Voice Analysis in Men with Benign Prostate Hyperplasia

Sedat Alagöz[1], Vedat Delibaş[1], Kemal Koray Bal[2], Ferhat Ortoğlu[1], Talih Özdaş[1], Gökhan Kuran[3], Orhan Görgülü[*], Betül Kahraman[1]

1 Adana City Training and Research Hospital, Department of ENT, Adana, Türkiye
2 Mersin City Hospital, Department of ENT, Mersin, Türkiye
3 Medicana Hospital, Department of ENT, Ankara, Türkiye

Abstract

Aim: In this study, we aimed to determine the differences by performing voice analysis in men with benign prostatic hyperplasia (BPH) and discussing it with the literature

Methods: The study included 77 male patients who came to the urology outpatient clinic and were diagnosed with BPH and consult to us for voice analysis. Patients' ages, testosterone, prostate specific antigen (PSA) levels, prostate volumes (milliliters) were recorded. International prostate symptom scoring (IPSS) was applied to the patients. Mild, moderate, severe patients according to IPSS scoring; were classify as group 1, group 2, group 3, respectively. Voice Handicap Index-10 Turkish version (VHI-10) was realized to the patients and the results were saved.

Results: 77 male patients were accepted to the study. The average age was 60. The mean prostate volume of the patients was 41.1 ml. The IPSS score of the patients was 16 on average. The mean VHI-10 scores were 9.14. The mean PSA levels of the patients were 1.43; testosterone levels were 3.04. F0 Hz (mean pitch) values were 157.74; jitter % values mean 0.26; shimmer % values mean 2.42; The mean HNR dB values were 22.91.

Conclusions: Maybe it would be more logical to think that many local factors, hormones and growth factors are efficient in place of a testosterone.

Keywords: *Benign prostatic hyperplasia, voice, analysis, frequency*

1. Introduction

Benign prostatic hyperplasia (BPH), is a histological diagnostic characterized by the cellular proliferation components of prostate gland, resulting in gland enlargement. BPH can cause retention of urinary, renal function impairment, continuing infections of urinary tract, macroscopic hematuria, and bladder stones[1]. The degree of BPH, analized by the International Prostate Symptom Score (IPSS)[1]. In individuals with indications of urinary retention or kidney failure, ultrasonography (USG) can help estimate prostate gland and bladder size, as well as the severity of hydronephrosis (if present).[1] Prostate hypertrophy is dependent on the dihydrotestosterone (DHT). In the prostate, type II 5-alpha-reductase metabolizes circulating testosterone to DHT, which works better locally rather than systemically.

Corresponding Author: Sedat Alagöz
e-mail: alagozsedat@gmail.com
Received: 04.09.2023, Accepted: 15.09.2023, Available Online Date: 06.10.2023
Cite this article as: Alagöz S, Delibaş V, Bal KK, et al E. Voice Analysis in Men with Benign Prostate Hyperplasia. J Cukurova Anesth Surg. 2023; 6(3): 402-5.
doi: 10.36516/jocass.1360835

DHT connect to androgen receptors in the nucleus, which may contribute to BPH.[2] PSA is a prostate gland-specific hormone and may increase in prostate cancer (CA) or BPH. It is commonly employed in prostate CA screening and follow-up, and it can have a high course in some BPH patients.[2]

Currently, voice examination in the clinic is done with objective methods such as acoustic analysis, videostroboscopy, and the evaluation of the clinician and the subjective evaluation of the patient. Among the many measurement methods, the most common one is the VHI (Voice Handicap Index) questionnaire developed by Jacobson et al. There is also a version of the test adapted to Turkish society, and its internal reliability is significant.[3-4] Testosterone becomes active in the prostate tissue, promoting hyperplasia and hypertrophy[2]. Testosterone also causes hyperplasia and hypertrophy of the vocal cords and surrounding tissue[5]. Jitter(%): It is the average of the absolute value of the difference of each period of the analyzed sound with the next period. It is the parameter that shows the change between periods. Jitter reflects the irregularity of the vocal cords and is also called frequency perturbation. Its normal value is below 1%.[6] Shimmer(%): It is obtained by dividing the average of the absolute value of the dif-

ference in intensity (amplitude) between each period and the following period by the average period intensity, and its normal value is below 3%.[6] Harmonic-to-Noise Ratio (HNR-dB): It is the ratio of the total energy of F0 and its multiples of harmonics to the noise energy.[6] Fundamental frequency (f0) (Hz): It is the number of opening-closing cycles that occur per second of sound folds. It reveals the thickness and thinness of the sound.[6] In our study, we aimed to examine the relationship between the degree of prostate obstruction and voice.

2. Materials and methods

The study comprised 77 male patients with benign prostatic hyperplasia (BPH) hospitalized at Adana City Hospital between January 1, 2021, and July 1, 2021. Urinary system ultrasonography was requested from the patients for prostate-specific antigen (PSA) level, testosterone level, prostate volume (in milliliters, ml), which are routine BPH examinations in Urology department. Testosterone (reference values 1.75-7.81 ng/mL), PSA (reference values 0-4 ng/mL) levels, and prostate volumes (ml) of the patients and their ages were recorded. International prostate symptom scoring (IPSS) was performed on the patients. According to the IPSS scoring, those with 0-7 points are grouped as mild (mild obstruction), those with 8-19 points as moderate (moderate obstruction), and those with 20-35 points as severe (severe obstruction). Mild, moderate, severe patients were categorized as group 1, group 2 and group 3, respectively. Voice Handicap Index-10 Turkish version (VHI-10) was realized to the patients and the results were saved.

Our study was approved by the Adana City Hospital Clinical Research Ethics Committee (Meeting Number: 80, Decision Number: 1404, Date: 06/05/2020). Written consent was obtained from the patient (or legal guardian) that her/his medical data can be published.

3. Results

The study involved 77 male patients. The ages of the patients ranged from 48 to 74, with an average of 60 years. There were 24 patients in Group 1, 26 patients in Group 2, and 27 patients in Group 3. The prostate volumes of the patients ranged from 27 ml to 62 ml, with an average of 41.1 ml. Patients' IPSS scores varied from 4 to 27, with a mean of 16. The patients' VHI-10 scores ranged from 0 to 21, with a mean of 9.14.

The PSA levels of the patients ranged from 0.2 to 3.1, with a mean of 1.43. Testosterone levels of the patients ranged between 1.78 and 5.32, and the mean was 3.04.

The patients' fundamental frequency F0 Hz (mean pitch) values ranged from 121.11 to 197.62, with a mean of 157.74. Jitter % (frequency perturbation jitter) values of the patients ranged from 0.22 to 0.34, and the mean was 0.26. The shimmer % (amplitude perturbation shimmer) values of the patients ranged between 1.82 and 3.44, with a mean of 2.42. The HNR dB values of the patients ranged from 20.37 to 24.81, and the mean was 22.91. The minimum, maximum, and average values are all presented in Table 1.

Among the three groups, there was a statistically significant difference in terms of prostate volume (p=0.001), Jitter % (p=0.001), Shimmer % (p<0.001), and HNR dB (p=0.002) variables.

For the prostate volume variable, the difference between Group 1 and Group 2 was statistically significant (p<0.001). Group 2 had a larger prostate volume than Group 1. For the jitter % variable, the difference between Group 2 and Group 3 was statistically significant (p<0.001). Jitter% was found to be higher in Group 2.

Table 1

Minimum and maximum values

Variables	Minimum	Maximum	Mean±SD
Age	48	74	60,08±8,76
Testosterone	1,78	5,32	3,04±1,12
PSA	0,2	3,10	1,43±0,95
Prostate Volume(ml)	27	62	41,1±9,62
VHI-10 Points	0	21	9,14±7,76
IPSS Score	4	27	16±7,52
Fundamental frequency F0 Hz(Mean Pitch)	121,11	197,62	157,74±25,95
Jitter % (frequency perturbation jitter)	0,22	0,34	0,26±0,05
Shimmer % (amplitude perturbation shimmer)	1,82	3,44	2,42±0,70
HNR dB	20,37	24,81	22,91±1,86

For the Shimmer% variable, the difference between Group 3 and Group 2 was statistically significant (p<0.001). The difference between Group 3 and Group 1 was statistically significant (p<0.001). Shimmer % value in Group 3 was statistically significantly lower than both other groups.

For the HNR dB variable, the difference between Group 1 and Group 2 was statistically significant (p=0.049). HNR dB values in group 1 were higher than the other groups. For the HNR dB variable, the difference between Group 2 and Group 3 was statistically significant (p=0.002). HNR dB values in Group 3 were higher than the other groups. The p values between the groups are shown in Table 2.

There was a weak negative linear correlation between PSA and fundamental frequency F0 Hz (Mean Pitch) (r=-0.312, p<0.01). There was a moderate positive linear correlation between PSA and jitter % (r=0.449, p<0.01) (The negative relationship represents an inverse relationship, that is, a relationship that decreases as one increases or increases as the other decreases, while a positive relationship represents a direct ratio, that is, a relationship that increases as one increases or decreases as the other decreases).

There was a strong positive linear correlation between prostate volume and jitter % (r=0.646, p<0.01). There was a weak negative linear correlation between prostate volume and HNR dB (r=-0.277, p<0.05).

There was a weak negative linear correlation between testosterone and fundamental frequency F0 Hz (Mean Pitch) (r=-0.246, p<0.05). There was a weak negative linear correlation between testosterone and jitter % (r=-0.339, p<0.01). There was a moderate linear correlation between testosterone and shimmer % (r=0.454, p<0.01). The p and r values are demonstrated in Table 3.

4. Discussions

Hormones are thought to have an effect on the voice function of the larynx.[7] Hormonal balance changes during adolescence, affecting body, provide one of the reasons for voice changes and form the source of hypotheses and studies regarding the effect of hormones.[8] Progesterone and testosterone ratios were high in Reinke's edema.

Table 2

Groups and p values

Variables	Groups			p values
	Group 1 [Q1:Q3] Median	Group 2 [Q1:Q3] Median	Group 3 [Q1:Q3] Median	
Age	[51.00:61.00] 56.00	[56.00:67.00] 61.00	[49.00:71.00] 64.00	0.310
Prostate Volume(ml)	[27.50:44.00] 34.00	[44.00:54.00] 44.00	[37.00:48.00] 42.00	0.001
PSA	[0.44:1.66] 0.48	[1.66:2.01] 1.66	[0.49:2.52] 1.64	0.071
Testosterone	[1.88:2.95] 2.72	[2.72:4.32] 2.95	[1.78:5.32] 2.88	0.353
Fundamental frequency F0 Hz(Mean Pitch)	[138.37:179.11] 149.48	[138.37:160.59] 160.59	[121.11:183.87] 183.87	0.864
Jitter % (frequency perturbation jitter)	[0.22:0.29] 0.23	[0.23:0.34] 0.34	[0.22:0.23] 0.23	0.001
Shimmer % (amplitude perturbation shimmer)	[1.90:3.07] 2.31	[1.93:3.44] 3.44	[1.82:1.93] 1.82	<0.001
HNR dB	[21.12:24.81] 23.32	[20.37:24.77] 20.37	[23.46:24.77] 23.46	0.002
VHI-10 Points	[3.50:16.00] 10.00	[0.00:21.00] 10.00	[0.00:18.00] 7.00	0.298

Table 3

p and r values

Variables	Fundamental frequency F0 Hz(Mean Pitch))	Jitter % (frequency perturbation jitter)	Shimmer % (amplitude perturbation shimmer)	HNR dB
PSA	-.312**	.449**	.151	-.005
Prostate Volume (ml)	.020	.646**	.055	-.277*
Testosterone	-.246*	-.339**	.454**	-.218

*P< 0.05 , ** P< 0.01, r<0.2 too weak, 0.2-0.4 weak, 0.4-0.6 moderate intensity, 0.6-0.8 high, 0.8> very high

These findings support the theory progesterone and testosterone hormones cause edema by affecting the larynx mucosa.[9] Nacci et al. hypothesized that in the larynx there are particular receptors for gender hormones. In a study, sample of vocal cords received from healthy people, cadavers and larynx cancer were research for the androgen, estrogen and progesterone receptors by immunohistochemically. However, while progesterone and mild estrogen receptors were found in cancerous samples, no receptors in other samples. According to this study, there is sex hormones no receptor in the larynx.[7] In our study, the effects of IPSS data, prostate volume, PSA and testosterone levels on voice in male BPH patients were examined. Among the 3 groups, we detected a statistically significant difference of prostate volume, Shimmer, Jitter and HNR dB variables in our study. When group 1 and group 2 were compared, it found that the prostate volume of group 2 was higher. When group 2 and group 3 were as per, jitter was found to be % higher in group 2. When the three groups were examined, it was observed that the group with the lowest average shimmer % value was group 3. As a result, as the prostate volume increased, the degree of obstruction and BPH also increased. Although PSA, testosterone, and prostate volume were not statistically strong in patients with a high BPH grade, a slope in the same direction was detected between them. While the shimmer and jitter values were advanced in group 2, which had the highest PSA and prostate volume, the HNR dB value was found to be lower. A negative weak linear relationship was seen between PSA and Testosterone with fundamental frequency F0 Hz (Mean Pitch). There was a negative weak linear relationship between prostate volume and HNR dB. While there was a weak negative linear relationship between testosterone and jitter %, we suggest that a positive moderate linear relationship between testosterone and shimmer %.

Pedersen et al. suggested that the fundamental frequency (f0) decreases in females at the transition to puberty, as in males, but decrease is less pronounced in females. The variety of downward in frequency related to the dissimilarity of testosterone or estrogen.[10] We suggest that a negative weak linear correlation was testosterone and F0 (Hz).

In order to better understand the effect of testosterone on the voice, it may be illuminating to examine the studies in which a female patient was given the hormone testosterone for any reason. Cler, reported that a transgender men treated testosterone therapy during one year, the f0 value fell into the normal range from female to male. In addition, it was found that the larynx structure of the patient showed changes (forward-sloping and longer larynx) seen in a male adolescent in the regular endoscopic examinations.[11] In another study, 10 female patients were given regular testosterone with a subcutaneous implant and voice analyzes were carried out at 3, 6, and 12 months. The results were evaluated and no significant changes were detected in the unbiased properties of the voice. In this study whereas, the testosterone dose is at the treatment dose level, not the advanced dosage used for transgender patients.[12] Bioavailable testosterone and DHEAS were seen to be related with less f0 in men.[13] In female-to-male transition subjects treated with testosterone, voice analysis showed that testosterone decreased f0. In another study, a significant decrease in mean pitch value was observed in the high-dose group, depending on dose and concentration, after the 24th week in women treated with testosterone.[14] Akcam et al., suggest that F0 value was between normal men and women in untreated Idiopathic Hypogonadotropic Hypogonadism (IHH) men. Those patients is treated with testosterone, the f0 value is close to that of a normal range. In other words, when testosterone

increases, the f0 value decreases.[15] In our study, the group with the highest testosterone average was group 2. We seen a negative weak linear correlation between testosterone and F0 Hz (Mean Pitch). While there was a negative weak linear relationship between testosterone and jitter %, we found a moderate positive relationship between testosterone and shimmer %. The highest Jitter % and shimmer % values were in group 2.

As far as the literature can be scanned, showed that studies on voice analysis in the field of otolaryngology are less than in other subjects.. By categorizing men with BPH according to testosterone, PSA and IPSS values, prostate volume measured by USG and performing voice analysis, we evaluate our article as different from previous literature and as the first. Studies on voice analysis in the literature have often been conducted on women with menstrual cycles, patients on hormone therapy, transgender people, or patients receiving treatment for acromegaly. [12-4,16-8]

The Voice Handicap Index is a 30-question personal feedback survey. It has 10 questions each of three subgroups: emotional, functional and physical. Each question is answered by the patient between 0-4 and the maximum score is 120. The score when increase, the greater the voice problem. This tool can supply adequate information to the physician.[4] Kılıç et al. They investigated the reliability and validity of the Turkish Voice Handicap Index and concluded that it is more suitable for use in clinics.[3] Our study found that the mean value of VHI-10 had the highest mean value with 10 points equally in group 1 and group 2. This score; 7 in group 3. Group 3 was the group with the highest IPSS score. This show that this group feels the voice problem not so much. This may have occurred as a result of the hormones and growth factors studied here.

In conclusion, although there is much debate about the effect of hormones on the voice, it is clear that nothing is clear. However, we currently believe that testosterone has a more pronounced effect on voice, in men. A combined thought that not only testosterone but other local and systemic hormonal factors are effective is more correct.

Statement of ethics

Adana City Hospital Clinical Research Ethics Committee (Meeting Number: 80, Decision Number: 1404, Date: 06/05/2020).

Conflict of interest statement

Author declare that they have no financial conflict of interest with regard to the content of this report.

Funding source

The authors received no financial support for the research, authorship, and/or publication of this article.

References

1.Logozzi M, Angelini DF, Giuliani A, et al. Increased Plasmatic Levels of PSA-Expressing Exosomes Distinguish Prostate Cancer Patients from Benign Prostatic Hyperplasia: A Prospective Study. Cancers (Basel). 2019; 11(10): 1449.
https://doi.org/10.3390/cancers11101449
2.Lein M, Stephan C, Jung K, et al. Relation of free PSA/total PSA in serum for differentiating between patients with prostatic cancer and benign hyperplasia of the prostate:which cutoff should be used?. Cancer Invest. 1998; 16(1): 45-9.
https://doi.org/10.3109/07357909809039753
3.Kilic MA, Okur E, Yildirim I, et al. Reliability and validity of the Turkish version of the Voice Handicap Index. Kulak Burun Bogaz Ihtis Derg. 2008; 18(3): 139-47.
4.Nanjundeswaran C, Jacobson BH, Gartner-Schmidt J, et al. Vocal Fatigue Index (VFI): Development and Validation. J Voice. 2015; 29(4): 433-40.
https://doi.org/10.1016/j.jvoice.2014.09.012
5.Kim JM, Shin SC, Park GC, et al. Effect of sex hormones on extracellular matrix of lamina propria in rat vocal fold. Laryngoscope. 2020; 130(3): 732-40.
https://doi.org/10.1002/lary.28086
6.Kilic MA. Evaluation of the patient with voice problem by objective and subjective methods. Curr Pract ORL. 2010; 6(2): 257-65.
7.Nacci A, Fattori B, Basolo F, et al. Sex hormone receptors in vocal fold tissue: a theory about the influence of sex hormones in the larynx. Folia Phoniatr Logop. 2011; 63(2): 77-82.
https://doi.org/10.1159/000316136
8.Ouyoung LM, Villegas BC, Liu C, et al. Effects of Resonance Voice Therapy on Hormone-Related Vocal Disorders in Professional Singers: A Pilot Study. Clin Med Insights Ear Nose Throat. 2018; 11:1179550618786934.
https://doi.org/10.1177/1179550618786934
9.Kravos A, Hočevar-Boltežar I, et al. Serum levels of sex hormones in males with Reinke's edema. Eur Arch Otorhinolaryngol. 2013; 270(1): 233-8.
https://doi.org/10.1007/s00405-012-2156-7
10.Pedersen MF, Møller S, Krabbe S, et al. Fundamental voice frequency in female puberty measured with electroglottography during continuous speech as a secondary sex characteristic. A comparison between voice, pubertal stages, oestrogens and androgens. Int J Pediatr Otorhinolaryngol. 1990; 20(1):17-24.
https://doi.org/10.1016/0165-5876(90)90331-K
11.Cler GJ, McKenna VS, Dahl KL, et al. Longitudinal Case Study of Transgender Voice Changes Under Testosterone Hormone Therapy. J Voice. 2020; 34(5): 748-62.
https://doi.org/10.1016/j.jvoice.2019.03.006
12.Glaser R, York A, Dimitrakakis C. Effect of testosterone therapy on the female voice.Climacteric. 2016; 19(2): 198-203.
https://doi.org/10.3109/13697137.2015.1136925
13.Jost L, Fuchs M, Loeffler M, et al. Associations of Sex Hormones and Anthropometry with the Speaking Voice Profile in the Adult General Population. J Voice. 2018; 32(3): 261-72.
https://doi.org/10.1016/j.jvoice.2017.06.011
14.Huang G, Pencina KM, Coady JA, et al. Functional Voice Testing Detects Early Changes in Vocal Pitch in Women During Testosterone Administration. J Clin Endocrinol Metab. 2015; 100(6): 2254-60.
https://doi.org/10.1210/jc.2015-1669
15.Akcam T, Bolu E, Merati AL, et al. Voice Changes after Androgen Therapy for Hypogonadotrophic Hypogonadism. Laryngoscope. 2004; 114(9): 1587-91.
https://doi.org/10.1097/00005537-200409000-00016
16.Hamdan A, Tabet G, Fakhri G, et al. Effect of Hormonal Replacement Therapy on Voice. J Voice. 2018; 32(1): 116-21.
https://doi.org/10.1016/j.jvoice.2017.02.019
17.Wolters TLC, Roerink SHPP, Drenthen LCA, et al. Voice Characteristics in Patients with Acromegaly during Treatment. J Voice. 2020; S0892-1997(19)30444-8.
18.Aydin K, Turkyilmaz D, Ozturk B, et al. Voice characteristics of acromegaly. Eur Arch Otorhinolaryngol. 2013; 270(4): 1391.
https://doi.org/10.1007/s00405-013-2369-4