A prospective survey of current prostate biopsy practices among oncological urologists

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Background: *Needle biopsy of the prostate is a common outpatient procedure. In March 2009, the European Association of Urology (EAU) published an updated, evidence-based "Guidelines on Prostate Cancer," including recommendations for this procedure.*

Objective: *To survey onco-urology specialists attending the 6th European Section of Oncological Urology (ESOU) meeting in Istanbul, Turkey in January 2009, to assess their biopsy practices and compare them with March 2009 EAU guidelines.*

Design, setting and participants: *The authors designed a questionnaire and distributed it to 606 conference delegates. It was completed by 298 delegates, of whom 156 were experienced onco-urological specialists.*

Measurements: *The survey results from the 156 experienced onco-urologist specialists were analyzed.*

Results and limitations: *Most (59%) of the 156 respondents worked in large (> 20 bed) units, and 76% said urologists always performed the biopsies. Transrectal ultrasound (TRUS)-guided biopsy was the preferred procedure for 78% of respondents. Prostate-specific antigen (PSA) cut-off points of 4 ng/mL, 3.5 ng/mL, 3 ng/mL, and 2.5 ng/ml were used by 42%, 18%, 23%, and 8% of respondents, respectively, to determine whether a biopsy was indicated. A total of 95% of respondents gave patients prophylactic antibiotics. Another of 15% and 17% of respondents did not advise patients to stop taking warfarin or clopidogrel, respectively. A total of 23% of respondents did not give patients pre-procedure anesthesia, while others gave patients periprostatic lidocaine (31% of respondents), topical lidocaine jelly (35%), or general or spinal anesthesia (5.7%). High grade prostatic intraepithelial neoplasia (HGPIN) was considered by 71% of respondents as being a pre-malignant condition requiring a repeat biopsy. If atypical small acinar proliferation (ASAP) was reported, 62% of respondents recommended a repeat biopsy. Magnetic resonance imaging (MRI) was used to help diagnose cancer (53% of respondents), help stage cancer (83%), or help diagnose cancer recurrence (62%). Study limitations include possible difficulties with the English questionnaire.*

Conclusions: *Many surveyed specialists were not performing prostate biopsies according to March 2009 evidence-based EAU practice guidelines, which could have adverse consequences for patients.*

Key Words: prostate cancer, transrectal ultrasound, prostate biopsy

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Introduction

The incidence of prostate cancer is rising in Europe, mainly due to the increasing use of prostate-specific antigen (PSA) screening in men presenting with or without lower urinary tract symptoms. The gold standard method to detect and diagnose prostate cancer in such men is transrectal ultrasound (TRUS)-guided needle biopsy, performed in an outpatient setting.[1] Since its introduction to clinical practice in the late 1980s,

issues such as the optimal number of biopsies,[2,3] the use of local anesthesia,[4,5] when to offer a repeat biopsy[6] and how to prevent complications[7] have all attracted much research interest. For example, the Vienna nomogram[8] was designed on the basis of a neural network aiming to identify the optimal number of biopsy cores based on a patient's age and prostate volume. Other methods by which histological diagnosis may be acquired include transperineal (with or without grid template) or TRUS-guided needle biopsy, extensive "saturation" needle sampling under general anesthesia,[9] or transurethral resection.[10] Although the research literature about biopsy procedures for the diagnosis of prostate cancer appears to show a consensus as to the best way to perform prostate biopsies, current clinical practices may vary widely.

To assess the standardization with respect to practicing this commonly performed diagnostic investigation, we conducted a survey of current practices and opinions among urologists who attended the 6th European Section of Oncological Urology (ESOU) meeting in Istanbul, Turkey, in January 2009. With the imminent publication of updated European Association of Urology (EAU) "Guidelines on Prostate Cancer",[11] we were keen to compare the results of this questionnaire with the recommendations contained in the guidelines.

Methods

A questionnaire was prepared and validated by members of the ESOU board before the ESOU meeting. All urologists who attended the ESOU meeting were given a copy of the survey. Responses were collected and analyzed. This article focuses on the replies from a subset of onco-urology specialists (excluding trainees).

Results

Of the 606 urologists who attended the ESOU meeting and were given questionnaires, 298 urologists from 30 different countries completed the questionnaires. Of the 298 respondents, 159 respondents came from 18 European Union (EU) and other countries. A total of 98% of the 159 respondents were onco-urologists, including 156 (52 %) who were trained specialists from 15 EU and 10 non-EU countries, Table 1. We report the questionnaire results obtained from this subset of 156 respondents.

Demographic characteristics

Most of the respondents (59%) worked in large (> 20 bed) units, and 55% worked with five or more colleagues, while 74% trained residents in their units.

TABLE 1. **Countries of origin of the 156 onco-urological specialists who replied to the survey**

Country	Number of survey respondents
Egypt	1
Estonia	1
Denmark	1
Jordan	1
Switzerland	1
Ireland	2
Latvia	2
Morocco	2
Portugal	2
Thailand	3
United States	3
Romania	3
Iran	4
Italy	5
Libya	5
Lithuania	6
Poland	7
Greece	8
Belgium	9
Russia	11
France	12
Ukraine	12
Spain	13
Turkey	18
Germany	19

Who performs the prostate biopsies?

Of 147 specialists who responded to this question, 76% said that the urologist always performed the biopsies, whereas 17% said urologists often performed the biopsies, and a minority of respondents said that a radiologist or a resident performed the biopsies. Two thirds (61%) of the respondents indicated that biopsies were never performed by a radiologist at their institution, while 25% stated that residents never performed biopsies.

Biopsy routes, biopsy numbers, and patient consent

To diagnose prostate cancer, a transrectal ultrasound (TRUS)-guided biopsy was the procedure of choice for 77.8% of respondents, while fewer preferred to

perform a transrectal digitally-guided biopsy (8.3% of respondents) or use a transperineal TRUS-guided route (6.7%) or perform a transurethral resection (7.2%). Almost two-thirds of respondents (61%) reported that they performed 200 or more biopsies a year, and 12% reported they performed more than 500 biopsies a year. Written, informed patient consent was obtained by 72% of survey respondents.

Use of PSA

To recommend a biopsy in men with a normal digital rectal examination (DRE), PSA cut-off points of 4 ng/mL, 3.5 ng/mL, 3ng/mL, and 2.5 ng/ml were used by 42%, 18%, 23%, and 8% of the respondents, respectively. A total of 8.7% of respondents used a PSA of 5 ng/mL or higher as the trigger point for sending a patient for a biopsy. A total of 63% of respondents indicated that PSA isoforms influenced their decision to perform an initial biopsy.

Preparation and prophylaxis

A total of 61% of respondents gave patients a prophylactic rectal enema and 95% of respondents gave patients prophylactic antibiotics before a biopsy. A total of 15% of specialists did not require patients to stop taking warfarin prior to undergoing a biopsy and similarly 17% of specialists did not require patients to stop taking clopidogrel, whereas 26% of specialists did not require patients to stop taking aspirin, Figure 1.

Anesthesia, patient position, and hospitalization

A total of 23% of respondents did not give patients any form of anesthesia for probe insertion or biopsy. Of the remaining specialists, 31% gave patients periprostatic lidocaine, 35% gave patients topical lidocaine jelly, and 5.7% gave patients general or spinal anesthesia for pain control. A total of 69% of specialists performed

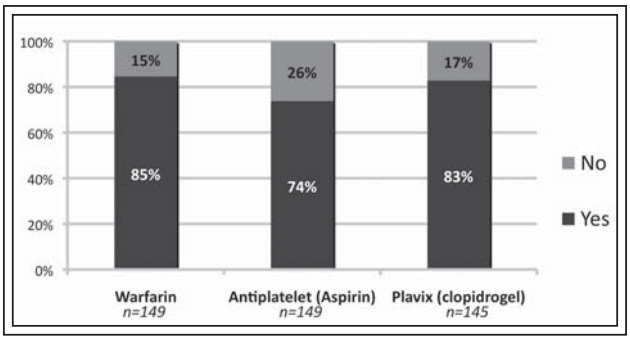

Figure 1. The percentages of oncological urologists who discontinue anticoagulant medication prior to prostatic biopsy.

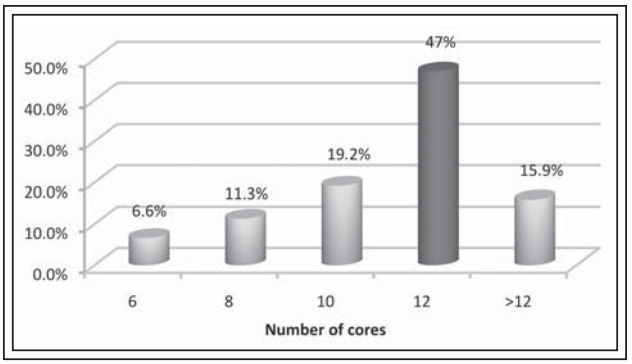

Figure 2. Number of biopsy cores routinely taken (n = 151).

prostate biopsy by placing the patient in the lateral position, while 31% placed patients in the lithotomy position. A total of 7% of respondents hospitalized patients for one or more days after a biopsy.

Number of cores

Sextant biopsies were performed by 7% of respondents, while 15.9% routinely obtained more than 12 cores. A total of 11.3%, 19.2%, and 47% of respondents reported routinely taking 8, 10, and 12 cores, respectively, Figure 2. A total of 72% of specialists did not use a published guide to determine the number of biopsies cores they took, and 47% of respondents performed transition zone (TZ) sampling for an initial biopsy.

Non-malignant histological findings and repeat biopsy

In cases of a negative initial biopsy, the preferred follow up strategies were repeat PSA measurements (48% of respondents), systematic repeat biopsy (31%), a repeat PSA measurement after antibiotic treatment (17%), and use of MRI to localize prostatic abnormalities (7%). Among respondents who indicated that a repeat PSA measurement was their preferred patient management strategy, 83.6% indicated they would wait 3 to 6 months. A total of 65% of respondents preferred to delay a repeat biopsy for 3 to 5 months, and 13% preferred to delay this for 6 months or more.

A total of 71% of respondents considered that high grade prostatic intraepithelial neoplasia (HGPIN) was a pre-malignant condition that required a repeat biopsy. Most respondents who would repeat a biopsy in such patients (74% of these respondents) indicated that they would wait at least 3 months, and 44% would wait at least 6 months. However, if a patient had a histological finding of atypical small acinar proliferation (ASAP), only 62% of respondents would recommend a repeat biopsy. In the presence

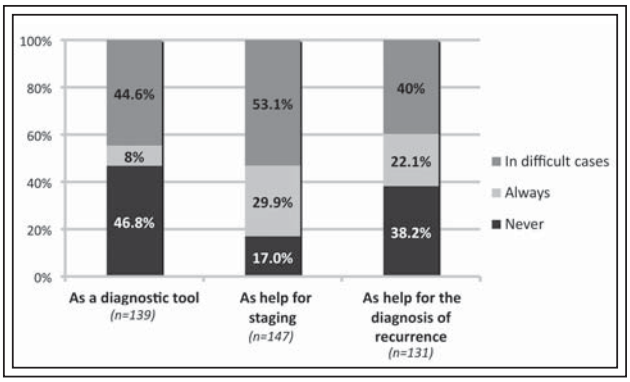

Figure 3. The role for MRI in diagnosis and investigation of prostate cancer.

of ASAP or prostatic intraepithelial neoplasia (PIN), 30% of respondents only take one or two biopsy sets to look for prostate cancer. On the other hand, for a patient with a normal DRE but persistently elevated PSA levels, 23.8% of respondents would stop taking biopsies after two sets of negative biopsies, and 58.3% of respondents would stop taking biopsies after three sets of negative biopsies.

Use of magnetic resonance imaging (MRI)

Of 147 respondents who answered the question about MRI, this tool was always or selectively used by 53% of the specialists to diagnose prostate cancer. It was used by 83% of the specialists to help stage cancer and by 62% of the specialists to help diagnose cancer recurrence, Figure 3.

Discussion

TRUS-guided, systematic needle biopsy is the state-of-the-art method to obtain prostatic tissue to diagnose prostate cancer in men who might have prostate cancer, based on an abnormal DRE and/or an elevated serum PSA level.

The 2009 EAU guidelines[11] state that results from transrectal and transperineal TRUS-guided prostate biopsies are similar and that a transurethral diagnostic prostate biopsy is "of minor importance" and "a poor tool for cancer detection." The guidelines do not mention the use of digitally-guided biopsies. They state that an ultrasound-guided perineal approach is a useful alternative to a transrectal TRUS-guided biopsy in special situations (for example, after rectal amputation). Thus, 15% of specialists in the present study were using biopsy routes that are not recommended, either digitally-guided (8.3%) or transperineal (6.7%). Digital-guided biopsies were historically used in the presence of a palpable abnormality. However, after multicore (> 8) ultrasound-guided biopsies became possible, this technique was abandoned.

A PSA level of 4ng/mL was used by 42% of respondents in this study as the trigger-point for recommending a biopsy, while 8.7% used a PSA level of 5 ng/mL or higher. The EAU guidelines state that a precise upper limit for a normal serum PSA level has not yet been determined, but 2 ng/mL-3 ng/mL are often used as the upper limits of normal serum PSA values for men aged 40 to 50 years. Awareness that many men harbor prostate cancer despite low serum PSA level has been underscored by results of the Prostate Cancer Prevention Trial.[12]

According to EAU guidelines, a set of repeat biopsies is warranted for patients with a persistent abnormal DRE, a persistent elevated serum PSA level, or abnormal histopathological findings (such as ASAP or multifocal HGPIN suggestive of malignancy) in an initial biopsy. Isolated HGPIN is no longer an absolute indication for a repeat prostate biopsy.[13] Conversely, ASAP is a strong indication for a repeat prostate biopsy, since it is highly associated with the presence of prostate cancer, although the optimal timing for a repeat biopsy remains to be determined. Surprisingly, 38% of specialists in this study said they did not repeat a biopsy if ASAP was found on an initial biopsy. As a result, these specialists may miss or delay detecting prostate cancer in such cases.

The EAU guidelines recommend taking a minimum of 10 systemic, laterally directed, core biopsy samples and possibly taking more core samples from patients with very large prostates. The guidelines also indicate that a sextant biopsy is no longer adequate. If a patient has a prostate volume that is greater than 30 cc, at least 8 cores should be sampled.[2] However, taking more than 12 cores does not provide significantly better determination of the presence or absence of prostate cancer. Thus, 7% of specialists in this study were out of date in their practice, since they still performed sextant biopsies. In addition, 18% of specialists in this study did not follow the recommendation of obtaining at least 10 systemic cores. Similarly, 47% of the specialists used TZ sampling for initial biopsies, whereas the updated EAU guidelines state that TZ sampling provides a very low detection rate and should be limited to repeat biopsies.[14]

A state-of-the-art prostate biopsy includes giving a patient prophylaxis with either oral or intravenous antibiotics, yet 5% of surveyed specialists did not do this, thus putting their patients at increased risk of postbiopsy sepsis.

Giving patients a TRUS-guided periprostatic lidocaine block to make them more comfortable is another part of a state-of-the-art prostate biopsy, yet less than a third of surveyed specialists reported that they provided this for their patients. Another third of respondents reported giving patients topical local anesthetic jelly (an ineffective form of anesthesia)[15] and 23% of respondents did not provide their patients with any anesthetic treatment!

Although the EAU guidelines do not recommend that patients discontinue aspirin, 74% of survey respondents stopped the use of aspirin in their patients. More than 80% of the specialists also instructed their patients to stop taking warfarin or clopidogrel anticoagulation therapy. Clopidogrel is frequently used to treat patients with drug-eluting coronary stents, and cardiologists are highly concerned that premature cessation of clopidogrel results in significantly higher cardiovascular event rates.[16-18] Further research may clarify if and when it is safe to discontinue these agents in patients who undergo prostate biopsies.

Another area of interest in this study is the use of MRI. Currently, the use of MRI to detect prostate cancer is at best investigational. However, MRI was used for this purpose in daily clinical practice by 53% of the specialists who replied to the questionnaire, which raising a serious concern about the cost of such treatment at a time of limited healthcare resources.

Study limitations include the possibility that some respondents did not understand the questions, which were in English. Some respondents who claimed to be specialists may have been trainees. In some countries in this study sample, TRUS devices may not be widely available and pathologists might lack sufficient training and expertise to be able to diagnose ASAP or even prostate cancer.

Conclusions

A prostate biopsy is one of the most common minor urological procedures, yet many specialists are not adhering to published European evidence-based guidelines for clinical practice. Causing unnecessary pain to patients undergoing prostate biopsy in this era is unforgivable. Serious consequences can occur when the procedure causes morbidity such as systemic infection or profuse bleeding or when a prostate biopsy fails to detect prostate cancer that is present. Not following guideline recommendations raises concern about unnecessary cost, given that healthcare resources are almost universally limited. The ESOU plans to undertake further surveys such as this one to investigate the impact of published guidelines on daily clinical practice, and it aims to strengthen the links between the EAU guidelines and clinical practice. Finally, we urge specialists who request and/or perform prostate biopsies to carefully read and consider applying the 2009 EAU guidelines, which almost entirely reflect evidence-based best standards of care. □

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