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Original Article

Does needle calibre affect pain and complication rates in patients undergoing transperineal prostate biopsy? A prospective, randomized trial

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Abstract

Transperineal prostate biopsy is a procedure that can be used to obtain histological samples from the prostate. To improve both the quality of the biopsy core samples and prostate cancer detection, we are currently performing a prospective, randomized trial comparing prostate biopsy samples obtained using an 18 G-needle to those obtained using a 16 G needle. The aim of this preliminary study was to evaluate pain and complication rates in both groups in order to assess whether performing a prostate biopsy with a larger calibre needle is a feasible procedure. One hundred and eighty-seven patients undergoing transperineal prostate biopsy were prospectively evaluated and divided into two groups. The first group (94 patients, Group A) received a transperineal prostate biopsy using a 16 G-needle and the second group (93 patients, Group B) underwent transperineal prostate biopsy with an 18 G-needle. Anaesthesia was obtained with a single perineal injection at the prostatic apex in all subjects. A visual analogue scale (VAS) and facial expression scale (FES) were used to assess pain during multiple steps of the procedure in each group. A detailed questionnaire was used to obtain information about drug use because it could potentially influence the pain and complications that patients experienced. Two weeks after the procedure, early and late complications were evaluated. Statistical analysis was carried out using non-parametric tests. Prostate Specific Antigen (PSA) and drug use were similar at baseline between the two groups. Pain during prostate biopsy, which was measured with both the VAS and FES instruments, did not differ significantly between the 18- and 16 G-needle groups, and no significant differences were found in early or late complication rates between the groups. Transperineal prostate biopsy with a 16 G-needle is a feasible procedure in terms of pain and complication rates. Further studies with larger patient populations are required to assess whether or not this procedure can improve prostate cancer detection rates.

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1 Introduction

Since the beginning of the last century, transrectal ultrasound-guided needle biopsy of the prostate has been used to diagnose prostate cancer, and it is considered to

be an accurate method for obtaining prostatic tissue for histological evaluation [1, 2]

The transperineal biopsy approach has been developed in more recent years, and is considered to be an adequate alternative to the transrectal approach [3]. In fact, no significant differences were found in terms of cancer detection or complication rates between the two approaches in a recent prospective, randomized study by Hara *et al*. [4]. An 18-G needle is the most common needle calibre used to obtain prostatic tissue, although this convention is derived from the transrectal approach, which requires this needle size. As reported in previous breast cancer trials, tissue harvested using smaller needles is frequently friable and tends to fragment more often than tissue harvested using larger ones [5]. The use of a larger calibre needle certainly increases the amount of tissue harvested during biopsy and could potentially improve histological sampling, thereby enhancing the accuracy of prostate cancer diagnosis. In a previous study, 14-G needles were compared with 16-G needles in patients undergoing breast biopsies, and the results indicated that patients who underwent breast biopsy using the larger calibre needle did not experience significantly worse side effects than patients whose biopsy was performed using the smaller needle [5]. On the basis of these findings, we sought to examine whether or not the same findings would hold true in prostate biopsies. Therefore, we are currently performing a prospective, randomized study comparing the use of 16-G versus 18-G needles in transperineal prostate biopsies. We present our preliminary findings with the use of 16-G needles in transperineal prostate biopsies, and critically analyze data regarding pain and complication rates.

2 Materials and methods

Between November 2006 and September 2007, 187 patients undergoing ultrasound-guided transperineal prostatic biopsy were enrolled in this study and randomly divided into two groups. One group underwent biopsy using a 16-G needle (94 patients, Group A) and the other underwent biopsy using an 18-G needle (93 patients, Group B). Local anaesthesia was administered by means of a single transperineal injection of mepivacaine (4 mL) plus 1 mL bicarbonate at the prostatic apex, which was administered using a 22-G needle.

The inclusion criteria for the study included the following characteristics: (1) prostate-specific antigen (PSA) > 2.5 ng mL^{-1}; (2) increasing PSA velocity; (3) PSA free: total ratio > 16; and (4) a suspicious digital rectal examination. Exclusion criteria were (1) previous prostatic biopsy; (2) age > 75 years; (3) presence of significant co-morbidities; and (4) biopsies performed by urologists not mentioned in this study.

All biopsies were performed by two skilled operators. A total of 12 samples (6 per side) were obtained from each biopsy. An automatic Pro-mag 2.2 device (ProMag, MD Tech, Gainesville, USA) was used for all biopsies. Transrectal ultrasound was performed using a 7.5 MHz biplanar probe. Each transrectal ultrasound that was performed included an assessment of prostatic diameter, the volume of the whole prostate, and the transition zone and capsular and seminal vesicle characteristics, as well as a morphological description of potential pathological features in the peripheral or transition zone. Antibiotic prophylaxis was performed in all patients using oral fluoroquinolones.

Needle cores were placed in tissue cassettes between two sponges that had been previously treated with 70% ethanol. Each core sample was numbered, and identified by biopsy site and prostate lobe. The core biopsies were distributed in pairs, and the tissue cassettes were then submitted to pathology in containers filled with 10% buffered formalin.

At the end of the procedure, the patients were administered two scales that analyzed the pain and discomfort domains. The first one was the visual analogue scale (VAS), which is easy to understand and scores pain from 0 to 10 depending on pain intensity. The second scale uses facial expressions to indicate pain intensity, and is graded from 0 to 10. Patients were asked to match the picture with his/her pain level. Finally, each subject was asked to answer several questions about drug use during the preceding 2 weeks (Did you take drugs that had anti-platelet activity, warfarin, dicumarolic agents, non-steroidal anti-inflammatory agents, steroids, or benzodiazepines during the past 2 weeks?). All anti-coagulants were stopped at least 8 days before the procedure. Patients whose anti-coagulant therapy could not be suspended had their regular anti-coagulant medication converted to low molecular weight heparin.

At 2 weeks after prostatic biopsy, the patients were interviewed and asked questions regarding pain persistence or the recurrence, and possible side effects (haematuria, urinary retention, fever, *etc*).

All data were entered into a database and statistically analyzed using Statistical Package for Social Sciences, version 13.0 for Windows (SPSS Inc., Chicago, Ill). A preliminary descriptive analysis of all the variables was performed. Statistical analyses were carried out using the unpaired *t*-test, Mann–Whitney *U*-test, Wilcoxon test and χ^2-test.

3 Results

The mean age of patients in Group A was 66.7 ± 7.1 years and the mean age of patients in Group B was 69.4 ± 8.7 years (P = 0.02). PSA levels, diabetes rates and overall drug consumption rates were similar between the two groups (P = 0.055, 0.8 and 0.3, respectively). This last finding may be of interest with regard to complication rates, and may even influence patients' feelings and subjective perception of pain.

Visual analogue scale pain scores are summarized in Table 1. Pain was assessed at three separate time points: at the time of perineal anaesthesia, at the time of the biopsy procedure and at the 15-day follow-up appointment. Pain, which was assessed by both the VAS score and the facial expression scale (FES), did not differ significantly between the two groups at any of the three time points (Table 1). The overall complication rate (which included haematuria, mild vagal symptoms/reaction, the need for more anaesthesia, acute urinary retention and fever) was 26.5% (26 points) in Group A and 24.4% (23 points) in Group B (P = 0.22). In both groups, the most common complication was haematuria.

A total of 26 prostate cancers were detected in each group (P = 0.547). In total, 15 cases of high-grade prostatic intraepithelial neoplasia (HGPIN) were found among patients in the 18-G needle group and 10 cases of HGPIN were identified among patients in the16-G needle group (P = 0.187). A single case of atypical small acinar proliferation (ASAP) was detected in Group A, whereas four cases of ASAP were detected in Group B (P = 0.181).

4 Discussion

Transperineal prostatic biopsy is a technique that can be used to adequately sample prostatic tissue. Although initially applied to patients who had previously undergone abdominoperineal resection, this approach has since been used more widely and has been found to have a significant cancer detection rate as well as acceptable morbidity. Transperineal prostate biopsy requires the use of local anaesthesia, which it is often also used for transrectal prostate biopsies to reduce discomfort and pain [6]. Injection of a local anaesthetic agent at the prostate apex is a common anaesthetic technique used in the transperineal biopsy approach. In fact, it seems to be easier to perform and less painful than the prostatic plexus block that is used during transrectal biopsies [7].

Patients' pain and discomfort during prostatic biopsy are interesting topics in the modern literature. To evaluate pain perception, Soyupek *et al*. [8] recently invoked the modified tourniquet test as a predictor of pain during prostate biopsy. Different anaesthetic strategies have also been evaluated. Cam *et al*. [9] recently assessed the role of intraprostatic injections of a local anaesthetic agent during transrectal prostate biopsy and found that intraprostatic injections provide better pain control than periprostatic injections.

Raber *et al*. [10] compared the pain control obtained by a single periprostatic nerve block both alone and in combination with topical prilocaine-lidocaine cream. As predicted, adding a topical anaesthetic agent was found to be beneficial in preventing pain, a finding that was particularly evident in younger patients.

The devices used to perform a prostate biopsy, such as the needle, may also influence patients' pain. Novella and co-workers [11] used a coaxial transperineal needle during transperineal prostate biopsy to see whether it could reduce patients' pain. The authors found that the use of a coaxial transperineal needle decreased the overall invasiveness of the procedure. The same

Table 1. Patients' pain scores at different time points, as assessed by the visual analogue scale (VAS) and facial expression scale (FES).

	Group A (16 G) (N = 94)	Group B (18 G) (N = 93)	P-value
Pain during anaesthesia (VAS)	4.02	4.09	0.5
Pain during biopsy (VAS)	2.07	2.34	0.37
Pain after 15 days (VAS)	0.06	0.07	0.91
Pain during anaesthesia (FES)	4.02	4.19	0.37
Pain during biopsy (FES)	2.03	2.1	0.7

authors analyzed the length of the cores obtained from transperineal biopsy with regard to pathological features. They concluded that the obtained core length was adequate and that the cores met the parameters of quality required by pathologists for the appropriate evaluation of the biopsy specimen [12].

To our knowledge, we report the first prospective and randomized trial evaluating the use of differing needle calibres in transperineal prostate biopsies. The lack of previous studies on this topic may be because of the higher popularity of the transrectal approach, which limits researchers' and clinicians' experiences with the transperineal approach. Transrectal biopsies are currently performed using a maximum needle calibre of 18 G. There have been no previous reports evaluating the use of larger calibre needles in transrectal prostate biopsies.

The effectiveness and safety of different needle sizes has been shown in breast cancer. In one study, the use of an 18-G needle provided a 6.4-mm^2 specimen, compared with the 9.6-mm^2 (mean values) sample obtained using a 16-G needle[5]. As a result, the quality of the tissue samples obtained during biopsy was significantly superior when a 16-G needle was used. Manju *et al*. [13] confirmed those findings, stating that a larger specimen may lead to an improved diagnostic sensitivity and cancer detection. In terms of prostate cancer, the only report concerning biopsy specimen size is the one from Iczkowski *et al*. [14], who found, in 2002, that needle core length on sextant biopsy may influence the cancer detection rate, especially at the apex.

Our study sought to take the first step in evaluating the feasibility of performing transperineal biopsies using a 16-G needle. Using a prospective, randomized study design, we compared two groups with similar baseline characteristics with regard to PSA levels, incidence of diabetes and drug use. Although age turned out to be significantly different between the groups, the mean value was older than 60 years in both groups. This finding has clinical importance, as several authors have found that patients under 60 years of age experience more discomfort during prostate biopsy than older patients [15, 16].

The two groups (those that received their biopsy using a 16-G needle and those who received their biopsy using an 18-G needle) did not differ in terms of the pain they experienced associated with prostate biopsy, which was assessed in two different ways (the VAS and FES pain scales) to provide more significant and detailed outcomes. Discomfort was assessed and recorded at the three separate steps that could be potentially distressing to patients, such as during anaesthesia, and during and 15 days after biopsy. Complication rates were not affected by needle calibre, even at the 15-day follow-up appointment. Our data confirm that 16-G transperineal prostate biopsy can be easily and safely performed. Although pathological analysis of the prostate biopsy cores obtained during this study did not reveal any statistically significant differences in overall cancer, HGPIN or ASAP-detection rates, we are currently continuing our research on this topic. There is a clear trend towards a significant improvement in diagnostic aptitude in patients who have undergone biopsy using a 16-G needle compared with those using an 18-G needle (data not presented). Despite the similar number of prostate cancers detected in both groups, the histological findings of uncertain malignant potential, such as ASAP, are encouraging, as those diagnoses seem to be more frequent in the 18-G needle group in which core quality and quantity is lower.

Therefore, although we have shown that this procedure is feasible and does not lead to increased side effects, further studies are required to better understand whether or not the use of a larger-calibre needle may potentially improve the detection rate of prostate cancers and reduce findings of ASAP and HGPIN, which represent serious concerns for both the urologist and the patient.

5 Conclusions

Pain assessment during prostatic biopsy is a popular topic in the recent literature. The modified transperineal technique using a 16-G needle is a feasible procedure that is well tolerated by patients in terms of both pain and side effects. The impact of a greater needle calibre on oncological outcomes remains to be determined. However, in addition to the increase in the number of biopsy cores obtained, we believe that this procedure may lead to a quantitative and qualitative improvement in histological sampling that may, in turn, potentially improve the diagnosis of prostate cancer.

References

1 Borley N, Feneley ML. Prostate cancer: diagnosis and staging. Asian J Androl 2009; 11: 74–80.

2 Scattoni V, Rossigno M, Raber M, Dehò F, Maga T, *et al*. Initial extended transrectal prostate biopsy–are more prostate cancers detected with 18 cores than with 12 cores? J Urol 2008; 179:1327–31.
3 Sartor AO, Hricak H, Wheeler TM, Coleman J, Penson DF, *et al*. Evaluating localized prostate cancer and identifying candidates for focal therapy. Urology 2008; 72: S12–24.
4 Hara R, Jo Y, Fujii T, Kondo N, Yokoyoma T, *et al*. Optimal approach for prostate cancer detection as initial biopsy: prospective randomized study comparing transperineal versus transrectal systematic 12-core biopsy. Urology. 2008; 71: 191–5.
5 Helbich TH, Rudas M, Haitel A, Kohlberger PD, Thurnher M, *et al*. Evalutation of needle size for breast biopsy: comparison of 14-, 16-, and 18 gauge biopsy needles. AJR Am J Roentgenol 1998; 171: 59–63.
6 Emiliozzi P, Longhi S, Scarpone P, Pansadoro A, Depaula F, *et al*. The value of a single biopsy with 12 transperineal cores for detecting prostate cancer in patients with elevated prostate specific antigen. J Urol 2001; 166: 845–50.
7 Shostack M, Cristoph F, Muller M, Heicappell R,Goessl G, *et al*. Optimizing local anesthesia duting 10 cores biopsy of the prostate. Urology 2002; 60: 253–7.
8 Soyupek S, Bozlu M, Armağan A, Ozorak A, Perk H. Does experimental pain assessment before biopsy predict for pain during transrectal ultrasound-guided prostate biopsy? Urology 2007; 70: 681–4.
9 Cam K, Sener M, Kayikci A, Akman Y, Erol A. Combined periprostatic and intraprostatic local anesthesia for prostate biopsy: a double-blind, placebo controlled, randomized trial. J Urol 2008; 180: 141–4.
10 Raber M, Scattoni V, Roscigno M, Dehò F, Briganti A, *et al*. Topical prilocaine-lidocaine cream combined with peripheral nerve block improves pain control in prostatic biopsy: results from a prospective randomized trial. Eur Urol 2008; 53: 967–73.
11 Novella G, Ficarra V, Galfano A, Ballario R, Novara G, *et al*. Pain assessment after original transperineal prostate biopsy using a coaxial needle. Urology 2003; 62: 689–92.
12 Ficarra V, Martignoni G, Novella G, Cerruto MA, Galfano A, *et al*. Needle Core Length is a Quality Indicator of Systematic Transperineal Prostate Biopsy. Eur Urol 2006; 50: 266–71.
13 Nath ME, Robinson TM, Tobon H, Chough DM, Sumkin JH. Automated large core needle biopsy of surgically removed breast lesions: comparson of samples obtained by 14–16 and 18-gauges needles. Radiology 1995; 197: 739–42.
14 Iczkowski KA, Casella G, Seppala RJ, Jones GL, Mishler BA, *et al*. Needle core length in sextant biopsy influences prostate cancer detection rate. Urology 2002; 59: 698–703.
15 Djavan B, Zlotta A, Remzi M, Ghawidel K, Basharkhah A, *et al*. Optimal predictors of prostate cancer in repeat prostate biopsy: a prospective study in 1051 men. J Urol 2000; 163: 1144–8.
16 Rodriguez LV, Terris MK. Risks and complications of transrectal ultrasound guided prostate needle biopsy: a prospective study and review of the literature. J Urol 1998; 160: 2115–20.