UROONCOLOGY
Original Article

Does the prostate volume always effect cancer detection rate in prostate biopsy? Additional role of prostate-specific antigen levels: A retrospective analysis of 2079 patients

Engin Kandıralı[1], Mustafa Zafer Temiz[2], Aykut Çolakerol[3], Emrah Yürük[1], Atilla Semercioöz[1], Ahmet Yaser Müslümanoğlu[1]

Cite this article as: Kandıralı E, Temiz MZ, Çolakerol A, Yürük E, Semercioöz A, Müslümanoğlu A. Does the prostate volume always effect cancer detection rate in prostate biopsy? Additional role of prostate-specific antigen levels: A retrospective analysis of 2079 patients. Turk J Urol 2019; 45(2): 103-7.

ABSTRACT

Objective: We aimed to determine whether the effect of prostate volume on cancer detection rates is influenced by serum prostate-specific antigen (PSA).

Material and methods: A total of 2465 men who underwent transrectal ultrasound-guided biopsy were retrospectively evaluated. Standard 10-core prostate biopsy was performed in all cases. Patients were divided into three groups according to the serum PSA levels: ≤10 ng/mL (Group 1), 10- 20 ng/mL (Group 2) and >20 ng/mL (Group 3). In each group age, serum PSA levels and prostate volumes were compared in patients with and without prostate cancer.

Results: A total of 2079 patients were included in the study group. Cancer detection rates were 16%, 25%, 53% in Groups 1, 2 and 3, respectively (p=0.001). In Group 1, there was a significant difference in mean prostate volume of patients with and without prostate cancer (p=0.01). However, this difference was not seen in Group 2 or 3 (p=0.06 and p=0.08, respectively). The mean age and PSA level which are the other determinants of prostate cancer diagnosis were similar between patients with and without cancer in the Group 1, thus prostate volume was the only determinant of the diagnosis.

Conclusion: According to our findings, prostate volume is an important factor for prostate cancer diagnosed with prostate biopsy only in patients with a PSA level of ≤10 ng/mL.

Keywords: Biopsy; prostate; prostate cancer; prostate-specific antigen.

ORCID IDs of the authors:
E.K. 0000-0003-0580-2144;
M.Z.T. 0000-0002-5736-5495;
A.Ç. 0000-0002-5076-5306;
E.Y. 0000-0002-2343-8828;
A.S. 0000-0001-8688-4772;
A.Y.M. 0000-0002-8691-0886.

The article was presented in 34th Congress of the Société Internationale d'Urologie (SIU), October 12-15, 2014, in Glasgow, Scotland

[1]Department of Urology, Bağcılar Training and Research Hospital, İstanbul, Turkey

[2]Department of Urology, Çatalca İlyas Çokay State Hospital, İstanbul, Turkey

[3]Department of Urology, Mehmet Akif İnan Training and Research Hospital, Şanlıurfa, Turkey

Submitted:
21.11.2017

Accepted:
15.01.2018

Available Online Date:
16.03.2018

Correspondence:
Mustafa Zafer Temiz
E-mail: dr_mustafazafertemiz@hotmail.com

Available online at www.turkishjournalofurology.com

Introduction

Prostate biopsy is the standard method for diagnosis of prostate cancer (PCa).[1] The original method described by Hodge et al.[2] comprised only six core biopsies and therefore called as 'sextant biopsy'. However, diagnostic sensitivity and specificity of transrectal ultrasound-guided prostate biopsy (TRUS-Bx) has been disappointing, with a reported false negative rates ranging from 30 to 45%.[3,4] The sensitivity of TRUS-Bx further decreases with increasing prostate volume.[5,6] Increasing the number of cores obtained resulted in higher PCa detection rates.[7,8] Therefore, modifications of the original method with extended-sampling protocols are now recommended.[9] In fact, nowadays magnetic resonance imaging (MRI)-guided transrectal prostate biopsies are in vogue but the current standard technique for PCadetection in men with a high prostate-specific antigen (PSA) or an abnormal finding on digital rectal examination (DRE) is a 10-12 core TRUS-Bx, especially at first diagnostic attempts.[9,10] According to the TRUS-Bx, the most controversial issue has been the number of biopsy cores. The most accepted attitude is that greater number of core biopsies are needed with larger prostate glands.[7-9] But, in the literature there is no clear consensus about this topic, additionally the role of PSA has been commonly ignored.

Prostate-specific antigen although first introduced for follow-up of PCa, is now widely

Turk J Urol 2019; 45(2): 103-7
DOI:10.5152/tud.2018.66909

used as a screening tool and a predictor of prostate biopsy results.[11] Previously, the relationship between PSA level and tumor volume was demonstrated.[12] Similarly, the correlation between PSA level and PCadetection rates is well described in the literature.[13,14] Consequently, it is not surprising that serum PSA levels have a significant impact on prostate biopsy outcomes. To our knowledge, although it is well known that PCa detection rates decrease with increasing prostate volume, the effects of PSA level on this correlation has not been studied before. In our large-scale cohort study, we aimed to determine whether the impact of prostate volume on cancer detection rates is influenced by serum PSA levels.

Material and methods

After obtaining institutional review board approval (Approval ID: 2013-97), data of patients who underwent TRUS-Bx between February 2009 and September 2014 in our tertiary referral center were retrospectively collected. The TRUS-Bx was indicated in patients with a PSA level above 2.5 ng/mL and/or suspicious findings on digital rectal examination.

Patients with a history of uncorrected coagulopathy, previous prostate biopsy or prostate surgery and patients under 5 alpha-reductase inhibitor treatments were excluded from the study. Moreover, the patients with a pathological report consistent with high- grade prostatic intraepithelial neoplasia (HGPIN) and atypical small aciner proliferation (ASAP) without evidence of PCa were also excluded.

All the procedures were performed by or under supervision of an urologist experienced in TRUS-Bx. Antibiotic prophylaxis was initiated the day before the procedure with oral 500mg ciprofloxacin twice daily, if not contraindicated and a rectal enema was prescribed four hours before the biopsy.

After completing the gross examination of the prostate and the surrounding structures with the Pro Focus 2202 Ultrasound system with 12-4 MHz prostate biplane and end-fire transducer 8818 transrectal probe (BK Medical, Herlev, Denmark), the PV were calculated using the prolate ellipse formula.[6] A 2% lidocaine solution was injected into the periprostatic space for local anesthesia. A 25 cm 18 Gauge tru-cut biopsy needle (Gallini Medical Devices, Mantova, Italy) with an automatic biopsy gun (Pro-Mag Ultra Angiotech, Stenlose, Denmark) were used for the procedures. A 10-core standard biopsy scheme comprising four laterally directed biopsies of the peripheral zone plus the conventional sextant biopsy template was preferred in all cases. All procedures were performed in outpatient settings and the antibiotic prophylaxis was continued for additional five days.

Statistical analysis

Patients were invited for follow-up visit on day 10. All procedure-related complications were noted. Patients were divided into three groups according to the serum PSA levels: PSA ≤10 ng/mL (Group 1), 10-20 ng/mL (Group 2) and >20 ng/mL (Group 3), respectively. For each PSA group, prostate volumes were compared in patients with and without PCa. All statistical analyses were performed using the Statistical Package for the Social Sciences version 16.0 (SPSS Inc.; Chicago, IL, USA). Unpaired t test, and Mann-Whitney U Test were used to compare the groups while significance was set at $p<0.05$.

Results

Overall 2465 patients underwent TRUS-Bx during the study period. Of these, 2079 patients who fulfill the inclusion criteria constituted the study group. Mean age, prostate volume and PSA level of the study cohort were 66.7 years, 56.42 mL and 10.07 ng/mL, respectively. Overall PCa detection rate was 22%. Mean patient age was similar among patients with and without cancer (65.8±25.2 years and 66.9±31 years, p=0.09). Mean prostate volume of all patients with cancer was significantly lower than patients without cancer (49.8±25.2 mL and 60.9±31.8 mL, respectively, p=0.08).

There were 1370, 440, 269 patients in Groups 1, 2, and 3, respectively. PCadetection rates were 16%, 25%, 53% in Groups 1, 2 and 3, respectively (p=0.001). In Group 1, there was a significant difference in mean prostate volume of patients with and without PCa (Table 1, p=0.01). However, this difference was not seen in patients in Group 2 or Group 3 (Table 1, p=0.08).

Despite the difference in prostate volumes of the patients with and without cancer in Group 1, the other parameters affecting biopsy outcomes such as mean age and PSA level were similar (67.73±32.4 years vs. 65.13±30 years, p=0.09 and 5.94±2.5 ng/mL vs. 5.47±2.3 ng/mL, p=0.06, respectively). Major complications including acute prostatitis, urinary retention, macroscopic hematuria, epididymitis, hypotension and prolonged rectal bleeding were seen in 161 (7.7%) patients (Table 2).

Discussion

Due to the insufficient sampling capabilities, the classical sextant biopsy scheme has been replaced with extended biopsy protocols consisting of 10 or more cores.[15] Eichler et al.[16] performed a systematic review of 20698 patients from 87 studies which compared the cancer detection rates of different extended prostate biopsy schemes with standard sextant scheme. The number of cores reported in individual studies ranged from 6 to 22 cores. The authors concluded

Table 1. Patient demographics, mean prostate volume and mean serum PSA levels

	Patients with PCa (n=472)	Patients without PCa (n=1607)	p
Age (year)			
Group 1	67.73±32.4	65.13±30	0.09*
Group 2	66.41±29.3	65.39±27	0.06*
Group 3	67.38±31.7	66.24±29.7	0.08*
Prostate volume (mL)			
Group 1	45.7±21.2	58.2±31.5	0.01**
Group 2	55.7±25.7	57.4±27.6	0.06**
Group 3	56.5±26.1	56.9±29.4	0.08**
PSA (ng/mL)			
Group 1	5.94±2.5	5.47±2.3	0.06**
Group 2	16.17±7.6	12.63±6.9	0.001**
Group 3	28.40±9.3	23.11±8.8	0.001**

**Mann-Whitney U test, *Unpaired t test. PCa: prostate cancer; PSA: prostate specific antigen. Group 1=patients with PSA <10 ng/mL, Group 2=patients with a PSA of 10-20 ng/mL, Group 3=patients with a PSA of >20 ng/mL

Table 2. Major complication rates in the study cohort

Complications	Number (%)
Acute prostatitis	65 (3.12)
Acute urinary retention	42 (2.02)
Gross hematuria	38 (1.82)
Acute epididymitis	10 (0.48)
Vasovagal hypotension	3 (0.14)
Rectal bleeding	3 (0.14)

that more extensive, laterally directed biopsy protocols have significantly higher diagnostic yield than the standard sextant scheme. However, increasing the biopsy core numbers over 18 to 24 did not provide additional benefit. Moreover, using 12 core schemes did not increase the complication rates while complications were poorly reported in studies performed with 18 to 24 cores. This review stated that the most proper biopsy scheme should balance the PCa detection rate, adverse events and cost-effectiveness. Although, the most efficient biopsy scheme with the optimal number of cores has not been yet defined[17], both American and European guideline panels recommend laterally directed biopsy schemes with 10 to 12 cores.[18,19] They also suggest that more than 12 core biopsies have no benefit for initial diagnostic biopsies.

The number of cores that should be sampled in large volume prostates is another controversial issue. The total prostatic tissue sampled with a standard sextant biopsy is only 90 mm in length (6x15 mm). As PCa is multifocal in most of the cases, larger prostate volume may significantly reduce the chance of detecting cancer.[20] The association between prostate volume and PCa detection rates of TRUS-Bx was first reported by Uzzo et al.[5] They observed a significant difference between PCa detection rates of large and small glands with sextant biopsy schemes and concluded that in order to overcome the significant sampling error seen in men with large glands increased number of cores should be sampled in these patients. This recommendation has also been supported by subsequent several studies.[21-23] However, it is well known that incidence of PCa increases with increasing PSA levels but none of these studies have evaluated the importance of prostate volume in different PSA subgroups. In the current study, we compared the mean prostate volume of the patients with and without PCa at different ranges of PSA levels of ≤10 ng/mL, 10-20 ng/mL and >20 ng/mL. Our findings revealed that the prostate volumes of the patients with and without PCa were significantly different in only patients with PSA ≤10 ng/mL. If the mean age , and PSA levels of the patients are comparable , then mean prostate volume seems to be the only predictor of PCa detection in this patient population. Moreover, such a correlation was not seen in patients with PSA levels more than 10 ng/mL.

Carvalhal et al.[24] evaluated the correlation between serum PSA levels and cancer volume in patients who underwent radical prostatectomy and reported that while the correlation between PSA and prostate size was only obvious in the largest prostate glands, and the association between tumor volumes was consistent in all prostate volumes. Therefore, we can say that increased PSA levels even in the larger prostates may indicate the existence of underlying PCa. We can also think that the effect of prostate volume on biopsy outcomes may be insignificant at increased serum PSA levels. Indeed, our results demonstrated that prostate volume has no effect on the PCa detection rate in patients with PSA level more than 10 ng/mL. It seems that increased tumor volume related to higher PSA levels masks the negative effects of prostate volume on the PCa detection rates. However, the probability of detecting cancer decreases in patients with PSA ≤10 ng/mL, and a greater prostate volume. So, this exactly like looking for a needle in a haystack and more cores are necessary during TRUS-Bx in these patients. We think that, extended biopsy templates may be recommended in patients with PSA level ≤10 ng/mL and large prostate gland, but not in patients with PSA levels more than 10

Turk J Urol 2019; 45(2): 103–7
DOI:10.5152/tud.2018.66909

ng/mL. Nevertheless, increasing the number of cores in patients with lower PSA levels possesses the risk of diagnosing more insignificant PCas and physicians should always discuss the pros and cons of such a diagnosis.

The current study has several limitations. First of all, the data were collected retrospectively. Second, all the patients in the study cohort underwent 10-core biopsy scheme and we did not have the results of extended biopsy templates. Moreover, information on clinically significant and insignificant PCa rates were not available. Finally, we did not consider the association between prostate volume and complications after biopsy. However, the present study has an important strength in terms of larger study population.

In conclusion, our results revealed that the prostate volume may interfere with the initial diagnostic value of prostate biopsy only in patients with PSA level of ≤10 ng/mL. Therefore, we can conclude that prostate volume may be ignored in the presence of higher PSA levels. Further prospective studies are necessary to find out the exact role of PSA on prostate biopsy outcomes.

Ethics Committee Approval: Ethics committee approval was received for this study from the Institutional Ethical Committee of Bagcilar Training and Research Hospital for Non-invasive Clinical Trials (14.01.3013/2013-97).

Informed Consent: The written patient informed consent was not obtained from the patients due to retrospective nature of the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.Z.T.; Design - E.K., M.Z.T.; Supervision - A.S., A.Y.M.; Resources - E.K., A.S.; Materials - E.K., A.S.; Data Collection and/or Processing - A.Ç., M.Z.T.; Analysis and/or Interpretation - T.E.K., A.Ç.; Literature Search -M.Z.T., E.Y.; Writing Manuscript - E.K., M.Z.T., E.Y.; Critical Review - E.Y., A.S., A.Y.M.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Refences

1. Chambó RC, Tsuji FH, de Oliveira Lima F, Yamamoto HA, de Jesus CM. What is the ideal core number for ultrasound-guided prostate biopsy? Korean J Urol 2014;55:725-31.
2. Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. J Urol 1989;142:71-5. [CrossRef]
3. Levine MA, Ittman M, Melamed J, Lepor H. Two consecutive sets of transrectal ultrasound guided sextant biopsies of the prostate for the detection of prostate cancer. J Urol 1998;159:471-6. [CrossRef]
4. Steven D, McCabe K, Peretsman S, Klein E, Levin H, Optenberg S, et al. Prostate rebiopsy is a poor surrogate of treatment efficacy in localized prostate cancer. J Urol 1998;159:1606-8. [CrossRef]
5. Uzzo RG, Wei JT, Waldbaum RS, Perlmutter AP, Byrne JC, Vaughan ED Jr. The influence of prostate size on cancer detection. Urology 1995;46:831-6. [CrossRef]
6. Letran JL, Meyer GE, Loberiza FR, Brawer MK. The effect of prostate gland volume on the yield of needle biopsy. J Urol 1998;160:1718-21. [CrossRef]
7. de la Taille A, Antiphon P, Salomon L, Cherfan M, Porcher R, Hoznek A, et al. Prospective evaluation of a 21-sample needle biopsy procedure designed to improve the prostate cancer detection rate. Urology 2003;61:1181-6. [CrossRef]
8. Inahara M, Suzuki H, Kojima S, Komiya A, Fukasawa S, Imamoto T, et al. Improved prostate cancer detection using systematic 14-core biopsy for large prostate glands with normal digital rectal examination findings. Urology 2006;68:815-9. [CrossRef]
9. N. Mottet, J. Bellmunt, E. Briers, M. Bolla, L. Bourke, P. Cornford, et al. Guidelines on Prostate Cancer. European Association of Urology, 2017.
10. Giganti F, Moore CM. A critical comparison of techniques for MRI-targeted biopsy of the prostate. Transl Androl Urol 2017;6:432-43. [CrossRef]
11. Grunkemeier MN, Vollmer RT. Predicting Prostate Biopsy Results: The Importance of PSA, Age, and Race. Am J Clin Pathol 2006;126:110-2. [CrossRef]
12. Kato RB, Srougi V, Salvadori FA, Ayres PPMR, Leite KM, Srougi M. Pretreatment tumor volume estimation based on total serum PSA in patients with localized prostate cancer. Clinics 2008;63:759-62. [CrossRef]
13. Woolf S. Screening for prostate cancer with prostate-specific antigen. An examination of the evidence. N Engl J Med 1995;333:1401-5.
14. Hayes JH, Barry MJ. Screening for prostate cancer with the prostate-specific antigen test: a review of current evidence. JAMA 2014;311:1143-9. [CrossRef]
15. Serefoglu EC, Altinova S, Ugras NS, Akincioglu E, Asil E, Balbay MD. How reliable is 12-core prostate biopsy procedure in the detection of prostate cancer? Can Urol Assoc J 2012;2:1-6.
16. Eichler K, Hempel S, Wilby J, Myers L, Bachmann LM, Kleijnen J. Diagnostic value of systematic biopsy methods in the investigation of prostate cancer: a systematic review. J Urol 2006;175:1605-12. [CrossRef]
17. Scattoni V, Raber M, Capitanio U, Abdollah F, Roscigno M, Angiolilli D, et al. The optimal rebiopsy prostatic scheme depends on patient clinical characteristics: results of a recursive partitioning analysis based on a 24-core systematic scheme. Eur Urol 2011;60:834-41. [CrossRef]
18. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Prostate Cancer Early Detection. Version 1.2012. 2012 [May 1, 2012]; Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.

19. Heidenreich A, Bastian PJ, Bellmunt J, Bolla M, Joniau S, van der Kwast T, et al. European Association of Urology. EAU guidelines on prostate cancer part 1: screening, diagnosis, and local treatment with curative intent-update 2013. Eur Urol 2014;65:124-37. [CrossRef]
20. Billebaud T, Villers A, Astier L, Boccon-Gibod L, Dauge MC, Sibert A, et al. Advantage of systematic random ultrasound-guided biopsies, measurement of serum specific antigen levels anddetermination of prostate volume in the early diagnosis of prostate cancer. Eur Urol 1992;21:6-14. [CrossRef]
21. Karakiewicz PI, Bazinet M, Aprikian AG, Trudel C, Aronson S, Nachabé M, et al. Outcome of sextant biopsy according to gland volume. Urology 1997;49:55-9. [CrossRef]
22. Mariappan P, Chong WL, Sundram M, Mohamed SR. Increasing prostate biopsy cores based on volume vs the sextant biopsy: a prospective randomized controlled clinical study on cancer detection rates and morbidity. BJU Int 2004;94:307-10. [CrossRef]
23. Ceylan C, Doluoglu OG, Aglamis E, Baytok O. Comparison of 8, 10, 12, 16, 20 cores prostate biopsies in the determination of prostate cancer and the importance of prostate volume. Can Urol Assoc J 2014;8:81-5. [CrossRef]
24. Carvalhal GF, Daudi SN, Kan D, Mondo D, Roehl KA, Loeb S, et al. Correlation between Serum PSA and Cancer Volume in Prostate Glands of Different Sizes. Urology 2010;76:1072-6. [CrossRef]