# Effect of Hormonal Replacement Therapy on Voice

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**Summary: Objective.** This study aimed to investigate the effect of hormonal therapy (HRT) on voice in a group of menopausal women, taking into consideration body mass index (BMI) as a confounding factor and its potential role as a substitute for HRT.

**Subjects and Methods.** A total of 53 menopausal women, 34 not on HRT and 19 on HRT, were recruited. Demographic variables included age, gender, smoking, and BMI. All subjects were asked about the presence or absence of the following symptoms: hoarseness, deepening of the voice, pitch breaks, throat clearing, dryness in the throat, and vocal fatigue. Acoustic analysis was performed, and Voice Handicap Index-10 was also completed.

**Results.** The mean BMI was 25.90 ± 5.39 and 25.77 ± 4.26 in patients on HRT and not on HRT, respectively. There was no statistical difference in the Voice Handicap Index-10 score and the prevalence of any of the phonatory symptoms in menopausal women not on HRT compared with menopausal women on HRT. However, menopausal women not on HRT had significantly lower habitual pitch than those on HRT (*P* value of 0.022). On the other hand, the jitter was significantly higher in those on HRT (*P* value of 0.033).

**Conclusion.** Hormonal therapy has an impact on the habitual pith in menopausal women with comparable BMI. Those on HRT have a higher habitual pitch than those not on HRT.

**Key Words:** Menopause–Hormonal therapy–Body mass index–Habitual pitch–Phonatory symptoms.

## INTRODUCTION

As a hormonal target, the larynx is heavily influenced by sex hormones. Major structural and anatomical changes occur at puberty leading to alterations in the vocal characteristics. In women, the cyclic fluctuation in hormonal levels in their reproductive years leads to a constellation of vocal symptoms mostly experienced in the last 7 days of the menstrual cycle. On the other hand, the decrease in estrogen and progesterone at menopause results in an array of vocal changes often referred to as the "postmenopausal vocal syndrome."[1,2] This syndrome includes phonatory symptoms such as loss of power, loss of high notes, decreased vocal range, vocal fatigue, and flattening of vocal timbre. Although the precise pathophysiological mechanism behind these symptoms is unclear, the most common vocal fold changes seen on laryngeal videostroboscopy in symptomatic women are edema, dilated varices, thickened mucus, and thinning of the vocal folds with atrophic changes. The aforementioned symptoms and laryngeal findings are mostly reported by professional voice users and more often than not are substantiated acoustically by a decrease in the speaking fundamental frequency (F0) and an increase in the perturbation parameters.[3]

To that end, over the last two decades, the intake of hormonal therapy (HRT) has been adopted as a treatment modality to mitigate these postmenopausal vocal symptoms and acoustic changes. In 1997, Lindholm et al have reported on the effect of HRT on the F0 and sound pressure level in a group of 43 postmenopausal women. The results indicated that those on HRT had a smaller decrease in F0 and sound pressure level than those who were not on treatment.[3] Similarly, D'haeseleer et al have also reported that the mean speaking fundamental frequency (SFF) in postmenopausal women on HRT is higher than in those not on HRT (187.7 Hz in the HRT *vs.* 178.9 Hz in the non-HRT group).[4] A year later, the same set of authors have reported on the impact of menopause on voice using a cross-sectional nonrandomized study showing again the favorable impact of HRT on both the speaking F0 and the vocal intensity.[5] These findings were further substantiated by the investigation of Caruso et al on the effect of estrogen replacement on voice quality and laryngeal cytology in menopausal women. The results indicated that HRT can prevent and treat vocal fold dystrophic changes.[6]

Despite the presence of a few studies on the effect of hormonal replacement on voice in menopausal women,[7–10] based on a PubMed search using words "Body Mass Index," "menopause," and "hormonal therapy," only three studies have accounted for body mass index (BMI) as a confounding variable in their analysis. In 2011, D'haeseleer et al, in their study on the relation between BMI and speaking F0, have reported a positive correlation between BMI and speaking F0 in menopausal women not on hormonal replacement.[4] This was followed by another report on the speaking F0 in premenopausal and postmenopausal women with and without HRT, taking into consideration BMI. The results indicated a significant difference in the SFF among the six groups. In particular, postmenopausal women with low BMI and not on HRT had lower SFF than postmenopausal women with low BMI and on HRT (174.5 Hz *vs.* 188.7 Hz).[11]

BMI is an important indicator of the amount of fat in the body, which is a major source of estrogen in postmenopausal women. Its effect in women in the reproductive age is often hidden by the high level of biologically potent estradiol. However, at menopause, the drastic drop in sex hormones unmasks the potential role of fat as an alternative source of estrogen, which can mitigate the vocal symptoms and acoustic changes often experienced by menopausal women. To that end, given the important effect of adipose tissue on voice and the rarity of reported studies on

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the acoustic changes in menopausal women with BMI as a confounding factor,[4,5,11] the authors of the present study have been intrigued to investigate the effect of HRT on voice in a group of menopausal women, taking into consideration BMI as a confounding factor and its potential role as a substitute for HRT.

## Subjects and methods

This was a prospective study where a total of 53 nonprofessional menopausal women, 34 not on HRT and 19 on HRT, were recruited. In this study, the HRT consisted of estrogen (seven patients), progesterone (four patients), and estrogen or progesterone (eight patients). All subjects have read and signed the informed consent approved by the institutional review board. Patients with recent history of upper respiratory tract infection, laryngeal manipulation, or laryngeal surgery were excluded from this study.

Demographic variables included age, gender, smoking, and BMI. BMI was defined as the weight in kilograms divided by the square of the height in meters ($kg/m^2$),[12] and accordingly, subjects were stratified as having either low BMI or high BMI with a cutoff figure of 25. Both age and BMI were considered as confounding variables in the analysis.

All subjects were asked about the presence or absence of the following symptoms: hoarseness defined as a change in voice quality and timbre, deepening of the voice, pitch breaks, throat clearing, dryness in the throat, and vocal fatigue. The Voice Handicap Index-10 (VHI-10) by Jacobson et al was filled out by all of the subjects.[13] Patients with a score above 11 were considered to have dysphonia of significant impact on quality of life.

All subjects underwent acoustic analysis using the VisiPitch IV by Pentax.[14] Sitting in a quiet room with the microphone placed 10 cm away from the mouth, patients were asked to sustain the vowel /a/ at a comfortable pitch and loudness, and the following parameters were retrieved using the multidimensional voice program: F0, habitual pitch, shimmer, relative average perturbation, harmonic-to-noise ratio, and voice turbulence index. By asking the patient to count to 10, the habitual pitch was measured using the real-time pitch module.

## Statistical analysis

Shapiro-Wilk test and a visual inspection of the histograms showed that the data are normally distributed. Independent sample *t* test was used to compare the means of the acoustic measures between the two groups of women: those who are on menopause not taking any hormonal treatment and the menopausal women on HRT. When the data were further segregated into menopausal women with high or low BMI, Mann-Whitney *U* test was used to compare the means of the acoustic parameters. Pearson chi-square test was used to analyze differences in the categorical variables, including the phonatory symptoms between the two groups of women (menopausal on hormonal treatment and menopausal women not on hormonal treatment). Fisher exact test was reported when more than 20% of the cells had a cell count less than 5. All statistical analysis was performed using IBM *SPSS Statistics* 22 (released 2013, IBM Corp, Armonk, NY). A two-tailed *P* value of less than 0.05 was considered statistically significant.

# RESULTS

## Demographic data

A total of 34 menopausal women not on HRT and 19 on HRT were included in the study. The mean age in the first group was 53.00 ± 6.76 years and in the second group was 53.5 ± 5.57 years. The average time lapse between age of menopause and time of the study was 3.4 years, with a range of 1–8 years. The BMI was also comparable in both groups (Table 1).

## Prevalence of phonatory symptoms and VHI score in menopausal women with and without hormonal therapy

There was no statistical difference in the prevalence of any of the phonatory symptoms in menopausal women not on HRT compared with menopausal women on HRT. The mean VHI-10 scores for menopausal women on HRT and those not on HRT were 1.89 and 0.88, respectively. Only one subject in each group had a VHI-10 score above 11 (5.3% in menopausal women in HRT *vs.* 2.9% in menopausal women not on HRT) (Table 2).

## Prevalence of phonatory symptoms in menopausal women with and without hormonal therapy, taking into consideration body mass index

Further analysis taking BMI into consideration revealed that there was no statistically significant difference in any of the phonatory symptoms in menopausal women with low BMI compared with menopausal women with high BMI. There was also no significant difference in the prevalence of phonatory symptoms in menopausal women not on HRT with either low or high BMI compared with menopausal women on HRT (Tables 3 and 4).

## Acoustic parameters in menopausal women with and without hormonal therapy

Menopausal women not on HRT had a significantly lower habitual pitch than those on HRT (*P* value of 0.022). On the other hand, the jitter was significantly higher in those on HRT (*P* value

**TABLE 1.**
**Demographic Data**

| | Menopausal Women on Hormonal Treatment (N = 19) | Menopausal Women Not on Hormonal Treatment (N = 34) |
|---|---|---|
| Mean ± SD | | |
| Age (y) | 53.00 ± 6.76 | 53.5 ± 5.57 |
| BMI* | 25.90 ± 5.39 | 25.77 ± 4.26 |
| Low BMI* | 22.42 ± 1.79 | 22.37 ± 1.77 |
| High BMI* | 30.99 ± 4.67 | 29.65 ± 2.53 |
| Frequency | | |
| Low BMI* | 9 (60%) | 16 (53.3%) |
| High BMI* | 6 (40.1%) | 14 (46.7%) |
| Smoking | 4 (21.1%) | 13 (38.2%) |

* Four patients from each group had missing BMI data.