

Factors Influencing Pain during Transrectal Prostate Biopsy

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| Received: 02.01.2019 | Accepted: 07.01.2019 | Published: 30.01.2019

DOI: [10.36348/sjmpps.2019.v05i01.008](https://doi.org/10.36348/sjmpps.2019.v05i01.008)

Abstract

Pain is the most common complaint from patients undergoing prostate biopsy. With the increase in patients requiring prostate biopsy following massive screening for prostate cancer, more men would therefore complain about pain. Observing that the perception of pain varies amongst patients, we set out to find the influence of these factors on pain experienced during prostate biopsy. We also sought the incidence of complications which may arise from this procedure. A total of 132 patients scheduled for transrectal prostate biopsy were randomly assigned to two groups. All patients had 20 mls of 2% lidocaine gel administered per rectum 10 minutes before transrectal ultrasound probe insertion. The severity of pain during the procedure was assessed using the 10-point numerical rating scale. A weak positive correlation was found between the prostate volume and level of pain perceived by patients ($r = 0.084$) & ($r = 0.339$). Pre-biopsy anxiety was found to have no influence on pain. There was moderate correlation ($r=0.497$) between pain and age of participants during needle insertion, whereas a weak correlation ($r=0.173$) was found between the latter and pain perceived during probe insertion. Age was found to be the only predictor of level of pain on regression analysis ($P = 0.016$). Post biopsy, 25% of patients had haematuria while 12% complained of rectal bleeding. Haematospermia and fever were seen in 5.5% and 0.8% of patients respectively. Increasing age was found to influence pain perceived during transrectal ultrasound-guided prostate biopsy. Haematuria and rectal bleeding were found to be the most common complications following TRUS-guided biopsy of the prostate.

Keywords: Factors; Prostate biopsy; Pain relief; Numerical rating scale; Prostate cancer; Complications.

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INTRODUCTION

The gold standard for diagnosis of cancer of the prostate gland is biopsy of the gland as empirical treatment without tissue diagnosis is no longer acceptable. Prostatic biopsy under transrectal ultrasound (TRUS) guidance is the technique of choice in tissue diagnosis of prostate cancer [1]. Transrectal ultrasound (TRUS) guided prostate biopsy is a well tolerated minor procedure and one of the most frequently performed procedures by urologists throughout Europe and the United states of America [2]. Though considered a safe procedure, it is beset by frequent minor complications such as haematuria, haematospermia, rectal bleeding, urinary tract infection and voiding symptoms in about half of patients, with pain as the most common complaint after the procedure [2, 3]. Nevertheless, the perception of pain associated with prostate biopsies varies widely amongst patients. Since the advent of Prostate specific antigen (PSA) estimation, the number of patients requiring prostate biopsy for the diagnosis of carcinoma of the prostate has markedly increased [4]. Recently, the tendency has been to increase the number of cores obtained during prostate biopsy, with the purpose of increasing the

diagnostic yield of the technique [5]. There has also been an increase in the number of patients requiring repeat prostate biopsies due to suspected false negative biopsies on initial testing, suspicious pathology or active surveillance [6]. These therefore translate to more pain experienced by more men during clinical evaluation for prostate cancer.

Only few studies have evaluated pre-biopsy clinical factors such as age, prostate volume as well as the number of biopsy punctures; and their impact on pain during the procedure [7-9]. However, the prediction of the level of pain to expect based on these pre-biopsy factors would be highly desirable in clinical practice and in planning for the appropriate anaesthesia for the procedure. In this study, we prospectively evaluated pre-biopsy factors which may be associated with the level of pain perceived during the two phases of ultrasound-guided transrectal biopsy of the prostate gland as well as the incidence of complications which may arise from the procedure.

PATIENTS AND METHODS

The study was a hospital-based cross-sectional prospective study carried out at the University of Uyo teaching hospital, Uyo, Nigeria. It spanned 14 months between 1st March 2015 and 30th April 2016. The ethical approval for the study was obtained from the hospital's Ethics Committee and written informed consent was obtained from the patients. The subject selection was by purposive criterion sampling method. Included in the study were all new patients aged 40 years and above with lower urinary tract symptoms attending the urology clinic with elevated PSA >4ng/ml and/or digital rectal examination findings suggestive of cancer of the prostate who voluntarily gave their consent to take part in the study.

After explanation of the aims of the study and obtaining written consent from the patient, demographic and clinical information were collected from each patient by the investigator using an interviewer-administered questionnaire. Patients had 20 mls of 2% lidocaine gel administered per rectum 10 minutes before transrectal ultrasound probe insertion. All patients underwent soap-water enema in the morning of the procedure as well as received prophylactic antibiotics (200mg of ciprofloxacin and 500mg of metronidazole) intravenously, 1 hour before the biopsy, followed by 500mg of ciprofloxacin and 400mg of metronidazole orally 12 hours after. All intrarectal instillations were done with the patients in the left lateral position. Subsequent to the intrarectal instillation of the gel, the gloved right index finger of the researcher was used to smear it over the prostate gland to maximize surface area covered by the gel.

Transrectal biopsy was carried out using an 18G trucut biopsy needle on a loaded biopsy gun

attached to and guided by a 7 MHz transrectal ultrasound probe, with the subject in the left lateral position. The transrectal ultrasonographic imaging was used to determine prostate volume using the ellipsoid formula (volume= $(\pi/6) \times \text{length} \times \text{width} \times \text{height}$). Ten (10) biopsy cores were taken from both lobes (sextant with two lateral cores on each side). Subjects were required to grade pain felt during transrectal probe insertion and pain felt during needle biopsy 2 minutes after these respective phases of the procedure using the 10-point numerical rating scale, NRS. The question concerning grading of pain was phrased in the same manner in all cases to minimize bias during data collection.

We used Student's *t*-test for continuous variables, Mann-Whitney test for qualitative variables. For multivariate analysis, ANOVA regression analysis was used and SPSS software (version 20) was employed for the analysis. *P* values < 0.05 were considered statistically significant.

RESULTS

In this study, a total of 132 men were recruited over a period of 14 months but 127 patients were studied after exclusion of 5 men. Of these, 3 men did not complete the prostate biopsy due to uncontrollable pain and 2 failed to show up for follow up. The results and findings of the men studied are shown in the following tables and figures.

The age range of patients was from 40 to 86 years with mean age of 66.5 ± 9.4 years. The peak age group was in the age range 60-69 years and accounted for 51 patients (40.2%) of the entire study population. Cumulatively, 82 (75.5%) of the patients were above 60 years of age (Table-1).

Table-1: Distribution of patients with age ranges in decades

Age (years)	Number of patients (%)
40 – 49	7 (5.5)
50 – 59	23 (18.1)
60 – 69	51 (40.2)
70 – 79	38 (29.9)
80 – 90	8 (6.3)
Total	127

In the study, the PSA ranged from 4.4ng/ml to 178ng/ml with mean PSA of 39.4 ± 30.2 ng/ml while prostate volume on ultrasound ranged from 22cm³ to

246cm³ with mean prostate size at 78.2 ± 42.2 cm³ (Table-2).

Table-2: Patient characteristics in the study

Patient characteristics	Mean (+/-) SD
Age	66.5 (± 9.4)
Prostate volume	78.2 (± 42.2)
PSA level	39.4 (± 30.2)
PSA density	0.51 (± 0.36)

The pain score range was 1 to 10 with a mean pain score of 4.1 ± 1.7 with 62.2% of patients having a pain score of 3 or less where as 3.9% scored ≥ 7 and above. As regards the age of the participants, moderate ($r = 0.497$) and weak ($r = 0.173$) correlations were found with pain on probe insertion and during biopsy needle

insertion respectively (Figures 1 & 2). Positive correlations, though weak, found between the prostate volume and level of pain perceived by patients in this study during probe insertion ($r = 0.084$) and needle insertion ($r = 0.339$) phases of the procedure (Figures 3 & 4).

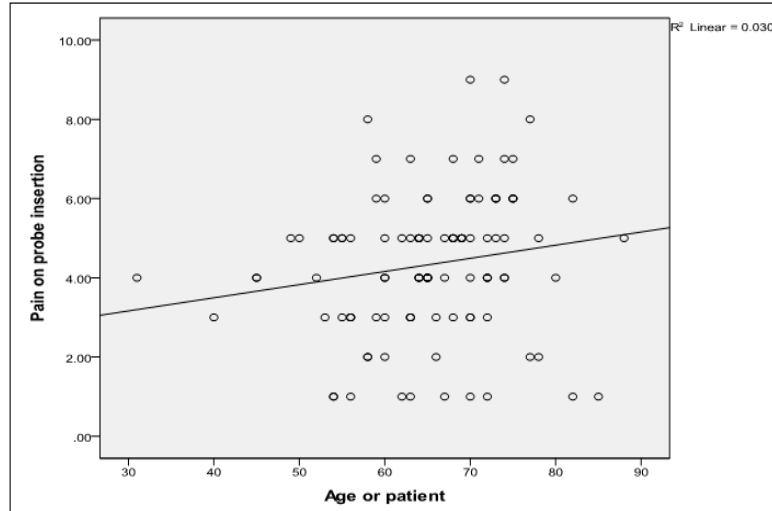


Fig-1: Scatter plot between pain on probe insertion and age

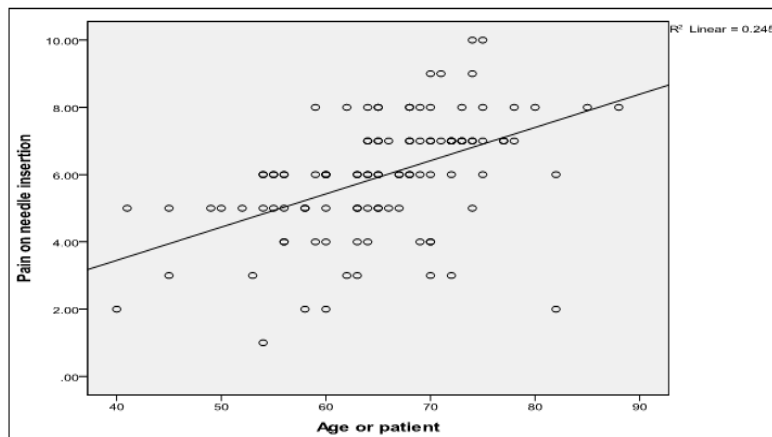


Fig-2: Scatter plot between pain on needle insertion and age

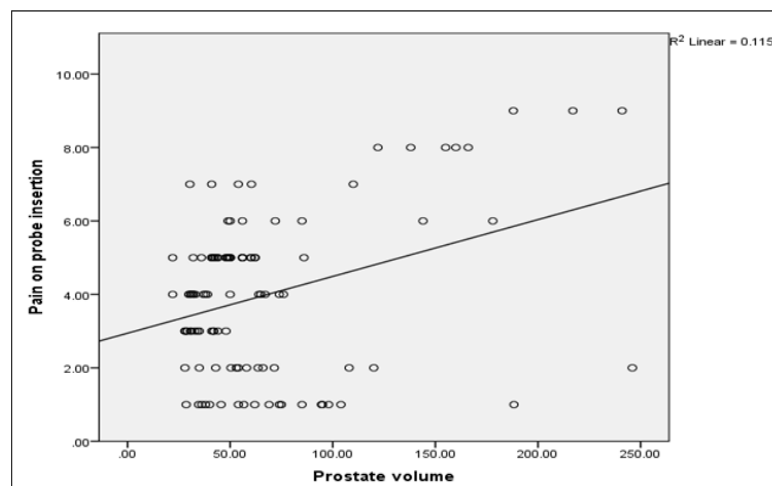


Fig-3: Scatter plot between pain on probe insertion and prostate volume

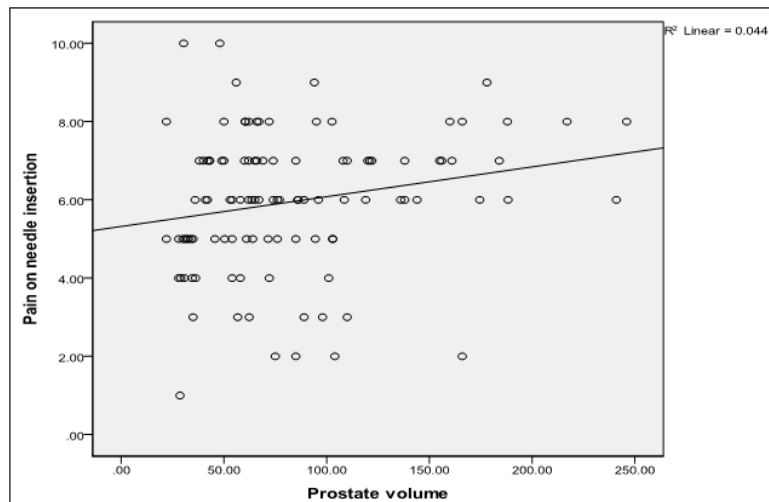


Fig-4: Scatter plot between pain on needle insertion and prostate volume

On analysis, the difference in mean pain scores of patients who experienced pre-biopsy anxiety and those that did not was found not to be statistically significant. ($p=0.73$, $U=1274.1$ respectively).

On analysis, the difference in mean pain scores of patients during probe insertion and needle insertion for patients who were anxious (pre-biopsy anxiety) and those who were not, were not statistically significant. ($p=0.73$, $U=1274.1$) and ($p=0.42$, $U=1311.5$) respectively.

On regression analysis of factors to determine their influence on pain perception, only age was to be a predictor of the pain during biopsy needle insertion ($P = 0.016$).

Fifty six patients (44%) reported post biopsy complications which included haematuria 32 (25.0%), rectal bleeding 15 (12.0%), haematospermia 7 (5.5%) and fever 1 (0.8%). However, no patient's complication necessitated hospitalization.

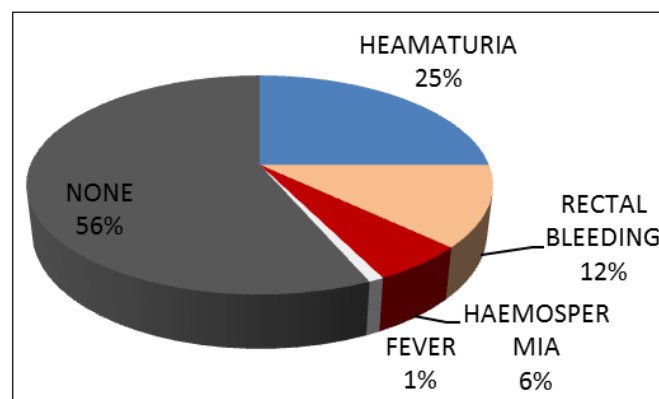


Fig-5: Post-biopsy complications

DISCUSSION

The transrectal route for biopsy of the prostate has been used widely as a technique since the mid 1950s, although Astraldi is credited with carrying out the first transrectal prostate biopsy in 1937 [10]. The most frequent complaint of the procedure is pain. Other common complications include: blood in the urine and stool for several days, clot retention, prostatic abscess, septicaemia as well as blood in the ejaculate for several weeks afterwards [3].

Factors which could influence pain during prostate biopsy could be categorized as patient-associated or procedure-associated factors. Examples of

patient-associated factors include age, pre-biopsy anxiety and prostate volume; while those of procedure-associated factors include cleansing enema, number of cores taken during biopsy as well as type of analgesia. Several studies have investigated the methods of analgesia for reducing the pain of prostate biopsy with minor emphasis focused on other clinical factors with the potential to influence the pain. This study aimed at evaluating patient-associated clinical factors that may influence the perception of pain experienced during the two phases of transrectal biopsy of the prostate. This stems from the paucity of such studies as well as the potential benefit from additional pain relief in the sub group of patient with identified factors. The factors we

investigated in this study included: age, prostate volume as well as pre-biopsy anxiety. In contrast to a report by Rodriguez *et al.*, [11] who reported more pain in younger patients, this study showed a statistically significant increase in pain experienced with increasing age ($P= 0.028$). Studies by Han *et al.*, [8] and Leibovichi *et al.*, [12] however did not observe any significant relationship between age and perceived pain. This relationship we observed between pain and age may be as a result of the decrease in inhibition to expression of pain with increasing age.

Though there was a positive correlation found between the prostate volume and level of pain perceived by patients in this study, it was not statistically significant. This is similar to what Leibovichi *et al.*, [12] and Bastide *et al.*, [9] observed in their study to determine the relationship between prostate volume and pain during transrectal ultrasound guided prostate biopsy. This however differs from the report of Yun *et al.*, [7] on 71 patients in which they found a strong positive and statistically significant relationship between prostate volume and pain. This finding may not be unconnected to the knowledge of the prostate volume by the investigators prior to the biopsy which may have induced some bias in the manner they interviewed the patients to determine pain scores after the procedure. This study, as well as Leibovichi's and Bastide's, was however double-blinded. Despite the statistically insignificant correlation observed, we presume that this finding may be attributed to the comparatively lower concentration per surface area of the anaesthetic gel on larger prostates thereby resulting in weaker anaesthetic effect and thus more pain.

Leibovichi *et al.*, [12] reported that pre-biopsy anxiety influenced the experience of pain during the procedure which contradicts the finding in our study. However, it is interesting to note that 26.7% of patients in Leibovichi's study had previous prostate biopsies which may have affected pre-biopsy anxiety in these patients and consequently, its correlation with perceived pain.

In consonance with the report by Shittu *et al.*, [13] on their complication rates after transrectal biopsy of the prostate, this study found haematuria and rectal bleeding to be the most common non-infective complications of the procedure. However, the slightly higher percentages in this study may be due to the relatively smaller sample size as well as the higher number of biopsy cores taken. In this study, none of the patients bled enough to require blood transfusion unlike in their study where four patients required blood transfusion following severe bleeding. This may be attributed to the relatively larger calibre of the biopsy needle used in their study.

CONCLUSION

In conclusion, increasing age was found to influence pain perceived during transrectal ultrasound-guided prostate biopsy. This finding suggests that additional analgesic strategies may be necessary for performing transrectal ultrasound-guided prostate biopsies in older patients. Haematuria and rectal bleeding were found to be the most common complications following TRUS-guided biopsy of the prostate.

Ethical committee approval

This study obtained the approval from the University of Uyo Teaching Hospital Institutional Health Research Ethics Committee.

Conflict of interest: None declared.

Source of funding

The research project was funded by the authors with no external source of funds or grant

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