## ORIGINAL ARTICLE

# Efficacy of radical prostatectomy on prostate cancer patients and analysis of risk factors for biochemical recurrence after radical prostatectomy

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## Summary

**Purpose:** To investigate the efficacy of radical prostatectomy on prostate cancer (PC) patients and analyze the risk factors for biochemical recurrence after radical prostatectomy.

**Methods:** A total of 168 PC patients aged 38-75 years admitted to and treated in our hospital from January 2017 to January 2018 underwent radical prostatectomy. Differences in the levels of prostate-specific antigen (PSA) and tumor markers in the patients before and after treatment were compared. The patients were divided into recurrence group (group 1) and non-recurrence group (group 2) according to postoperative recurrence. The risk factors for biochemical recurrence were analyzed by comparing the PC stage, body mass index (BMI), Gleason score and the positive resection margin between the two groups of patients.

**Results:** There was a significant difference in the expression level of serum PSA in PC patients before and after treatment, and the PSA level was decreased remarkably after treatment, which was lower than that before treatment (p<0.05). The expression levels of tumor markers, neuron-specific enolases (NSE), carbohydrate antigen 19-9 (CA19-9) and lactate dehydrogenase (LDH) in PC patients after treatment were decreased and were obviously lower than those before treatment (p<0.05). The proportion of patients with tumors in stage T3 was the largest in group 1, and the proportion of patients

with tumors in stage T1 was the largest in group 2. Through comparison, it was found that the disease condition of the patients in group 2 was better than that in group 1 (p<0.05). The results showed that the proportion of patients with BMI ≥30 in group 1 was the largest, while that of patients with BMI <30 in group 2 was the largest, displaying a statistically significant difference (p<0.05). There were 29 patients with Gleason score >8 points in group 1 and 34 patients with Gleason score ≤6 points in group 2, showing a statistically significant difference (p<0.05). The number of patients with positive resection margin ≥60% in group 1 was larger than that in group 2 (p<0.05). It was also discovered from the multivariate analysis that Gleason score, cancer stage, BMI and resection margin were all the risk factors for biochemical recurrence of patients after radical prostatectomy (p<0.05).

**Conclusions:** Radical prostatectomy brings good efficacy in the treatment of the disease, which can evidently reduce the PSA and tumor marker levels in the patients. In the meantime, the positive resection margin, BMI, Gleason score and cancer stage are found to be related to the biochemical recurrence of PC patients.

**Key words:** biochemical recurrence, radical prostatectomy, risk factor analysis, prostate cancer

## Introduction

Prostate cancer (PC) is a relatively common malignant tumor in males [1-4]. As no specific symptoms appear in the early stage of disease, patients have generally been in the advanced stage of cancer at the time of diagnosis [5-7]. Studies in China and abroad have revealed that the incidence rate of PC is highest among malignant tumors in males in European and American countries, and the incidence

rate of PC in China is far lower than that in European countries [8]. However, with the gradually aging population, changes in the diet structure and progress in disease diagnosis in recent years, the incidence rate shows an obvious uptrend [9]. The incidence rate of PC is gradually increased world over [10]. PC in the early stage has no obvious clinical manifestation. With the development of PC, the disease is gradually manifested as incomplete urination and hematuria [11]. PC is triggered by many causes and in clinical research is shown to be related to genetic factors, sexual life and other factors [12]. Currently, PC can be clinically diagnosed through prostate-specific antigen (PSA) level, related instrument examination and rectal examination [13]. Due to the high metastasis rate and proneness to transferring cancer cells to other parts of the body, isotope scanning of cancer cells is also required during the examination and diagnosis of PC [14]. In contemporary medicine, common treatment methods for PC include particle implantation and radical resection, among which only surgical treatment can fundamentally treat the disease, so radical prostatectomy is widely applied in the clinic [15]. During radical prostatectomy, prostate and part of the spermaducts and ejaculatory ducts around them are excised, pelvic lymph nodes metastases are observed and removed [16].

This study, therefore, explores the efficacy of radical prostatectomy in the treatment of PC patients and analyzes the risk factors for the patient biochemical recurrence after radical prostatectomy through analyzing inflammatory cytokines, PC stage, body weight index (BMI), Gleason score, positive resection margin of PC patients as well as univariate and multivariate analyses.

## Methods

### General data

A total of 168 PC patients aged 38-75 years admitted to and treated in our hospital from January 2017 to January 2018 were subjected to radical prostatectomy. Inclusion criteria: 1) patients definitely diagnosed with PC through preoperative biopsy; 2) patients whose pathological stage was T1-T3; 3) patients with no metastasis in other parts of the body; 4) patients without other cancers; and 5) patients who and whose family members signed the informed consent. Exclusion criteria: 1) patients unwilling to participate in this study; 2) patients receiving treatment before operation; or 3) patients whose clinical data were incomplete. This study was approved by the Ethics Committee of Jilin Province Cancer Hospital. Signed informed consents were obtained from all participants before the study entry.

### Biochemical recurrence criteria

Criteria for biochemical recurrence of PC: The biochemical recurrence of PC were determined if the serum PSA level of patients with postoperative recurrence was relatively high or gradually increased in a stepwise manner, the postoperative PSA was ≥0.4 ng/mL, or the PSA exceeded the minimum value of above 0.2 ng/mL.

### Detection of tumor markers and PSA

A total of 5 mL of fasting venous blood was extracted from the elbow of all patients in the early morning at admission and after treatment, respectively. The expression levels of serum neuron-specific enolase (NSE), carbohydrate antigen 19-9 (CA19-9) and lactate dehydrogenase (LDH) were detected by ROCHE Elecsys 2010 automatic electrochemiluminescence immunoassay analyzer. All specimens were detected within 2 h in strict accordance with the requirements of standard operation procedure (SOP) documents, and the results were recorded. Five mL of patient peripheral blood was taken before and after operation, respectively, and the concentration of serum PSA was detected.

### Tumor node metastasis (TNM) stage

Staging was performed according to the pathological examination results of PC patients. Stage T1: The prostate mass was only present in the prostate and did not metastasize to other parts, with a relatively low malignancy. Stage T2: The prostate mass was present in the prostate but could be clearly detected by rectal fingerprinting and CT. Stage T3: The prostate mass was not present in the prostate but had gradually invaded the prostate capsule and even had created lymph node metastasis.

### Gleason score

Gleason score is a commonly used histological grading method for PC in the clinic. With Gleason score ≤6 points, PC is clinically manifested as infiltrative growth of small glands or acini in the prostate or prostate peripheral area, which is relatively common (low risk). With Gleason score =7 points, PC is clinically manifested as irregular, back-to-back dense and large glands, non-fusion of glands in nodules and poor tumor differentiation (moderate risk). With Gleason score >8 points, PC is clinically manifested as concurrent large glands, with a clear boundary and in close alignment (high risk).

### Positive resection margin

Positive postoperative resection margin indicated that cancer cells still existed in patients. The higher the positive rate of postoperative resection margin, the greater the recurrence probability.

### Observational indicators

1) PSA and tumor markers in the patient serum before and after treatment were measured. 2) The relationship between the PC stage and biochemical recurrence of patients in group 1 and group 2 was observed and recorded. 3) The BMI of patients in group 1 and group 2 was measured, and its correlation with biochemical recurrence was determined. 4) The association between Gleason score of patients in group 1 and group 2 and

biochemical recurrence was observed and recorded. 5) Univariate analysis was conducted clinically. 6) The positive rate of resection margin of patients in group 1 and group 2 was recorded. 7) Multivariate analysis was carried out for the postoperative biochemical recurrence of patients.

*Statistics*

SPSS 22.0 (IBM, Armonk, NY, USA) was used for statistical analyses. Independent samples *t*-test was employed to observe the differences in PC stage, BMI, positive resection margin and Gleason score of patients between group 1 and group 2. Data were expressed as mean±SD and p<0.05 suggested statistically significant difference.

# Results

*Comparison of PSA of PC patients before and after treatment*

The results revealed a significant difference in the expression level of serum PSA in PC patients before and after treatment, and the PSA level was decreased remarkably after treatment, and was lower than that before treatment (p<0.05) (Table 1).

*Tumor markers of PC patients before and after treatment*

It was found that the expression levels of tumor markers NSE, CA19-9 and LDH in PC patients after treatment were decreased and were obviously lower than those after treatment (p<0.05) (Table 2).

*Analysis of risk factors for postoperative biochemical recurrence of PC patients*

*Comparison of the patient PC stage between group 1 and group 2*

Among 168 PC patients, 69 (group 1) suffered from recurrence within 5 years after operation, and 99 (group 2) did not develop recurrence. It was discovered that the proportion of T3 stage patients was largest in group 1, and the proportion of patients with T1 stage was largest in group 2.

**Table 1.** Comparison of the PSA of prostate cancer patients before and after treatment (mean±SD)

| Time | PSA | t | p |
|---|---|---|---|
| Before treatment | 6.14±0.46 | 7.358 | <0.001 |
| After treatment | 1.02±0.35 | | |

**Table 2.** Tumor markers of prostate cancer patients before and after treatment (mean±SD)

| Time | NSE (ng/mL) | CA19-9 (U/mL) | LDH (IU/mL) |
|---|---|---|---|
| Before treatment | 13.45±5.89 | 21.98±4.98 | 198.34±25.07 |
| After treatment | 10.95±5.24 | 14.06±4.58 | 146.84±25.86 |
| t | 2.634 | 9.724 | 11.886 |
| p | 0.009 | <0.001 | <0.001 |

**Table 3.** Comparison of the prostate cancer stage of patients between group 1 and group 2

| Group | n | T1 | T2 | T3 | $x^2$ | p |
|---|---|---|---|---|---|---|
| Group 1, n (%) | 69 | 18 (26.08) | 12 (17.39) | 39 (56.52) | 40.124 | <0.001 |
| Group 2, n (%) | 99 | 54 (54.54)* | 34 (34.34)* | 11 (11.11)* | | |

*p<0.05 *vs.* group 1

**Table 4.** Comparison of the BMI of patients between group 1 and group 2

| Group | n | BMI (kg/m²) | | | $x^2$ | p |
|---|---|---|---|---|---|---|
| | | <25 | 25-30 | ≤30 | | |
| Group 1, n (%) | 69 | 17 (24.63) | 21 (30.43) | 31 (44.92) | 28.778 | <0.001 |
| Group 2, n (%) | 99 | 53 (53.53)* | 36 (36.36)* | 10 (10.10)* | | |

*p<0.05 *vs.* group 1

**Table 5.** Comparison of the Gleason score of patients between group 1 and group 2 [(n) %]

| Group | n | ≤6 points | 7 points | >8 points | $x^2$ | p |
|---|---|---|---|---|---|---|
| Group 1, n (%) | 69 | 16 (23.18) | 24 (34.78) | 29 (42.02) | 16.605 | <0.001 |
| Group 2, n (%) | 99 | 34 (34.34)* | 51 (51.51)* | 14 (14.14)* | | |

**Table 6.** Comparison of the positive resection margin between group 1 and group 2

| Group | n | ≤30% | 30-60% | ≥60% | $x^2$ | p |
|---|---|---|---|---|---|---|
| Group 1, n (%) | 69 | 22 (31.88) | 17 (24.63) | 30 (43.47) | 11.366 | 0.003* |
| Group 2, n (%) | 99 | 29 (29.29)* | 48 (48.48)* | 23 (23.23)* | | |

*p<0.05 *vs.* group 1

**Table 7.** Multivariate analysis

| Factor | OR | p | 95% CI |
|---|---|---|---|
| Stage | 3.358 | 0.034 | 1.175-9.631 |
| BMI | 1.047 | 0.026 | 1.761-3.245 |
| Gleason score | 2.345 | 0.038 | 1.473-6.319 |
| Resection margin | 2.469 | 0.017 | 1.831-2.465 |

Comparison showed that the disease condition of the patients in group 2 was better than in group 1 (p<0.05) (Table 3).

*Comparison of BMI of patients between group 1 and group 2*

The results showed that the proportion of patients with BMI ≥30 in group 1 was largest, while that of patients with BMI <30 in group 2 was largest, displaying a statistically significant difference (p<0.05) (Table 4).

*Comparison of Gleason score of patients between group 1 and group 2*

There were 29 patients with Gleason score >8 points in group 1 and 34 with Gleason score ≤6 points in group 2, showing a statistically significant difference (p<0.05) (Table 5).

*Comparison of positive resection margin of patients between group 1 and group 2*

The number of patients with positive resection margin ≥60% in group 1 was larger than that in group 2 (p<0.05) (Table 6).

*Univariate and multivariate analysis*

Univariate and multivariate analysis demonstrated that the Gleason score, cancer stage, BMI and resection margin were all independent risk factors for biochemical recurrence after radical prostatectomy (p<0.05) (Table 7).

## Discussion

PC is a tumor that severely threatens the health of males [17]. When the tumor grows and develops too fast, causing lower urinary tract occlusion or irritation symptoms, the patients start to attach importance to the disease condition. When definitely diagnosed, the cancer has been in middle or advanced stage, with an increased treatment difficulty [18]. PC growth depends on androgen, so endocrine therapy for PC patients is an effective and conservative method. Drugs can suppress androgen secretion of patients, thus hindering the proliferation of cancer cells [19]. However, as the treatment time of the disease is prolonged, cancer may progress to androgen-independent PC, seriously affecting the prognosis of patients. Therefore, surgical treatment is the best treatment method. Currently, radical prostatectomy is considered to be one of the preferred treatment methods for PC in clinical practice [20].

The levels of PSA and tumor markers in serum of PC patients before and after treatment were significantly different. They were notably decreased

after treatment and lower than those before treatment (p<0.05). Studies have verified that radical prostatectomy produces more remarkable clinical efficacy with better prognosis compared with conventional treatment [15]. Radical prostatectomy has advantages such as minimal surgical trauma, little bleeding, rapid postoperative recovery and small incision scar which can improve the patient quality of life and reduce complications after treatment, so it is of great significance to PC [17]. Postoperative follow-up results showed that the patients in group 2 were sicker than in group 1. It was also found that the proportion of patients with BMI ≥30 in group 1 was the largest, while that of patients with BMI <30 in group 2 was largest, displaying a statistically significant difference. It could be concluded from Table 3 that the cases of high-risk disease in group 1 were more than those in group 2. Moreover, the number of patients with a higher positive percentage of resection margins in group 1 was relatively large, while that in group 2 was relatively low, showing a statistically significant difference. Multivariate analysis results demonstrated that the Gleason score, cancer stage, BMI and resection margin were all independent risk factors for biochemical recurrence after radical prostatectomy. A study of Dang et al [21] showed that the positive resection margin of the patients selected in the experiment had no significant relationship with the postoperative biochemical recurrence rate and survival. However, after excluding the interference of other irrelevant factors, multivariate analysis indicates that the Gleason score, positive resection margin and clinical stage are all independent relevant factors for postoperative recurrence of PC patients.

It is reported in a study that obese patients (BMI ≥30 kg/m$^2$) have a higher risk coefficient than normal people (BMI <25 kg/m$^2$), which increases the possibility of biochemical recurrence after radical prostatectomy [1]. Dall'Era et al [22] conducted a multivariate analysis for accurate clinical staging of PC in patients, the results of which had significant correlations with the time of biochemical recurrence. In another study it has been found that cancer stage is the main risk factor for recurrence of patients after radical prostatectomy [23]. Clinical experimental studies have stressed that positive resection margin is an independent factor for biochemical recurrence after operation, but the incidence rate of biochemical recurrence could be reduced through regular postoperative adjuvant therapy, such as chemotherapy. At present, the related factors that lead to biochemical recurrence of PC are rarely researched in China. The experimental results in this study play crucial roles in the clinical treatment and the improvement of the cure rate of PC in patients [24]. Clinically, the study of independent factors related to biochemical recurrence of PC patients after operation can effectively strengthen the postoperative recovery of patients and provide a basis for the medical staff to treat recurrence [25].

## Conclusions

Radical prostatectomy has good efficacy in the treatment of this disease, which can evidently reduce the PSA and tumor marker levels in the patients. In the meantime, the positive resection margin, BMI, Gleason score and cancer stage are found to be related to the postoperative biochemical recurrence of PC patients..

## Conflict of interests

The authors declare no conflict of interests.

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