Management of Localized Prostate Cancer in Elderly Patients

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Abstract

There are uncertainties concerning treatment management in elderly patients diagnosed with localized prostate cancer. The patient's age and morbidity are the most important factors affecting the treatment to be applied. Many screening scales are used for this purpose. It is reported that standard definitive treatments are suitable for patients with a life expectancy of more than 10 years, who are considered fit according to these screening scales. However, treatment options should be discussed in detail with patients in this group, which are already old and getting older. Therefore, elderly patients can be considered as the group that should be given the most information about the side effects of treatments. It is very important to properly evaluate the current state of the patient prior to treatment and inform them well to ensure that they have more rational expectations.

Keywords: Elderly patients, management, prostate cancer

Introduction

According to the global cancer statistics data, in 2020, prostate cancer was the second most common type of cancer after lung cancer in men, with approximately 1.4 million new cases. It is also the fifth leading cause of death due to cancer (1). At the time of diagnosis, 60% of patients are over the age of 65 years, and 70% of prostate cancer-related deaths occur in those aged 75 years and over (2). It is predicted that these rates will gradually increase as the world population ages (3).

Patients Selection

Age is an important factor in both the etiology and treatment selection of prostate cancer. However, in elderly patients that are planned to be treated for prostate cancer, treatment selection should be planned according to the biological age and health status of the patient, not according to chronological age (4). When determining the health status of this patient group, it is recommended to perform a comprehensive geriatric evaluation, including data on their comorbidities, nutritional status, physical functions, and cognitive-mental status (5). Studies have shown that a comprehensive geriatric evaluation has positive effects on the survival and quality of life of these patients (6). However, this type of evaluation requires specialist geriatricians and is a very time-consuming process. In addition, not all elderly patients need a comprehensive geriatric evaluation. Therefore, a number of geriatric screening tools have been developed to determine which patients need this evaluation, with the most accepted being the Geriatric-8 (G8) screening scale (Table 1) (7,8).

Patients who have a score above 14 on the G-8 screening scale, which also has Turkish validation, do not require a comprehensive geriatric evaluation. However, a score of ≤14 has been reported to be associated with three-year mortality, and therefore a comprehensive geriatric evaluation is recommended for these patients (7,9,10).

The International Society of Geriatric Oncology (SIOG) recommends evaluating the capacity of elderly cancer patients to properly evaluate the information provided for them and make informed decisions about their treatment processes. There are many screening scales developed for this purpose. SIOG recommends the use of the Mini-Cog™ test (Table 2) for the evaluation of cognitive functions in elderly patients with prostate cancer (11). This is a short test consisting of a combination of three word registration, clock drawing and three word recall tasks to distinguish patients with dementia from those without dementia. The evaluation is made over a total of 5 points. Patients with a score of ≤3 should be further evaluated for dementia (12).

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Table 1. G8 screening tool (7)	
Item	**Score**
Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?	0= Severe decrease in food intake 1= Moderate decrease in food intake 2= No decrease in food intake
Weight loss during the last 3 months	0= Weight loss greater than 3 kg 1= Does not know 2= Weight loss between 1 and 3 kg 3= No weight loss
Mobility	0= Bed or chair bound 1= Able to get out of bed/chair but does not go out 2= Goes out
Neuropsychological problems	0= Severe dementia or depression 1= Mild dementia 2= No psychological problems
BMI = Weight in kg/(height in m)^2	0= BMI less than 19 1= BMI 19 to less than 21 2= BMI 21 to less than 23 3= BMI 23 or greater
Takes more than 3 prescription drugs per day	0= Yes 1= No
In comparison with other people of the same age, how does the patient consider his/her health status?	0= Not as good 0.5= Does not know 1= As good 2= Better
Age	0= >85 years 1= 80-85 years 2= <80 years
BMI: Body mass index	

The European Association of Urology (EAU) and the SIOG Prostate Cancer Working Group recommend the use of a decision tree model (Figure 1) using the G8 screening scale and the Mini-Cog™ test for the treatment planning of prostate cancer cases aged over 70 years (13,14). According to the decision tree model, patients are divided into three groups: Group 1, fit; group 2, vulnerable (sensitive and susceptible); and group 3, frail (weak, fragile). All patients in group 1 and those with reversible disorders in group 2 should receive the same treatment as younger patients after their existing problems have been resolved. The treatment of patients in group 3 with irreversible disorders should be managed with treatment models tailored to each patient. For patients whose condition is even more severe, only palliative treatments are recommended (13).

Most patients with prostate cancer over the age of 65 years die due to co-morbidities (15). The most common co-morbidities in elderly patients with prostate cancer are lung and heart diseases, followed by vascular diseases, kidney diseases, and diabetes mellitus (16). These co-morbid conditions are known to be independent prognostic factors for survival in patients with cancer (17). Therefore, in order to decide how the current co-morbidities of elderly patients will affect the selection of treatment, first, these co-morbidities need to be evaluated systematically. Various methods have been developed for this purpose, with the most commonly used examples being the Charlson co-morbidity index (CCI) (Table 3) and the Cumulative Illness Rating Scale for Geriatric Individuals (Table 4) (18).

In CCI, the patient's co-morbid conditions are scored from 1 to 6, depending on the risk of death with which they are associated, and the total score obtained is used to predict mortality risk (19). There are studies showing that CCI can also be used to predict progression-free survival, postoperative complications, and length of hospital stay (20).

Localized prostate cancer treatment options should be reviewed by evaluating all these factors of patients. The most appropriate treatment method should be decided after informing the patient about the advantages and disadvantages of treatment options, such as active surveillance, watchful waiting, radical prostatectomy, and radiotherapy.

Treatment Options

Active Surveillance and Watchful Waiting

Treatment decisions concerning elderly patients with localized prostate cancer should be based on the risk evaluation. In this group of patients, the risk of death due to prostate cancer and the risk of death due to co-morbidities should be evaluated, and the potential risks and side effects of the treatment to be applied, as well as patient preferences should be considered (21).

Active surveillance aims to delay curative treatment as much as possible in patients with clinically localized prostate cancer. Here, the aim is to protect the patient from the potential side effects of curative therapy. Meanwhile, patients are followed up closely based on the prostate-specific antigen (PSA) value, digital rectal examination and multiparametric magnetic resonance imaging findings, and recurrent prostate biopsies. The aim of active surveillance is to identify and treat patients who will need active treatment during the follow-up protocol before missing
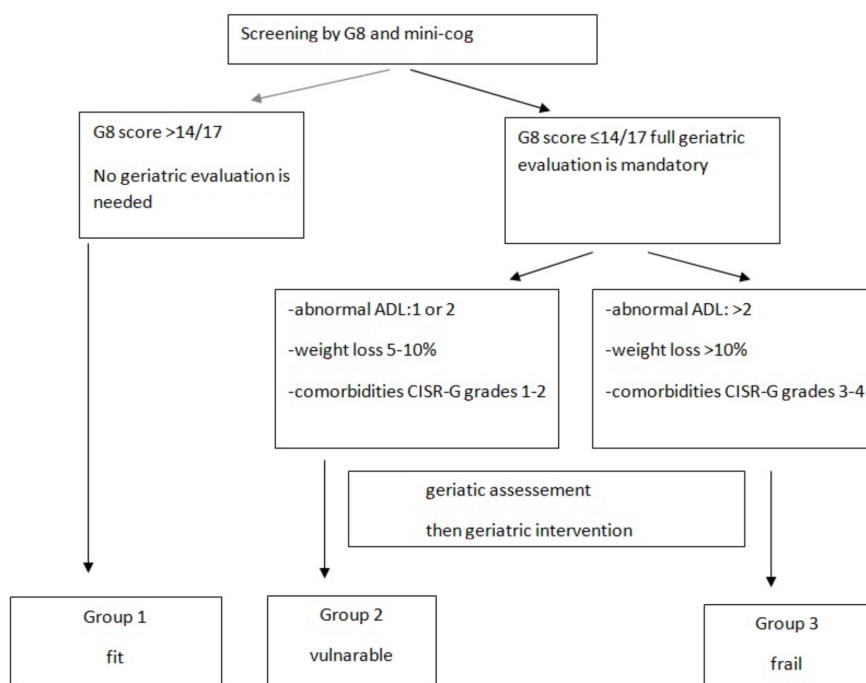
Figure 1. EAU geriatric assessment flow-chart (13). Decision tree for health status screening (men >70 years)

EAU: European Association of Urology

the chance for curative treatment (22). In a study including 993 patients under active surveillance, four factors associated with general mortality were defined: >70 years of age, high Gleason score, high prostate volume, and high PSA level. It was reported that among elderly patients, mortality mostly occurred for reasons other than prostate cancer, and when evaluated in terms of cancer-specific survival, patients aged <70 years did not differ from those aged <70 years (23).

It is also necessary to mention some of the disadvantages of the active surveillance option. An important handicap of the active surveillance option is the need for repeat biopsy procedures during the follow-up. Each biopsy poses a higher risk for sepsis and bleeding for the elderly group of patients compared to the younger patient group. Therefore, the patient should be well informed about the risks involved. In addition, the patient, who is already old and is getting older, may develop further co-morbidities during the process of transition to definitive treatment. Delaying definitive treatment constitutes a further problem due to the possibility of the risk group of the patient changing during this process. Therefore, active surveillance may have to switch to watchful waiting. Active surveillance can be considered as the treatment option that is most difficult to decide in the elderly patient group. In light of all these findings, active surveillance can be regarded as a rational treatment option in elderly patients with a low risk.

In watchful waiting, patients that are considered unsuitable for curative treatment due to their general health conditions and have a life expectancy of less than 10 years are followed up without treatment until the development of symptoms related to local or systemic progression. After this stage, palliative treatments are applied to these patients (24). Considering older

age and scoring system parameters, watchful waiting may be the most accurate option for patients in the frail group.

According to the SIOG prostate cancer study group, elderly patients with prostate cancer that are in the low and intermediate risk groups according to the D'Amico classification can be followed up with either active surveillance or watchful waiting depending on their individually determined life expectancy (13).

Radical Prostatectomy

There are studies showing that patients aged ≥75 years who have undergone open radical prostatectomy have higher rates of mortality and morbidity, as well as more perioperative and postoperative complications compared to those aged <75 years (25,26). Due to these high morbidity and mortality rates, elderly patients are often not considered suitable for curative treatment options for prostate cancer and are followed up with conservative methods. However, prostate cancer detected in older men tend to pose a higher risk (27). It is known that patients with high-risk diseases face a greater risk of death when followed up with conservative treatments (28). Studies show that patients who are not given local curative treatment only due to their chronological age have increased mortality rates associated with prostate cancer, as well as significant morbidities, such as long-term urethral catheterization, development of hydronephrosis, nephrostomy opening, and colostomy opening due to the local progression of prostate cancer (28,29). Recently, there has been growing awareness that elderly patients with cancer are under-treated, especially in terms of local curative therapy (30). Developments in the surgical technique and the increasing adoption of minimally invasive methods have encouraged the

Table 2. Mini-Cog™ test (10)					
Step 1. Three word registration					
Look directly at person and say, "Please listen carefully. I am going to say three words that I want you to repeat back to me now and try to remember. The words are (select a list of words from the versions below). Please say them for me now." If the person is unable to repeat the words after three attempts, move on to Step 2 (clock drawing)					
The following and other word lists have been used in one or more clinical studies.1-3 for repeated administrations, use of an alternative word list is recommended					
Version 1	**Version 2**	**Version 3**	**Version 4**	**Version 5**	**Version 6**
Banana	Leader	Village	River	Captain	Daughter
Sunrise	Season	Kitchen	Nation	Garden	Heaven
Chair	Table	Baby	Finger	Picture	Mountain
Step 2. Clock drawing					
Say: "Next, I want you to draw a clock for me. First, put in all of the numbers where they go." When that is completed, say: "Now, set the hands to 10 past 11."					
Use preprinted circle (see next page) for this exercise. Repeat instructions as needed as this is not a memory test. Move to step 3 if the clock is not complete with in three minutes					
Step 3. Three word recall					
Ask the person to recall the three words you stated in step 1. Say: "What were the three words I asked you to remember?" Record the word list version number and the person's answers below					
Word list version: _____ Person's answers: _____ _____ _____					
Scoring					
Word recall: _____ (0-3 points)			1 point for each word spontaneously recalled without cueing		
Clock draw: _____ (0 or 2 points)			Normal clock = 2 points. A normal clock has all numbers placed in the correct sequence and approximately correct position (e.g., 12, 3, 6 and 9 are in anchor positions) with no missing or duplicate numbers. Hands are pointing to the 11 and 2 (11:10). Hand length is not scored. Inability or refusal to draw a clock (abnormal) = 0 points		
Total score: _____ (0-5 points)			Total score = Word recall score + Clock draw score. A cut point of <3 on the Mini-Cog™ has been validated for dementia screening, but many individual swithc clinically meaningful cognitive impairment will score higher. When greater sensitivity is desired, a cut point of <4 is recommended as it may indicate a need for further evaluation of cognitive status		

widespread use of radical prostatectomy in elderly patients (31). In a study evaluating 800 patients who underwent robot-assisted laparoscopic radical prostatectomy, the patients were divided into two groups as <70 years and ≥70 years. At the end of the study, no difference was found between the groups in terms of perioperative complications (32). In another study, Iguchi et al. (33) compared the results of 28 patients over 70 years of age and 47 patients under 70 years who underwent robotic radical prostatectomy for prostate cancer. All patients underwent a urodynamic examination preoperatively and at three months after the operation. The presence of persistent overactive bladder symptoms in the group with ongoing postoperative urinary incontinence was reported to be significantly higher in the elderly patient group. It was also determined that the presence of overactive bladder symptoms before the operation was associated with incontinence regardless of age. Therefore, the preoperative evaluation of continence status, overactive bladder symptoms, and evaluation of urethral closure pressure with urodynamic studies, if necessary, may be useful in terms of more rational expectations (33). A recent study published in Turkey evaluated the results of robot-assisted laparoscopic radical prostatectomy performed in patients aged <70 years (n=819) and ≥70 years (n=151). At the end of the study, the authors reported that they did not detect any difference in terms of oncological and operative results, although the functional results were statistically significantly worse in the elderly group (34). In another study conducted in our country; as emphasized by Tavukçu and Kaplan (35), in the elderly patient group with frail but treatable disease, standard treatment can be applied after existing comorbidities are corrected or improved. Considering all these findings, patients aged ≥75 years should be informed about the increased risk of perioperative morbidity and mortality compared to younger patients.

Age is an independent risk factor for urinary incontinence in patients undergoing radical prostatectomy (36). Studies have demonstrated an inverse relationship between advancing age and continence rates (37,38). The rate of erectile dysfunction development after radical prostatectomy is also negatively affected by age (39).

While the EAU guidelines suggest that patients who will undergo radical prostatectomy should have a life expectancy of at least 10 years, the National Comprehensive Cancer Network guidelines state that this period is 10-20 years depending on the

Table 3. Charlson co-morbidity index	
Score	Comorbid condition
1	Myocardial infarction Congestive heart failure Cerebro vascular disease Peripheral vascular disease Dementia Chronic obstructive pulmonary disease Connective tissue disease Peptic ulcer disease Mild liver disease Age[a]
2	Diabetes Hemiplegia Moderate/severe renal disease Diabetes with end-organ damage Any solid tumour Leukemia Lymphoma
3	Moderate/severe liver disease
6	Metastatic solid tumour Acquired immunodeficiency syndrome
[a]For each decade after 40 years, a point is added (1 point for age group 41-50, 2 points for age group 51-60, 3 points for 61-70, 4 points for 71 or older)	

risk groups (40). In a review of radical prostatectomy performed in patients over 75 years of age, Mandel et al. (41) reported that biological age should not constitute a definite contraindication to radical prostatectomy. The authors stated that the perioperative morbidity and mortality rates were higher and oncological and functional outcomes were worse in the elderly group but the results were still acceptable. Considering all these factors, the authors emphasized that radical prostatectomy was a viable treatment option in a well-selected patient group aged 75 and over (41). In a study including 2,000 patients who underwent radical prostatectomy, Porres et al. (42) evaluated the functional outcomes of 45 patients aged 75 years and older. In the third month, the continence rate was 18.0% in the elderly patient group and 37.5% in the younger group. However, at the 12th-month evaluation, the authors determined these rates to be 76.7% and 85.7%, respectively, indicating no statistically significant difference (p=0.084). As a result, although the authors found no difference between the continence rates of the groups in the first year, they emphasized that the elderly patients needed more time to achieve continence.

When evaluated in terms of impotence, it is not surprising that the functional results of elderly patients are worse. The most important factors in impotence are pre-operative potency status and whether a nerve-sparing approach is applied. A study evaluating patients who underwent bilateral nerve-sparing surgery by Mandel et al. (41) was reported the postoperative potency rates as 66.2% for the young patient group and 39.6% for the elderly patient group. Similarly, in a study conducted by Sokolov et al. (43) with 117 patients over 65 years of age who underwent radical prostatectomy, it was observed that age had no effect on oncological outcomes and the potency ratios of the cases, especially those in which the bilateral nerve-sparing approach was used improved earlier regardless of age.

Table 4. Cumulative Illness Rating Scale (17)	
Rating strategy of comorbidity	
0= No problem	Organ system not compromised
1= Mild	Illness/impairment with or without Requirement of therapy, excellent prognosis, patient with normal activity
2= Moderate	Illness/impairment requiring therapy, good prognosis, compromised activity
3= Severe	Illness/impairment with urgent requirement of therapy, prognosis unclear, marked restriction in activity
4= Extremely severe	Life threatening illness/impairment, emergency case of therapy, adverse prognosis
Assess illness/impairment in each of the following systems on a scale from 1 to 4:	
System	Score
Heart	
Blood pressure	
Vascular	
Respiratory	
Eye/ear/nose/throat/larynx	
Upper gastrointestinal	
Lower gastrointestinal	
Liver	
Renal	
Genitourinary	
Musculoskeletal	
Endocrine/metabolic	
Neurological	
Psychiatric	
Total	

Compared to younger patient groups; worse postoperative functional results are expected in elderly patients due to longer recovery times and worse preoperative erectile functions and urinary continence. In brief, radical prostatectomy is a strong option in well-selected elderly patients. However, it is important to inform the patient well that this option has worse functional outcomes.

Radiotherapy

In localized prostate cancer, radiotherapy is an important treatment modality with cancer control rates similar to radical prostatectomy (44). In the literature, modifications of radiotherapy applications due to age-related specific toxicities in elderly patients have been evaluated. In a recent study including 3,216 patients divided into two groups as <75 and ≥75 years, each group was further randomized into three groups as 74 Gy-37 fraction (conventional method), 60 Gy-20 fraction, and 57 Gy-19 fraction. As a result of the study, no difference was found between the <75 and ≥75 years groups in relation to the biochemical or clinical failure (BCF)-free rates after radiotherapy. In the ≥75 years group, the BCF-free rates were 84.7% for the

74 Gy subgroup, 91% for the 60 Gy subgroup, and 87.7% for the 57 Gy group. In the same study, the authors reported that there was no increased risk of radiation-induced acute bowel and bladder toxicity in the ≥75 years group (45).

In another study evaluating 902 patients who underwent external beam radiotherapy and 1,527 patients who underwent brachytherapy for clinically localized prostate cancer, the patients were divided into two groups as ≥80 years and <80 years. As a result of the study, no significant difference was found between the age groups in terms of the five-year biochemical failure-free survival rates (91.3% vs. 85.9%, p=0.6171) and cancer-specific survival rates (100% vs. 99.3%, p=0.6171). The long-term results of the study that the gastrointestinal toxicity rates were similar between the groups. The authors stated that among the patients that received brachytherapy, the rate of late genitourinary toxicity was significantly higher in the ≥80 years group than in the <80 years group, and the former required sensitive care in terms of late genitourinary toxicity (46).

Considering the similar efficacy and acceptable side-effect profile, radiotherapy is a strong treatment candidate in the curative treatment of localized disease in elderly patients. However, it should be kept in mind that a closer follow-up is required in terms of postoperative genitourinary and intestinal toxicity.

Conclusion

There are many factors that should be considered when deciding on treatment in elderly patients with prostate cancer. The basic principle in treatment management should be to take action according to co-morbidity risk scores, which may change depending on the co-morbidity status of the patient during the treatment process. The elderly constitute a patient group in which the advantages and disadvantages of each treatment option should be discussed with utmost sensitivity. Accurate and proper patient information is valuable in preventing irrational expectations. This process should be managed by evaluating all factors, and follow-up should be personalized according to the current co-morbidities of patients. This will help patients achieve the highest benefit from the treatment and keep their comfort at an optimal level.

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Short Quiz

1- Which of the following is the most accurate nodal staging method?

A) CT or MR imaging

B) PSMA/PET CT imaging

C) Extended lymph node dissection

D) Abdominal ultrasonography

E) Transrectal ultrasonography

Answer: C

2- Which of the following is incorrect about a 78-year-old patient diagnosed with localized prostate cancer?

A) It is not suitable for definitive treatment, watch full waiting treatment should be applied.

B) Comorbidity scores should be used in making the treatment decision.

C) Oncological outcomes after radical surgery are similar to younger patients.

D) It should be informed that the postoperative functional results are worse than the younger patient group.

E) Radiotherapy has high success rates.

Answer: A

3- Which of the following is incorrect for a diagnosis of advanced age localized prostate cancer?
A) Patients with a life expectancy of more than 10 years can be treated with standard treatment methods.
B) Longer follow-up is required in terms of intestinal toxicity in elderly patients who received radiotherapy.
C) Active surveillance is not accepted as a treatment option due to advanced age.

D) Watch full waiting can be applied to patients with a life expectancy of less than 10 years.

E) Hypofractionation can be used for radiotherapy.

Answer: C

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