Original Article

Clinical Preferences of Turkish Urologists in Screening and Diagnosis of Prostate Cancer and Adherence to European Association of Urology Guidelines

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Abstract

Objective: To compare the clinical preferences of urologists in prostate cancer screening and diagnosis with current guideline recommendations.

Materials and Methods: The study is based on an online survey that consists of 21 single response or multiple response questions. By e-mail, 2,305 certified urologists in active practice as well as urology residents in their last year of training were invited to participate in the study. Descriptive statistics were used to analyze practice patterns and demographics. The respondents were divided into groups based on their experience in urology, hospital type and academic title.

Results: Our results show that preferences of the majority of urologists conflicts with recommendations of European Association of Urology Prostate Cancer Guidelines regarding prostate biopsy method, management of a patient with high prostate-specific antigen value, use of additional test and performance scoring systems, role of multiparametric prostate magnetic resonance imaging.

Conclusion: Urologists act in the direction of their habits or clinical experience rather than current guidelines regardless of their experience. Both clinicians and professional organizations should work on what can be done about the reflection of rapidly changing scientific knowledge on the field and the improvement of the health service provided.

Keywords: Diagnosis, guidelines, prostate cancer, screening

Introduction

Prostate cancer is the most common cancer among men (1). Therefore, screening and diagnosis of prostate cancer is one of the most frequent tasks of urologists in daily practice. Clinical practice guidelines are commonly used by clinicians for the standardization of these applications. Clinical practice guidelines were first formally defined in 1990 by "Clinical Practice Guidelines: Directions for a New Program" published by the Institute of Medicine of the United States (2). Nowadays, the need for using these guidelines has increased due to medico-legal concerns, the need to reduce cost, the need to reduce overdiagnosis and overtreatment, and the need to have a universally accepted approach to the diseases (3). Many studies show that adherence to guidelines increases interventions that show benefit, while at the same time reducing ineffective or harmful treatment, potentially reducing mortality and morbidity

(4,5,6). European Association of Urology (EAU) Guidelines on Prostate Cancer have been prepared to assist medical professionals in the evidence-based management of prostate cancer (7). With the development of information technologies, it has become easier to reach these guides. However, it is questionable to what extent these guidelines are known and applied by clinicians in real-world practice. In our study, we aimed to compare the clinical preferences of urologists in prostate cancer screening and diagnosis with current guideline recommendations.

Materials and Methods

The study is based on an online survey that consists of 21 single response or multiple response questions. The questionnaire was prepared using the checklist for reporting results of internet E-Surveys (8). Questions about the respondents' baseline

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characteristics make up the first section. In the second part, the urologists were asked whether they perform a biopsy and if they do, their preferences regarding the biopsy method. The third part includes urologists' preferences for managing a patient with a high prostate-specific antigen (PSA) value. In the fourth part, the participants were asked about their preferences to use additional tests to PSA, performance status tests, and multiparametric prostate magnetic resonance imaging (mpMRI). In the last section, re-biopsy preferences of the participants were evaluated. After testing for feasibility with 10 responders, e-mail invitations were sent to 2,305 certified urologists who are currently in practice as well as urology residents who are in their last year of training. Reminder e-mails were also sent out after four weeks. Since the study was not based on patient groups, informed permission was not required. The survey was accessible between June and October 2020 through the web program Google Forms (Alphabet Co., Mountain View, CA). The Zonguldak Bülent Ecevit University Non-Invasive Clinical Research Ethics Committee approved this study (decision no: 2020/10, date: 13.05.2020).

Statistical Analysis

Demographics and practice patterns were analyzed using descriptive statistics. Respondents who perform prostate biopsy were asked about their preferences of prostate biopsy methods. We demonstrated the numbers and percentages of answers and respondents separately for multiple response questions. Statistical analyses were performed by using IBM Statistical Package for Social Sciences, version 26.0, software (IBM SPSS Corp., Armonk, NY, USA). A post hoc power analysis was conducted using the software package, GPower (Faul and Erdfelder, 2009). A p-value less than 0.05 were considered statistically significant.

Results

A total of 351 out of 2,305 urologists participated. The response rate was 15.2%. Fourty four incomplete questionnaires were excluded from the study and 306 responses were evaluated. To check if our sample size represents all urologist in Turkey, we conducted post hoc power analyses which showed us an n of 270 would be enough with power (1-β) set at 0.80 and α=0.05.

The median age of the responders was 36 (27-66). The responders had a urology practice for a median of 10 (4-39) years. Demographics and other practice patterns are shown in Table 1.

In their hospital, 230 (75.2%) of 306 respondents perform prostate biopsy. As for the hospital type, percentages of performing biopsy in university hospitals, training and research hospitals, Private hospitals, and state hospitals were 100%, 85%, 84.4%, 49.6% respectively (p<0.001). When 76 (24.8%) urologists who do not perform biopsy were asked about the reason they are not performing, the main reason was lack of equipment (71.1%), followed by risk of complication (23.7%), other (19.7%), lack of auxiliary staff (18.4%), financial concerns (5.3%%) (percentages are based on respondents, total 138.2% as it is a multi-response question).

In their hospital or city, 175 (57.2%) of the urologists do not have a targeted magnetic resonance imaging-transrectal

ultrasound (MRI-TRUS) fusion prostate biopsy to which they can refer patients if needed.

Prostate Biopsy Method

Table 2 shows the preferences of urologists about enema administration, rectal cleansing, oral restriction prior to biopsy, and number of cores they get in a standard prostate biopsy. In subgroup analyzes made according to academic title and experience in urology, no statistical significant difference was found in the pre-procedure enema administration (titles: residents 73.3%, specialists: 72.6%, academicians: 76.2% p=0.901; years of experience: 0-5: 71.9%, 5-10: 78.4%, 10-15: 69.2%, 15-20: 72%, >20: 71.4% p=0.836). There was no statistical significant difference in rectal cleansing prior to the biopsy in subgroup analyses based on academic title and years of experience in urology (titles: residents: 37.3%, specialists: 39.8%, academicians: 35.7% p=0.852; years of experience: 0-5: 38.6%, 5-10: 41.9%, 10-15: 38.4%, 15-20: 16%, >20: 45.7% p=0.178). There was no statistical significant difference in oral restriction prior to biopsy in subgroup analyses based on academic title and experience in urology (titles: residents: 20%, specialists: 22.1%, academicians: 23.8% p=0.861; years

Table 1. Demographic data of the respondents		
Academic titles	**n**	**%**
Resident	76	24.8
Specialist	185	60.5
Academician	45	15.7
Total	306	100
Hospital type	**n**	**%**
University	78	25.5
Research hospital	60	19.6
Private hospital	51	16.7
State hospital	117	38.2
Total	306	100
Geographic location	**n**	**%**
Marmara	88	28.8
Aegean	44	14.4
Central Anatolia	54	17.6
Eastern Anatolia	18	5.9
Southeastern Anatolia	12	3.9
Black sea	54	17.6
Mediterranean	36	11.8
Total	306	100.0
Experience in urology (years)	**n**	**%**
0-5	63	20.6
5-10	110	35.9
10-15	48	15.7
15-20	32	10.5
20 and more	53	17.3
Total	306	100.0

Table 2. Urologists' preferences about enema administration, rectal cleansing, oral restriction prior to biopsy and number of cores they get in a standard prostate biopsy

Do you administer an enema prior to the biopsy?

	n	%
Yes	169	73.5
No	61	26.5
Total	230	100.0

Do you perform rectal cleansing with povidone-iodine or chlorhexidine prior to the biopsy?

	n	%
Yes	88	38.3
No	142	61.7
Total	230	100.0

Do you restrict the patient's oral intake prior to the biopsy?

	n	%
Yes	50	21.7
No	180	78.3
Total	230	100.0

How many cores do you get in a standard biopsy procedure?

	n	%
6-9	4	1.3
10-11	19	6.2
12	260	85.0
More than 12	23	7.5
Total	306	100.0

of experience: 0-5: 21.1%, 5-10: 20.3%, 10-15: 15.4%, 15-20: 28%, >20: 28.6% p=0.501).

Regarding prophylactic antibiotics, urologists prefer 69.6% fluoroquinolones, 24.8% cephalosporins, 14.8% fosfomycin, 14.3% aminoglycoside, 3.9% other, 0.4% none (percentages are based on respondents, total 127.8% as it is a multi-response question). When the antibiotic preferences of the participants were compared according to their academic titles and experience in urology, no statistically significant diference was found (p=0.137, p=0.381 respectively).

As for the anesthetic methods, urologists prefer rectal anesthetic agents 69.6%, sedation 24.8%, periprostatic blockage 14.8% (percentages are based on respondents, total 132.2% as it is a multi-response question).

Preferences for Managing a Patient with a High PSA Value

Table 3 compares urologists' preferences for managing patients with PSA values of 3 ng/mL and 9 ng/mL. When we performed subgroup analyzes for patients with a PSA value of 3 ng/mL according to academic title statistical significant differences were found for the answers; antibiotics administration (titles: residents: 6.6%, specialists: 16.8%, academicians: 6.7% p=0.034), digital rectal examination (titles: residents: 93.4%, specialists: 77.3%, academicians: 88.9% p=0.004), mpMRI (titles: residents: 11.8%, specialists: 12.4%, academicians: 33.3% p=0.002) and, additional tests (titles: residents: 18.4%, specialists: 6.5%, academicians: 11.1% p=0.014). When we performed subgroup analyzes for patients with a PSA value of 3 ng/mL according to years of experience in urology, statistical significant differences were found for the answers; antibiotics administration (years of experience: 0-5: 4.8%, 5-10: %9.1, 10-15: 18.8%, 15-20: 28.1%, >20: 15.1% p=0.009) and, digital rectal examination (years of experience: 0-5: 92.1%, 5-10: 90%, 10-15: 75%, 15-20: 71.9%, >20: 71.7% p=0.002). When we performed subgroup analyzes for patients with a PSA value of 9 ng/mL according to academic title statistical significant differences were found for the answers; antibiotics administration (titles: residents: 19.7%, specialists: 33.5%, academicians: 15.6% p=0.012), digital rectal examination (titles: residents: 92.1%, specialists: 81.6%, academicians: 71.1% p=0.011), mpMRI (titles: residents: 31.6%, specialists: 28.6%, academicians: 48.9% p=0.033). When we performed subgroup analyzes for patients with a PSA value of 9 ng/mL according to years of experience in urology, only statistical significant difference were found for the answer; digital rectal examination (years of experience: 0-5: 88.9%, 5-10: 88.2%, 10-15: 85.4%, 15-20: 75%, >20: 66.7% p=0.003). It was determined that as experience increased, the tendency to perform digital rectal examination (DRE) decreased, for both PSA values. No statistically significant difference was found between the subgroups for any of the other responses.

Table 3. Urologists' preferences for managing patients with PSA values of 3 ng/mL and 9 ng/mL

	PSA: 3 ng/mL			PSA: 9 ng/mL		
	n	%	% of respondents	n	%	% of respondents
Antibiotherapy	39	6.3%	12.7%	84	11.1%	27.5%
Repeat PSA after 6 weeks	192	31.0%	62.7%	139	18.3%	45.4%
DRE	254	41.0%	83.0%	253	33.3%	82.7%
MpMRI	47	7.6%	15.4%	99	13.0%	32.4%
Biopsy	12	1.9%	3.9%	147	19.4%	48.0%
Additional test	31	5.0%	10.1%	35	4.6%	11.4%
Annual follow-up	45	7.3%	14.7%	2	0.3%	0.7%
Total	620	100.0%	202.6%	759	100.0%	248.0%
PSA: Prostate-specific antigen, DRE: Digital rectal examination, MpMRI: Multiparametric prostate magnetic resonance imaging						

Use of Additional Tests and Performance Scoring Systems

Urologists were asked at what PSA levels they use additional tests to help in their biopsy decision in a patient with normal DRE. Answers were 2-10 ng/mL for 25.2%, 4-10 ng/mL for 66.7%, 10-20 ng/mL for 4.2%, other for 3.9%.

Additional tests that urologists use in this patient group are shown in Table 4. When we performed subgroup analyzes academic titles and experience in urology, residents, academicians and urologist with experience less than five years tended to use mpMRI more than other groups (titles: residents: 78.9%, specialists: 59.5%, academicians: 88.9% p<0.001; years of experience: 0-5: 81%, 5-10: 66.4%, 10-15: 56.3%, 15-20: 68.8%, >20: 69.8% p=0.006). No statistically significant difference was found between the subgroups for any of the other tests.

When respondents were asked which scoring system they use to evaluate geriatric patients' performance status when making a biopsy decision, answers were Eastern Cooperative Oncology Group (ECOG) for 24.8%, Karnofsky for 24.8%, G8 for 5.6%, mini-cog for 1.0%, other for 2.9%, none for 65.0% (percentages are based on respondents, total 112.7% as it is a multi-response question).

Role of mpMRI

When urologists were asked their opinions about area of usage of multiparametric MRI in biopsy planning, the most common answer was before re-biopsy (Table 5).

Re-biopsy Preferences

Most of the urologists (42.8%) prefer to wait 6 months before re-biopsy after a previous biopsy. Followed by 3 months (34.6%), 12 months (17%) and 1 month (5.6%).

Methods used by the urologist for re-biopsy were determined as saturation biopsy 44.4%, MRI-TRUS fusion biopsy 25.8%, standard biopsy 17.6%, and cognitive fusion biopsy 12.1%, respectively.

Discussion

The main finding of our study was low adherence to guidelines in prostate cancer screening and diagnosis among Turkish urologists. Although there were statistically significant differences in some preferences, it was observed that there was not enough compliance with the guidelines regardless of experience or academic title.

There are studies showing similarly low adherence to guidelines by urologists in North America, Canada, and Europe (9,10,11,12). Reasons for this are complex. Makarov et al. (13) investigated the reasons for guideline-discordant use of

Table 4. Urologists' preferences for using additional tests			
Which of the following do you use in addition to PSA in the biopsy decision?			
	n	%	% of respondents
PSA density	80	13.0%	26.1%
PSA velocity/doubling time	79	12.8%	25.8%
F/T PSA ratio	225	36.6%	73.5%
PCA3 marker/SelectMDX/Mi prostate score /ExoDX	1	0.2%	0.3%
MpMRI	210	34.1%	68.6%
None	20	3.3%	6.5%
Total	615	100.0%	201.0%
PSA: Prostate-specific antigen, PCA3: *Prostate cancer antigen 3* gene, MpMRI: Multiparametric prostate magnetic resonance imaging			

Table 5. Urologists' preferences for using multiparametric prostate magnetic resonance imaging				
At which stage do you think multiparametric MRI should be used first in biopsy planning?				
	Screening n (%)	Before the first biopsy n (%)	Before re-biopsy n (%)	During re-biopsy method (targeted MR-TRUS fusion biopsy) n (%)
Academic title				
Resident	2 (2.6%)	12 (15.8%)	48 (63.2%)	14 (18.4%)
Specialist	0 (0%)	56 (30.3%)	67 (36.2%)	62 (33.5%)
Academician	0 (0%)	19 (42.2%)	16 (35.6%)	10 (22.2%)
p<0.001				
Experience in urology				
0-5 years	1 (1.6%)	12 (19.0%)	38 (60.3%)	12 (19%)
5-10 years	1 (0.9%)	30 (27.3%)	52 (47.3%)	27 (24.5%)
10-15 years	0 (0%)	13 (27.1%)	19 (39.6%)	16 (33.3%)
15-20 years	0 (0%)	14 (43.8%)	8 (25%)	10 (31.3%)
>20 years	0 (0%)	18 (34%)	14 (26.4%)	21 (39.6%)
p=0.025				
Total	2 (0.7%)	87 (28.4%)	131 (42.8%)	86 (28.1%)
MRI: Magnetic resonance imaging, TRUS: Transrectal ultrasound				

imaging to stage incident prostate cancer. Most physicians self-reported that they know and trust imaging guidelines yet some were still likely to follow their own intuition, whether due to clinical suspicion or years of experience. Additionally, physicians reported that medico-legal concerns, fear of missing associated diagnoses, tendency to practice in line with more senior colleagues, influences rates of imaging despite guidelines (13).

Passive dissemination via publication of guidelines alone is rarely enough to effect widespread guideline adherence (14). Nowadays, it is anticipated that social media may play an important role in disseminating the guidelines (15).

Prostate Biopsy Method

A meta-analysis of eight RCTs demonstrated that use of a rectal povidone-iodine cleansing prior to biopsy, in addition to antimicrobial prophylaxis, led to a significant decrease of infectious complications (16,17,18). EAU guidelines on prostate cancer recommends the use of rectal cleansing with povidone-iodine before transrectal prostate biopsy strongly (7). However, only 38.6% of the respondents use rectal cleansing.

A meta-analysis evaluating the use of rectal enema preparation before transrectal biopsy, showed no significant benefit in terms of infectious complications (7). 73.5% of the urologists who perform biopsy administer enema prior to transrectal biopsy.

Fluoroquinolones are widely used as antibiotic prophylaxis before transrectal biopsy. However, fluoroquinolone resistance has increased as a result of overuse of the drugs. Furthermore, the European Commission has implemented strict regulations on the use of fluoroquinolones for perioperative antibiotic prophylaxis (7). EAU prostate cancer guidelines recommends using either target prophylaxis (based on a rectal swab or stool culture); augmented prophylaxis; or alternative antibiotics for antibiotic prophylaxis for transrectal biopsy (7). A recent study shows 67.6% fluoroquinolone resistance in patients with urinary tract infections in Turkey (19). Half of the urologists that perform prostate biopsy uses only fluoroquinolone as prophylaxis.

EAU prostate cancer guidelines recommends Ultrasound-guided peri-prostatic block for pain control (7). Intra-rectal instillation of local anesthesia was shown to be inferior to peri-prostatic infiltration (20). However, our study showed that majority of the urologists do not perform peri-prostatic block.

Preferences for Managing a Patient with a High PSA Value

In asymptomatic men with a PSA value between 2-10 ng/mL and a normal DRE, EAU guidelines recommends use of a risk calculator, imaging, or an additional serum, urine, or tissue-based test (7). Clinicians should not perform biopsy immediately with only a limited increase in PSA. After a few weeks PSA value should be confirmed under standardized conditions (21,22). Antibiotics should not be used in asymptomatic patients to reduce PSA levels (23). Two questions were asked to the respondents about what to do when a PSA value of 3.0 ng/mL and 9.0 ng/mL of a patient who meets the screening and treatment conditions for prostate cancer and does not have active complaints. According to recent EAU guidelines, there is no difference in recommendations for these PSA values (7). However, our study showed that there is a

considerable difference in the clinical preferences of urologists. The percentage of the respondents who prefer DRE, and an additional test did not change significantly. For a patient with a PSA value of 3 ng/mL, respondents were more likely to repeat PSA after 6 weeks and follow patients annually. For a patient with a PSA value of 9 ng/mL, respondents were more likely to administer antibiotherapy, perform mpMRI, perform biopsy. It is understood that the 2-10 ng/mL psa treshold is not accepted among urologists yet.

In clinical decisions about prostate cancer, not only age, but also individual life expectancy, health status and comorbidities of the patient should be considered. Patients who are frail and above the age of 70 should have a full geriatric evaluation. EAU guidelines recommends the use of a performance scoring system for geriatric patients to determine patients' life expectancy, health status, and co-morbidities. Scoring systems that are mentioned in EAU guidelines are Geriatric 8 (G8) screening tool for a systematic evaluation of health status minicog for cognitive function, Karnofsky and ECOG for physical function (24,25,26). However, the majority of urologists do not use any performance scoring system when evaluating elderly patients.

Role of mpMRI

Recent guidelines do not recommend mpMRI as a screening tool. For biopsy naive patients, mpMRI is strongly recommended before the biopsy. And it is also recommended for patients with prior negative biopsy if no mpMRI has been performed before the initial biopsy (7). Majority of the respondents think that mpMRI should be used before re-biopsy. Although most of the academicians and urologist with experience of 15-20 years think that mpMRI should be used before first biopsy, the percentages do not exceed 44%.

Study Limitations

First, as with any survey study, there is a possible recall and response bias. Only individuals who are interested in or are not interested in prostate cancer and biopsy may have answered, we cannot exclude the possibility of a systematic bias as the reason for response vs. nonresponse. Another limitation is, due to demographic bias, the findings cannot be expanded. Like all survey data, the quality of our data is dependent on the truthfulness and/or potential biases of the respondent. As our study is descriptive in nature, it cannot determine the causes and clinical outcomes of low adherence to guidelines.

Conclusion

Studies show that it takes time for changes in guidelines to enter clinical practice. In some cases, it can be explained by the late spread of technology and the difficulty of accessing equipment, or the lack of training in use. However, in subjects such as patient management or antibiotic prophylaxis, it was seen that urologists act in the direction of their habits or clinical experience rather than current knowledge regardless of their experience. We think that urologists should be more active in following up-to-date information which is easy to access directly and online. Both clinicians and professional organizations should work on

what can be done about the reflection of rapidly changing scientific knowledge on the field and the improvement of the health service provided.

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