

A SINGLE CENTRE STUDY ON PREVALENCE AND PREDICTIVE FACTORS FOR INCIDENTAL PROSTATE CANCER FOLLOWING TRANSURETHRAL RESECTION OF PROSTATE

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Abstract

Background: Many prostate cancers remain undiagnosed until benign prostatic hyperplasia (BPH) surgeries are performed. Transurethral resection of the prostate (TURP) renders subsequent radical prostatectomy technically challenging. Therefore, it is advantageous to identify high-risk patients and consider further investigations prior to BPH surgery.

Objectives: This study aims to report the prevalence of incidental prostate cancer (IPC) following TURP at Penang General Hospital and to develop predictive factors for IPC.

Methods: This retrospective observational study reviewed patients who underwent TURP for presumed BPH over the past five years. Clinicopathological variables studied included patient age, serum prostate-specific antigen (PSA) level, prostate volume, PSA density, resected prostatic tissue weight, and histopathological assessment of the resected specimen.

Results: A total of 220 patients underwent TURP for presumed BPH from April 2018 to April 2023. Thirteen patients (5.9%) had IPC, including seven patients with T1a disease and six patients with T1b disease. The most common cancer detected was ISUP grade group 1 (n = 6), followed by grade groups 2 (n = 4), 3 (n = 2), and 4 (n = 1). Stepwise binary logistic regression analysis revealed that a PSA density of >0.15 ng/ml² (p = 0.001) and low resected prostatic tissue weight (p = 0.024) correlated with an increased prevalence of IPC, with odds ratios of 26.1 and 0.9, respectively.

Conclusions: The prevalence of IPC at Penang General Hospital is 5.9%. A PSA density of >0.15 ng/ml² and low resected prostate volume are associated with a higher risk of IPC following TURP. Patients at risk should be offered further investigations, such as mpMRI of the prostate and/or repeat prostatic needle biopsy prior to BPH surgeries. Additionally, pathologists should consider examining the specimens of at-risk patients in their entirety rather than using standard handling procedures.

Keywords: Incidental Prostate Cancer, Risk Factors, PSA, TURP, BPH Surgery

Introduction

Incidental prostate cancers (IPC) are tumors diagnosed unintentionally after surgery for benign prostatic hyperplasia (BPH), incidentally found after radical cystoprostatectomy in patients with bladder cancer, or detected as latent tumors in autopsies (1-3). Most patients with BPH are screened for prostate cancer before BPH surgery, as the detection of incidental prostate cancer would alter the treatment course. Despite the availability of current screening strategies, some prostate cancers remain undiagnosed until BPH surgeries are performed. This study is the first to report on the prevalence of IPC in Malaysia and aims to develop predictive factors for IPC following TURP.

Patients and Methods

This study has been reviewed and approved by the Medical Research Ethics Committee (MREC) Malaysia and registered with the National Medical Research Registry (NMRR ID: NMRR ID-23-01145-JDO). It is a retrospective observational study reviewing patients who underwent TURP for presumed BPH over the past five years, from April 2018 to April 2023, at Penang General Hospital, Malaysia. All TURP procedures were performed using bipolar resection under continuous normal saline irrigation. The indications for TURP included recurrent urinary retention, recurrent urinary tract infection, renal impairment, bladder stones, recurrent haematuria, and failed medical therapy.

At our center, all patients with raised serum prostate-specific antigen (PSA) levels > 4 ng/ml and/or abnormal DRE findings were offered prostatic needle biopsy before proceeding with TURP. Following a negative prostatic needle biopsy, those requiring TURP proceeded accordingly. If the prostatic needle biopsy was positive for malignancy, TURP was deferred until further workup for prostate cancer was completed, i.e., completion of staging for the disease. Patients with presumed BPH included all patients with normal DRE findings and PSA levels < 4 ng/ml, as well as those with PSA levels > 4 ng/ml and/or abnormal DRE findings and a negative prostatic needle biopsy.

A computerized operation registry was used to identify all patients who underwent TURP within the mentioned period, and their identifiers were used to trace their clinical notes and files, laboratory, and histological results. Patients' demographics and other clinicopathological variables, including age, ethnicity, serum PSA level, prostate volume, PSA density, resected prostatic tissue weight, and histopathological assessment of resected specimens, were recorded.

Based on a confidence level of 95%, an expected prevalence of 14% within an infinite population, and an expected

precision of 0.05, the calculated minimum sample size required was 186 (4). The association of IPC with various factors studied was evaluated using stepwise binary logistic regression analysis with SPSS version 23. P values < 0.05 were considered significant.

Results

A total of 220 patients underwent TURP for presumed BPH from April 2018 to April 2023. The median age of the patients was 75 years (ranging from 57 to 90 years). The most common indication for TURP among these patients was urinary retention, followed by bladder stones, failed medical therapy, renal impairment, and haematuria. The median prostate volume and PSA level were 71.0 ml (11.0 to 300.0 ml) and 3.4 ng/ml (0.15 to 97.9 ng/ml), respectively. Due to raised PSA levels, 61 patients (27.7%) underwent transrectal ultrasound (TRUS) guided biopsy of the prostate before TURP. The median weight of resected prostatic tissues was 25.0 grams (ranging from 1.1 to 68.0 grams). This study considers resected prostate volume of less than 25.0 grams low. A summary of patients' demographic and clinical information is described in Table 1.

Table 1: Patient characteristics.

Patient demographics and characteristics	Total (n = 220)	BPH (n = 207)	IPC (n = 13)
Age – year			
Median (range)	75 (57 – 90)	74 (57 – 90)	79 (65 – 87)
Ethnicity – no. (%)			
Malay	106 (48.2)	99 (47.8)	7 (53.8)
Chinese	91 (41.4)	86 (41.5)	5 (38.5)
Indian	23 (10.5)	22 (10.6)	1 (7.7)
Indication for BPH surgery – no. (%)			
Urinary retention	105 (47.7)	95 (45.9)	10 (76.9)
Stone disease	57 (25.9)	54 (26.1)	3 (23.1)
Haematuria	10 (4.5)	10 (4.8)	0 (0)
Renal impairment	13 (5.9)	13 (6.3)	0 (0)
Failed medical therapy	35 (15.9)	35 (16.9)	0 (0)
Prostate volume – ml			
Median (range)	71.0 (11.0 – 300.0)	72.0 (11.0 – 300.0)	55.0 (29.0 – 112.0)
PSA – ng/ml			
Median (range)	3.4 (0.15 – 97.9)	3.2 (0.15 – 75.0)	9.8 (0.72 – 97.9)
PSA density > 0.15 ng/ml² – no. (%)			
No	183 (83.2)	180 (87.0)	3 (23.1)
Yes	37 (16.8)	27 (13.0)	10 (76.9)
Resected prostatic tissue weight – gram			
Median (range)	25.0 (1.1 – 68.0)	25.5 (1.1 – 68.0)	17.0 (5.7 – 41.0)
Incidental prostate cancer – no. (%)			
No	207 (94.1)		
Yes	13 (5.9)		

Thirteen patients (5.9%) had IPC, including seven patients with T1a disease and six patients with T1b disease. The most common cancer detected was ISUP grade group 1 (n = 6), followed by grade group 2 (n = 4), grade group 3 (n = 2), and grade group 4 (n = 1). Stepwise binary logistic regression analysis revealed that PSA density > 0.15 ng/ml² (p = 0.001) and low resected prostatic tissue weight (p = 0.024) were associated with IPC, with odds ratios of 26.1 and 0.9, respectively. The logistic regression analysis results on predicting prostate cancer factors are summarized in Table 2.

Table 2: Logistic regression analysis on predicting factors for prostate cancer.

Factors	p-value
Age	0.130
Ethnicity	0.128
Indication for BPH surgery	0.666
Prostate volume	0.167
PSA – ng/ml	0.947
PSA density > 0.15 ng/ml ²	0.001
Resected prostatic tissue weight	0.024

Discussion

In our study population, 5.9% of patients were recorded with IPC. This finding corresponds to the prevalence of IPC reported in the literature, which ranges from 5% to 14% (5, 6). It has significantly reduced compared to the pre-PSA era when the prevalence of IPC was reported as high as 27% (7). Nevertheless, it remains concerning as more than half of these cases warrant radical treatment. BPH surgery renders subsequent radical prostatectomy technically challenging. Thus, early detection of prostate cancer prior to BPH surgery is vital to keeping patients' cancer treatment options open.

Prostate cancer is the third most common cancer in Malaysia. Most prostate cancer patients are ethnic Chinese, followed by Malays, Indians, and others, with reported percentages of 45.2%, 38.3%, 6.7%, and 9.8%, respectively (8). We found no correlation between ethnicity and the prevalence of incidental prostate cancer.

Prostate cancer incidence increases with age (9). In 2014, Sakamoto and colleagues reported that older patients, particularly those over 75, are at an independent risk of detecting IPC following TURP (10). This finding is consistent with those reported by Gunda and Bright (11, 12). However, recent studies have shown no relationship between age and IPC following BPH surgery (13, 14). Our study results align with the latter studies, finding no association between age and IPC.

It is well accepted that a high PSA density is associated with the detection of clinically significant prostate cancer during prostatic needle biopsy, often using a cutoff of PSA density > 0.15 ng/ml² (15). Similar trends were observed in our study, where PSA density > 0.15 ng/ml² was significantly associated with a higher prevalence of IPC (OR = 26.1, p = 0.001). Notably, 10 out of 13 patients diagnosed with IPC had a PSA density > 0.15 ng/ml². Despite opportunistic screening of prostate cancer in those with PSA levels > 4 ng/ml and/or abnormal DRE findings, 11 out of 61 patients (18%) who required TRUS biopsy prior to TURP were found to have incidental prostate cancer. This suggests that a single TRUS-guided biopsy of the prostate is insufficient to rule out prostate cancer, especially in those with PSA density > 0.15 ng/ml². Further investigations such as mpMRI prostate and/or transperineal biopsy of the prostate should be considered.

An increasing body of studies suggests that smaller resected specimen volumes are associated with a higher risk of IPC. A Taiwan-based study by Liu reported a higher risk of IPC in patients with smaller resected specimens compared to those with larger volumes (HR = 1.221) (16). This relationship was consistently observed in a study by Mohamed et al. (17). Similarly, we observed an association between lower resected prostatic tissue weight and a higher prevalence of IPC (OR = 0.9, p = 0.024).

In the histopathological laboratories of many centers, not all prostatic chips are grossed, processed, and examined, especially for samples with large volumes of prostatic chips. This could contribute to our finding that larger resected prostate weights correlate with lower risks of incidental prostate cancer, suggesting that incidental prostate cancer may be under-reported. Nevertheless, this interpretation is hypothetical and does not conclusively establish this relationship. Therefore, patients at risk should be highlighted to pathologists so their specimens can be examined in their entirety, potentially aiding in the detection of incidental prostate cancer.

We acknowledge several limitations within our study. As a single-center study, its generalizability to the broader Malaysian population is limited. However, it serves as a stepping stone for larger-scale epidemiological studies. The identified factors associated with a higher prevalence of IPC, including PSA density and resected prostate volume, require further validation to conclude their significance. Additionally, mpMRI prostate was difficult to access during the study period at our center. Due to the retrospective design of our study, the disease progression or survival of patients with IPC was not examined.

Conclusion

The prevalence of IPC in Penang General Hospital is 5.9%. A PSA density of > 0.15 ng/ml² and low resected prostate volume are independent predictive factors for IPC following TURP. Further investigations, such as mpMRI prostate and

trans-perineal biopsy of the prostate, should be considered in patients at risk prior to BPH surgeries. Additionally, patients at risk should be highlighted to pathologists to ensure their specimens are examined in their entirety rather than standard handling.

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Competing interest

The authors declare no conflict of interest.

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