African Journal of Urology (2015) **21**, 62–66

HOSTED BY

Pan African Urological Surgeons' Association

African Journal of Urology

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Original article

A review of transrectal ultrasound guided prostate biopsies: Is there still a role for finger guided prostate biopsies?

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Received 14 July 2013; received in revised form 30 November 2014; accepted 11 December 2014

KEYWORDS
Prostate cancer;
Prostate biopsy;
Transrectal ultrasound;
Finger-guided prostate biopsy

Abstract

Objective: We compared our institution's initial experience with transrectal ultrasound-guided (TRUS) prostate biopsies in a single arm prospective study to a historical cohort of finger guided (FG) biopsies. The primary outcome measure was prostate cancer detection. We documented our findings on TRUS including the findings of peripheral calcifications, hypoechoic lesions and capsular distortion and evaluated whether these had any significance in prostate cancer detection.

Patients and methods: All patients presenting to our institution for prostate biopsy were included. Indications included raised PSA and/or abnormal DRE or other suspicion of prostate cancer. Data on 12-core TRUS guided biopsies were prospectively collected and compared to a historical cohort of 6-core FG biopsies obtained from the pathology database of all prostate biopsies performed at Groote Schuur Hospital within the study period.

Results: One hundred and ninety-two patients were included in the TRUS group over a 25-month period (2008–2010) and 262 FG biopsies were reviewed between 2006 and 2008. Abnormal DRE findings were present in 56.2% of FG and 43.3% of TRUS biopsies. Histology was available in 97.8% of cases. The incidence of prostate cancer was 42%. Malignant or suspicious histology was found in 45.6% of the FG group compared to 48.6% in the TRUS group ($p = 0.27$). In patients with a normal DRE there was a trend that favoured TRUS for improved cancer detection, which is significant if the PSA was below 10 ng/mL.

Conclusion: Our study did not show superiority of TRUS over FG biopsies except when the patient had a low PSA (below 10 ng/mL) and a normal DRE. Systematic FG biopsies may be underutilised in the TRUS era, and may be of benefit in patients presenting with a PSA over 10 ng/mL or an abnormal DRE. This may be of value in a limited resource setting where access to TRUS is restricted.

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Peer review under responsibility of Pan African Urological Surgeons' Association.

http://dx.doi.org/10.1016/j.afju.2014.12.002

Introduction

Prostate cancer is the commonest malignancy among black males in South Africa and the second commonest among white males [1,2]. Although the incidence of prostate cancer is increasing in the developed world, it remains under-diagnosed in the developing world where it often presents late [3]. Biopsy of the prostate forms the cornerstone in diagnosing and treating this disease. Historically, needle biopsies of the prostate were performed either transrectally or trans-perineally, with digital palpation of the gland and guidance of the biopsy needle per rectum [4]. Three important developments significantly changed the way the prostate cancer was diagnosed in the early 1990s. Firstly, the adoption of a systematic rather than random biopsy scheme as described by Hodge et al. [5]. Secondly, the use of a biopsy gun as opposed to hand-operated Tru-cut needles and thirdly, the advent of the transrectal ultrasound (TRUS) probe enabling the clinician to visually guide the biopsy needle [6].

Over the last two decades, TRUS has become the gold standard in performing prostate biopsies [7,8]. The initial work from Stanford University demonstrated that TRUS biopsies diagnosed cancer in 23 of 43 patients who had previous negative FG biopsies while confirming previously digitally diagnosed cancer in 94% [9]. In a further publication in the same journal, they showed that the yield of prostate cancer was better with six systematic random biopsies than FG biopsies of abnormal areas in the prostate [5]. The benefits of ultrasound in guiding biopsy needles became more apparent as the understanding of prostate anatomy and distribution of carcinoma improved, assisted by McNeal's description of the different zones [10]. Since then much work has been done to determine the optimal sites and numbers of prostate biopsies to maximise cancer detection of what remains a test with a significant sampling error. The consensus today for initial biopsies is to use a minimum of 10–12 laterally directed biopsies from the peripheral zones with the use of TRUS [11,12].

Our institution only acquired a transrectal ultrasound probe in 2008, enabling us to perform TRUS guided biopsies. We prospectively collected data on all TRUS guided prostate biopsies since the inception of this service, using a standard proforma. The aim of this review was to investigate our hypothesis that TRUS would increase the yield of our prostate biopsies which were previously performed with 6 finger-guided (FG) cores. At the same time we wanted to evaluate the extent to which the trainees were able to detect abnormalities of the prostate on TRUS by recording the findings and correlating them with cancer diagnoses.

Patients and methods

Approval was obtained from the Human Research Ethics Committee of the Faculty of Health Sciences of the University of Cape Town.

The study population included all patients undergoing prostate biopsy at our institution during the study period July 2006 to February 2010. The first group was the FG biopsy group identified from pathological records of needle biopsies of the prostate performed in the time period immediately preceding the introduction of TRUS at our hospital. The second group was the TRUS guided biopsy group where data were prospectively collected since the start of TRUS, on a standardised proforma at the time of biopsy and combined with the histological findings. Only patients with complete data sets were included in the study. Patients who underwent FG biopsy during the TRUS period were excluded.

Clinical parameters included patient demographics including age, reason for intervention (screening or symptoms), PSA value, and clinical findings on DRE. DRE findings were classified from clinical stage 1 to 4 according to the AJCC [13] staging system as found on initial examination by a member of our Urology Department. Absolute PSA values were recorded and subsequently subdivided for the purposes of analyses into five groups: 0–4, 4–9.9, 10–19.9, 20–99.9 and >100 ng/mL.

TRUS was performed using a Toshiba diagnostic ultrasound machine with a 7.5-MHz transrectal probe. Informed consent was obtained and antibiotic prophylaxis administered orally 30 min before the procedure. Local anaesthetic with intrarectal instillation of 20 mL 2% lignocaine jelly (Remicaine®, AI Generics, South Africa) was used without periprostatic needle infiltration. The findings on TRUS were documented for both the right and left lobe as follows: the presence of hypoechoic areas and/or calcifications in the periphery and the centre of the glands as well as the presence of capsular distortion or the visualisation of a palpable irregularity. The prostate gland was assessed in the axial plane where the transverse and antero-posterior measurements were taken at the point of maximum diameter, followed by a paramedian longitudinal measurement in the sagittal plane. The volume was calculated using a standard pre-programmed formula $\{\pi/6 \times (\text{transverse diameter}) \times (\text{antero-posterior diameter}) \times (\text{superior–inferior diameter})\}$ based on an ellipsoid shape. The number of biopsies taken was documented prospectively in the TRUS group as either the routine 12 cores (2 cores from apex, mid-zone and base of prostate on the periphery of either lobe) or the routine 12 cores plus additional biopsies of suspicious areas (on ultrasound or digital examination).

Finger-guided biopsies were performed similarly to TRUS biopsies using a Magnum Biopsy Instrument (C.R. Bard Inc., USA) with 18 G 25 cm Tru-cut needles. However, with finger-guided biopsies, there was a maximum of 6 cores taken, 3 in each lateral lobe. Cores were transferred in 2 specimen bottles for FG biopsies (left and right lobes) and in 6 pots for TRUS biopsies (left and right apex, mid-zone and base respectively).

Histological diagnoses were classified for the purposes of analysis into benign if reported as normal prostate or benign prostatic hyperplasia or inflammation and as suspicious for malignancy if reported as atypical, atypical small acinar proliferation (ASAP) or high grade prostatic intraepithelial neoplasia (PIN). Gleason scores below 6 were classified as suspicious for malignancy and 6 and higher were classified as malignant. To differentiate between negative biopsies and those with pathological findings, patients with suspicious findings were grouped together with the confirmed carcinomas.

Data were compiled using MicroSoft Excel® and statistical analysis was performed by a biostatistician on Stata® software using the Mann–Whitney U test for continuous variables and the Pearson's chi-squared test for categorical variables. A two-tailed p-value <0.05 was accepted as significant with a power of 80%.

Results

Over a 25-month period complete data sheets and pathology reports were collected in 192 patients who underwent TRUS guided biopsies

Table 1 Patient age, PSA and histology.

	Finger guided ($n = 262$)	TRUS guided ($n = 192$)	p-Value
Age (mean ± SD)	68.4 ± 8.38	65.6 ± 7.87	0.0005
PSA (median + IQR)	12 (8.8–52.8)	17.5 (6.5–24.2)	0.0001
DRE suspicious or malignant	109/194 (56.2%)	78/180 (43.3%)	0.013
Benign histology	141 (54.4%)	94 (51.4%)	0.32
Malignant histology	118 (45.6%)	89 (48.6%)	0.27
Gleason 6	31.3%	41.3%	
Gleason 7	23.6%	30.7%	
Gleason 8–10	45.3%	28%	

at one hospital. The FG cohort comprised 262 patients over a 17-month period preceding the start of TRUS guided biopsies.

Presenting features

Patients in the TRUS group presented mostly with obstructive lower urinary tract symptoms (65.2%) followed by referral with raised PSA (21.5%), irritative or mixed lower urinary tract symptoms (11.6%) and other symptoms (1.6%) such as haematuria or paralysis.

Patient age, presenting PSA value and clinical findings are presented in Table 1 together with diagnosis of biopsy. Twenty-four patients had a PSA value less than or equal to 4 and 399 patients a raised PSA. In the FG and TRUS guided groups, the numbers of patients with normal PSA (4 ng/mL and lower) were 12 (5%) and 12 (6.6%) respectively, and with a raised PSA (more than 4 ng/mL) in 229 (95%) and 182 (93.4%) patients respectively. Statistically however, when looking at the whole group, both age and PSA values were significantly different.

Biopsies performed

Biopsies were performed by an equal number of trainees [6] and specialists [2] with similar level of experience in both finger guided and TRUS guided biopsy groups, as shown in Table 2. Trainees performed 97.9% of the TRUS guided biopsies during the study period.

The number of biopsies taken differed in the two groups. In the finger guided group the average number of cores was 6.24 (range 2–12). In the TRUS group all but 15 patients had 12 or more cores, taken in a systematic sextant fashion as described above. All but 3 patients (due to technical failure of biopsy gun and patient being unable to tolerate biopsy under local anaesthetic) who had less than 12 cores taken with TRUS guidance had raised PSA above 50 ng/mL, with a clinically malignant feeling prostate.

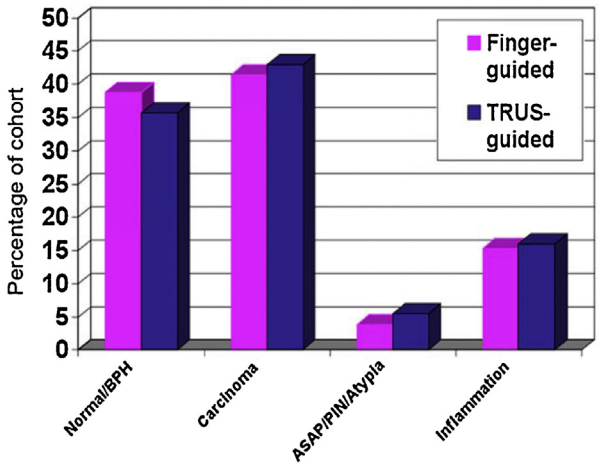

Figure 1 Histological findings in FG and TRUS guided groups.

Histology

Histology was available in 444 cases. The cancer detection rate was 42% overall, followed by benign prostatic hypertrophy, prostatitis (mostly chronic) and atypia, ASAP and PIN. Results are shown in Fig. 1. When comparing the FG with the TRUS group, there was no difference in the cancer detection rate between the two groups. When analysing the results according to DRE findings, more patients with a normal feeling prostate in TRUS group had carcinoma ($p = 0.03$). Among the patients with an abnormal DRE and a PSA value of less than 10 ng/mL, there was statistically an advantage in using TRUS guided over FG biopsies.

Prostatitis was diagnosed in 69 (15.2%) patients, evenly distributed between the two groups. The mean age (±SD) for patients with histological evidence of prostatitis was 69.4 (±8.1) years with a mean PSA of 16.9 ng/mL (IQR 7.1–19.8 ng/mL).

Eighty-eight patients had a palpable nodule on rectal examination of which 48.9% were diagnosed with malignancy. When analysing patients with an abnormal DRE in whom carcinoma was diagnosed, the yield using TRUS was significantly better only if the PSA was less the 10 ng/dL.

Features identified on TRUS of the prostate

The average size of prostates measured was 38.6 g. The findings are presented in Table 3. The probability ratios (with a 95% confidence interval) are presented to show the association between TRUS findings and the incidence of malignancy on biopsy. Findings included hypoechoic areas, peripheral calcifications, and a distorted or irregular capsule with probability ratios of 1.34 (0.98–1.8), 0.9 (0.7–1.3) and 29.0 (4.0–210.5) respectively. The findings of hypoechoic areas or calcifications were therefore not associated with a

Table 2 Clinicians (A–P) performing prostate biopsies with finger guidance (FG) and transrectal ultrasound (TRUS) guidance.

	Clinician															
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
FG (262)	10	53	27	24	74	24	18	6	3	7	10	5	0	0	0	0
TRUS (181)	0	0	3	0	31	15	15	3	11	4	0	30	21	13	30	5

Table 3 Findings on transrectal ultrasound with histological diagnosis.

TRUS findings	Total	Cancer	No cancer
Capsule distorted	22 (13.0%)	21	1
Capsule intact	147 (87.0%)	50	97
Calcification PZ	108 (60.3%)	27	81
No calcification PZ	71 (39.7%)	21	50
Calcification centre	36 (21.3%)	17	19
No central calcif	133 (79.7%)	55	78
Hypoechoic PZ	100 (54.6%)	54	46
No hypoechoic PZ	83 (45.4%)	24	59

PZ, peripheral zone; calcif, calcification

higher probability of finding malignancy in the prostate biopsy. However, when a distorted capsule was seen on TRUS, the probability was at least 4 times higher, and on average 29 times higher than the general population. In all the cases where capsular distortion or irregularity was seen on TRUS, the DRE was also documented as abnormal.

Discussion

Cancer detection

The yield of prostate cancer overall was 42% in our study population with no difference in the incidence between the FG and the TRUS guided groups. This is in keeping with published figures, in spite of the fact that there was, on average, double the number of biopsies done in the TRUS group (12 cores) compared to the FG group (6 cores) [14,15]. This finding was contrary to our expectations, as we believed TRUS not only to be sampling the prostate more precisely, but also obtaining double the number of cores.

We also postulated that TRUS might be of more benefit where the DRE was normal but when analysing these patients, there was a trend favouring TRUS only if the PSA was lower than 20 ng/mL, which was statistically significant only when the PSA was below 10 ng/mL. The subgroup of "normal" PSA below 4 ng/mL did not reach significance, likely because of the small number of patients in this group.

Digital rectal examination

The DRE was found to be abnormal in 50%. Among the patients who had a normal DRE, 63 were diagnosed with carcinoma and these patients were equally distributed between the FG and TRUS groups. However, when stratifying these results according to PSA values as shown in Figs. 2 and 3, this difference in diagnosis only approaches statistical significance when the PSA value is less than 10 ng/mL. This trend is maintained whether or not the diagnoses of PIN and ASAP are included in the malignant group. This finding suggests that TRUS biopsy is not superior to FG biopsies for patients with a PSA value of more than 10 ng/mL, irrespective of the DRE findings. According to our data, TRUS should be reserved for patients with a normal DRE and a PSA value below 10 ng/mL.

Of note is the finding that patients were either screened with PSA once they presented to the urological service with urinary symptoms or were referred with a raised PSA. No patient was referred with an abnormal DRE despite almost 50% of patients having a palpable nodule. We found that, in keeping with the literature, a nodule

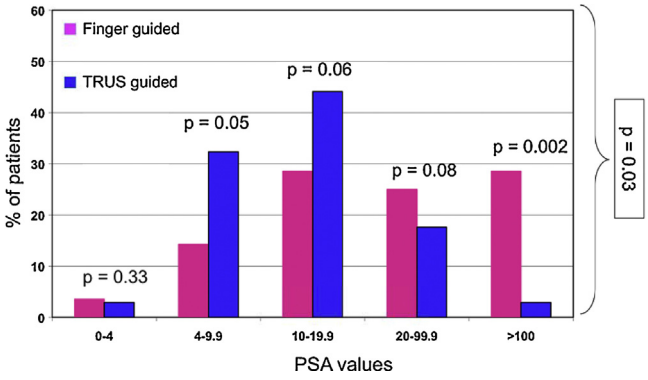

Figure 2 Incidence of cancer in patients presenting with a benign feeling prostate gland shown by PSA categories.

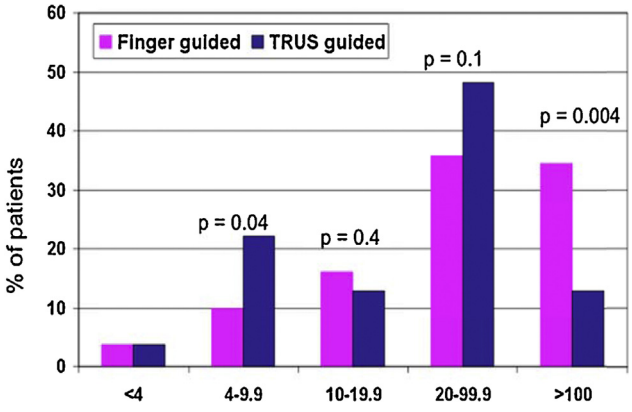

Figure 3 Incidence of cancer in patients presenting with an abnormal DRE shown by PSA categories.

has a 49% chance of being malignant. In a resource limited setting the performance of DRE is cost-effective and may prompt earlier detection of disease and thus earlier referral for assessment.

Study population

In our single arm prospective study of TRUS there were fewer biopsies performed over a 25-month period than was the case with the 17-month retrospective control group. Two factors can account for this: excluded patients who underwent FG biopsies in the TRUS era, and secondly, the increased time needed to perform TRUS compared to FG biopsies. One weakness of this study is that our two study groups were found to be statistically different in terms of age and PSA value at presentation, even though our department's clinical indications for prostate biopsy have not changed over the course of this study period. Although the mean patient age was significantly higher in the FG biopsy group, the median PSA in this group was, contrary to expectation, significantly lower than in the TRUS guided biopsy group. This might be accounted for by the higher percentage of high Gleason grade cancers (Grade 8–10) in the retrospective group. Whether the statistical difference in age and PSA is clinically relevant, is debatable.

Number of biopsies

Although the current guidelines from leading professional bodies [7,16] suggest at least 10-core biopsies, there is evidence

to suggest that fewer cores are adequate [14,17]. The literature has however shown that 6-core biopsies, in contrast to our findings, are inferior to 10 and 12-core biopsies [18–20]. Although urology trainees performed both FG and TRUS biopsies, with equal experience in both approaches, the learning curve associated with TRUS biopsy might impact the quality of the TRUS biopsies in our study. Investigators have, however, found no learning curve associated with the procedure in studies that assessed the cancer detection rate [21,22].

Finger guided targeted biopsies

Initially the trials comparing FG with TRUS guided biopsies after Hodge's publication [5] consisted of small retrospective series, showing conflicting results. Most trials investigating FG biopsies involved only patients with abnormal DRE findings. Among these, there is evidence to show that FG biopsies have a role to play in the era of TRUS guided biopsies, especially in patients presenting with an abnormal DRE [23–26].

Conclusion

While TRUS guided biopsies remain the gold standard, in centres where TRUS is not available, a systematic finger guided biopsy with a minimum of 6 cores, is a suitable alternative in patients who present with an abnormal feeling prostate gland on DRE. It should also be considered when there is a raised PSA, especially a PSA level more than 10 ng/mL.

Our findings are limited by the study design, which due to its retrospective nature limits the conclusions we can derive. However, the benefits of FG biopsies are: that it is quick, requires fewer cores and is readily available in resource limited settings where there is not access to TRUS. In the absence of a prospective randomised controlled trial directly comparing TRUS with FG biopsies, the role of FG biopsies remains unproven.

Conflict of interest

The authors report no conflict of interest.

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