ORIGINAL RESEARCH—ONCOLOGY

The Effects of Long-Term Androgen Deprivation Therapy on Penile Length in Patients with Prostate Cancer: A Single-Center, Prospective, Open-Label, Observational Study

Kyung Kgi Park, MD,* Seung Hwan Lee, MD,† and Byung Ha Chung, MD, PhD†

*Department of Urology, Yongin Severance Hospital, Urological Science Institute, Yonsei University Health System, Yongin, Korea; †Department of Urology, Gangnam Severance Hospital, Urological Science Institute, Yonsei University Health System, Seoul, Korea

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ABSTRACT

Introduction. The adverse effects of long-term drug therapy for prostate cancer (PCa) can dramatically impact patient quality of life and are considered to be important factors when selecting treatment.

Aim. To assess stretched penile length before and after long-term androgen deprivation therapy (ADT) for treatment of PCa.

Methods. From January 2008 to June 2010 at a single institution, 39 consecutive patients without distant metastases who were elected to receive ADT as initial therapy for PCa were prospectively enrolled. Exclusion criteria were history of penile anomalies and/or trauma, and prior radical prostate surgery or radiation therapy. Erectile functions were evaluated at baseline according to the International Index of Erectile Function (IIEF). Vertically stretched penile length was measured every 3 months from the pubopenile junction to the meatus with a spring scale.

Main Outcome Measure. After ADT, significant 3-month interval changes in stretched penile length were noted for up to 15 months ($P < 0.001$). The relationship between potency and penile shortening was not significant ($P = 0.45$).

Results. The mean patient age was 67.1 years. Before therapy, the mean stretched penile length was 10.76 cm. After 24 months of ADT, mean penile length had decreased to 8.05 cm. However, these changes plateaued after 15 months. Normal erectile function (EF) was reported by 41% of patients before therapy, while 10.5% reported normal EF at the 24-month follow-up. The relationship between potency and penile shortening was not significant. However, patients who preserved their potency tended to experience less penile shortening.

Conclusions. The administration of luteinizing hormone-releasing hormone (LHRH) agonists induced significant decreases in penile length for only up to 15 months in the absence of the confounding effects of surgery and radiation. **Park KK, Lee SH, and Chung BH. The effects of long-term androgen deprivation therapy on penile length in patients with prostate cancer: A single-center, prospective, open label, observational study. J Sex Med 2011;8:3214–3219.**

Key Words. Prostate Carcinoma; Androgen Antagonists; Body Measures; Penis; Penile Length

Introduction

Since the pivotal studies of Huggins and Hodges [1] that showed that the development and growth of prostate cancer (PCa) cells are dependent on androgens, androgen deprivation therapy (ADT) has been increasingly used for the treatment of PCa. Until recently, ADT was reserved for patients with PCa that had spread beyond the prostate. The increases in frequency and length of ADT administration over the past decade have contributed to increased attention to quality of life issues in these patients. In patients who require long-term drug therapy for PCa, these adverse effects dramatically impact quality of life and are thus considered important factors

when selecting treatment. Much research has been carried out on the side effects of primary treatments for PCa [2], but little is known about the potentially negative effects of ADT itself on the male genitalia. Haliloglu et al. [3] investigated the effects of ADT on penile length in 2007. However, they enrolled subjects who received three times of neoadjuvant hormonal therapy and external radiotherapy [3]. Thus, they actually evaluated the short-term effects of ADT in combination with other treatments on penile length [3]. In this study, we investigated the isolated effects of long-term ADT on penile length in patients with PCa.

Materials and Methods

Patients

This study was approved by our institutional review board. Between January 2008 and June 2010 at a single institute, 42 patients (mean age 67.1 years, range 55–80 years) who were not candidates for curative treatment with surgery or radiation were enrolled in this prospective study to evaluate penile length following hormone therapy for PCa. All subjects provided informed consent. Exclusion criteria were history of penile or urethral surgery or trauma, history of penile abnormalities, current use of medications known to affect EF (i.e., phosphodiesterase type 5 inhibitors), and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. All Gleason scores were acceptable, and clinical stage ranged from T3a to T4 (Tumor, Node, Metastases [TNM] System Stage, 2007). All patients were required to have a negative bone scan and a pelvic lymph node assessment based on a computerized tomography scan of the abdomen and pelvis. Normal baseline hepatic and renal function were required, in addition to an estimated life expectancy of more than 5 years. Three subjects whose serum prostate-specific antigen (PSA) levels were not controlled with only the initial luteinizing hormone-releasing hormone (LHRH) agonist were excluded from the study after enrollment.

Hormone Therapy

An LHRH agonist (leuprolide acetate 11.25 mg) was injected intramuscularly every 3 months for a total of eight injections. Oral bicalutamide (50 mg) was administered daily, beginning 7 days before the initial LHRH agonist injection and ending 7 days after injection.

Assessments

All eligible subjects provided baseline medical histories and underwent physical examinations. International Index of Erectile Function (IIEF)-5 assessments were completed at baseline and at 12 and 24 months. The reference period on the IIEF-5 was the most recent 4 weeks. We defined normal erectile function as an IIEF score of greater than 21. Other measurements such as serum testosterone, serum PSA, and stretched penile length were taken at baseline and repeated every 3 months thereafter.

All penile measurements and evaluations were performed by the same investigator (KKP) with a paper ruler and were recorded to the nearest 0.5 cm. To avoid interobserver variation, we used a spring scale to assure that each measurement was taken with uniform stretching force (450 g) using a technique previously described by Chen et al. [4]. The measurements were conducted in a dimly lit and warm private room, with the patient in a supine position. Stretched penile length was measured from the pubopenile skin junction to the tip of the glans while applying perpendicular tension.

Study End Point and Statistical Analysis

For the analyses at 2 years, the primary end point was the change in penile length from baseline and the reduction in the total length of the penis. Secondary end points were to evaluate the effect of maintenance of potency on changes in penile length. We categorized the patients into three groups according to the maintenance of potency. The statistical comparisons were post hoc analyses of the effects of baseline parameters on mean change in penile length from baseline to each post-baseline assessment up to and including month 24. Differences between penile length measurements before and after treatment were evaluated using Bonferroni-corrected Wilcoxon's signed rank tests. Group I showed potency at 12 and 24 months; group II showed potency at baseline and impotency at 12 or 24 months; and Group III showed impotency from baseline to 24 months. Differences in changes in penile length according to pretreatment and post-treatment potency groups were evaluated using the general linear model. To avoid the presence of missing data, we designed the study simply. However, if the nonobservation data was present, we planned to consider missing data last observation carried forward. Fortunately, observation data at 24 months was obtained from all subjects. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.