

Contemporary Approach to Active Surveillance by Urologists: Is There a Need for a Postgraduate Education Program?

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What's known on the subject? and What does the study add?

Active surveillance (AS) in prostate cancer is an increasingly popular approach. There are differences in AS criteria worldwide and there is no study on urologists' approach to AS in Türkiye. This is a pioneering study evaluating the knowledge, attitudes and practices of urologists in our country on AS. In addition, some of our data can be considered noteworthy such as AS recommendation rates, the effect of patient age and comorbidities on AS preference, and the use of mpMRI. AS preference rates are lower in our country compared to developed countries. Establishment of a validated AS follow-up protocol by urology organizations, continuous AS education programs for urologists and patient awareness programs may increase AS preference in appropriate patients.

Abstract

Objective: Active surveillance (AS) is an appropriate primary treatment option for low-risk prostate cancer (LRPCa) and selected intermediate-risk prostate cancer. In the current series, a considerable number of patients with LRPCa undergo radical prostatectomy instead of AS. We aim to evaluate the approaches of urologists in Türkiye and to document whether postgraduate courses on AS are necessary.

Materials and Methods: A survey was conducted among urologists registered in the Society of Urological Surgery database. A 27-question survey, including items on current management strategies for descriptive cancer cases, was created on the Research Electronic Data Capture website and sent via an online messaging application.

Results: A total of 1211 urologists received the message. Only 172 (14%) participants responded. About 2/3 (66.9%) of the participants prioritized AS for very LRPCa (vLRPCa). However, the AS rate was significantly lower for LRPCa in patients with high-core (>50%) involvement and high number of core (>3 cores) positivity in prostate biopsies (42.4%, 34.9%, respectively). Most of the (73.8%) urologists declared that they utilized multiparametric magnetic resonance imaging of the prostate (mpMRI) in the decision to perform AS, and 62.2% utilized it during follow-up. Over 92% of urologists do not recommend AS patients with for The Prostate Imaging Reporting and Data System 4-5 lesions. It was observed that urologists tended to prefer a more curative treatment as the patient's age decreased and more AS as their comorbidities increased.

Conclusion: The results suggest that, contrary to current guidelines, AS is relatively underutilized in patients with LRPCa. Interestingly, mpMRI seems to play a significant role in the decision and follow-up of patients with AS in daily practice. Postgraduate courses on AS for urologists may improve their attitudes toward AS. At least a certain need exists to establish standardized AS protocols to increase urologists' attention to AS.

Keywords: Prostate cancer, active surveillance, surveys and questionnaires

Introduction

Prostate cancer (PCa) is the most common cancer among men and the second most common cause of death after lung cancer (1). PCa exhibits a biologically slow progression. Given that 59%

were found in autopsy series of patients aged >79 years, there is likely no effect on overall survival in some patients (2). Therefore, the use of radical curative treatments (RCT) in some patients leads to overtreatment. Active surveillance (AS) is recommended for eligible patients so they are not exposed to the side effects

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of RCTs. The European Association of Urology and National Comprehensive Cancer Network (NCCN) guidelines recommend AS as a primary option for localized low-risk prostate cancer (LRPCa) and for favorable intermediate-risk prostate cancer (IRPCa) after explaining the risks (3,4).

There are differences between the criteria for enrollment and follow-up in the AS cohort studies due to the lack of randomized controlled trials (3). In addition, patients may require RCT during follow-up. Furthermore, these patients are at risk of progression and metastasis during follow-up despite a success rate of >90% (5). In addition to the doctor's approach, patient treatment desires, patient anxiety, and legal issues also influence the decision for AS. Considering these situations, clinicians' recommendations for AS and follow-up approaches differ. Nevertheless, AS is the primary and effective option for LRPCa and is widely used worldwide. However, a large proportion of men with LRPCa eligible for AS do not undergo AS at the time of diagnosis but instead undergo radical prostatectomy or radiotherapy (6).

On the other hand, the use of multiparametric prostate magnetic resonance imaging (mpMRI) has become necessary for the diagnosis and follow-up of PCa. However, its use in the AS protocol remains unclear. There are differences between centers and even physicians in the same center regarding many topics on AS, such as prostate-specific antigen (PSA) usage, timing of prostate biopsy (PB), evaluation of PB pathologies, use of mpMRI, and conversion to treatment. Due to the heterogeneity of studies, there are different approaches to patient selection and follow-up in AS in our country, similar to those in other countries. Such studies on the current attitudes of urologists may suggest the need for postgraduate education courses for urologists.

The main aim of this study was to evaluate the approaches of urologists in our country to AS and follow-up strategies for patients with PCa.

Materials and Methods

A cross-sectional survey was conducted among urologists registered in the Society of Urological Surgery (UCD) database in Türkiye. The study was conducted in accordance with the Declaration of Helsinki. The study was approved by the Marmara University Faculty of Medicine Pharmaceutical and Non-Medical Device Research Ethics Committee (date: 20.09.2024, protocol no: 09.2024.972). The survey was created online as multiple-choice questions via the Research Electronic Data Capture (REDCap) website (7). The survey were then sent to urologists registered with the UCD via an online message application. Informed consent was obtained from the participants in the survey.

The survey consisted of 27 questions in three parts. The first part included demographic information about the participants, such as gender, age, workplace type, academic qualifications, and career duration. The second part analyzed the participants' attitudes toward AS using index PCa cases. This section categorizes cases according to NCCN guidelines for very low-risk Pca (vLRPCa), LRPCa, and IRPCa patients, along with the patient's comorbidity status (4). Patients' comorbidity status in the cases was calculated using the Charlson comorbidity index (CCI) (8). Patients with comorbidities were selected from those with a CCI score of 4 (estimated 10-year life expectancy-53%). The third section's questions were about participants' approaches to include and follow-up of patients with AS. The study also evaluated the participants' approach to mpMRI in AS and the transition to curative treatment.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 22.0. The numbers and percentages of categorical variables were calculated for descriptive analyses. The data were analyzed using the chi-square test for the analysis of categorical variables. P-value <0.05 was accepted as indicative of statistical significance.

Results

The survey was sent to 1211 urologists. Data from 172 (14%) participants who completed the survey were included in the study. There were 171 (99.4%) men and only one woman urologist. Just 23 (13.4%) participants are <35 years of age, 53 (30.8%) between 35-45 years, 47 (27.3%) between 46-55 years and 49 (28.5%) >55 years. Regarding the participants' professional experience, 89 (51%) had been working as urologists for >15 years. Of the participants, 90 (52.3%) were working as a specialist in urology, 28 (16.3%) as an associate professor, and 39 (22.7%) as a professor. According to place of work, 50 (29.1%) were working in public hospitals, 38 (22.1%) in training and research hospitals, 47 (27.3%) in university hospitals, and 37 (21.5%) in private hospitals. There were 50 (29.1%) participants who primarily treated patients with urologic cancer in their daily practice and identified themselves as uro-oncologist (Table 1).

Cases were used to evaluate the participants' AS approaches. In vLRPCa patients, 115 (66.9%) participants stated that they primarily recommend AS, while others (33.1%) recommend RCT. Participants who recommended AS for patients with LRPCa but not vLRPCa due to high core positivity or high number of positive cores decreased to 73 (42.3%) and 60 (34.9%), respectively. However, participants who recommended AS for a LRPCa patient with comorbidities was 157 (91.3%). In IRPCa patients with Grade Group-(GG) 1 disease and elevated PSA, GG-2 favorable IRPCa and GG-2 favorable IRPCa with comorbidities,

108 (62.8%), 97 (56.4%), and 100 (58.1%) participants preferred AS, respectively. 39 (22.7%) participants stated that they preferred AS in IRPCa despite GG-3 pathology in patients with comorbidities in prostate-confined disease (Table 2).

When all other criteria were met, 142 (82.6%) of the participants recommended AS for patients with PSA<10.7 (4.1%) for patients with PSA<15 and 1 (0.6%) for patients with PSA<20. Only 31 (18%) participants did not consider the number of PB-

positive cores for AS. In comparison, the remaining 141 (82%) participants preferred a lower number of positive cores in the PB for AS. One hundred and fourteen (66.3%) participants selected to perform a confirmation prostate biopsy (cPB) within 1 year after the initial diagnosis. In comparison, 44 (25.6%) participants performed follow-up PB within the first 2 years. However, 14 (8.1%) participants did not suggest a cPB or even a follow-up PB. In follow-up PB, annual PB (62.8%) is most commonly preferred. However, 33 (19.1%) participants did not

Variables		n=172	%
Gender	Male	171	99.4
	Female	1	0.6
Age	<35	23	13.4
	35-45	53	30.8
	46-55	47	27.3
	>55	49	28.5
Worked as a urologist (years)	< 5	31	18
	5-10	26	15.1
	11-15	26	15.1
	>15	89	51
Academic qualifications	Specialist	90	52.3
	Assistant professor	15	8.7
	Associate professor	28	16.3
	Professor	39	22.7
Workplaces	Public hospital	50	29.1
	Training and research hospital	38	22.1
	University hospital	47	27.3
	Private hospital	37	21.5
Do you focus mainly on urologic cancers? (describing yourself as a uro-oncologist)	Yes	50	29.1
	No	122	70.9

Clinical cases	Active surveillance		Curative treatment (RP/RT)	
	n	%	n	%
1. vLRPCa	115	66.9	57	33.1
2. LRPCA (excluding from vLRPCA due to high core involment in PB)	73	42.4	99	57.6
3. LRPCA (excluding from vLRPCA due to high number of core positivity in PB)	60	34.9	112	65.1
4. LRPCA with comorbidities	157	91.3	15	8.7
5. IRPCa (due to PSA level between 10 and 20 ng/dL)	108	62.8	64	37.2
6. Favorable IRPCa	97	56.4	75	43.6
7. Favorable IRPCa with comorbidities	100	58.1	72	41.9
8. IRPCa due to GG 3 pathology with comorbidities	39	22.7	133	77.3

*: Comorbidity status was calculated using the Charlson Comorbidity index.

vLRPCa: Very low risk prostate cancer, LRPCA: Low risk prostate cancer, IRPCa: Intermediate risk prostate cancer, GG: Gleason grade, PB: Prostate biopsy, RP: Radical prostatectomy, RT: Radiotherapy

perform routine follow-up PB and recommended to undergo PB after cPB in the presence of elevated PSA or clinical necessity. Although only 127 (73. %) participants reported that mpMRI influenced their AS decision, in a different question, over 90% of the participants answered that they do not recommend AS for The Prostate Imaging Reporting and Data System (PIRADS) 4/5 lesions. Furthermore, 107 (62.2%) participants performed mpMRI control within a 2-year period during routine follow-up (Table 3).

Interestingly, the rate of participants recommending AS decreased as the patient age decreased, even if the patients met the criteria for AS. In other words, participants tended to recommend more RCTs as their patient age decreased (Table 3). The 3 most common factors that prevented participants from recommending AS to patients were patient anxiety (55.2%), concern on patient compliance to follow-up protocol (54.7%), and risk of missing the chance of treatment (45.9%). The most common reason for 91.3% of participants to convert AS to RCT was disease progression due to GG upgrading. Participants also reported that elevated and persistently elevated PSA (52.3%), DRE findings (50%), and radiological tumor growth on imaging (51.2%) triggered the RCT.

We asked the participants whether they focused mainly on urologic cancers in their daily practice and whether they would describe themselves as uro-oncologists (UO). Based on the answers, the participants were divided into two groups: UO and other urologists (OU). There were no significant differences between the ages and professional experience of the participants ($p>0.05$). The approaches of these two groups to vLRPca, LRPCa, and favorable IRPCa patients were similar ($p>0.05$). There was no difference between the distributions of follow-up protocol approaches, such as the use of mpMRI, the approach to cPB, and follow-up biopsies ($p>0.05$). Participants who identified themselves as UO were mostly associate professors and professors ($p<0.001$). Moreover, they primarily worked in university and private hospitals ($p<0.001$). In terms of the reasons preventing participants from recommending AS, patient anxiety was more important (68% vs. 50%) for UO than OU ($p=0.023$). However, OU were more concerned (39% vs. 14%) about legal issues ($p=0.01$) in AS. Although there were no difference in the age groups of other patients, UO recommends more AS than OU (50% vs. 30.3%) between 50 and 60 years old patients ($p=0.012$). Compared with UOs, OUs were more likely to recommend curative treatment for a one- (13.1% vs. 2%) or two-time PSA elevation (57% vs. 40%) without PB ($p=0.018$, $p=0.028$, respectively).

Secondly, we divided the participants into two groups: group 1 (<15 years of work-time) and group 2 (>15 years of work-time). Experienced urologists were more likely to work in private hospitals (30.3% vs. 12%) and university hospitals (29.2% vs. 25.3%) ($p=0.011$). Despite no difference in the other risks of

PCa patients, Group 2 recommended AS more than Group 1 (76.4% vs. 48.2%) in patients with GG-1 and PSA:10-20 ng/dL ($p<0.001$). Participants in Group 1 tended to recommend AS at a greater rate in patients <50 years old (31.3% vs. 12.4%) and 50-60 (45.8% vs. 27%) years old compared to group 2 ($p=0.002$, $p=0.008$, respectively).

Discussion

AS of PCa is an increasingly popular approach. Initially considered only for LRPCa, AS has recently been considered as an option for favorable IRPCa (3). It has been promoted as the only treatment option for patients with vLRPca in the latest NCCN guidelines (4). In other words, we will see many more patients with AS in the future. Although there is a general approach to AS worldwide, a consensus has not yet been reached. There have been no studies on the differences in approaches to AS in the Turkiye yet. Therefore, we believe our study is valuable as it is a pioneering study of AS in our country. In addition, some of the data can be considered noteworthy. Despite having the same disease characteristics, participants tend to prefer a more curative treatment as the patient's age decreases and prefer more AS as their comorbidities increases. Nowadays, studies on the use of mpMRI have increased, and it was observed that 73.8% of participants utilized mpMRI in the decision to perform AS and 62.2% utilized mpMRI during follow-up in our study. Moreover, over 92% of the participants did not recommend AS for patients with PIRADS 4 and 5 lesions on mpMRI. Thus, if mpMRI-based AS protocols are introduced, participants may not experience difficulties in adapting.

The survey was sent to 1211 urologists, and 172 (14%) participants eligible for analysis returned. Similar survey studies have reported response rates in different ranges, such as 36% and 8.2% (9,10). According to studies involving 35, 52, 225, and 413 participants, the number of participants in our study was sufficient (9-12). When we look at the number of participants in other studies and demographic data, such as age, workplace, and position of the participants, our data may reflect the general approach in Turkiye. In the survey studies, 95.9 % and 94.2 % of the participants were male among urologists in the USA and among urologists, oncologists, and radiation oncologists in Lebanon, respectively (9,11). 99.4% of our participants were male. The participants were 99.4% male. Our participants' age distribution and professional experience were similar to those of the survey studies in the literature. The workplaces of our participants are homogeneous, covering all hospitals in our country.

Patient selection is crucial in AS. Guidelines recommend as a first-line treatment option in patients with vLRPca and LRPCa (3,4). However, there are some differences in AS selection criteria,

Variables	n	%	
PSA level as recommended (provided that all other criteria are appropriate)	<10 ng/dL	142	82.6
	<15 ng/dL	7	4.1
	<20 ng/dL	1	0.6
	<30 ng/dL	0	0
	GG 1 patients (regardless of PSA)	22	12.8
Number of prostate biopsy-positive cores (provided that all other criteria are appropriate)	≤2 core	76	44.2
	≤3 core	42	24.4
	1/3 of the number of biopsies	20	11.6
	Less than 1/2 of the number of biopsies	3	1.7
	GG 1 patients (regardless of number of positive cores)	31	18
Confirmatory biopsy time	The first 3 months	23	13.4
	First 6 months	35	20.3
	The first 12 months	56	32.6
	No confirmatory biopsy	58	33.7
Follow-up biopsy time (month)	12	108	62.8
	18	5	2.9
	24	12	7
	No routine biopsy (unless psa elevation or clinical necessity)	47	27.3
No confirmation or follow-up biopsy	unless PSA elevation or clinical necessity	14	8.1
Does mpMRI influence the decision to perform AS?	Yes	127	73.8
	No	45	26.2
Frequency of patient visits	3 months	90	52.3
	6 months	34	19.8
	First, 1 year, 3 months, then rare	35	20.3
	First 2 years, 3 months, then rare	12	7
	Different follow-up	1	0.6
mpMRI during follow-up	No	18	10.5
	No unless the PSA rises	47	27.3
	Yes, every 6 months	19	11
	Yes, once per year	78	45.3
	Yes, every 2 years	10	5.8
	Yes ≥3 years	0	0
Influence of patient age on the decision to acquire AS	<50	37	21.5
	50-60	62	36
	60-75	91	52.9
	>75	99	57.6
Influence of mpMRI findings on the decision to undergo AS	No lesion	86	50
	PIRADS 1	84	48.8
	PIRADS 2	82	47.7
	PIRADS 3	64	39
	PIRADS 4	13	7.6
	PIRADS 5	4	2.3

AS: Active surveillance, PSA: Prostate-specific antigen, GG: Glenn grade, mpMRI: Multiparametric prostate magnetic resonance imaging, PIRADS: Prostate Imaging Reporting and Data System

such as PSA level, number of positive cores, and extent of core involvement. In the present study, 66.9% of the participants prioritized AS for vLRPCa. The AS rate was lower in patients with LRPCa who were not categorized as having vLRPCa due to high core involvement or high number of core positivity in PB. This rate declined to 42.4% and 34.9%, respectively. Considering that guidelines strongly recommend AS for patients with vLRPCa and LRPCa, we can conclude that AS recommendation rates among urologists are low in Türkiye. It should also be kept in mind that the NCCN guidelines recommend AS as the only option for vLRPCa (4). However, this situation may not be specific to our country. Similar to our country, the rate of AS recommendations among urologists is low in Brazil (53% for vLRPCa and LRPCa) and in Lebanon (58% for LRPCa (10,11). The rate of AS recommendations may be higher in developed countries. Because 74.7% of urologists in the USA recommend AS for vLRPCa and 43.5% for LRPCa, which is slightly higher than that of us (13). In Sweden, the AS recommendation rate has increased over the years to 94% for vLRPCa and 74% for LRPCa (14). Interestingly, although the rate of recommending AS in patients aged 50-59 years was 36% in our country, it was 88% in Sweden (14). Urologists in Türkiye recommend more AS as the patient's age increases and more curative treatment as the patient's age decreases. In contrast, in the UK, more AS is preferred for younger patients (12).

Approximately 83% of the participants preferred a PSA level of 10 ng/dL, even if the other features were the same in AS. In Brazil, most urologists (87.7%) also indicate PSA<10 ng/dL for AS (10). Although only 18% of the participants did not care about the number of positive cores in LRPCa patients, the remaining 82% preferred AS in patients with less core involvement, in accordance with at least one of the criteria in AS studies. Moreover, most of our participants (44.2%) reported that they prefer ≤ 2 core positives for AS. Additionally, 11% wanted the number of positive cores to be less than 1/3 of the cores taken at biopsy. Similarly, among Brazilian urologists, 44.3% considered ≤ 2 positive cores and 9.9% considered <34% of total cores as inclusion criteria (10). When we compared participants according to self-identification as UO and OU or experience (>15 years) and inexperience, both groups had similar approaches to AS in vLRPCa, LRPCa, and eligible IRPCa patients ($p>0.05$).

Patients will be monitored in AS with a scheduled follow-up protocol. It is essential to conduct RCTs early when treatment is necessary due to disease progression. PSA measurements, regular biopsies, and tests such as mpMRI are used for monitoring. In particular, in the first year, 72.6% of our participants chose to monitor the patients at 3-monthly. Urologists in Türkiye closely follow AS patients. When RP is performed in patients who meet the AS criteria, 29.7% have GG upgrading (15). NCCN guidelines recommend cPB within the first 6-12 months to avoid these reclassification mistakes (4). 66.3% of our participants prefer to

perform cPB within the first year and 13.4 % within the first 3 months. The rate of early PB within 3 months is 29.2%, and that within 1 year is nearly 40% in the United Kingdom (UK) (12). Although the remaining 33.7% did not perform cPB, the majority preferred to perform annual or biannual PB without cPB, as in some studies (16). Furthermore, 72.7% of the participants stated that they performed follow-up PB in the following 1-2 years in parallel with the NCCN recommendation. In contrast to the guideline recommendations, 8.1% of the participants stated that they did not perform cPB or follow-up PB unless there was PSA elevation or clinical necessity. Using mpMRI in both initial and follow-up PB contributes to accurate patient selection by increasing the diagnosis of clinically significant PCa (csPCa) (17). Although PB-based follow-up protocols are not yet available, studies on this issue are increasing. In our study, 73.8% of urologists utilized mpMRI in the decision to perform AS, and 62.2% had mpMRI control within a 2-year period during routine follow-up. In the UK, 58.3% of patients routinely undergo mpMRI to facilitate the selection of suitable patients for AS (12). The higher the number of PIRADS lesions on MRI, the higher the risk of csPCa (3). The risk of detecting csPCa was 16% in PIRADS-3 lesions, whereas the risk increased to 59% in PIRADS-4 lesions and 85% in PIRADS-5 lesions (18). In our study, although PIRADS-1/-2/-3 lesions did not significantly affect the AS decisions of the participants, the rates of their AS recommendations decreased to 7.6% for PIRADS-4 lesions and 2.3% for PIRADS-5 lesions. There was no difference between the UO/OU and experience/inexperience groups in the use of mpMRI, approach cPB, and follow-up biopsies ($p>0.05$). Similar to the literature, the most common reasons for urologists in Türkiye to convert AS to RCTs are disease progression due to GG upgrade, PSA elevation, DRE findings, and radiological tumor growth on imaging.

All similar studies confirmed the considerable variety in selecting appropriate patients for AS and applying a standard follow-up protocol worldwide. A national postgraduate education program and national guidelines may help overcome the current drawbacks of AS. Furthermore, using biomarkers may provide a standard and convenient approach for AS in the following years (19).

Study Limitations

There are some limitations in our study. First, we could only send messages to urologists registered in the database of a national urological association. Therefore, we could not reach all urologists in Türkiye. Second, although this is not a low percentage compared with the studies in the literature, we achieved a response rate of 14% from the urologists. However, we believe that the homogenous distribution of our participants will be sufficient to understand the approaches of urologists in Türkiye regarding AS.

Conclusion

In Türkiye, there is no current protocol for patient selection, enrollment, and follow-up in AS. As shown in our survey, urologists in Türkiye manage the follow-up and treatment of their AS patients by synthesizing the criteria in AS studies accepted worldwide. Thus, this situation leads to differences in the approaches to AS patients. AS preference rates are lower than those in developed countries. Establishing a standardized AS protocol increases urologists' attention to AS and encourages them to recommend AS for appropriate patients. Therefore, urological organizations are critical in establishing a validated follow-up AS protocol. Continuous AS education programs for urologists and patient awareness programs may increase the preference of AS for appropriate patients. Therefore, offering AS to appropriate patients not only saves them from the potentially harmful adverse effects of treatments but also reduces their economic burden.

Ethics

Ethics Committee Approval: The study was approved by the Marmara University Faculty of Medicine Pharmaceutical and Non-Medical Device Research Ethics Committee (date: 20.09.2024, protocol no: 09.2024.972).

Informed Consent: Written informed consent was obtained from all patients.

Footnotes

Authorship Contributions

Surgical and Medical Practices: G.Ö., M.K., Y.Ş., K.Ç., Concept: G.Ö., M.K., O.C.Ö., K.Ç., Design: G.Ö., M.K., Y.Ş., B.Ş., K.Ç., Data Collection or Processing: G.Ö., Y.Ş., B.Ş., K.Ç., Analysis or Interpretation: G.Ö., M.K., O.C.Ö., B.Ş., K.Ç., Literature Search: G.Ö., M.K., Writing: G.Ö., M.K., Y.Ş., K.Ç.

Informed Consent: All patients signed a written consent form before the operation.

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