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Prevalence and risk factors for incidental prostate cancer in patients after transurethral resection of the prostate with negative results on prostate biopsy: A retrospective study

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Purpose: This study aimed to explore the prevalence and predictors of incidental prostate cancer (IPC) after transurethral resection of the prostate (TURP) with negative results on transperineal magnetic resonance imaging (MRI)/transrectal ultrasonography (TRUS) fusion prostate biopsy or TRUS-guided prostate biopsy.

Materials and Methods: Data of 253 patients who underwent TURP with a preliminary diagnosis of benign prostatic hyperplasia (BPH) were evaluated. The prevalence of IPC was calculated. Univariate and multivariate logistic regression analyses were conducted to explore independent predictive factors of IPC.

Results: A total of 253 patients were included. IPC was diagnosed in 12 patients (4.7%). The mean age of the patients and the mean prostate volume were 69.8±7.07 years and 89.3±49.29 mL, respectively. The prevalence of IPC was higher in the TRUS guided prostate biopsy group than in the transperineal MRI/TRUS fusion prostate biopsy group (11 of 203 [5.4%] vs. 1 of 50 [2.0%], p=0.47), but the difference was not statistically significant. Our results indicated that older age (≥70 y) (odds ratio [OR], 1.14; 95% confidence interval [CI], 1.02–1.27; p=0.025) and smaller prostate volume (OR, 0.97; 95% CI, 0.938–0.998; p=0.039) were associated with an increased incidence of IPC after TURP.

Conclusions: Our findings indicate that the prevalence of IPC may be higher among patients who undergo transrectal prostate biopsy before TURP than among those who undergo transperineal MRI/TRUS fusion prostate biopsy. Older age and smaller prostate volume were independent predictors of increasing the risk for IPC after TURP.

Keywords: Biopsy; Prevalence; Prostatic neoplasms; Risk factors; Transurethral resection of prostate

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INTRODUCTION

Prostate cancer is one of the leading causes of cancer-related death among the aging male population, and its incidence rate varies globally depending on diagnostic advancements [1,2]. Incidental prostate cancer (IPC) is the diagnosis of prostate cancer with histopathologic examination of resected prostate tissue previously considered to be benign prostatic hyperplasia (BPH) [3,4]. Surgical therapy is still the most effective treatment for patients diagnosed with BPH when medical treatment fails to resolve symptoms of lower urinary tract obstruction or in the presence of absolute indications to relieve the obstruction [5]. For many years, transurethral resection of the prostate (TURP) was a standard surgical treatment for symptomatic BPH [6]. Moreover, prostate-specific antigen (PSA), digital rectal examination (DRE), and magnetic resonance imaging (MRI) were routinely evaluated before TURP to exclude prostate cancer. Transrectal ultrasonography-guided (TRUS-guided) prostate biopsy is the gold standard to exclude prostate cancer in high-risk patients and has been widely used. Interestingly, recent research indicated more advantages, including good tolerance and higher positive rate, of transperineal MRI/TRUS fusion prostate biopsy [7-10]. However, negative results may be observed in the histopathologic examination when the prostate biopsy is performed with fusion or TRUS guidance, even though PSA levels are high or the MRI findings are positive.

Overall, IPC is still a challenge for physicians and patients with high expectations. In our study, all patients had elevated PSA levels or suspicious DRE findings. Thus, they underwent prostate biopsy to rule out any carcinoma before any further treatment. Hence, we conducted a retrospective study to investigate the prevalence and potential risk factors for IPC in patients who were diagnosed with suspected BPH after TURP and had negative results for transperineal MRI/TRUS fusion prostate biopsy or TRUS-guided prostate biopsy.

MATERIALS AND METHODS

1. Population and study design

The study protocol was approved by the Institutional Review Board of the Second Affiliated Hospital of Guangzhou University of Chinese Medicine (approval number: ZE2021–155–01). The written informed consent was waived by the board.

We consulted a retrospective clinical database of 253 patients who had undergone prostate biopsy because of elevated PSA levels, suspicious DRE findings, or a Prostate Imaging Reporting and Data System version 2.0 (PI-RADS-v2) score of 3 or higher in the peripheral zone between January 2016 and May 2021. All patients undergoing TURP for symptomatic bladder outlet obstruction after previous negative prostate biopsy results (transperineal MRI/TRUS fusion prostate biopsy or TRUS-guided prostate biopsy) were identified in our study. Moreover, 217 patients who underwent prostate biopsy had pre-interventional multiparametric MRI examination of the prostate at 3T and lesions were scored according to PI-RADS-v2 [11]. We did not exclude patients with a previous history of medication for lower urinary tract symptoms, because the baseline PSA levels of all patients were not statistically different. Moreover, each targeted lesion in the peripheral zone was previously classified by radiologists according to the MRI PI-RADS score and grouped according to level of suspicion as probably benign (PI-RADS 1–2), indeterminate (PI-RADS 3), or probably malignant (PI-RADS 4–5). Furthermore, systematic biopsies were performed in all patients, and targeted biopsies from the regions of interest were obtained in addition to the systematic cores in patients with suspicious MRI findings [12]. Generally, the 12-core needle biopsies and TURP were performed by an experienced urologist (Zhaohui Wang). Moreover, the specimens from biopsy and TURP were analyzed by professional pathologists (Shusheng Wang) at our hospital, and the findings of IPC were recorded rigorously. Patients previously diagnosed with prostate cancer were excluded from the study. Finally, potential risk factors were collected from each patient: age, DRE findings, body mass index (BMI), total and free/total PSA value, prostate volume (PV) at MRI or TRUS examination, biopsy methods, histopathologic findings of TURP, and TNM stage.

2. Biopsy procedure

For transperineal MRI/TRUS fusion prostate biopsy, patients who underwent general anesthesia were placed in the lithotomy position with well-disinfected perineum preparation. The scrotum was lifted from the perineum using microporous tape. The biplanar TRUS probe was clamped on a stepper and then pushed into the rectum. The full grid of the biopsy perineum was set on the stepper by the perineum. The grid guides the operator to ensure accurate positioning and targeting of the lesion. The prostate edges were contoured and the images of the MRI were superimposed on the TRUS images. Then, the suspicious lesions could be easily identified and defined on the three-dimensional prostate shape. Finally, the 12-core targeted and random needle biopsies were performed. For TRUS-guided prostate biopsy,

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the biopsy was performed with the patients under general anesthesia, positioned in the left lateral decubitus position. All patients received the same antibiotic prophylaxis and a povidone-iodine aqueous solution enema before the procedure. Sampling was performed with an 18-gauge Tru-Cut needle powered by an automatic spring-loaded disposable biopsy gun after images of the prostate were obtained and PV measured. Subsequently, 12 core biopsies were taken: 6 cores from each side of the prostate at the base, mid, apex, upper lateral, and lower lateral regions. None of the patients underwent repeat biopsies in our study.

3. Statistical analysis

All eligible patients were divided into two groups, Non-IPC (n=241) and IPC (n=12) according to the histopathologic findings of TURP. Means with standard deviations (SDs) of continuous variables with normally or nonnormally distributions were reported. Moreover, frequencies with associated proportions (%) were used for categorical variables. A univariate and multivariate logistic regression model was applied to investigate any potential risk factors (age, PSA value, PV, BMI, biopsy methods, and MRI findings) that could be associated with IPC after TURP in patients with suspected BPH. Data were analyzed by using Student's t-test and Mann–Whitney U-test for continuous variables, whereas the chi-square test was used for categorical variables. Analysis was performed on SPSS version 22 (IBM Corp., Armonk, NY, USA) with a two-sided significance level set at $p<0.05$.

RESULTS

1. Patient characteristics

The basic characteristics of all patients are described in Table 1. In summary, 253 patients with symptomatic bladder outlet obstruction who underwent TURP after preoperative negative prostate biopsy findings were included in the present study. Specifically, 50 patients were identified after previous negative findings on transperineal MRI/TRUS fusion prostate biopsy and 203 were identified after TRUS-guided prostate biopsy. The patients' mean±SD age was 69.8±7.07 years. The mean total PSA value was 17.4±15.13 ng/mL, the mean PV was 89.3±49.29 mL, and the mean BMI was 23.0±3.03 kg/m^2. Suspicious DRE findings were recorded in 43 patients, whereas negative findings were obtained in 210 patients (p=0.44). Furthermore, 72 of 217 patients had no suspicious findings on MRI examination and 145 patients had suspicious MRI findings (p=0.50), of which 70 patients were assigned a PI-RADS score of 3, 55 a PI-RADS score of 4, and 25 a PI-RADS score of 5.

2. Prevalence of incidental prostate cancer

In general, IPC was detected in 12 of 253 (4.7%) patients (Table 2). Of the 12 patients with IPC, 9 had stage T1a tumors and 3 had T1b. Eight patients with IPC in TURP specimens had a Gleason score of 3+3=6, and the four other patients with IPC had a Gleason score of 7. In detail, the prevalence of IPC was higher in the TRUS-guided prostate biopsy group than in the transperineal MRI/TRUS fusion prostate biopsy group (11 of 203 [5.4%] vs. 1 of 50 [2.0%], p=0.47), but the difference was not significant. Moreover, the prevalence of IPC was higher in patients with suspicious findings on the preoperative MRI examination than in those without suspicious MRI findings (8 of 145 [5.5%] vs. 2 of 72 [2.8%], p=0.50). In the same manner, IPC after TURP was detected more often in the suspicious DRE group than in the not suspicious DRE group (3 of 43 [7.0%] vs. 9 of 210 [4.3%], p=0.44).

3. Risk factors for incidental prostate cancer

To investigate the potential risk factors for IPC detection, we conducted logistic regression analyses using univariate and multivariate methods. In the univariate logistic regression, only age was significantly associated with IPC after TURP (odds ratio [OR], 1.11; 95% confidence interval [CI], 1.02–1.21; p=0.023), whereas no effect of other predictors

Table 1. Basic characteristics of all patients

Variable	Total (n=253)	BPH (n=241)	IPC (n=12; T1a=9, T1b=3)	p-value
Age (y)	69.8±7.07	69.6±7.06	74.4±6.10	0.02
BMI (kg/m^2)	23.0±3.03	23.0±3.06	23.5±2.28	0.55
Total PSA value (ng/mL)	17.4±15.13	17.1±14.69	22.8±22.34	0.21
Free/total PSA value (ng/mL)	0.19±0.08	0.19±0.08	0.15±0.05	0.16
PV (mL)	89.3±49.29	90.4±50.02	67.7±23.28	0.12

Values are presented as mean±standard deviation.
BPH, benign prostatic hyperplasia; IPC, incidental prostate cancer; BMI, body mass index; PSA, prostate-specific antigen; PV, prostate volume.
A p-value of <0.05 was considered statistically significant.

Table 2. Prevalence of IPC after TURP

Variable	Total	BPH	IPC	p-value
Biopsy methods				0.47
Transperineal MRI/TRUS fusion prostate biopsy	50	49	1	
TRUS-guided prostate biopsy	203	192	11	
MRI findings				0.50
Suspicious	145	137	8	
Non-suspicious	72	70	2	
DRE findings				0.44
Suspicious	43	40	3	
Non-suspicious	210	201	9	

Values are presented as number only.
IPC, incidental prostate cancer; TURP, transurethral resection of the prostate; BPH, benign prostatic hyperplasia; MRI, magnetic resonance imaging; TRUS, transrectal ultrasonography; DRE, digital rectal examination.
A p-value of <0.05 was considered statistically significant.

Table 3. Univariate and multivariate logistic regression analyses of predictors of IPC after TURP

Variable	TURP			
	Univariate		Multivariate	
	p-value	OR (95% CI)	p-value	OR (95% CI)
Age	0.023	1.11 (1.02–1.21)	0.025	1.14 (1.02–1.27)
BMI	0.551	1.06 (0.88–1.27)	-	-
Total PSA value	0.217	1.02 (0.99–1.05)	0.138	1.03 (0.99–1.06)
Free/total PSA value	0.159	0.002 (0.00–11.76)	-	-
PV	0.087	0.98 (0.96–1.00)	0.039	0.97 (0.938–0.998)
Biopsy methods	0.888	1.11 (0.26–4.86)	-	-
MRI findings	0.374	2.04 (0.42–9.88)	0.637	1.51 (0.27–8.46)

IPC, incidental prostate cancer; TURP, transurethral resection of the prostate; OR, odds ratio; CI, confidence interval; BMI, body mass index; PSA, prostate-specific antigen; PV, prostate volume; MRI, magnetic resonance imaging; -, not available.
A p-value of <0.05 was considered statistically significant.

was observed. Interestingly, the present study indicated that older age (≥70 y) was a significant independent predictive factor with an OR of 1.14 (95% CI, 1.02–1.27; p=0.025) for IPC after TURP. In addition, smaller PV was associated with increased incidence of IPC (OR, 0.97; 95% CI, 0.938–0.998; p=0.039) after TURP in patients diagnosed with BPH. However, PSA value, BMI, biopsy methods, and MRI findings did not reach statistical significance in the multivariate analysis (Table 3).

DISCUSSION

This retrospective clinical study aimed to explore the prevalence and predictors of IPC after TURP in patients who underwent preoperative biopsy because of abnormal PSA levels or suspicious DRE and MRI findings. After screening all the TURP cases in the electronic databases of our hospital, we identified 253 patients who met the inclusion criteria. We recorded 12 findings of IPC in the TURP specimens, of which 11 were detected in the TRUS-guided prostate biopsy group and 1 in the transperineal MRI/TRUS fusion prostate biopsy group. Age and PV were independent predictors of IPC in the multivariate logistic regression analysis.

Our IPC detection rate was 4.7% after TURP, consistent with other previously published data, in which detection rates for IPC ranged from 1.4% to 17% [13-16]. Among the patients diagnosed with IPC, the majority of cases were assigned a Gleason score of 6, which represents low-risk cancer. In general, these populations with a mean age of 69.8 years at our center can be managed with active surveillance because of its good long-term survival rates. Moreover, active surveillance seems to be an adequate choice for the majority of our patients with IPC. For instance, Elkoushy et al. [17] demonstrated that the overall survival rate of patients with IPC was 72.8% at 5 years and 63.5% at 10 years by means of active surveillance. However, radiotherapy is also safe for patients with a history of TURP and is related to an acceptable

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quality of life. On the other hand, undergoing radical prostatectomy is technically challenging for this population [18].

Although no significant effect of biopsy was observed, the prevalence of IPC was higher in the TRUS-guided prostate biopsy group than in the transperineal MRI/TRUS fusion prostate biopsy group. Therefore, our study strongly revealed the refusal to use TURP as a diagnostic tool and emphasizes the importance of MRI fusion target biopsy, especially for patients who are suspected of having tumors after the initial biopsy [19]. For example, Radtke et al. [20] concluded that MRI fusion targeted biopsy has a higher detection rate of prostate cancer (97%) than any single biopsy method. Moreover, Siddiqui et al. [8] reported a similar result that the detection rate of prostate cancer was higher in the MRI/TRUS fusion biopsy group than in the standard TRUS-guided biopsy group.

To explore the predictors of IPC, we conducted a logistic regression analysis and demonstrated that older age and small PV were independent predictive factors of IPC after TURP, consistent with previous publications [16,21] and confirming the representative value of our patients. However, no significant association was observed for PSA values in the multivariate regression analysis, in contrast with other studies [22,23]. The small sample size might have contributed to this significant difference. Future studies are still needed to confirm our results.

This study has some limitations that should be considered. First, our study was based on retrospective data from 253 patients in a single center and lacked power owing to the limited sample size, which may affect the statistical power of the results. Hence, future prospective multicenter studies with larger sample sizes should be implemented to explore comprehensive and valuable predictive factors of IPC. Second, although approximately 60% of the prostate gland was removed, TURP specimens represent only a part of the whole prostate. Third, other specific measurable parameters such as TRUS transitional zone volume, intravesical prostatic protrusion, voiding symptoms, overall volume of cancer, location of cancer, and resected volume after TURP could not be further investigated by use of the current database of our hospital, because these variables were not completely captured in our database. Hence, we will continue to improve and supplement the hospital's database to make it more comprehensive and we will carry out high-quality prospective clinical studies in the future. Finally, we were unable to investigate the effect of the different proportions of IPC on long-term oncologic outcomes because of a lack of follow-up data.

CONCLUSIONS

Our study strongly indicates that the prevalence of IPC may be higher among patients who underwent transrectal prostate biopsy before TURP than among those who underwent transperineal MRI/TRUS fusion prostate biopsy. Older age and smaller PV were associated with increased risk of IPC after TURP. Further prospective randomized trials and high-quality studies are needed to explore other predictors and determine the optimal treatment for patients diagnosed with IPC.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS' CONTRIBUTIONS

Research conception and design: Zhenlang Guo and Junwei He. Data acquisition: Lijuan Huang. Statistical analysis: Jiadong Cao and Zunguang Bai. Data analysis and interpretation: Shusheng Wang, Songtao Xiang, Chiming Gu, and Zhaohui Wang. Drafting of the manuscript: Zhenlang Guo. Critical revision of the manuscript: Junwei He. Approval of the final manuscript: Zhaohui Wang and Jun Pan.

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