

## RESEARCH ARTICLE

# Incidentally Detected Adenocarcinoma Prostate in Transurethral Resection of Prostate Specimens: a Hospital Based Study from India

Jophy Varghese<sup>1</sup>, Priya Mariam Kuruvilla<sup>1</sup>, Nisarg Mehta<sup>2</sup>, Ranjeet Singh Rathore<sup>2</sup>, Manas Babu<sup>2</sup>, Devesh Bansal<sup>2</sup>, Biju Pillai<sup>2</sup>, Mohan P Sam<sup>2</sup>, H Krishnamorthy<sup>2\*</sup>

## Abstract

**Background:** Awareness about prostate cancer has increased in the community, and prostate cancer screening examinations, including prostate specific antigen (PSA) assays, are now widely available. Prior to the PSA era, up to 27% of prostate cancers were detected incidentally at the time of transurethral resection of prostate (TURP). After PSA testing became widely available, the incidence of incidentally detected carcinoma prostate in TURP specimens without prior diagnosis reduced to 5-13%. However, the incidence of incidentally detected carcinoma prostate has been reported to vary across the globe since various factors can influence the identification of this malignancy in TURP specimens. In this paper, we focus on rates of incidentally detected prostate cancer in TURP specimens in our hospital and correlate it with various parameters. **Materials and Methods:** This retrospective study of histopathological findings of biopsy specimens was conducted for patients undergoing TURP during a period of 5 years from April 2010. The inclusion criteria were patients diagnosed with benign prostatic hyperplasia (BPH) (digital rectal examination (DRE) not showing any abnormally hard areas and normal age adjusted PSA values). Patients with elevated PSA, abnormal DRE, documented urinary tract infection and proved adenocarcinoma prostate (CaP) were excluded from the study. The total weight of prostatectomy specimen, occurrence of carcinoma prostate in the chips, percentage of total tissue resected showing malignancy and Gleason's scores were recorded. **Results:** A total of 597 patients belonging to the inclusion criteria were studied. The incidence of occult CaP in the study group was 5.2 % (31/597). Out of these, 8 belonged to T1a and 23 belonged to T1b stages. The age group 70 - 79 years had the maximum incidence of occult CaP. It was observed that the clinical grading of prostate did not have a bearing on the incidence of occult CaP whereas the weight of resected specimen correlated with the incidence of CaP. The incidence of occult CaP was greater with low volume prostates (<20 g). (P=0.15). **Conclusions:** The rate of incidentally detected adenocarcinoma prostate in patients undergoing TURP for clinically diagnosed BPH was found to be only 5.2 % in our study which is low when compared with similar studies done elsewhere. The age of the patient and weight of the resected specimen correlated with incidence of occult prostate cancer. The clinical grading of prostate by DRE however, demonstrated no correlation.

**Keywords:** Incidental prostate cancer - transurethral resection of prostate (TURP) - prostate specific antigen (PSA)

*Asian Pac J Cancer Prev*, 17 (4), 2255-2258

## Introduction

Prostate cancer is the fourth leading cancer in both sexes and the second most common cancer in males. The incidence of prostate cancer is on the rise. The reasons for the increase of this disease are not known, but increasing life expectancy and modified diagnostic techniques have been suggested as causes. The established risk factors for this disease are advancing age, race, positive family history of prostate cancer and western diet (use of fat items). Several other risk factors, such as obesity, physical

activity, sexual activity, smoking and occupation have been also associated with prostate cancer risk, but their roles in prostate cancer etiology remain uncertain. (Saleh et al., 2015).

Clinical T1 or incidental prostate cancer is defined as clinically inapparent tumour that is neither palpable nor visible by imaging. Clinical T1a and T1b prostate cancer are diagnosed at the time of transurethral resection of the prostate (TURP) for benign prostatic disease. T1a disease (formerly A1 under the Whitmore-Jewett staging system) involves 5% or less of the resected tissue whereas

<sup>1</sup>Department of Pathology, <sup>2</sup>Department of Urology, Lourdes Hospital, Cochin, Kerala, India \*For correspondence: dr.moorthy65@gmail.com

T1b disease (formerly A2) involves more than 5% of the resected tissue (Edge et al., 2010). Prior to the PSA era, up to 27% of prostate cancers were detected incidentally at the time of TURP (Tombal et al., 1999). With an increase in PSA screening, there has been a decrease in T1a and T1b lesions (Fowler et al., 1997). It may therefore be necessary to redefine “true” incidental prostate cancer as carcinoma associated with a normal digital rectal examination (DRE) and a normal PSA level. Although most of the incidental prostate cancers are considered clinically insignificant, recent studies have suggested that in some of them, the clinical course can become more unfavorable. In this study, we sought to identify the rates of incidentally detected prostate cancer in TURP specimens in our hospital and correlate it with various parameters like age of the patient, weight of resected gland and clinical grading of prostate according to DRE.

### Materials and Methods

This was a retrospective study of the histopathological findings of biopsy of patients undergoing TURP for obstructive urinary symptoms due to BPH in our hospital during a period of 5 years from April 2010. The inclusion criteria were patients diagnosed with pure BPH (Digital Rectal Examination had not shown any abnormally hard areas and normal age adjusted PSA values, Oosterling JE et al., 1993). Patients with elevated age adjusted PSA values, abnormal DRE, those with documented UTI and proved adenocarcinoma prostate (CaP) were excluded from the study. TURP was performed by consultants with more than 5 years of clinical experience and it was ensured that complete resection was done in all individuals in a single sitting. Entire TURP chips were processed and subjected to histopathological examination by Consultant Pathologist having more than 5 years of clinical experience. For an accurate pathological diagnosis, tumour extent (stage) in TURP specimens was determined by calculating the fraction of all TURP chips involved by tumour, and Gleason scores were assigned to the diagnosed CaP. (Epstein et al., 2005). The total weight of prostatectomy specimen, occurrence of CaP in the chips, percentage of total tissue resected showing malignancy and Gleason’s scores were recorded. The findings were also correlated with the clinical grading of prostate (based on DRE, Barnes’ Classification). The statistical analysis was done using MedCalc Statistical Software version 14.8.1 (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>; 2014). Pearson’s correlation coefficient and Chi squared test were used to correlate the occurrence of incidental CaP with various clinical parameters.

### Results

A total of 597 patients belonging to the inclusion criteria were studied. The age of patients ranged from 41 to 90 years (Mean 66.79 ± 8.7 years). The incidence of occult CaP in the study group was 5.2 % (31/597). Out of these, 8 belonged to T1a (25.8 %) and 23 belonged to T1b (74.2 %).

Correlating the age of the patients with the incidence

**Table 1. Age-wise Incidence of Incidental Prostate Cancer**

Age (years)	No. of patients studied	Incidental CaP detected (% incidence)	P value
40-49	13	0 (0)	0.001
50-59	101	3 (9.6)	
60-69	247	6 (19.3)	
70-79	190	18 (58)	
>79	46	4 (12.9)	
Total No. of patients	597	31 (5.2 %)	

**Table 2. DRE Grading vs. Incidence of Prostate Cancer**

DRE Grade	No. of patients studied	Incidental CaP detected (% incidence)	P value
1	252	12 (38.7)	0.18
2	249	15 (48.3)	
3	96	4 (12.9)	
Total No. of patients	597	31 (5.2 %)	

**Table 3. Resected Weight of Prostatectomy Specimen vs. Incidence of Prostate Cancer**

Resected weight (g)	No. of patients studied	Incidental CaP detected (% incidence)	P value
<20	356	23 (74.1)	0.15
20-40	163	5 (16.1)	
>40	78	3 (9.6)	
Total No. of patients	597	31 (5.2 %)	

of incidental CaP, it was observed that the age group 70 - 79 years had the maximum incidence of incidental CaP (58.06%) and the age group 40 - 49 years had no patients detected with CaP. (P=0.001). Age wise incidence of occult CaP is depicted in Table 1.

Correlating the clinical grade of prostate and incidental CaP, it was observed that the clinical grading of prostate did not have a bearing on the incidence of occult CaP. (Table 2).

When the weight of resected specimen was correlated with the incidence of occult CaP, it was observed that the incidence was highest when the total weight of resected gland was <20 g. Hence the incidence of an occult CaP was inversely proportional to the weight of resected gland (P=0.15) (Table 3).

Of all the patients detected with incidental CaP, 15 had a Gleason’s score of 6/10, 6 had a score of 7/10 (4 with 3+4 and 2 with 4+3), 4 had score of 8/10 and 6 with score of 9/10.

### Discussion

It is well known that the main preoperative diagnostic tools to confirm prostate cancer include serum PSA, DRE and imaging modalities. PSA is considered a better predictor of cancer than DRE or TRUS (Catalona et al., 1994, Kash et al., 2014) and it can be complemented with parameters, such as PSA velocity, PSA density, and free/total PSA. However, serum PSA levels may be elevated in the presence of BPH, prostatitis, and other non-malignant

conditions.

Ziguener et al. reported that in the PSA era, the rate of incidental prostate cancer has decreased by more than 50%. In their study, incidental prostate cancer was diagnosed in 314 (13%) of 2422 patients. However, the rate of incidental prostate cancer in patients with both negative age-specific PSA levels and negative DRE findings was 6.4% (72 of 1127) (Ziguener et al., 2003). The rate of incidental cancer in our study was only 5.2% (31 of 597).

Jones et al. from Cleveland Clinic compared the frequency of incidental prostate cancer among patients undergoing TURP between the pre-PSA era and the PSA era, and showed a decrease in frequency from 14.9% (34 of 228) to 5.2% (26 of 501) with clinically significant drop in stage T1b. They suggested that men considering surgical or medical management of BPH be informed that it should be infrequent that they harbor clinically significant undetected malignancy (Jones et al., 2009).

In a Multi-Center review done in 11 centers in Korea by Yoo and coworkers, Incidental prostate cancer was detected in 4.8% (78 of 1613) of the patients who underwent surgical treatment for BPH and more than half of them showed clinically significant prostate cancer. They also showed that in addition to DRE findings, a combination of transition zone volume and PSA can be used as useful predictive factors of incidental prostate cancer. In our study the age of the patient was a positive predictor for incidence of occult CaP whereas DRE findings had no correlation with presence of incidental CaP similar to the studies by Yoo and colleagues. (Yoo et al., 2012).

In the study by Melchior and colleagues, the rate of incidental prostate cancer was found to be 5.4 % (104 of 1931 patients). They concluded that there is currently no possibility to reliably predict the absence of aggressive prostate cancer after TURP, and thus safely recommend observation instead of further therapy. Therefore, patients with incidental prostate cancer need to be counselled individually (Melchior et al., 2008).

In a study on 1648 patients undergoing surgery for BPH (1199 – TURP, 449 – open enucleation), Tombal and coworkers found T1 prostate cancers in 11 % patients (182 of 1648). They concluded that the use of PSA assays have decreased but not suppressed the incidence of T1 prostate cancer, with a greater effect on those tumours at a higher risk of progression (T1b) (Tombal et al., 1999).

In our study, we focused on identifying incidence and preoperative risk factors for incidental prostate cancer in the current clinical setting in our hospital. We found that 2 simple parameters (age =70 to 79 years, weight of resected gland <20g) were unfavorably linked to incidental prostate cancers. The difference in the rates of incidental cancers in our study as compared to some others may be because of varied epidemiological background as well as better diagnostic tools employed for detection of prostate cancer as suggested by Esfahani et al., 2015 and Bashir, 2015. The outcomes of prostate cancer have been well known to show geographical disparities. (Baade et al., 15). The age wise levels of PSA as well as cut offs for prostate biopsy were different in each study.

In conclusions, The incidence of occult CaP in patients undergoing TURP for clinically diagnosed BPH was found to be only 5.2 % in our study which was found to be low when compared with similar studies done elsewhere. The age of the patient was a positive predictor for incidence of occult CaP whereas the total weight of resected specimen had a statistically insignificant correlation with the presence of incidental CaP. The clinical grading of prostate by DRE however, had no correlation with incidence of occult CaP. The low incidence of occult CaP could further reduce due to the availability of better diagnostic tools preoperatively namely MR Spectroscopy, Transrectal ultrasound (TRUS) and newer forms of PSA.

## References

- Baade PD, Yu XQ, Smith DP, et al (2015). Geographic disparities in prostate cancer outcomes - review of international patterns. *Asian Pac J Cancer Prev*, **16**, 1259-75.
- Bashir NM (2015). Epidemiology of prostate cancer. *Asian Pac J Cancer Prev*, **16**, 5137-41.
- Catalona WJ, Richie JP, Ahmann FR, et al (1994). Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: Results of a multicenter clinical trial of 6,630 men. *J Urol* **151**, 1283-90.
- Edge SB, Byrd DR, Compton CC, et al (2010). (Eds.) American joint committee on cancer (AJCC). Cancer staging manual. 7<sup>th</sup> edition. Springer, New York, NY.
- Epstein JI, Allsbrook WC Jr, Amin MB, et al (2005). ISUP Grading Committee. The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. *Am J Surg Pathol*, **29**, 1228-42.
- Esfahani M, Ataei N, Panjehpour M (2015). Biomarkers for evaluation of prostate cancer prognosis. *Asian Pac J Cancer Prev*, **16**, 2601-11.
- Fowler JE Jr, Pandey P, Bigler SA, et al (1997). Trends in diagnosis of stage T1a-b prostate cancer. *J Urol*, **158**, 1849-52.
- Jones JS, Follis HW, Johnson JR (2009). Probability of finding T1a and T1b (incidental) prostate cancer during TURP has decreased in the PSA era. *Prostate Cancer Prostatic Dis*; **12**, 57-60.
- Kash DP, Lal M, Hashmi AH, et al (2014). Utility of digital rectal examination, serum prostate specific antigen, and transrectal ultrasound in the detection of prostate cancer: a developing country perspective. *Asian Pac J Cancer Prev*, **15**, 3087-91.
- Melchior S, Hadaschik B, Thuroff S, et al (2008). Outcome of radical prostatectomy for incidental carcinoma of the prostate. *BJU International*, **103**, 1478-81.
- Oesterling JE, Jacobsen SJ, Chute CG et al (1993). Serum prostate-specific antigen in a community-based population of healthy men. Establishment of age-specific reference ranges. *JAMA*, **270**, 860-4.
- Saleh AM, Fooladi MM, Nustas WP, et al (2015). Enhancing knowledge, beliefs, and intention to screen for prostate cancer via different health educational interventions: a literature review. *Asian Pac J Cancer Prev*, **16**, 5137-41.
- Tombal B, De Visccher L, Cosyns JP, et al (1999). Assessing the risk of unsuspected prostate cancer in patients with benign prostatic hypertrophy: a 13-year retrospective study of the incidence and natural history of T1a-T1b prostate cancers, *BJU International*, **84**, 1015-20.
- Yoo C, Oh CY, Kim SJ, et al (2012). Preoperative clinical factors for diagnosis of incidental prostate cancer in the era of tissue-ablative surgery for benign prostatic hyperplasia: A Korean

*Jophy Varghese et al*

multi-center review. *Korean J Urol*, **53**, 391-5.

Zigeuner RE, Lipsky K, Riedler I et al (2003). Did the rate of incidental prostate cancer change in the era of PSA testing? A retrospective study of 1127 patients. *Urol*, **624**, 451-5.