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Original Research / Özgün Araştırma

Palliative Care Decision in Aging Male With Prostate Cancer

Prostat Kanserli Yaşlanan Erkekte Palyatif Bakım Kararı

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Özet

Amaç: Çalışmamızın amacı, prostat kanserinde hastanın geliş hasta yaşı ve PSA değeri ilepalyatif yaklaşım veya küratif tedavi kararının verilebileceğini göstermektir.

Gereç ve Yöntemler: 2007 ve 2012 kliniğimizde prostat kanseri tanısı almış hastalar retrospektif olarak tarandı. Hastaların yaşı, prostat hacimleri, transrektal ultrasonografi eşliğinde prostat biyopsi sonuçları, metastaz taraması için yapılan görüntülemeleri ve radikal prostatektomi yapılan hastaların patoloji sonuçları kaydedildi.

Bulgular: Hastaların yaş ortalaması 70.85 ± 8.40 idi. Ortalama yaş, PSA seviyeleri, yüzde kadran oranları ve Gleason skorları metastaz varlığına bağlı olarak anlamlı farklılık gösterdi ($p<0.01$). Bir hastada prostat kanseri varlığı açısından, 75 yaş kesme değerinde özgüllük % 77,17, duyarlılık % 68,18, pozitif öngörü değeri (PPV) % 48,28, negatif öngörü değeri (NPV) % 88,58 ve doğruluk % 70,68 idi; 20 PSA kesme noktasında duyarlılık % 92,13, özgüllük % 91,52, PPV % 80,69, NPV % 96,79 ve doğruluk % 91,68 idi; 0,41 Çeyreksel kesme değerinde, özgüllük % 75,59, PPV % 52,17, NPV % 88,64 ve duyarlılık % 73,96 idi.

Sonuç: Geriatrik yaş grubunda, palyatif bakım veya küratif tedavi kararında hastaların yaş ve PSA değeri değerlendirilerek hasta yönetiminde karar verilmelidir.

Anahtar Kelimeler: Prostat kanseri, palyatif bakım, metastaz, yaşlanan erkek

Abstract

Objective: The aim of our study is to demonstrate that differentiating patients receiving a palliative approach to prostate cancer from candidates for definitive treatment using age and PSA value at initial presentation.

Material and Methods: The records of patients diagnosed with prostate cancer in our clinic and external centers and presenting to our clinic for treatment between 2007 and 2012 were examined retrospectively. Information was collected concerning patients' ages at presentation, presentation PSA values, rectal examination findings at time of presentation, prostate volumes, transrectal ultrasonography (TRUS)-guided prostate biopsy results, imaging findings performed for staging purposes in patients with prostate cancer, and pathological specimens in operated patients.

Results: Mean age of patients was 70.85±8.40. Mean ages, PSA levels, percentage quadrant rates, and Gleason scores differed significantly depending on presence of metastasis ($p<0.01$). In terms of the presence of prostate cancer in a patient, at a cut-off value of age 75, specificity was 77.17%, sensitivity 68.18%, positive predictive value (PPV) 48.28%, negative predictive value (NPV) 88.58%, and accuracy 70.68%; a PSA cut-off point of 20 exhibited sensitivity of 92.13%, specificity of 91.52%, PPV of 80.69%, NPV of 96.79%, and accuracy of 91.68%; and also sensitivity at a percentage of quadrant cut-off value of 0.41, specificity was 75.59%, PPV 52.17%, NPV 88.64%, and accuracy 73.96%.

Conclusion: Decision in management should be made by evaluating age and PSA value whether to apply palliative care or curative treatments in the geriatric age group without performing a biopsy.

Keywords: Prostate cancer, palliative care, metastasis, aging male

INTRODUCTION

Prostate cancer is the second most common cancer among men in terms of new case numbers, although incidence and mortality rates vary among countries (1). Prostate cancer has been determined in one in three or four men aged 40-50 years in autopsy studies (2). An incidence study in Turkey performed by the Association of Urooncology described prostate cancer as the most common urological cancer, and the second most common of all cancers, after lung cancer (3).

Definitive treatments and close follow-up including radical prostatectomy, radiotherapy and brachytherapy, and palliative approaches such as hormonal therapy, are applied in the treatment of prostate cancer, depending on the stage. Experimental therapeutic methods such as cryotherapy and high-intensity focused ultrasound (HIFU) are also available. Experimental approaches shown to prolong general survival in controlled randomized studies include radical prostatectomy in localized prostate cancer and radiotherapy together with neoadjuvant hormonal therapy, and adjuvant hormonal therapy in local advanced prostate cancer (4,5,6,7). However, systemic androgen deprivation therapy entails severe comorbidities (8).

Elderly patients with high-risk prostate cancer and poor performance are generally potentially suitable candidates for a palliative approach, such as close monitoring or hormonal therapy. Prostate biopsy morbidity is higher in this patient group due to general performance conditions (9).

Our study examined the possibility of differentiating patients receiving a palliative approach to prostate cancer from candidates for definitive treatment using age at initial presentation, presentation PSA value, and rectal examination findings without prostate biopsy.

MATERIAL AND METHODS

The records of all patients new diagnosed with prostate cancer in our clinic and external centers, and presenting to our clinic for treatment between 2007 and 2012 were examined, retrospectively. The patients have atypical form of prostate cancer except adenocarcinoma were excluded, except this all the patients were included.

Information was collected concerning patients' ages at presentation, PSA values, rectal examination findings, prostate volumes, transrectal ultrasonography (TRUS)-guided prostate biopsy results, imaging findings performed for staging purposes in patients with prostate cancer, and pathological specimens in operated patients.

Rectal examination findings were coded as benign or malign, and size was disregarded. Total Gleason score and percentage quadrant rates were noted for subjects with prostate cancer determined at TRUS-biopsy. Abdominopelvic tomography, pelvic magnetic resonance imaging (MRI) and whole-body bone scintigraphy were recorded as presence or absence of local invasion and distant metastasis.

Patients were grouped as palliative or definitive, depending on the type of treatment received. Patients receiving radical prostatectomy and radiotherapy were included in the definitive treatment group. The palliative group included patients receiving hormonal therapy (maximal androgen blockage, LHRH analog monotherapy, antiandrogen monotherapy, and surgical castration), close monitoring, or transurethral resection due to intravesical obstruction.

Statistical analyses were performed on Number Cruncher Statistical System 2007&Power Analysis and Sample Size 2008 Statistical Software (Utah, USA). In addition to descriptive statistical methods (mean, standard deviation, median, frequency, minimum, and maximum), Student's t test was used in two-group comparisons of normally distributed quantitative variables and the Mann Whitney U test for non-normally distributed parameters. One-Way ANOVA was applied in the comparison of three or more groups exhibiting normal distribution, and Tukey's HSD was applied to identify the group responsible for variation. The Kruskal Wallis test was applied in the comparison of three or more groups not exhibiting normal distribution, and the Mann Whitney U test was used to identify the group responsible for variation. Pearson's chi-square test and the Yates Continuity Correction test (Yates corrected chi-square) were used in the comparison of qualitative data. Diagnostic screening tests (sensitivity, specificity, PPV, and NPV) and ROC Curve analysis were used to determine parameter cut-off points. Significance was set at $p<0.01$ and $p<0.05$.

RESULTS

The study was performed with 457 male patients diagnosed with prostate cancer at our clinic and at external centers between 2007 and 2012 and presenting for treatment. Cases ranged between 45 and 88 years in age, with a mean age of 70.85±8.40.

PSA measurements, the presence of metastasis, local invasion and rectal examination results were summarized in the table below (Table 1).

Mean ages, PSA levels, percentage quadrant rates, and Gleason scores differed significantly depending on presence of metastasis (p<0.01).

Gleason Score & Metastasis

Gleason scores based on biopsy results depending on presence of metastasis are shown in Table 1; Gleason scores were 6 in cases without metastasis, while much higher numbers of Gleason scores of 7, 8, and 9 were observed in metastatic cases (Table 2).

Age & Metastasis

The best cut-off point for age by groups was 75. At a cut-off value of age 75, specificity was 77.17%, specificity 68.18%, positive predictive value (PPV) 48.28%, negative predictive value (NPV) 88.58%, and accuracy 70.68% (Table 3)

PSA & Metastasis

We considered calculating a cut-off point for PSA based on the significance of PSA depending on presence of metastasis. ROC analysis and diagnostic screening tests were used to determine a cut-off point by groups. The best cut-off point for PSA by groups was 20. A PSA cut-off point of 20 exhibited sensitivity of 92.13%, specificity of 91.52%, PPV of 80.69%, NPV of 96.79%, and accuracy of 91.68%. A statistically highly significant relation was determined between presence of metastasis and a PSA cut-off point of 20 (p<0.01). The ODDS ratio for presence of metastasis was 126,193 (95% CI: 59,435-267,932), so in cases with PSA levels of 20 or more, we found that the risk of metastasis is 126 times higher.

Percentage of Quadrant & Metastasis

The best cut-off point for percentage of quadrant by groups was 0.41 (p<0.01). Sensitivity at a percentage of quadrant cut-off value of 0.41, specificity was 75.59%, PPV 52.17%, NPV 88.64%, and accuracy 73.96%.

The ODDS ratio for presence of metastasis was 8,516 (95% CI: 5308-13,663), so in cases with a percentage of quadrant of 0.41 or above, found that the risk of metastasis is 8.5 times higher.

Table 1. Descriptive properties of 457 patients

		Min-Max	Mean±STD	Median
Age (year)		45-88	70,85±8,40	72,0
PSA		1,5-178	25,71±31,60	10,6
Percentage of quadrant		0,08-1,00	0,44±0,33	0,3
		N	**%**	
Metastasis	**No**	330	72,2	
	Yes	127	27,8	
Biopsy	**Gleason Score 6**	225	49,2	
	Gleason Score 7	144	31,5	
	Gleason Score 8	51	11,2	
	Gleason Score 9	37	8,1	
Rectal Examination (n=292)	**Benign**	184	63,0	
	Malign	108	37,0	
Local Invasion	**No**	300	65,6	
	Yes	157	34,4	

PSA: *prostate spesific antigen* ***STD:*** *Standart Deviation* ***p<0,01*
aStudent t Test *bMann Whitney U Test*

Table 2. Age, PSA, percentage of quadrant and gleason scores according to the metastasis presence

		Metastasis		
		Yes (n=127)	**No (n=330)**	***p***
		Mean±STD	**Mean±STD**	
Age (year)		68,71±8,21	76,43±6,00	***[a]0,001****
PSA		10,13±6,72 (7,80)	66,18±34,79 (62,00)	***[b]0,001****
Percentage of quadrant *(Median)*		0,33±0,27 (0,25)	0,71±0,32 (0,83)	***[b]0,001****
Gleason Score; *(Median)*		6,44±0,68 (6,0)	7,67±0,94 (8,0)	***[b]0,001****
		n (%)	**n (%)**	
Biopsy	**Gleason Score 6**	213 (%64,5)	12 (%9,4)	
	Gleason Score 7	96 (%29,1)	48 (%37,8)	
	Gleason Score 8	14 (%4,2)	37 (%29,1)	
	Gleason Score 9	7 (%2,1)	30 (%23,6)	

PSA: *prostate spesific antigen* ***STD:*** *Standart Deviation* ***p<0,01*

aStudent t Test *bMann Whitney U Test*

Table 3. Relationship between metastasis and age (Cut-off value 75)

	Age (year)				
	< 75		**≥ 75**		***[a]p***
	n	***%***	**n**	***%***	
Metastasis	**No**	*229*	*69,4*	101	*30,6*
	Yes	31	*24,4*	96	*75,6*

0,001**

aPearson Chi-square test ***p<0,01*

DISCUSSION

Prostate cancer is one of the most common types of cancer worldwide. It has become more frequently seen due to the increase in life spans in recent years, and an even more important public health problem. While some patients live with prostate cancer for extended periods without treatment, in others the cancer progresses rapidly, no response to treatment is achieved, and mortality occurs within a few years. Prostate cancer is the most frequent type of cancer in men and the

second most common cancer-related cause of death in men (10). Major advances and progress in the diagnosis and treatment of prostate cancer began being seen from the mid-1980s onward. In parallel to these developments, prostate cancer consists of consecutive stages of organ-limited disease, local advanced stage disease, metastatic disease, and hormonal therapy-resistant disease. Our study concerning parameters predicting metastatic disease in patients newly diagnosed with prostate cancer yielded important findings.

Diagnosis of prostate cancer is based on confirmation with tissue diagnosis of clinical suspicion raised by the combined use of serum PSA values and digital rectal examination (11). First of all, in our study we evaluated the PSA levels for diagnosis and find the best option for prostate cancer treatment. In nomograms, it was full-filled at the beginning of evaluations. The mean PSA value in this study of 25.71±31.60 ng/mL exhibits a significant parallel with Merril and Stephenson's (12) results. Some studies have shown that no significant benefit is obtained from bone scintigraphy in cases with PSA values less than 10 ng/ ml (13). However, the results from our study suggest that bone scintigraphy is appropriate.

PSA elevation may be seen in such prostate pathologies as prostate cancer, prostatitis, and benign prostatic hyperplasia; in addition, various prostatic manipulations can also cause a rise in PSA. One of the most important problems concerning PSA is that it is organ-specific rather than cancer-specific, and its specificity is therefore inadequate (14). We determined a statistically significant difference between PSA levels depending on metastasis. We therefore considered a cut-off point for PSA and calculated this at 20. A statistically highly significant relation was determined between presence of metastasis and the PSA cut-off value. Analysis of the data obtained from this study showed that the risk of metastasis was approximately 126-fold higher in patients with PSA levels of 20 or more (ODDS = 126,193). Serum PSA elevation occurs due to PSA entering the blood from the prostate as a result of impaired prostate tissue integrity. PSA levels were 66.18±34.79 ng/mL in metastatic cases and 10.13±6.72 ng/mL in non-metastatic patients. These results show that PSA levels increase considerably in line with metastasis. Although PSA levels are a practical marker for avoiding unnecessary scintigraphy in patients followed up with treatment, insufficient clinical data are available concerning the optimal PSA level for use as a definitive marker in patients with potential metastasis. We think that the PSA values obtained in our study will make a significant contribution to the decision whether to employ bone scintigraphy. A Gleason score above 6 in cases with and without metastasis will also support this. We also determined a high level of statistical significance between presence of metastasis and a PSA cut-off value of 20. Data analysis revealed that the risk of metastasis was approximately 126-fold higher in cases with PSA levels of 20 and above, and this also shows the importance of PSA in terms of diagnosis of the disease and determining treatment.

Based on the significant mean ages of patients according to presence of metastasis, cut-off value calculations were performed for age. The best cut-off point for age by groups was 75. A cut-off point for age of 75 exhibited sensitivity of 77.17%, specificity of 68.18%, PPV 18.28%, NPV 88.58% and accuracy of 70.68%. These values indicated a statistically significant relation between presence of metastasis and a cut-off value of age of 75. The ODDS ratio for presence of metastasis was calculated at 7.021, and the risk of metastasis was approximately seven times higher in cases aged 75 or over. This indicated that the rate of metastasis increases in an age-dependent manner, and this finding is in agreement with Boyle and Dresler's findings (15,16).

The Gleason score is the most commonly employed system for classifying prostate adenocarcinoma (15); and also a highly important prognostic factor in predicting pathological stage (17); and also of proven importance in the Partin table, used to predict pathological stage by means of clinical stage, serum PSA value, and biopsy Gleason score (18); and also of the very greatest importance in the selection of one of the options of wait and see, radical surgery, or radiotherapy, and in deciding on the form of radical surgery (19). Chan et al. (20) evaluated 570 patients with Gleason

scores of 7 in radical prostatectomy materials and reported that the risk of progression increased in subjects with Gleason scores 4+3. In this study, we aimed to find the predictive values of metastasis of prostate cancer without perform a biopsy, so that we know and all the studies showed the importance of Gleason, it is a biopsial predictive factor.

The highest tumor percentage in cores in which cancer is determined by means of biopsy is an important prognostic risk factor in PSA recurrence in the postoperative period (18). We also evaluated this parameter, and we found it is an important prognostic and predictive factor for prostate cancer metastasis.

This study has several limitations. First of all, it was a retrospective study and we discussed the treatment on pathological findings. Secondly, the study does not include only geriatric age group, and this reduce the strength of our study. Also, this study has low number patient relatively; it will be more accurate to conclude with a relatively higher number of studies in oncological outcomes.

CONCLUSION

Our study findings were compatible with results from the literature concerning parameters predicting metastatic disease in patients diagnosed with prostate cancer. According to our findings, PSA value, Gleason score, and percentage of quadrant may be quite effective in predicting metastatic disease and deciding on imaging techniques. Decision in management should be made by evaluating age and PSA value whether to apply palliative care or curative treatments in the geriatric age group without performing a biopsy.

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