ORIGINAL RESEARCH PAPER

Urology

INCIDENTAL DETECTION OF PROSTATE CANCER IN TRANSURETHRAL RESECTION OF PROSTATE (TURP) SPECIMENS: A RETROSPECTIVE STUDY.

KEY WORDS: TURP, BPH, incidental adenocarcinomaprostate

Dr. Neha Kumari Senior Resident, Department of Urology, Yenepoya Medical College, Mangalore, Karnataka, India

Dr. Farhana Zakaria Professor in Pathology, Kanachur Institute of Medical Sciences, Mangalore, Karnataka, India

Dr. Altaf Khan* Professor, Department of Urology, Yenepoya Medical College, Mangalore, Karnataka, India *Corresponding Author

Dr. Mujeeb urahiman Professor, Department of Urology, Yenepoya Medical College, Mangalore, Karnataka, India

Dr. Nischih Dsouza Professor, Department of Urology, Yenepoya Medical College, Mangalore, Karnataka, India

ABSTRACT

Introduction: Transurethral Resection of Prostate (TURP) is a surgery commonly done for Benign Prostatic Hyperplasia (BPH) which mainly targets the transitional zone of prostate gland. T1a and T1b prostate cancer are diagnosed at the time of transurethral resection of the prostate (TURP) for benign prostatic disease. Prior to the PSA era, up to 27% of prostate cancers were detected incidentally at the time of TURP. With an increase in PSA screening, there has been a decrease in pT1a and pT1b lesions. **Methods:** A 2-year retrospective analysis of TURP specimens collected between from January 2021 till December 2022 was conducted at the institute of Nephro-Urology Yenepoya Medical College Mangalore. TURP specimens were examined and reported by pathologists. **Results:** A total of 250 patients belonging to the inclusion criteria were studied. The incidence of occult adenocarcinoma prostate in the study group was 2%. Correlating the age of the patients with the incidence of incidental adenocarcinoma prostate, it was observed that the age group 70 - 79 years had the maximum incidence of incidental adenocarcinoma prostate (13.0%, P-value <0.001). The incidence of adenocarcinoma prostate was found to be inversely proportional to the weight of resected gland, but this was not statistically significant. **Conclusion:** Even if the preliminary diagnosis of BPH is made, processing of all the TURP specimen especially those obtained from elderly patientsand evaluating pre-operative PSA level are important not to miss any tumour. The age of the patient was a positive predictor for incidence of occult adenocarcinoma prostate. The clinical grading of prostate by DRE however, had no correlation with incidence of occult adenocarcinoma prostate.

INTRODUCTION

Prostate cancer is the second most commonly diagnosed cancer and the fifth leading cause of cancer death among men worldwide, with an estimated 1,414,000 new cancer cases and 375,304 deaths in 2020 (1).

Prostate is a fibro-musculo-glandular organ encircling the neck of the urinary bladder. So, enlargement or growth of prostate due to nodular hyperplasia or prostatic intraepithelial neoplasia or adenocarcinoma may give rise to bladder outlet obstruction (2).

Transurethral resection of the prostate (TURP) is considered the standard method of surgical treatment for benign prostatic hyperplasia (BPH) (3). TURP targets the transitional zone of the prostate. The majority of prostate cancers arise in the peripheral zones, and transrectal needle core biopsy is the gold standard for confirming the diagnosis in patients with elevated levels of Prostate Specific Antigen (PSA). Prostate cancer isolated exclusively in the transitional zone is uncommon, and a minority of tumours may not cause a rise in PSA, especially those of low volume (4).

Benign Prostatic Hyperplasia (BPH) is a histological diagnosis associated with unregulated proliferation of connective tissue, smooth muscle and glandular epithelium within the prostatic transition zone(5).Incidental prostatic adenocarcinoma is described as a tumour diagnosed incidentally after surgery for benign prostate hyperplasia (without previous suspicion of Prostate Cancer) or found after autopsy or detected incidentally after radical cysto-prostatectomy for bladder cancer (6).Most incidental prostatic adenocarcinomas are considered clinically insignificant, but recent studies have suggested that in some the clinical course becomes more unfavourable (7,8).

Clinical T1a and T1b prostate cancer are diagnosed at the time of transurethral resection of the prostate (TURP) for benign prostatic disease. T1a disease involves 5% or less of the resected tissue, whereas T1b disease involves more than 5% of the resected tissue. Prior to the PSA era, up to 27% of prostate cancers were detected incidentally at the time of TURP (9).

With an increase in PSA screening, there has been a decrease in pT1a and pT1b lesions (10). Some incidental prostate cancers have been shown to be clinically relevant, specifically tumours with a higher Gleason score and stage pT1b (11).Prostate cancer can be detected incidentally in patients undergoing transurethral resection of the prostate for benign prostatic hyperplasia. Therefore, it is very important that the transurethral resection of the prostate specimen is evaluated carefully for accurate grading and staging (12).

A systematic review of autopsy studies reported a prevalence of Prostate Carcinoma at age < 30 years of 5% (95% confidence interval [CI]: 3–8%), increasing by an odds ratio (OR) of 1.7 (1.6–1.8) per decade, to a prevalence of 59% (48–71%) by age > 79 year (13).

MATERIALS AND METHODS

A 2-year retrospective analysis of TURP specimens collected from January 2021 till December 2022 was conducted at a tertiary care centre. TURP specimens were examined and reported by experienced pathologists.

All the TURP specimens were weighed. The method recommended in the college of Americanpathologist's guidelines was used for the sampling of specimens. TUR-P specimens weighing ≤12 g were submitted in entirety, usually in 6–8 cassettes.

For specimens weighing >12 g, the initial 12 g was submitted and 1 cassette was submitted for every additional 5 g of remaining tissue. In addition, in patients with incidental prostatic carcinoma, resampling was performed and all remaining tissue was submitted for histopathological evaluation. 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.

Inclusion and exclusion criteria:
Patients in whom Digital Rectal Examination (DRE) had not shown any abnormally hard areas and normal age and volume adjusted PSA values were included in this study.

Patients with elevated age adjusted PSA values, abnormal DRE, those with documented urinary tract infection (UTI) and proved adenocarcinoma prostate were excluded from the study.

SPSS 22 software was used for data collection and analysis.

RESULTS

A total of 250 patients satisfying the inclusion criteria were studied.The age of patients ranged from 40 to 80 years (mean 66.79 ± 8.7 years). The incidence of occult adenocarcinoma prostate in the study group was 2% (5/250). Out of these, two belonged to T1a (40.0%) and three belonged to T1b (60.0%).

Correlating the age of the patients with the incidence of incidental adenocarcinoma prostate, it was observed that the age group 70 - 79 years had the maximum incidence of incidental adenocarcinoma prostate (13.0%) and the age group 40 - 59 years had no patients detected with adenocarcinoma prostate. (Table 1)

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

When the weight of resected specimen was correlated with the incidence of occult adenocarcinoma prostate, it was observed that the incidence was highest when the total weight of resected gland was < 20 g. Hence the incidence of an occult adenocarcinoma prostate was inversely proportional to the weight of resected gland. (Table 3) Of all the patients detected with incidental prostate cancer, one had a Gleason score of 7, two had score of 8 and another two with score of 9.

DISCUSSION

BPH and carcinoma of the prostate are more frequent after the age of 50 and the prevalence of Prostate cancer doubles every 14 years (14, 15). Clinically, T1 or incidental PC is known to be a tumour that cannot be detected by clinical examination and imaging methods (16).

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 trans rectal ultrasound (TRUS) (17, 18).

A study by Bostwick DG et al found that 10.0% of participants undergoing transurethral removal of prostate had an incidental detection of carcinoma (19).

Di Silverio F et al studied more than 3900 cases with benign prostatic hyperplasia and found that as the age increases, the incidental finding of carcinoma increases (20).

Our study showed an incidental prostate cancer rate of 2% the Gleason sum of which ranged from 7 to 9. This detection rate is lower than several other recently published series; however, it is consistent with the overall decrease in incidental prostate cancer in the PSA era.

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 harbour clinically significant undetected malignancy (21).

In a Multi-Centre review done in 11 centres in Korea by Yoo et al, 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 prostate cancer whereas DRE findings had no correlation with presence of incidental prostate cancer similar to the studies by Yoo et al. (22).

In the study by Melchior et al, 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. Therefore, patients with incidental prostate cancer need to be counselled individually (23).

Mai et al. also showed similar results in their review of almost 1000 TURP specimens. They found significant decreases in the overall detection rate, 12.9 to 8%, and the amount of pT1b lesions, 10% to 5% (24). More recently, Jones et al.'s comparison found a decrease of incidental prostate cancer from 14.9% to 5.2% (pre versus post PSA era) in over 700 patients (25). They saw significant decreases in both pT1a and pT1b incidental prostate cancer (4.4% to 2.2% and 10.5% to 2.8%, resp.) between the pre-PSA and the PSA eras (21).

Dellavedova et al. found an incidental prostate cancer detection rate of 7% when they reviewed 100 patients who underwent bipolar TURP. Six patients had Gleason grade 3 + 3 pT1a disease and one patient had Gleason grade 3 + 4 pT1b disease (25).

In a study on 1648 patients undergoing surgery for BPH (1199 – TURP, 449 – open enucleation), Visccher et alfound 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) (26).

Among the population of 250 patients who took treatment at our institute, the demographic distribution of patients coming to the centre for treatment may affect the prevalence of incidental carcinoma in the current study.

CONCLUSION

In our study, we observed that the occurrence of incidental carcinoma of the prostate in transurethral resection of the prostate (TURP) procedures was 2%. This incidence was particularly higher in patients aged 70 years and above. It is crucial to process all TURP material, especially from elderly patients, and assess pre-operative prostate-specific antigen

(PSA) levels to avoid missing any tumours, even if a preliminary diagnosis of benign prostatic hyperplasia (BPH) has been made. We discovered that patient age was a positive indicator for the occurrence of hidden adenocarcinoma of the prostate, but the total weight of the removed specimen was not significantly correlated with the presence of incidental adenocarcinoma of the prostate. Moreover, the clinical grading of the prostate by digital rectal examination (DRE) did not have any correlation with the incidence of hidden adenocarcinoma of the prostate. Therefore, we recommend conducting further studies involving larger case series, including data on patient follow-up, treatment, and prognosis, in order to obtain more conclusive results.

Abbreviations

TURP = trans urethral resection of prostate
BPH = benign prostatic hyperplasia
UTI = urinary tract infection
PSA = prostate specific antigen
TRUS = trans rectal ultrasound
DRE = digital rectal examination

REFERENCES:

1. Wang L, Lu B, He M, Wang Y, Wang Z, Du L. Prostate Cancer Incidence and Mortality: Global Status and Temporal Trends in 89 Countries From 2000 to 2019. Front Public Health. 2022 Feb 16;10:811044.
2. Kantikundo SNS, Bhattacharyya NK, Bhattacharyya PK, Kundu AK. Astudy to correlate histopathology, biochemical marker and immunohistochemical expression of sex-steroid receptor in prostatic growth. Indian J Med PaediatrOncol. 2014 jan-mar;35(1):40- 43.
3. Trpkov K, Thompson J, Kulaga A, Yilmaz A (2008) How much tissue sampling is required when unsuspected minimal prostate carcinoma is identifed on transurethral resection? Arch Pathol Lab Med 132:1313–1316
4. Rajab R, Fisher G, Kattan MW, Foster CS, Møller H, Oliver T et al (2011) Transatlantic Prostate Group. An improved prognostic model for stage T1a and T1b prostate cancer by assessments of cancer extent. Mod Pathol 24:58–63
5. Auffenberg GB, Helfand BT, McVary KT. Established medical therapy for benign prostatic hyperplasia. UrolClin North Am. 2009;36:443-59.
6. Kimura T, Egawa S. Epidemiology of prostate cancer in Asian countries. *Int J Urol*. 2018;25(6):524–531. doi:10.1111/iju.2018.25.issue-6
7. Otto B, Barbieri C, Lee R, Te AE, Kaplan SA, Robinson B et al (2014) Incidental prostate cancer in transurethral resection of the prostate specimens in the modern era. AdvUrol 2014:627290.
8. Sakamoto H, Matsumoto K, Hayakawa N, Maeda T, Sato A, Ninomiya A et al (2014) Preoperative parameters to predict incidental (T1a and T1b) prostate cancer. Can UrolAssoc J 8:E815–E820
9. Visccher D, Cangh V. 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. 1999 Dec;84(9):1015-20.
10. Fowler JE, Pandey P, Bigler SA, Yee DT, Kolski JM. Trends in diagnosis of stage T1a-b prostate cancer. The Journal of urology. 1997 Nov;158(5):1849-52.
11. Voigt S, Hüttig F, Koch R, Propping S, Propping C, Grimm M-O, et al. Risk factors for incidental prostate cancer-who should not undergo vaporization of the prostate for benign prostate hyperplasia? The Prostate. 2011;71(12):1325-31.
12. Nergiz, D., Yıldırım, H.T. & Yıldırım, . Incidence of incidental cancer in transurethral resection of prostate specimens: a 10-year retrospective analysis. *Afr J Urol* **27**, 120 (2021).
13. Bell, K.J., et al. Prevalence of incidental prostate cancer: A systematic review of autopsy studies. Int J Cancer, 2015. 137: 1749. https://pubmed. ncbi.nlm. nih.gov/25821151/
14. Haas, G.P. and Sakr, W.A. (1997), Epidemiology of prostate cancer. CA: A Cancer Journal for Clinicians, 47:273-287.
15. Bell KJ, Del Mar C, Wright G, Dickinson J, Glasziou P. Prevalence of incidental prostate cancer: A systematic review of autopsy studies. Int J Cancer 2015;137:1749-1757.
16. Varghese J, Kuruvilla PM, Mehta N, Rathore RS, Babu M, Bansal D, Pillai B, Sam MP, Krishnamorthy H. Incidentally Detected Adenocarcinoma Prostate in Transurethral Resection of Prostate Specimens: a Hospital Based Study from India. AsianPac J Cancer Prev 2016;17:2255-2258.
17. Catalona WJ. Comparison of digital rectal examination of prostate cancer: results of multicenter clinical trial of 6,630 men. J. Urol.. 1994;151:1283-90.
18. Kash DP, Lal M, Hashmi AH, Mubarak M. Utility of digital rectal examination, serum prostate specific antigen, and transrectal ultrasound in the detection of prostate cancer: a developing country perspective. Asian Pacific Journal of Cancer Prevention. 2014;15(7):3087-91.
19. Bostwick DG, Cooner WH, Denis L, Jones GW, Scardino PT, Murphy GP. The association of benign prostatic hyperplasia and cancer of the prostate. Cancer. 1992 Jul 1;70(S1):291-301.
20. Di Silverio F, Gentile V, De Matteis A, Mariotti G, Giuseppe V, Luigi PA, Sciarra A. Distribution of inflammation, pre-malignant lesions, incidental carcinoma in histologically confirmed benign prostatic hyperplasia: a retrospective analysis. European urology. 2003 Feb 1;43(2):164-75.
21. Jones JS, Follis HW, Johnson JR. Probability of finding T1a and T1b (incidental) prostate cancer during TURP has decreased in the PSA era. Prostate cancer and prostatic diseases. 2009 Mar;12(1):57-60.
22. Yoo C, Oh CY, Kim SJ, Kim SI, Kim YS, Park JY, Song YS, Yang WJ, Chung HC, Cho IR, Cho SY. Preoperative clinical factors for diagnosis of incidental prostate cancer in the era of tissue-ablative surgery for benign prostatic hyperplasia: a korean multi-center review. Korean journal of urology. 2012 Jun 1;53(6):391-5.
23. Melchior S, Hadaschik B, Thüroff S, Thomas C, Gillitzer R, Thüroff J. Outcome of radical prostatectomy for incidental carcinoma of the prostate. BJU international. 2009 Jun;103(11):1478-81.
24. Mai KT, Isotalo PA, Green J, Perkins DG, Morash C, Collins JP. Incidental prostatic adenocarcinomas and putative premalignant lesions in TURP specimens collected before and after the introduction of prostate-specific antigen screening. *Archives of Pathology and Laboratory Medicine*. 2000;**124**(10):1454–1456.
25. Dellavedova T, Ponzano R, Racca L, Minuzzi F, Dominguez M. Prostate cancer as incidental finding in transurethral resection. *ArchivosEspanoles de Urologia*.2010;**63**(10):855–861.
26. Visccher D, Cangh V. 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. 1999 Dec;84(9):1015-20.