

# Subjective and Objective Effects of Androgen Ablation Therapy on Voice

\*Ziya Salturk, \*Ozan Çakır, \*Tolgar Lütü Kumral, \*Güven Yıldırım, †Alper Ötünçtemur, \*İmran Aydoğdu, and \*Yavuz Uyar, \*†Istanbul, Turkey

**Summary: Objectives.** The aim of present study was to evaluate possible side effects of androgen deprivation therapy (ADT) on voice quality by means of objective and subjective measures.

**Study Design.** Cross-sectional.

**Methods.** Thirty-five male patients who had been diagnosed with prostate cancer and who had been using bicalutamide and goserelin acetate combination for at least 12 months were included in the study. Thirty healthy nonsmoker males of similar age and without any laryngeal pathology constituted the control group. Acoustic and aerodynamic voice analyses and voice handicap index-10 were applied to both groups. Maximum phonation time, fundamental frequency, jitter, shimmer, and noise-to-harmonic ratio were determined during acoustic and aerodynamic voice analyses.

**Results.** Maximum phonation times were  $18.86 \pm 5.24$  and  $24.20 \pm 3.59$  in ADT and control groups, respectively. It was significantly higher in the control group. Fundamental frequencies were  $143.73 \pm 18.47$  and  $135.00 \pm 13.18$  in ADT and control groups, respectively. Jitter values were  $2.72 \pm 0.62$  and  $1.99 \pm 0.27$  in ADT and control groups, respectively. Shimmer values were  $11.50 \pm 1.81$  and  $10.48 \pm 1.36$  in ADT and control groups, respectively. Fundamental frequency, jitter, and shimmer values were significantly higher in the ADT group. Noise-to-harmonic ratio values did not differ between groups. Voice handicap index-10 result was significantly higher in the ADT group.

**Conclusions.** ADT has adverse effects on the human voice. Prospective studies with long-term follow-up of a larger cohort are required for more detailed analysis.

**Key Words:** Androgen deprivation therapy–Acoustic voice analysis–Prostate cancer–Adverse effect–Voice handicap index.

## INTRODUCTION

Voice is one of the main tools in human communication and professional life.<sup>1</sup> Development of the human voice does not differ between males and females until puberty. The onset of puberty, under the influence of sex hormones, causes differentiation of the human larynx and voice. In males, sex hormones result in more elongated and thicker vocal cords, increased sagittal diameter of the larynx, and a lower angle of thyroid cartilage in comparison with females. This development causes a lower fundamental frequency ( $F_0$ ) in males.<sup>2,3</sup> Aging has also effects on the human voice, resulting in atrophy of the extralaryngeal muscles, dehydration of the mucosa, decreased elasticity of ligaments, calcification of cartilage, and loose vocal cords.<sup>2</sup> These changes are also related to hormonal changes and physical status.<sup>4</sup>

Prostate cancer is the most common cancer in the male population and the second most common cause of death from cancer in Western countries.<sup>5,6</sup>

The treatment of localized prostate cancer commonly involves a radical retropubic prostatectomy with pelvic lymph node dissection with or without radiotherapy in the form of external beam radiation or brachytherapy. However, surgical resection is not suitable for most patients with advanced

prostate cancer; these patients are commonly treated with androgen ablation hormonal therapy or androgen deprivation therapy (ADT).<sup>7,8</sup>

Bicalutamide is an oral nonsteroidal antiandrogen drug that competitively antagonizes the actions of androgens of both testicular and adrenal origin at the receptor level, thereby inhibiting the growth of prostate tumors.<sup>9</sup> Although it does not inhibit gonadotropin and testosterone production, it results in side effects related to androgen deficiency, including gynecomastia and decreased libido.<sup>9,10</sup> Goserelin acetate is a depot luteinizing hormone-releasing hormone superagonist that suppresses release of gonadotropins from the pituitary gland by downregulation.<sup>11</sup>

This study aimed to evaluate possible side effects of ADT on voice quality by means of objective and subjective measures.

## MATERIALS AND METHODS

Institutional Review Board approval was obtained from the Okmeydanı Training and Research Hospital Ethical Committee. Thirty-five male patients who had been diagnosed with prostate cancer and who had been using bicalutamide for at least 12 months were included in the study (ADT group). Patients with upper respiratory tract infection, history of laryngeal surgery or pathology, pulmonary problems, history of head and neck radiotherapy, smoking, reflux, or obstructive sleep apnea were excluded. None of the patients had obesity problem; all of them had body mass index below 30. All of the patients had been using a dosage of 50 mg/day bicalutamide orally and 10.8 mg per 3 months of goserelin acetate intramuscularly. Thirty healthy nonsmoker males of similar age and without any laryngeal pathology constituted the control group. All subjects in both groups underwent complete

Accepted for publication September 8, 2014.

This study has not been published partially or totally.

From the \*Okmeydanı Training and Research Hospital ENT Clinic, Istanbul, Turkey; and the †Okmeydanı Training and Research Hospital Urology Clinic, Istanbul, Turkey.

Address correspondence and reprint requests to Ziya Salturk, Okmeydanı Training and Research Hospital ENT Clinic, Darulaceze cad, Şişli, Istanbul, Turkey. E-mail: ziyasalturk@gmail.com

Journal of Voice, Vol. 29, No. 4, pp. 490–493

0892-1997/\$36.00

© 2015 The Voice Foundation

<http://dx.doi.org/10.1016/j.jvoice.2014.09.010>

head and neck examinations, as well as acoustic and aerodynamic analyses. Voices were recorded using a dynamic microphone kept at a distance of 15 cm from the lips. Following a deep inspiration, the subject tried to say the vowel “ah” for as long as he could and repeated it three times, and the longest recording time was accepted as the maximum phonation time (MPT). Additionally, subjects were asked to read a phonetically balanced passage from a famous Turkish story titled “Diyet” for 40 seconds in a relaxed voice. The *Praat* software (version 4.4.13, Boersma and Weenink, University of Amsterdam, Amsterdam, The Netherlands) was used for acoustic analysis. The fundamental frequency ( $F_0$ ), jitter, shimmer, and noise-to-harmonics ratio (NHR) were determined during acoustic voice analysis. Subjective evaluation was performed using the Voice Handicap Index-10 (VHI-10). The Turkish version of VHI-10 was validated by Kılıç et al<sup>12</sup> VHI-10 comprises 10 questions and is scored between 0 (never) and 4 (always). It has emotional, functional, and physical subscales with four, three, and three questions, respectively.

Statistical analysis of the data was conducted using SPSS version 17.0 (SPSS, IBM, NY). Data were analyzed using descriptive statistical methods (mean and standard deviation). Parametric independent sample *t* test was used for the comparison of independent groups. Results were evaluated using the 95% confidence intervals, and the level of significance was set at  $P < 0.05$ .

## RESULTS

The mean age of the ADT group was  $57.57 \pm 3.01$  years, and the mean period of bicalutamide use was  $16.57 \pm 3.07$ ; range (13–24) months. The mean age of the control group was  $57.95 \pm 2.81$  years. Age did not differ significantly between the two groups.

Results of acoustic and aerodynamic analyses are shown in Table 1. MPT was significantly higher in the control group.  $F_0$ , jitter, and shimmer values were significantly higher in the ADT group. NHR values did not differ between groups. Subjects in the ADT group had significantly higher VHI-10 scores, which indicated that they were more dissatisfied with their voices.

## DISCUSSION

Voice is a secondary sexual characteristic that completes its maturation at the end of puberty. It completes its development at age 16 to 17 years in males. Sex hormones are the main determinants of laryngeal maturation.<sup>2</sup> Newman et al<sup>13</sup> performed a study with fresh cadavers and reported that there are hormone receptors in the cytoplasm and nucleus of vocal cords with differences in distribution depending on age and sex. Animal studies also proved that androgens cause hypertrophy and hyperplasia of the laryngeal muscles.<sup>14</sup> Two studies performed on juvenile *Xenopus laevis* revealed that androgens induce myogenesis and chondrogenesis. In addition, these effects are more dominant than innervations.<sup>15,16</sup>

Efforts have been made to assess voice changes depending on testosterone.<sup>17–23</sup> Dabbs et al<sup>18</sup> performed instant testosterone level measurements and found that higher testosterone levels

**TABLE 1.**  
**Comparison of Vocal Parameters**

Test	ADT Group (n = 35)	Control Group (n = 30)	P
	Mean ± SD	Mean ± SD	
MPT	18.86 ± 5.24	24.20 ± 3.59	0.000
$F_0$	143.73 ± 18.47	135.00 ± 13.18	0.030
Jitter	2.72 ± 0.62	1.99 ± 0.27	0.000
Shimmer	11.50 ± 1.81	10.48 ± 1.36	0.012
NHR	0.14 ± 0.94	0.15 ± 0.02	0.099
VHI-10	5.86 ± 2.89	4.00 ± 1.31	0.002

Notes: Independent samples *t* test \* $P < 0.05$ .

Abbreviations: ADT, androgen deprivation therapy;  $F_0$ , fundamental frequency; NHR, noise-to-harmonic ratio; VHI-10, voice handicap index 10.

cause lower pitch. It was reported that the vocal characteristics of a professional singer were converted to baritone from tenor with use of testosterone for hypogonadotropic hypogonadism.<sup>17</sup>  $F_0$  values of male patients with isolated hypogonadotropic hypogonadism declined significantly at the end of testosterone replacement therapy.<sup>19</sup> Evans et al<sup>20</sup> claimed that  $F_0$  values were inversely proportional to the daily changes in testosterone level. Table 2 illustrates the studies<sup>17–20</sup> which evaluated  $F_0$  changes related to testosterone. On the other hand, Gugatschka et al<sup>21</sup> did not find differences in voice parameters, including  $F_0$  and mean voice range, of osteoporotic patients with low and normal testosterone levels, but they found differences in  $F_0$  between patients with low and normal estradiol levels. Androgens cause a decrease in  $F_0$  and increase of voice instability.<sup>22,23</sup> Gerritsma et al<sup>22</sup> explained that this situation results from histologic changes and problems in adaptation to these changes. Hormone replacement therapies applied for female-to-male sex conversion cause decreases in voice pitch range and  $F_0$ .<sup>24,25</sup> Nakamura et al<sup>26</sup> investigated testosterone replacement therapy in persons who changed sex from female to male and showed that higher testosterone dosage was more effective in producing male characteristics, including voice, at 1 month, but at 6 months, the three groups exhibited identical results. This study showed that the acute phase of hormonal changes causes a more unstable situation.

ADT can be applied to patients by maximal androgen blockade and peripheral androgen blockade. The antiandrogen bicalutamide is the leading agent used in both regimens. Because this agent inhibits androgen receptors competitively, all side effects that depend on androgen blockade might be observed in patients. These include hot flashes, osteoporosis, anemia, loss of libido, erectile dysfunction, metabolic syndrome, and so forth. As a secondary sex characteristic, the voice might be affected by ADT because of lower testosterone level.<sup>9,10</sup> Goserelin acetate is added to therapy to maximize the efficacy of bicalutamide; because it has effects similar to those of orchiectomy, it could also increase the incidence of side effects.<sup>11,27</sup>

MPT reflects prolonged vocalization and continuous speech; it is related to the resistance and force generated at the glottal

Download English Version:

<https://daneshyari.com/en/article/1101480>

Download Persian Version:

<https://daneshyari.com/article/1101480>

[Daneshyari.com](https://daneshyari.com)