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ORIGINAL ARTICLE

Effect of age on biochemical recurrence after radical prostatectomy

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Abstract The aim of the study was to evaluate the relationship between patient's age and biochemical recurrence (BCR) after radical retropubic prostatectomy (RRP). Data from RRP applied to 305 patients with clinically localized prostate cancer were included in the study. Patients were divided into the three age groups, $<$ 60 years, 60–70 years, and $>$ 70 years. The groups were compared regarding adverse pathological findings on RRP specimen, BCR, and biochemical recurrence-free survival (bRFS) rates. The rates of positive surgical margin, seminal vesicle invasion, lymph node involvement, RRP specimens' Gleason score, and BCR were not significantly different among the three age groups. bRFS rates were not different either. Nonorgan-confined disease and extracapsular extension (ECE) rates were significantly higher in the group of 60–70 years group than in the other two age groups. Factors associated with BCR in multivariate Cox regression analysis were ECE, seminal vesicle invasion, positive surgical margin, and RRP specimens' Gleason score of $\geq 4+3$. Patient age and preoperative prostate specific antigen levels were not identified to be associated with BCR. Post-RRP nonorgan-confined disease and ECE are more frequently seen in patients of 60–70 years of age group than in other age groups. However, patient age is not an independent prognostic factor associated with bRFS.

Introduction

Prostate cancer (PCa) is the most frequently diagnosed and the second most mortal cancer in men aged $>$ 60 years [1]. With its high success and low morbidity rates, radical prostatectomy is the most appropriate treatment method for patients with clinically localized PCa with a life expectancy of more than 10 years. Radical prostatectomy is associated with local recurrence-free rates of 83.9% and

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75.6% for 5 years and 10 years, respectively [2]. Changes in the demographic and socioeconomic structure of the world and widespread use of prostate-specific antigen (PSA) have considerably changed the epidemiology of PCa. Unlike today's earlier stage diagnoses, PCa was often diagnosed in the metastatic stage in the past. Because of the continuous increase in the aging population, the number of older patients who will receive treatment for PCa is expected to increase in the next couple of years [3].

The process of population aging is occurring much more rapidly in Turkey. Between 2008 and 2040, the elderly population in Turkey is expected to increase by more than 200%. The ageing index is a demographic indicator, defined as the percentage between the elderly ($>$ 65 years) and the young ($<$ 15 years) populations. While the aging index of Turkey was 8.6 in 1950, it had reached 12.2 in 1990, and by 2025 it is estimated to rise to 21.2 [4]. Today, advances in medical treatments and awareness of healthier lifestyles have increased the average life expectancy of men [5]. Although it is generally accepted that older age is a positive predictive factor for PCa detection at biopsy, its role in PCa prognosis is yet to be established [6,7].

Advanced age was identified as an independent risk factor associated with biochemical recurrence (BCR) after radical retropubic prostatectomy (RRP) in some studies [8,9]. However, the results obtained in other studies have not confirmed this association [10,11]. In the present study, we have evaluated the possible effect of advanced age on biochemical recurrence-free survival (bRFS) after RRP in a Turkish population of clinically localized PCa patients.

Methods

Patients and pathological features

In the study, 305 patients with clinically localized PCa who had undergone RRP between January 2000 and May 2014 were included. The clinical and pathological findings of patients were evaluated retrospectively. The patients who received adjuvant hormonal therapy or radiotherapy after RRP were excluded. Applicable local Ethics Committee Approval was achieved at the beginning of the study; however, informed consent forms could not be obtained due to the retrospective nature of the study. Diagnosis of PCa was achieved through the pathology of prostate biopsies or transurethral resection of prostate specimens. All patients had undergone preoperative evaluation, including digital rectal examination, transrectal ultrasonography, routine biochemistry blood tests, PSA, and chest X-rays. A pelvic computed tomography or a radioisotope bone scan was performed if clinically indicated. Biopsy and surgical specimens were histologically classified by the Gleason grading system, and clinical staging was based on the 2002 TNM system. A positive surgical margin (PSM) was identified as the cancer cells extending to the inked surface of the resected specimen, whereas observation of cancer cells outside the prostatic capsule was identified as extracapsular extension (ECE). Seminal vesicle invasion (SVI) and lymph node invasion (LNI) were simply defined as the presence of tumor in the muscular wall of the seminal vesicles and lymph nodes, respectively. These pathological features, including PSM, ECE, SVI, and LNI, were accepted as "adverse pathological features." Follow-up examinations were performed every 3 months for the postoperative 1st year, every 6 months for the next 5 years, and annually thereafter. At least 4 weeks following the RRP surgery, two consecutive elevations of serum PSA levels, 0.2 ng/mL or over, were accepted as BCR. The patients were classified into three groups according to their age at the time of RRP: $<$ 60 years, 60–70 years, and $>$ 70 years. The patients' PSA levels were stratified into three levels: $<$ 10 ng/mL, 10–20 ng/mL, and $>$ 10 ng/mL. Gleason scores (GS) were subgrouped as $\leq 3+4$ or $\geq 4+3$. The three age groups were compared according to the patient ratios with nonorgan-confined disease, adverse pathological findings, BCR, three different PSA levels, and two GS subgroups.

Statistical analysis

All statistical analyses were performed using SPSS version 18 (IBM Corporation, NY, USA). Qualitative data were presented as the number and percentage of patients, whereas continuous variables were expressed as mean $\pm$ standard deviation. Chi-square test was used for categorical comparisons. Univarite and multivariate Cox regression analyses were performed to determine factors associated with bRFS. For each independent variable, a relative risk (RR) and a 95% confidence interval (CI) were calculated. Kaplan–Meier method and log-rank test were used for the evaluation of bRFS. A p value $<$ 0.05 was considered to be statistically significant.

Results

Preoperative clinical and biopsy parameters of the 305 patients are shown in Table 1. Of these, 103 (33.8%) patients were aged $<$ 60 years, 157 (51.5%) patients were aged 60–70 years, and 45 (14.8%) patients were aged $>$ 70 years. There was no statistically significant difference among the three age groups in terms of PSM, SVI, LNI, BCR rates, PSA, and RRP specimens' GS subgroups. Nonorgan-confined disease and ECE were significantly more prevalent in the group with patients in the age range 60–70 years (Table 2).

Following the mean follow-up period of 71.2 ± 37.3 months, BCR was identified in 55 (20.9%) patients. The bRFS rates at 3 years, 5 years, and 10 years were 88.9%, 84.6%, and 78.6% for all patients, respectively. The mean bRFS duration was calculated as 106.3 ± 3.1 months (95% CI: 100.3–112.4), and the bRFS rate was not different among the three age groups ($p = 0.44$; Kaplan–Meier method; Figure 1).

In univariate Cox regression analysis, factors associated with BCR were preoperative serum PSA level of more than 20 ng/mL (RR = 3.89; 95% CI = 2.00–7.56; $p = 0.0001$), ECE (RR = 4.59; 95% CI = 2.67–7.89, $p = 0.0001$), SVI (RR = 8.58; 95% CI = 5.03–14.62, $p = 0.0001$), PSM (RR = 9.9; 95% CI = 5.75–17.24, $p = 0.0001$), LNI (RR = 8.10; 95% CI = 4.03 to 16.2, $p = 0.0001$), and RRP specimens' GS of $\geq 4+3$ (RR = 5.05; 95% CI = 2.96–8.61, $p = 0.0001$). Being above the age of 70 years (RR = 1.50;