grade prostate cancer [9–12]. High-grade prostate cancer can be divided into GS 8 and GS 9–10 [13]. GS 9–10 prostate cancer is more aggressive and is associated with obviously poorer survival when compared with GS 8 diseases [14–16]. The survival differences of PSA levels in GS 8 and GS 9–10 have not been revealed in previous studies. The aim of this study was to evaluate the prognostic differences of PSA levels (PSA < 4.0 ng/ml,

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Table 1
Baseline characteristics of patients with different PSA levels.

Characteristic	< 4.0 ng/ml	4.0–10.0 ng/ml	10.1–20.0 ng/ml	> 20.0 ng/ml	Total
N	4119	27388	13830	6649	59336
Age (years)					
Median	69	68	71	71	70
IQR	62–75	63–74	64–78	64–79	63–76
Age, n (%)					
≤65	1482(36)	10075(36.8)	4151(30)	4414(31.5)	20122(33.9)
> 65	2637(64)	17313(63.2)	9679(70)	9585(68.5)	39214(66.1)
Race, n (%)					
White	3503(85)	21640(79)	10573(76.4)	9827(70.2)	45543(76.8)
Black	404(9.8)	3613(13.2)	1988(14.4)	2878(20.6)	8883(15)
Others	172(4.2)	1805(6.6)	1109(8)	1101(7.9)	4187(7.1)
Unknown	40(1)	330(1.2)	160(1.2)	193(1.4)	723(1.2)
Marriage, n (%)					
Married	3030(73.6)	19533(71.3)	9172(66.3)	8014(57.2)	39749(67)
Unmarried	316(7.7)	2290(8.4)	1367(9.9)	1715(12.3)	5688(9.6)
Divorced or Separated	454(11)	3368(12.3)	2016(14.6)	2499(17.9)	8337(14.1)
unclear	319(7.7)	2197(8)	1275(9.2)	1771(12.7)	5562(9.4)
T stage, n (%)					
T1	919(22.3)	9438(34.5)	5208(37.7)	5182(37)	20747(35)
T2	2130(51.7)	11960(43.7)	5657(40.9)	5976(42.7)	25723(43.4)
T3	949(23)	5562(20.3)	2655(19.2)	2342(16.7)	11508(19.4)
T4	121(2.9)	428(1.6)	310(2.2)	499(3.6)	1358(2.3)
Gleason score, n (%)					
8	2301(55.9)	16697(61)	7662(55.4)	6891(49.2)	33551(56.5)
9	1628(39.5)	9994(36.5)	5650(40.9)	6380(45.6)	23652(39.9)
10	190(4.6)	697(2.5)	518(3.7)	728(5.2)	2133(3.6)
Therapy, n (%)					
RP	1476(35.8)	9620(35.1)	4077(29.5)	3498(25)	18671(31.5)
EBRT	1105(26.8)	7549(27.6)	4316(31.2)	4322(30.9)	17292(29.1)
Prostatectomy	156(3.8)	861(3.1)	492(3.6)	588(4.2)	2097(3.5)
Radiation	491(11.9)	3461(12.6)	1626(11.8)	1633(11.7)	7211(12.2)
Prostatectomy + radiation	312(7.6)	2061(7.5)	1361(9.8)	1873(13.4)	5607(9.4)
No definitive therapy	579(14.1)	3836(14)	1958(14.2)	2085(14.9)	8458(14.3)
Survival time (months)					
Median	69	71	63	54	64
IQR	33–102	36–104	29–95	27–91	31–98

PSA, prostate-specific antigen; N/n, number; IQR, interquartile range; RP, radical prostatectomy; EBRT, external beam radiotherapy.

4.0–10.0 ng/ml, 10.1–20.0 ng/ml, > 20.0 ng/ml) in men with high-grade (GS 8–10, GS8, GS9, GS10) prostate cancer.

2. Materials and methods

2.1. Data source

The Surveillance, Epidemiology and End Results (SEER) program collects and publishes cancer incidence, treatment and survival data from population-based cancer registries, which includes approximately 28% of all cancer cases in the United States population. In our study, patients with clinically localized (cT1-4N0M0) prostate cancer from January 2004 to December 2015 were retrospectively identified. Patients were divided into 4 groups according to their PSA levels (< 4.0 ng/ml, 4.0–10.0 ng/ml, 10.1–20.0 ng/ml, > 20.0 ng/ml). This work has been reported in accordance with the STROCSS criteria [17].

2.2. Selection criteria

Patients were considered eligible if they met the following criteria: (1) clinical localized (cT1-4N0M0) prostate cancer. (2) High-grade (GS 8–10) detected by needle core biopsy, transurethral resection of the prostate, or prostatectomy. (3) The survival status at the end of the follow-up were clearly known.

The following criteria were used for data exclusion: (1) Multiple tumor; (2) Tumor had Lymph nodes and/or distant metastases; (3) the information of PSA or GS was unclear or missing; (3) the follow-up time was unclear or incomplete.

2.3. Variables and main outcomes

The general characteristics, tumor information, and survival outcomes were collected. The variables included age at diagnosis, race (white, black, other race including American Indian and Asian/Pacific Islander), marital status (married, unmarried, divorced or separated), T stage (T1, T2, T3, T4), pretreated serum PSA values, Gleason score (8,9,10), therapy, survival time, living status (alive or dead), and prostate cancer-specific survival status (alive, dead for prostate cancer, dead for other reasons). The PSA values were divided into levels of < 4.0 ng/ml, 4.0–10.0 ng/ml, 10.1–20.0 ng/ml, > 20 ng/ml. Treatments included radical prostatectomy (RP), external beam radiotherapy (EBRT), prostatectomy but not including RP, radiations but not including EBRT, prostatectomy + radiation and no definitive therapy. The main outcomes were PCSS in GS 8–10, GS 8, GS 9, and GS 10. The survival time was defined as the time from the patient's first diagnosis to the patient's death or the last follow-up time (December 31, 2015).

2.4. Statistical analyses

Baseline characteristics including age, race, marital status, tumor cell differentiation, T stage, GS, PSA level, and follow-up time were described in different PSA levels. The differences were calculated with the chi-square test or *t*-test. The Kaplan-Meier analysis was used to evaluate the PCSS and construct the survival curves of PSA levels. Long rank P values were calculated to determine statistical significance. Univariate COX analysis was adopted to obtain the hazard ratio (HR) values with 95% confidence interval (95% CI) of each variable. Multivariate Cox analysis was performed on the variable with $P < 0.1$

in the univariate COX analysis. All statistical analyses were performed with the software of SPSS 25.0 and Graph prism 7.0. P < 0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

59,336 men with high-grade prostate cancer were identified. The median (interquartile range, IQR) age was 70 (63–76) years. There were 4,119 patients in PSA < 4.0 ng/ml group, 27,388 in PSA 4.0–10.0 ng/ml group, 13,830 in PSA 10.1–20.0 ng/ml group, and 13999 in PSA > 20.0 ng/ml group. The median follow-up time was 64 (31–98) months. The basic characteristics of patients with different PSA levels were presented in Table 1.

3.2. Survival outcomes

3.2.1. Estimation of PCSS by PSA levels, stratified by Gleason score

Among the overall cohort, patients with PSA 4.0–10.0 ng/ml had the best PCSS, followed by patients with PSA < 4.0 ng/ml, 10.1–20 ng/ml, and > 20.0 ng/ml. The survival outcomes of patients with PSA < 4.0 ng/ml were obviously worse than that of patients whose PSA levels 4.0–10.0 ng/ml [HR: 0.7 (0.63–0.78)], and were significantly better than that of patients with PSA 10.1–20.0 ng/ml [HR: 1.18 (1.06–1.31)] and PSA > 20 ng/ml [HR: 2.23 (2.01–2.48)]. With patients who had PSA levels of 4.0–10.0 ng/ml as the reference, the HR and 95%CI for patients with PSA < 4.0 ng/ml, 10.1–20.0 ng/ml and > 20.0 ng/ml were 1.43 (1.28–1.58), 1.68 (1.57–1.79), 3.18 (3.01–3.37), respectively. These results were presented in Fig. 1A and Table 2.

When stratified by GS, patients with 4.0–10.0 ng/ml had better PCSS than patients with other PSA levels in GS 8 disease. However, the differences between patients with PSA 4.0–10.0 and PSA < 4.0 ng/ml ng/ml were not significant [HR: 1.04 (0.95–1.14); P = 0.092]. Moreover, patients with PSA < 4.0 ng/ml had significantly better PCSS than those with 10.1–20.0 ng/ml [HR: 1.47 (1.34–1.61)] and PSA > 20.0 ng/ml [HR: 2.48 (2.24–2.74)]. With patients whose PSA levels 4.0–10.0 ng/ml as the reference, the HR and 95%CI for patients with PSA < 4.0 ng/ml, 10.1–20 ng/ml, and > 20.0 ng/ml were 1.04 (0.95–1.14), 1.54 (1.46–1.62), and 2.59 (2.43–2.76), respectively (Fig. 1B and Table 2).

In GS 9 diseases, patients who had PSA levels of < 4.0 ng/ml had significantly worse PCSS than patients with 4.0–10.0 ng/ml [HR: 1.49 (1.28–1.72)], and had similar results of PCSS with patients whose PSA levels 10.1–20.0 ng/ml [HR: 1.06 (0.91–1.23)]. With patients whose PSA levels < 4.0 ng/ml as the reference, the HR and 95%CI for patients with PSA 4.0–10.0 ng/ml, 10.1–20.0 ng/ml, and > 20.0 ng/ml were 0.67 (0.58–0.78), 1.06 (0.91–1.23), 2.62 (2.25–3.04), respectively (Fig. 1C and Table 2).

For GS 10 prostate cancer, the PCSS of patients with PSA < 4 ng/ml were significantly worse than that of patients with PSA 4.0–10.0 ng/ml [HR: 1.42 (1.12–1.8)], and was similar to that of patients with PSA 10.1–20.0 ng/ml [HR: 1.13 (0.89–1.44)]. Patients who had PSA levels of 4.0–10.0 ng/ml showed the highest PCSS, while those of > 20 ng/ml presented the lowest. With patients whose PSA levels < 4.0 ng/ml as the reference, the HR and 95%CI for patients with 4.0–10.0 ng/ml, 10.1–20 ng/ml and PSA > 20 ng/ml were 0.71 (0.56–0.89), 1.13 (0.89–1.44), 1.67 (1.19–2.35), respectively. These results were shown in Fig. 1D and Table 2.

3.2.2. Multivariate Cox regression analysis for PCSS

The results of multivariate Cox regression analysis of PCSS were presented in Table 3. The variables of age, race, marital status, T stage, PSA, GS and treatment were independent risk factors of prostate cancer-specific mortality. For PSA levels, the risk of PSA < 4.0 ng/ml was significantly higher that of PSA 4.0–10.0 ng/ml, and was similar to that of PSA 10.1–20.0 ng/ml. With PSA < 4.0 as the reference, the HR and 95% CI of PSA 4.0–10.0 ng/ml, 10.1–20.0 ng/ml, > 20.0 ng/ml were 0.73 (0.65–0.81), 1.07 (0.96–1.19), and 1.86 (1.67–2.06), respectively.

4. Discussion

The factors of GS and PSA are widely used for the risk classification of prostate cancer and the guidance of treatment decisions [18]. High GS is an important prognostic factor for prostate cancer with aggressive tumor characterizes. In general, higher PSA levels are associated with poorer survival, but there are exceptions in high-grade prostate cancer [12,19,20].

In our study, 59,336 patients with localized high-grade prostate cancer were included. According to the analysis results, we found that the best PCSS was observed in patients with PSA 4.0–10.0 ng/ml. Patients with PSA < 4.0 ng/ml had significantly worse survival outcomes than those with 4.0–10.0 ng/ml. It revealed that men with high-grade prostate cancer and low PSA levels were associated with poor prognosis. Falchook et al. [19] analyzed 37,283 patients and found that

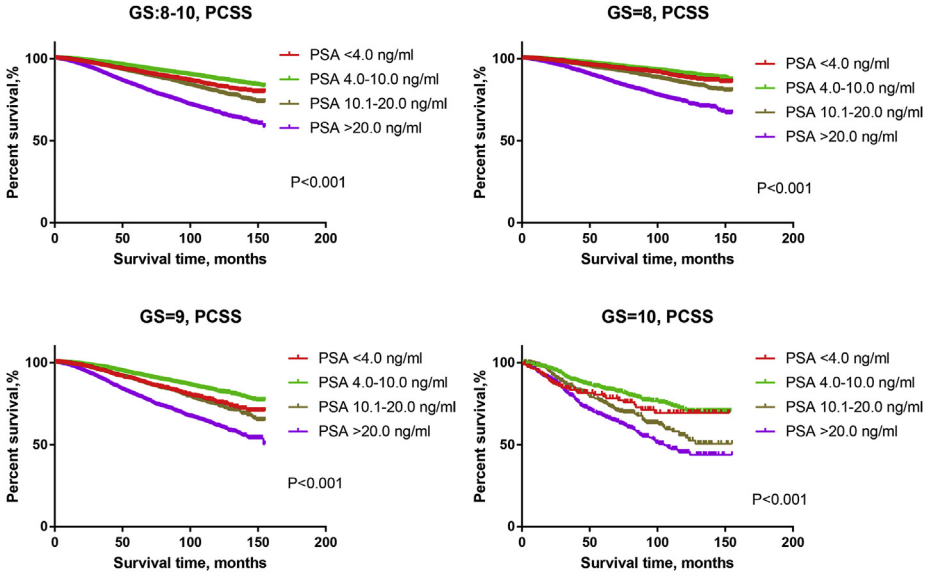


Fig. 1. The prostate cancer-specific survival (PCSS) of PSA levels in men with high-grade prostate cancer. (A) The PCSS of PSA levels in men with GS 8–10 prostate cancer. (B) The PCSS of PSA levels in men with GS 8 prostate cancer. (C) The PCSS of PSA levels in men with GS 9 prostate cancer. (D) The PCSS of PSA levels in men with GS 10 prostate cancer.

Table 2
Hazard ratios of prostate cancer-specific survival for men with different PSA levels.

HR(95%CI)	< 4.0 ng/ml	4.0–10.0 ng/ml	10.1–20.0 ng/ml	> 20.0 ng/ml
GS:8–10				
< 4.0 ng/ml	1	1.43(1.28–1.58)	0.85(0.76–0.95)	0.47(0.42–0.52)
4.0–10.0 ng/ml	0.7(0.63–0.78)	1	0.6(0.56–0.64)	0.34(0.32–0.36)
10.1–20.0 ng/ml	1.18(1.06–1.31)	1.68(1.57–1.79)	1	0.55(0.51–0.59)
> 20.0 ng/ml	2.23(2.01–2.48)	3.18(3–3.37)	1.9(1.78–2.02)	1
GS:8				
< 4.0 ng/ml	1	1.04(0.95–1.14)	0.68(0.62–0.75)	0.4(0.37–0.45)
4.0–10.0 ng/ml	0.96(0.88–1.05)	1	0.65(0.62–0.69)	0.39(0.36–0.41)
10.1–20.0 ng/ml	1.47(1.34–1.61)	1.54(1.46–1.62)	1	0.59(0.55–0.63)
> 20.0 ng/ml	2.48(2.24–2.74)	2.59(2.43–2.76)	1.69(1.57–1.8)	1
GS:9				
< 4.0 ng/ml	1	1.49(1.28–1.72)	0.94(0.81–1.1)	0.38(0.33–0.44)
4.0–10.0 ng/ml	0.67(0.58–0.78)	1	0.63(0.58–0.7)	0.26(0.23–0.28)
10.1–20.0 ng/ml	1.06(0.91–1.23)	1.58(1.43–1.73)	1	0.41(0.37–0.45)
> 20.0 ng/ml	2.62(2.25–3.04)	3.89(3.54–4.28)	2.47(2.23–2.73)	1
GS:10				
< 4.0 ng/ml	1	1.42(1.12–1.8)	0.88(0.7–1.12)	0.62(0.48–0.79)
4.0–10.0 ng/ml	0.71(0.56–0.89)	1	0.62(0.53–0.74)	0.43(0.37–0.52)
10.1–20.0 ng/ml	1.13(0.89–1.44)	1.6(1.36–1.89)	1	0.7(0.59–0.83)
> 20.0 ng/ml	1.67(1.19–2.35)	2.44(1.78–3.35)	2.12(1.52–2.97)	1

HR: Hazard ratios; CI: confidence interval; GS: Gleeson score.

Table 3
Multivariate COX analysis for PCSS.

Risk factors	PCSS		
	HR	95%CI	P
Age			
< 55	1		Ref.
55–65	0.99	(0.89–1.11)	0.922
65–75	1.24	(1.11–1.38)	< 0.001
> 75	2.1	(1.88–2.35)	< 0.001
Race			
White	1		Ref.
Black	1.22	(1.14–1.31)	< 0.001
Others	0.76	(0.68–0.84)	< 0.001
Marital status			
Married	1		Ref.
Unmarried	1.31	(1.2–1.42)	< 0.001
Divorced	1.32	(1.23–1.41)	< 0.001
T staging			
T1	1		Ref.
T2	0.97	(0.91–1.02)	0.260
T3	1.04	(0.96–1.12)	0.330
T4	2.07	(1.82–2.36)	< 0.001
PSA			
< 4.0 ng/ml	1		Ref.
4.0–10.0 ng/ml	0.73	(0.65–0.81)	< 0.001
10.1–20.0 ng/ml	1.07	(0.96–1.19)	0.248
> 20.0 ng/ml	1.86	(1.67–2.06)	< 0.001
Gleason score			
8	1		Ref.
9	1.83	(1.74–1.93)	< 0.001
10	3.21	(2.92–3.53)	< 0.001
Treatment			
RP	1		Ref.
EBRT	1.16	(1.09–1.24)	< 0.001
Prostatectomy	1.31	(1.16–1.49)	0.337
Radiation	1.04	(0.96–1.13)	< 0.001
No definitive therapy	1.49	(1.35–1.65)	< 0.001

PCSS, prostate cancer-specific survival; HR, hazard ratio; Ref, reference; PSA, prostate-specific antigen; RP, radical prostatectomy; EBRT, external beam radiotherapy.

high-grade prostate cancer with PSA < 4.0 ng/ml was more aggressive than the disease with PSA 4–9.9 ng/ml. In another study, Mahal et al. [20] analyzed 494,793 patients from the National Cancer Data Base and 136,113 patients from the SEER database with $cT_{1\text{-}4}N_0M_0$ prostate cancer. They found that using patients with PSA 4.1–10.0 ng/ml as the reference, the adjusted HR of PSA ≤2.5, 2.6–4.0, 10.1–20.0, > 20.0 ng/ml in GS 8–10 disease were 2.70, 1.97, 1.36 and 2.56, respectively.

When stratified by GS, patients with PSA 4.0–10.0 ng/ml had significantly better PCSS than patients with PSA < 4.0 ng/ml in GS 9 and GS 10 prostate cancer, but not in GS 8. In addition, the PCSS of patients with PSA < 4 ng/ml was obviously better than that of patients with PSA 10.0–20.0 ng/ml in GS 8 disease, but such difference between the two groups were not found in GS9 and 10 diseases. As we know, it has not been reported in previous studies.

Low PSA levels in high-grade prostate cancer are indicators of poor differentiation and aggressive tumor behavior. It may represent a feature of potential dedifferentiation biology and may be poorly responding to current treatments, particularly for androgen deprivation therapy [20]. However, little evidence supports this hypothesis [9,11,12]. Compared with other high-grade patients, men with low PSA levels are related to high expression of neuroendocrine/small cell disease and low AR signaling markers. These patients are often associated with neuroendocrine phenotypes, and have a poor response to hormonal therapy [12,20–22]. Even though GS 8 and GS 9–10 are generally considered to be high-grade diseases, their invasiveness and prognosis are not similar. Prostate cancer of GS 9 and 10 are more aggressive and have poorer prognoses than that of GS 8. Our results indicated that low PSA levels (PSA < 4.0 ng/ml) in GS 9–10 prostate cancer are more aggressive and men with low PSA levels in GS 9–10 prostate cancer have obviously poorer prognoses than those in GS 8 diseases.

There were still some limitations in our study. Firstly, even with a large number of patients, our study is a retrospective analysis which means there are some unavoidable confounders and risk biases. It may have an impact and interference on the results. Secondly, we only included the clinical localized ($T_{1\text{-}4}N_0M_0$) disease. With the exclusion of patients with N_+, N_x and $N_{1\text{-}2}$, our study may have some biases. Thirdly, our study only focused on the analysis of survival and did not analyze many other important outcomes such as comorbidities, quality of life. Therefore, more high-quality studies are needed to evaluate these results in future studies.

5. Conclusion

The PCSS of patients with PSA < 4.0 ng/ml is significantly worse than that of patients with PSA 4.0–10.0 ng/ml, and is similar to patients

with PSA 10.1–20.0 ng/ml in GS 9–10 prostate cancer. However, with the limitations of our study, high-quality studies are needed for future evaluations.

Ethical approval

All data are from the public database, the data use agreement has been designed. No ethical approval and patient consent are required.

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Author contribution

Pan Song, Bo Yang and Qiang Dong: Design the protocol, acquisition and interpretation of data, technical procedures, drafted the initial manuscript, and approved the final manuscript, revise the manuscript, supervised all phases of the study.

Zhufeng Peng, Zhengju Ren: technical procedures, drafted the initial manuscript, revise the manuscript, and approved the final manuscript.

Kun Fang, Luchen Yang, Jing Zhou and Linchuan Wang: drafted the initial manuscript, revise the manuscript, and approved the final manuscript.

Research registry number

1. Name of the registry: Research Registry
2. Unique Identifying number or registration ID: researchregistry5172
3. Hyperlink to the registration (must be publicly accessible): https://www.researchregistry.com/register-now#user-researchregistry/registerresearchdetails/5da131c3cf73960015c78613/Data statement

Guarantor

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Data statement

The raw data for this study was from the SEER database, which is available in public. All detailed data contained in the study can be obtained through the request to contact the corresponding author.

CRediT authorship contribution statement

Pan Song: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization. **Bo Yang:** Conceptualization, Methodology, Software, Validation, Formal analysis, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization. **Zhufeng Peng:** Conceptualization, Methodology, Validation, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization. **Jing Zhou:** Writing - original draft, Writing - review & editing, Visualization. **Zhengju Ren:** Methodology, Software, Validation, Formal analysis, Data curation, Writing - original draft, Writing - review & editing. **Kun Fang:** Methodology, Investigation, Writing - original draft, Writing - review & editing, Visualization. **Luchen Yang:** Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization. **Linchuan Wang:** Writing - original draft, Writing - review & editing, Visualization. **Qiang Dong:** Conceptualization, Methodology, Investigation, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ijsu.2020.02.024.

References

[1] J. Ferlay, I. Soerjomataram, R. Dikshit, et al., Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012, Int. J. Canc. 136 (5) (2015) E359–E386.
[2] L.A. Torre, R.L. Siegel, E.M. Ward, A. Jemal, Global cancer incidence and mortality rates and trends–an update, Cancer Epidemiol. Biomark. Prev. 25 (1) (2016) 16–27.
[3] R.L. Siegel, K.D. Miller, A. Jemal, Cancer statistics, 2019, Ca - Cancer J. Clin. 69 (1) (2019) 7–34.
[4] F. Dong, C. Wang, A.B. Farris, et al., Impact on the clinical outcome of prostate cancer by the 2005 international society of urological pathology modified Gleason grading system, Am. J. Surg. Pathol. 36 (6) (2012) 838–843.
[5] A.J. Armstrong, I.F. Tannock, R. de Wit, et al., The development of risk groups in men with metastatic castration-resistant prostate cancer based on risk factors for PSA decline and survival, Eur. J. Canc. 46 (3) (2010) 517–525.
[6] K. Fizazi, C. Massard, M. Smith, et al., Bone-related parameters are the main prognostic factors for overall survival in men with bone metastases from castration-resistant prostate cancer, Eur. Urol. 68 (1) (2015) 42–50.
[7] A.J. Vickers, D.D. Sjoberg, D. Ulmert, et al., Empirical estimates of prostate cancer overdiagnosis by age and prostate-specific antigen, BMC Med. 12 (1) (2014) 26.
[8] J.A. Halpern, C. Oromendia, J.E. Shoag, et al., Use of digital rectal examination as an adjunct to Prostate Specific Antigen in the detection of clinically significant Prostate Cancer, J. Urol. 199 (4) (2018) 947–953.
[9] A.V. D'Amico, M.H. Chen, S.B. Malkowicz, et al., Lower prostate specific antigen outcome than expected following radical prostatectomy in patients with high grade prostate and a prostatic specific antigen level of 4 ng/ml. Or less, J. Urol. 167 (5) (2002) 2025–2030 discussion 2030-2021.
[10] R.K. Berglund, A.J. Stephenson, A.M. Cronin, et al., Comparison of observed biochemical recurrence-free survival in patients with low PSA values undergoing radical prostatectomy and predictions of preoperative nomogram, Urology 73 (5) (2009) 1098–1103.
[11] B.B. McGuire, B.T. Helfand, S. Loeb, et al., Outcomes in patients with Gleason score 8-10 prostate cancer: relation to preoperative PSA level, BJU Int. 109 (12) (2012) 1764–1769.
[12] B.A. Mahal, A.A. Aizer, J.A. Efstathiou, P.L. Nguyen, Association of very low prostate-specific antigen levels with increased cancer-specific death in men with high-grade prostate cancer, Cancer 122 (1) (2016) 78–83.
[13] P.M. Pierorazio, P.C. Walsh, A.W. Partin, J.I. Epstein, Prognostic Gleason grade grouping: data based on the modified Gleason scoring system, BJU Int. 111 (5) (2013) 753–760.
[14] J.I. Epstein, L. Egevad, M.B. Amin, et al., The 2014 international society of urological pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma: definition of grading patterns and proposal for a new grading system, Am. J. Surg. Pathol. 40 (2) (2016) 244–252.
[15] J.I. Epstein, M.J. Zelefsky, D.D. Sjoberg, et al., A contemporary prostate cancer grading system: a validated alternative to the Gleason score, Eur. Urol. 69 (3) (2016) 428–435.
[16] J.J. Safdieh, D. Schwartz, J.P. Weiner, E. Nwokedi, D. Schreiber, The need for more aggressive therapy for men with Gleason 9-10 disease compared to Gleason < /=8 high-risk prostate cancer, Tumori 102 (2) (2016) 168–173.
[17] R. Agha, A. Abdall-Razak, E. Crossley, N. Dowlut, C. Iosifidis, G. Mathewfor the STROCSS Group, The STROCSS 2019 guideline: strengthening the reporting of cohort studies in surgery, Int. J. Surg. 72 (2019) 156–165.
[18] M.K. Buyyounouski, P.L. Choyke, J.K. McKenney, et al., Prostate cancer - major changes in the American Joint Committee on Cancer eighth edition cancer staging manual, Ca - Cancer J. Clin. 67 (3) (2017) 245–253.
[19] A.D. Falchook, N.E. Martin, R. Basak, et al., Stage at presentation and survival outcomes of patients with Gleason 8-10 prostate cancer and low prostate-specific antigen, Urol. Oncol. 34 (3) (2016) 119 e119-126.
[20] B.A. Mahal, D.D. Yang, N.Q. Wang, et al., Clinical and genomic characterization of low-prostate-specific antigen, high-grade prostate cancer, Eur. Urol. 74 (2) (2018) 146–154.
[21] T. Gilligan, Decision making in a data-poor environment: management of brain metastases from testicular and extragonadal germ cell tumors, J. Clin. Oncol. 34 (4) (2016) 303–306.
[22] M. Alshalalfa, M. Santiago-Jimenez, N. Erho, et al., Relationships between an androgen receptor output signature (ARoS), AR expression, and poor prostate cancer prognosis in RP tissues, Am. Soc. Clin. Oncol. 35 (6 Suppl) (2018) 38.