Do I sound dry? Comparative voice analysis of primary Sjögren's syndrome

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ABSTRACT

Objective. *Desiccation of the vocal tract can cause many voice problems. Therefore, we aimed to investigate whether patients with primary Sjögren's syndrome (pSS) with dry mouth have more voice-related problems than controls without the disease and to determine the factors affecting voice in pSS patients.*

Methods. *Patients with pSS and controls complaining of voice-related symptoms underwent acoustic analysis, aerodynamic study and stroboscopic analysis. They also completed the voice handicap index (VHI) questionnaire and perceptual voice analysis (GRBAS). Various disease-related parameters were obtained from pSS registry data.*

Results. *Fifty-five pSS patients and 52 controls were analysed. The subjects were all female, and mean age was 53.9 years. VHI score was significantly higher in the pSS patient group (median [interquartile range], 11 [3-30] vs. 5.5[0-15.75], p=0.014). However, the results of acoustic analysis aerodynamic study and stroboscopic findings were not different between the two groups. Disease-related parameters were available in 47 pSS patients. Correlation analysis revealed that jitter value positively correlated with ESSDAI (spearman's rho = 0.29, p=0.048) and patient global assessment (rho=0.3, p= 0.04). High VHI score was associated with low quality of life measured by EQ5D (rho=-0.493, p=0.0001). Of note, patients with longer disease duration (≥40 months) showed higher noise-to-harmonics ratio (NHR).*

Conclusion. *Patients with pSS had higher VHI score, which was associated with low quality of life and longer disease duration was associated with increased noise in pSS patients. The likelihood of voice problems should be addressed with pSS patients, and vocal hygiene education will be important in those patients.*

Introduction

It is well known that laryngeal lesions can occur in conjunction with autoimmune disease. Such laryngeal abnormalities, including mucosal edema, laryngitis, cricoarytenoid arthritis, and vocal cord paralysis, have commonly occurred during periods of acute exacerbation of the autoimmune condition (1, 2). In particular, patients with rheumatic arthritis (RA) frequently complain of laryngeal manifestations including voice changes, globus symptoms, and throat pain due to arthritis of the cricoarytenoid joint, other myositis, and neuropathy (3).

Sjögren's syndrome (SS) is an autoimmune disease characterised by infiltration of lymphocytes in the salivary and lacrimal glands (4). The exact pathophysiology of SS is unknown, and the reported prevalence of pSS ranges from 0.03% to 2.7%, and it varies according to the race and age of the subject population (5). SS is divided into primary (p) SS, defined as occurring in the absence of another inflammatory autoimmune disease, and secondary SS, which occurs as a result of other autoimmune disease. Up to 60% of SS cases are classified as secondary. With the progression of SS, patients were more likely to experience reduced function of the exocrine glands, including the salivary and lacrimal glands; the pharynx and larynx also could be affected (6, 7). Desiccation of the vocal tract can cause many voice problems, but few studies have examined the prevalence of voice problems in SS patients, with mixed methodologies and results. These vocal problems could cause a significant decrease in quality of life.

In the current study, we aimed to investigate vocal alteration in pSS patients and to identify the contribution of vocal status to quality of life in those patients.

Methods

Study population

A prospective study of patients diagnosed with pSS was performed from September 2016 to January 2017 in Seoul St. Mary's Hospital, a tertiary care University Hospital and referral centre in Seoul, Korea. Patients with pSS who complained voice-related symptoms were enrolled to the study. All of the pSS patients in the study were registered in the pSS registry named Korean Initiative Sjögren's Syndrome (KISS). The KISS registry was founded in 2013 with the goals of establishing a nationwide prospective cohort that contains overall clinical data and samples from patients with pSS and developing diagnostic and treatment tools for pSS. Informed consent was obtained from all patients according to the principles of the Declaration of Helsinki. This study was approved by the Institutional Review Board of Seoul St. Mary's Hospital (KC13ONMI0646). All data were collected and managed using the Clinical Research and Trial Management System (Korea National Institutes of Health, Korea Centers for Disease Control and Prevention). Patients were classified to have pSS according to either the 2002 American-European Consensus Group classification criteria for pSS (8) or the 2012 American College of Rheumatology classification criteria for pSS (9).

We included only female patients to exclude sex-related differences in voice analyses. A total of 55 pSS patients were included in this study; 52 patients who visited the otorhinolaryngology department for throat discomfort without evidence of autoimmune disease over the same time period were enrolled in a control group as potential comparators.

Perceptual voice analysis

The grade, roughness, breathiness, asthenia, and strain (GRBAS) score is widely used by many professional bodies. Each voice in the present study was scored using the five GRBAS parameters: grade = overall degree of voice deviance from normal; roughness = irregular fluctuation of the fundamental frequency; breathiness = turbulent noise produced by air leakage; asthenia = overall voice weakness; and strain = impression of tenseness or excess effort when speaking. Each parameter was scored on a scale of 0–3 (0, normal; 1, slight disturbance; 2, moderate disturbance; and 3, severe disturbance). Voice samples were recorded for all patients, who were instructed to read "Sanchaek" ("A Walk") at a comfortable volume and rate. Each patient's voice was also perceptually evaluated during conversation. The patients provided information on their voice history and social history. A GRBAS score was assigned at the end of the evaluation session. Recorded audiotapes were replayed after the evaluation session to reconsider the GRBAS scores. The voices were judged by two speech therapists and one otolaryngologist by consensus.

Acoustic analysis

Patients were instructed to produce the vowel "a" at a comfortable volume and constant pitch. Each vowel pronunciation was recorded with a constant mouth-to microphone distance of 5 cm using Computerized Speech Lab (CSL, model 4150; KayPENTAX, Lincoln Park, NJ, USA). All digital recordings were produced in a quiet room. Each patient sustained an "a" for at least 3 sec at a comfortable pitch level. The task was repeated at least four times, and the fourth trial was often the recorded sample. Each analysis was performed using the Multi-Dimensional Voice Program (MDVP, model 5105, ver. 3.1.7; KayPENTAX). The parameters considered in the analysis were fundamental frequency (F0), perturbations of fundamental frequency (jitter), amplitude (shimmer), noise-to-harmonics ratio (NHR), and speaking fundamental frequency (SFF). The software defines normal jitter values up to <1.1% and shimmer values up to <3.8%. The normal NHR is <0.2.

VHI questionnaire

All patients completed a Voice Handicap Index (VHI) questionnaire with a five-point scale from 0 (never) to 4 (always) for each question. VHI is composed of three categories that evaluate the functional, physical, and emotional aspects of subjective voice status. The VHI had a minimum total score of 0 and a maximum total score of 120, with higher scores indicating greater perceived disability due to the patient's voice problem.

Fiber-optic laryngoscopic and videostroboscopic examination

We examined the entire larynx, including the mucosal status and the presence of vocal fold diseases, using fiberoptic laryngoscopy (Machida Instruments, Tokyo, Japan) and videolaryngostroboscopy (model 9200C; KayPENTAX). The diagnosis of vocal fold disease was judged by two speech therapists and one otolaryngologist by consensus.

Reflux Symptom Index (RSI) questionnaire

We recorded symptom scores using the RSI. The items were hoarseness or a problem with voice, throat clearing, excess throat mucus or postnasal drip, difficulty swallowing (food, liquids, or pills), coughing after eating or lying down, breathing difficulties with choking episodes, troublesome or annoying cough, sensation of a lump or something sticking in the throat, heartburn, chest pain, indigestion, and regurgitation. Study patients were evaluated using the RSI at each visit and rated from 0 to 5 (0 = no problem, 5 = severe problem), with a maximum total score of 45.

Sjögren's Syndrome Disease Related Index

Disease activity was assessed with EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and patient-reported outcome was EULAR Sjögren's syndrome patient-reported index (ESSPRI). Disease related damage was scored with SSDDI, Sjögren's syndrome disease damage index.

Statistical analysis

Statistical analyses were performed using SPSS software (v. 22.0 for Windows; SPSS, Chicago, IL, USA). As many of the clinical parameters were not normally distributed, continuous variables were expressed as median and interquartile ranges (IQRs) and compar-

ison between the two groups was made by Mann-Whitney test. Categorical variables were compared using the chi-square test. Bivariate correlation was determined using the Spearman correlation. A p-value <0.05 was considered to indicate statistical significance.

Results

Overall patient characteristics

A total of 55 pSS patients and 52 controls were enrolled in the study. Median age (IQR) was 54.5 years (47–61) in the pSS group and 53.7 years (47–62) in the control group. Table I shows baseline vocal characteristics of the subjects. The total VHI score was significantly higher in the SS group than in the control group (median, 17.10 *vs.* 9.35, p=0.014). Among the three categories (functional, physical, emotional) of the VHI score, the functional and physical VHI scores were significantly higher in the SS group than in the control group (mean value of VHI-F was 4.75 in SS group and 2.08 in the control group, p=0.014; VHI-P was 8.20 in SS group and 5.50 in the control group, p=0.048). Subjective perceptual voice quality was evaluated using the GRBAS scale; there was no statistical difference in the five parameters. The RSI was significantly higher in the SS group than in the control group (median, 14.22 *vs.* 9.83, p=0.004). Acoustic analysis was conducted for all patients, and F0, SFF, jitter, shimmer, and NHR were reviewed. The mean values of F0 and SFF were 188.2 Hz and 183.4 Hz, respectively, in the SS group and 193.8 Hz and 185.5 Hz in the control group. Comparative analysis between the two groups showed no statistical difference in acoustic parameters. In the aerodynamic examination of maximal phonation time (MPT), mean flow rate (MFR), and subglottic pressure, there was no statistically significant difference.

Table II summarises the results of SS-related parameters of the patients. Median disease duration was 40 months.

Overall videostroboscopic findings

Table III summarises the results of videostroboscopic findings. We evaluated videostroboscopic findings of SS patients in four categories (symmetry, regularity, glottis closure, amplitude) and compared the data with that of the control group by Chi-square test. Three pSS patients (5.5%) showed asymmetrical mucosal wave, 13 (23.6%) showed incomplete glottal closure, and 10 (18.3%) had decreased mucosal wave amplitude. However, we found no statistical difference between the pSS group and the control group in the four categories, and no abnormal laryngeal findings (vocal nodule, polyp, cyst) were detected by videostroboscopic examination in either group.

Table I. Baseline characteristics of the study subjects.

Parameter	Sjögren's syndrome (n=55)	Control (n=52)	p-value
Age (years)	55 [47-61]	54.5 [47-62]	0.822
Gender			
Female	55	52	
VHI (total score)	11 [3-30]	5.5 [0-15.75]	0.014*
VHI-F (functional)	2 [0-10]	0 [0-4]	0.009*
VHI-P (physical)	7 [3-13]	4 [0-10]	0.048*
VHI-E (emotional)	0 [0-6]	0 [0-3.5]	0.055
RSI	14.22 [0-29]	9.83 [0-33]	0.004*
Auditory-Perceptual analysis			
G(grade)	0.49	0.5	0.932
R(rough)	0.29	0.33	0.802
A(asthenic)	0.05	0.04	885
B(breathy)	0.21	0.19	0.695
S(strained)	0	0.04	0.144
Acoustic analysis			
F0	191 [173-203]	195 [185.75-205.5]	0.181
SFF	182 [170-196]	190 [170-196.75]	0.545
Jitter	1.3050 [0.693-2.412]	1.297 [0.60-2.16]	0.667
Shimmer	0.3577 [2.843-4.727]	3.46 [2.83-4.67]	0.607
NHR	0.13 [0.118-0.152]	0.128 [0.1098-0.1398]	0.218
Aerodynamic study			
MPT	14.37 [10.56-17.891]	15.29 [12.495-21.035]	0.123
MFR	120 [70-170]	110 [80-150]	0.508
Subglottic pressure	7.41 [6.23-8.79]	7.375 [6.1725-8.0775]	0.36

VHI: voice handicap index; RSI: reflux symptom index; SFF: speaking fundamental frequency; NHR: noise to harmonic ratio; MPT: maximal phonation time; MFR: mean flow rate. Data are presented with median and interquartile range.

Table II. Sjögren's syndrome-related parameters of subjects.

Parameter	Sjögren's syndrome (n=47)
Age (years)	56 [48-61]
Female	47 (100%)
Disease duration(months)	40 [12-64]
ESSPRI	5 [4-6.3]
ESSDAI	1 [0-2]
SSDDI	3 [2-3]
Physician GA (mm)	15 [4-31]
Patient GA (mm)	62 [50-71]
Anti Ro positivity	37/47 (78.7%)
Anti La positivity	22/46 (47.8%)
ESR (mm/hr)	19 [11-42]
CRP (mg/dL)	0.04 [0.02-0.1]
IgG (mg/dL)	1473 [1186-1876]
EQ5d (TTO)	0.766 [0.72-0.833]
uSFR (mL/5min)	0.6 [0-1.8]

ESSDAI: EULAR Sjögren's syndrome disease activity index; ESSPRI: EULAR Sjögren's syndrome patient-reported index; GA: global assessment; SFR: salivary flow rate; SSDDI: Sjögren's syndrome disease damage index. Data are presented with median and interquartile range.

Table III. Overall stroboscopic laryngeal findings.

Parameter	Sjögren's syndrome (n=55)	Control (n=52)	*p*-value
Symmetry			0.694
symmetric	52 (94.5%)	50 (96.2%)	
asymmetric	3 (5.5%)	2 (3.8%)	
Regularity			1.000
regular	55 (100%)	52 (100%)	
irregular	0 (0%)	0 (0%)	
Glottic closure			0.283
complete	42 (76.4%)	44 (84.6%)	
incomplete	13 (23.6%)	8 (15.4%)	
Amplitude			0.699
normal	45 (81.8%)	44 (84.6%)	
decreased	10 (18.2%)	8 (15.4%)	
increased	0 (0%)	0 (0%)	

Correlations between disease activity markers and voice status in SS patients

To investigate the correlation between disease activity and voice status in SS patients, we analysed three SS disease activity markers (ESSDAI, SSDDI and ESSPRI). Additionally, we tested for correlations between SS-related parameters included in the questionnaire (severity of dry mouth (xerostomia inventory [XI]), global assessment (GA) of the disease by physician/ patient, unstimulated salivary flow rate (uSFR), and quality of life (QoL) (EQ5d)) and the results of VHI, acoustic analysis, and aerodynamic study. The summarised results are shown in Table IV. Among acoustic analysis parameters, jitter score showed positive correlation with ESSDAI and patient GA score (rho=0.29, p=0.048 and rho=0.3, p=0.04, respectively). Subglottic pressure was negatively correlated with ESSDAI score (rho=-0.339, p=0.02). VHI score showed the negative correlation with EQ5d score, which suggests that patients with voice problems reported low QoL (rho= -0.493, p=0.0001).

Associations between VHI score and SS disease-related parameters

VHI is widely used as a sensitive screening tool for voice problems, but it is difficult to define cut-off values for detecting vocal disorders. Recently, Moradi *et al*. (10) reported that a VHI score of 14.5 could be used as a sensitive cut-off point to distinguish voice disorders from normal voice status. Following the recommendation from this report, we categorised SS patients into two subgroups by VHI score (patients with VHI scores under and over 15) and analysed voice status param-

Table IV. Correlation analysis between disease activity markers of Sjögren's and acoustic, aerodynamic study parameters.

Parameter	VHI	RSI	F0	SFF	Jitter	Shimmer	NHR	MPT	MFR	Subglottic pressure
ESSDAI										
Rho	0.082	0.105	0.209	0.236	0.29	-0.111	-0.063	0.101	0.083	-0.339
p-value	0.585	0.482	0.159	0.11	0.048*	0.458	0.675	0.501	0.577	0.020*
SSDDI										
Rho	-0.023	0.045	-0.12	-0.1	-0.026	0.081	0.167	0.01	-0.086	0.099
p-value	0.877	0.762	0.42	0.503	0.861	0.589	0.263	0.945	0.564	0.508
ESSPRI										
Rho	0.218	0.117	0.034	0.029	0.137	0.045	-0.105	0.126	0.097	0.065
p-value	0.14	0.433	0.819	0.847	0.358	0.765	0.484	0.398	0.516	0.662
XI										
Rho	0.055	-0.061	-0.007	-0.067	-0.056	-0.152	-0.012	-0.101	-0.032	0.159
p-value	0.711	0.685	0.961	0.657	0.71	0.309	0.938	0.501	0.832	0.286
Physician GA										
Rho	-0.086	0.074	0.125	0.131	-0.098	-0.063	0.112	0.101	0.013	0.232
p-value	0.565	0.621	0.401	0.379	0.514	0.674	0.452	0.5	0.93	0.116
Patient GA										
Rho	0.028	0.149	-0.171	-0.153	0.3	0.148	0.113	0.105	-0.068	0.189
p-value	0.854	0.319	0.251	0.306	0.04*	0.321	0.449	0.483	0.647	0.204
CRP										
Rho	0.035	-0.057	0.165	-0.039	-0.005	-0.108	-0.096	-0.125	0.005	-0.012
p-value	0.817	0.703	0.267	0.794	0.973	0.472	0.52	0.404	0.975	0.934
uSFR										
Rho	-0.164	-0.069	-0.045	0.111	-0.062	-0.081	-0.017	0.057	-0.043	-0.16
p-value	0.346	0.695	0.796	0.525	0.724	0.645	0.923	0.745	0.806	0.357
EQ5d										
Rho	-0.493	-0.429	0.095	0.074	-0.044	-0.046	0.053	-0.033	0.194	-0.123
p-value	<0.0001*	0.003*	0.526	0.622	0.769	0.758	0.722	0.823	0.192	0.41

ESSDAI: EULAR Sjögren's syndrome disease activity index; ESSPRI: EULAR Sjögren's syndrome patient-reported index; GA: global assessment; MFR: mean flow rate; MPT: maximal phonation time; NHR: noise to harmonic ratio; RSI: reflux symptom index; SFR: salivary flow rate; SFF: speaking fundamental frequency; SSDDI: Sjögren's syndrome disease damage index; VHI: voice handicap index; XI: xerostomia inventory.

Table V. Comparative analysis of voice parameters and SS activity parameters according to VHI score.

Parameter	Normal VHI score (<15) (n=28)	Abnormal VHI score (>15) (n=19)	*p*-value
Mean VHI score	5.18	30.79	
Disease period (months)	37.93	78.84	0.014*
Voice parameter			
F0(Hz)	184.13	185.26	0.603
SFF(Hz)	186.36	178.95	0.193
Jitter	1.342	1.775	0.298
Shimmer	3.535	4.538	0.065
NHR	0.128	0.144	0.374
MPT (sec)	16.28	13.196	0.083
MFR (ml/sec)	123.93	143.68	0.753
SS activity parameter			
ESSDAI	1.61	2.68	0.287
Physician VAS	20.11	16.89	0.515
SSDDI	2.43	2.53	0.955
ESSPRI	4.893	5.705	0.134
pain	2.86	4.32	0.08
dryness	4.96	5.53	0.221
fatigue	6.86	7.26	0.475
Patient VAS	60.29	61.89	0.914
XI	37.18	39.68	0.349
uSFR	1.461	0.722	0.367
ESR	25.29	26.74	0.803
CRP	0.186	0.076	0.912
IgG	1589.86	1718.26	0.502
C3	85	88.89	0.095
OSDI	35.54	40.58	0.356
QoL			
EQ5D	0.796	0.718	0.001*

ESSDAI: EULAR Sjögren's syndrome disease activity index; ESSPRI: EULAR Sjögren's syndrome patient-reported index; GA: global assessment; OSDI: ocular surface damage index; QoL: quality of life; SFR: salivary flow rate; SSDDI: Sjögren's syndrome disease damage index; VHI: voice handicap index; XI: xerostomia inventory.

Table VI. Comparative analysis according to disease period of Sjögren's syndrome.

Parameter	Disease period < 40mo (n=23)	Disease period≥40mo (n=24)	*p*-value
Acoustic analysis			
F0	192 [173-201]	189 [171.75-203.25]	0.831
SFF	184 [171-194]	181 [170.5-197.5]	0.873
Jitter	1.419 [0.799-2.531]	1.0785 [0.53425-1.90550]	0.097
Shimmer	3.283 [2.705-4.173]	3.90050 [3.0455-5.56375]	0.154
NHR	0.125 [0.108-0.135]	0.146 [0124-0.1585]	0.042*
Aerodynamic study			
MPT	14.37 [11.1-17.79]	14.5 [10.7275-18.915]	0.602
MFR	150 [120-170]	90 [62.5-177.5]	0.178
Subglottic pressure	6.54 [6.11-8.95]	7.565 [6.2375-8.155]	0.509

MFR: mean flow rate; MPT: maximal phonation time; NHR: noise to harmonic ratio; SFF: speaking fundamental frequency; VHI: voice handicap index. Data are presented with median and interquartile range.

eters, SS-related parameters, and QoL by EQ5d score. The voice parameters (F0, SFF, jitter, shimmer, NHR, MPT, and MFR) showed no difference between the two subgroups (Table V). SS disease activity markers also showed no statistical difference, but mean SS disease duration was much longer in patients with high VHI score than patients with low VHI score (78.84 months *vs*. 37.93 months, p=0.014). Also, a significantly lower EQ5d score was observed in the high-VHI subgroup (p=0.001).

Effect of disease duration on voice status in SS patients

Based on the fore mentioned results, we determined that VHI score and vocal status were closely related to SS disease duration. Accordingly, we investigated the effect of disease duration on the objective voice parameters of SS patients by classifying SS patients into two groups (patients with disease duration greater than and less than the median disease duration of 40 months) for acoustic analysis and aerodynamic study. The results are summarised in Table VI. The values of F0, SFF, jitter, and shimmer were not affected by disease duration. Of note, NHR was much higher in the longer disease duration group (0.145 *vs*. 0.125, p=0.042), suggesting the more noise in voice of patients with longer disease duration. The results of aerodynamic study were comparable between the two groups.

Discussion

In the current study, we demonstrated that pSS patients may have voice problems, which can result in low QoL.

Patients with pSS usually suffer from hyposalivation. Decreased saliva can cause voice alteration, as well as other problems including dental caries, oral candidiasis, and taste change (11). The prevalence of current and lifetime voice disorders in SS patients ranges from 12 to 41.9% (12, 13). A recent report found that up to 59% of SS patients had a current voice disorder (14), but the exact cause of voice alteration is not yet understood.

Stroboscopic findings of pSS patients in our study revealed decreased mucosal wave amplitude and incomplete glottis closure. However, we did not find any pathologic condition in the larynx of pSS patients such as bamboo nodule or joint ankylosis, which are typical pathologic findings in other autoimmune disease patients. Previously, there has been debate over the laryngostroboscopic findings of SS patients. Salturk *et al*. (15) reported that smoothness and straightness were affected in SS patients, but found no difference in amplitude or phase asymmetry. Another study reported abnormal rippling of mucosa and decreased amplitude in 90.32% of

SS patients, but no abnormal findings in vocal cord or pyriform sinus in those patients (12). Heller, *et al*. (16) found no obvious structural changes but frequent supraglottic compression, thick mucus, and vascular markings in SS patients. They suggested that the lack of obvious structural changes might indicate that the voice alteration in SS patients was a result of inflammation, dryness, or muscle tension problems (*e.g*. supraglottic adduction). Moreover, perturbation of the protective mechanism of the esophagus could allow reflux to irritate the dry laryngeal mucosa, leading to laryngeal edema with high values of jitter, PPQ, APQ, and shimmer in SS patients (17). Similarly, in our study, significantly higher RSI scores were observed in pSS patients without any pathologic laryngeal findings. This result may indicate that an inflammatory condition resulting from reflux combined with dry mucosa could contribute to alteration of the voice in SS patients.

Long periods of dehydration also cause changes in the biochemical properties of vocal cord tissue and the dynamic mechanism of vibration. Titze *et al*. (18) proposed that the minimum lung pressure required to produce small-amplitude oscillations of the vocal folds, known as phonation threshold pressure (PTP), depends on tissue biomechanical properties including tissue thickness, elasticity, and viscosity. PTP is a measure of ease of phonation (19-21), and theoretically increases when the viscosity of the vocal fold mucosa increases relative to its elasticity (22). Viscosity is an important biomechanical property involved in vocal fold hydration and may have a linear relationship with PTP (18). Hydration of the vocal fold reduces vocal fold viscosity and should decrease PTP. Therefore, dehydrated vocal folds caused by SS lead to a stiffer, more viscous condition that requires more energy to produce sound, resulting in easier vocal fatigue (23).

In our study, high ESSDAI was associated with high jitter. ESSDAI is a composite index that addresses the systemic involvement of SS; jitter index reflects the perturbation of F0. Therefore, high systemic activity could potentially affect vocal frequency stability.

In addition, one can expect that patients with longer disease duration may have more voice problems. Persistent desiccation of the vocal tract can easily cause vocal fatigue, resulting in instability of F0 (jitter) and higher NHR without any pathologic laryngeal disease (18-23).

In addition to disease related parameters, we also tried to investigate lifestyle or occupational factors that may increase the risk of voice problems such as smoking or job. However, there were only two smokers in our study population – one per each group – and the effect of smoking could not be determined. With respect to job-related risk, most of the subjects were housewives – 73.1% in controls and 72.7% in pSS group. The list of the jobs of the subjects includes teacher, salesman, retailer, counsellor, etc. As the frequency of a certain job is too small to consider its effect, this could not be take into account in the current study as well.

To treat dehydrated vocal cords, both systemic and topical hydration should be applied to improve quality of voice and reduce vocal fatigue. Although the effectiveness of systemic hydration by drinking water has been disputed, Solomon *et al*. (23, 24) demonstrated that increased water consumption could reduce vocal fatigue, and that, especially in women, it could delay or attenuate the detrimental effects of the strenuous phonation task. Therefore, education on vocal hygiene appears to be important for improving this condition and should be considered in pSS patients with voice problems (25, 26).

Conclusion

Primary SS patients had higher VHI scores than the control group, and patients with disease duration longer than 40 months had higher NHR. High VHI score was associated with low QOL, while ESSDAI and patient GA had strong positive correlations with jitter score. This is the first report to investigate the relationships between disease activity markers and vocal status in pSS patients, and we suggest that pSS patients are more likely to experience vocal problems than the general population, which could lead to low QOL. Probability of voice problems should be addressed in pSS patients, and vocal hygiene education will be important in those who have voice problems.

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