2019-1003 IJOI
http://www.ijoi-online.org/

THE CLINICALLY PREDICTIVE FACTORS FOR THE AERODYNAMICS OF VOCAL FOLD ATROPHY IN ELDERLY

Wei-Kang Tung*
MD, EMBA
Department of Otorhinolaryngology, Kaohsiung Municipal United Hospital, Kaohsiung, Taiwan, 80457
PhD Student, Industrial Management Department, I-Shou University
Kaohsiung, Taiwan, 84001
*Corresponding Author: ent88882001@gmail.com

Hsiang-Chen Hsu
PhD, Professor
Industrial Management Department, I-Shou University
Kaohsiung, Taiwan, 84001

Shiao-Wen Tung
Kaohsiung Municipal Kaohsiung Girls' Senior High School,
Kaohsiung, Taiwan, 80148

Abstract

Background: Hoarseness due to vocal fold atrophy (VFA) embraced a substantial part of vocal clinic's patients. Frailty seemed common in the elderly with vocal fold atrophy. We aimed to find out: 1. The Maximum phonation time (MPT) in VFA and in normal vocal folds (NVF); the incidence rate of frailty in NVF and VFA. 2. The association of Clinical Frailty Scale (CFS), Study of Osteoporotic Fracture Criteria for Frailty (SOF), Charlson Comorbidity index(CCI) and MPT in all patients. 3. The predictive factors for MPT in NVF and VFA. 4. The sports-days per week (SDW) in NVF and VFA.

METHOD: This was a retrospective medical chart review with 212 patients 65 years or older enrolled. 112 patients in this study were all diagnosed as VFA. 100 patients were with NVF. All the patients were recorded with MPT, AGE, CCI, CFS, SOF, SDW. Pearson correlation was used to find the correlation of AGE, GENDER, SOF,

CFS, CCI, SDW and MPT in all patients. Stepwise regression and Area Under the ROC Curve (AUC) were used to find out the predictive factors for MPT in NVF and VFA..
Results: Comparing with patients with NVF, the MPT was shorter in patients with VFA. The incidence rate of frailty was higher in patients with VFA than those with NVF. In elderly patients of both genders with VFA, MPT was moderately to highly negatively correlated with CFS, SOF, and CCI. In elderly patients of both genders with NVF, MPT was modestly to moderately negatively correlated with CFS ,SOF and CCI. In all elderly patients with VFA, SOF, SDW, AGE, and CFS were the predictive factors for MPT. In patients with NVF, the predictive factors for MPT were SOF, SDW, and CFS. The SDW of VFA was less than that of NVF.
Conclusions: The MPT of VFA was shorter than that of NVF. The MPT was a valid and excellent indicator of physical condition for the patients with VFA. The predictive factors for the MPT were SOF, SDW, AGE, and CFS in patients with vocal fold atrophy. It could be found that more amount of exercise, although which exerted muscles unrelated to the intrinsic laryngeal muscles, would be correlated with longer MPT and lower incidence rate of frailty in normal vocal folds groups. Besides, less amount of exercise would be correlated with shorter MPT and higher incidence rate of frailty in vocal fold atrophy groups.

Keywords: Clinical Frailty Scale, Maximum Phonation Time, Vocal Fold Atrophy, Study of Osteoporotic Fracture Criteria for Frailty, Charlson Comorbidity Index

Introduction

Vocal fold atrophy was one of the aging phenomena. The muscles of the vocal folds might become weaker, thinner and looser overtime. Besides, the soft tissue of vocal folds would lose volume with aging. There was no real effective treatment for restoring the tension of tissue quality in the vocal folds. The current common practices were voice rehabilitation (Fujimaki Y *et al*., 2017), intracordal injection, various thyroplasties, and pulsed dye laser. (Koo, Y.C., Chung, H.J., Suh, M.J., Choi, H., & Murthy, P.D., 2012) Voice rehabilitation could improve voicing techniques and/or increase vocal fold muscle bulk. Some surgery could restore some of the bulk lost overtime by injecting some material into the vocal folds. They were not necessarily effective due to inherent limitations in the vocal mechanism. Besides, not all patients could accept voice therapy and/or the vocal surgery (Gartner- Schmidt, J.

and Rosen, C., 2011).

Molecular Mechanisms

Exercise training (Bowen TS, Schuler G, Adams V., 2015) could increase IGF-1 (Husmann I, Soulet L, Gautron J, Martelly I, Barritault D., 1996, Cassano M *et al.*, 2009, Sacheck JM, Ohtsuka A, McLary SC, Goldberg AL., 2004, Chrysis D, Underwood LE., 1999, Hong D, Forsberg NE., 1994), PGC-1α4 (Bowen TS. *et al.*, 2015), PGC-1α (Wenz T, Rossi SG, Rotundo RL, Spiegelman BM, Moraes CT., 2009), satellite cell regeneration (Husmann I.*et al*., 1996, Cassano M *et al*., 2009), which increased the muscle growth. On the other hand, exercise could inhibit the effect of inflammatory cytokines, reactive oxygen species (ROS), myostatin signalling, which collectively repressed the transcription of atrogenes and consequent protein degradation (Bowen TS. *et al.*, 2015). Exercise training represented an intervention that could attenuate or even reverse the process of muscle wasting with protein degradation and activate molecules associated with protein synthesis (Bowen TS. *et al.*, 2015).We really want to know if exercise which exerted muscles unrelated to the intrinsic laryngeal muscles could help for the prevention of VFA besides the current common methods. But before that, we should investigate the association of SDW and the MPT in both of NVF and VFA. Besides, the difference of SDW in NVF and VFA should also be investigated.

Assessment of Frailty

Frailty was a common clinical syndrome in elderly that carried an increased risk for poor health outcomes including falls, incident disability, hospitalization, and mortality (Bandeen-Roche K, Xue QL, Ferrucci L, *et al*., 2006, Fried LP, Tangen CM, Walston J, *et al*., 2001, Gill TM, Gahbauer EA, Allore HG, *et al*., 2006, Graham JE, Snih SA, Berges IM, *et al*., 2009, Ensrud KE, EwingSK, Cawthon PM, *et al*., 2009, Qian-Li Xue, 2011). Frailty was also a predictive factor of readmission within 90 days of hospitalization for acute exacerbations of chronic obstructive pulmonary disease (Roberto BM. *Et al*., 2017). When the frail elderly were admitted to hospital, they were at increased risk of adverse events including falls, delirium, and disability (Juma S, Taabazuing MM, Montero-Odasso M., 2016, Eeles E, White SV, O'Mahony SM, *et al*., 2012, Gill T, Allore HG, Gahbauer EA, *et al.*, 2010, Joosten E, Demuynck M, Detroyer E, *et al.*, 2014). Although many frailty scores (FS) had been proposed, no single score was considered the generally accepted standard (Rockwood K, Song

X, MacKnight C, *et al*., 2005).

The CSHA Clinical Frailty Scale (CFS) was developed by Kenneth Rockwood at 2005 and could predict the medium-term risk of death and entry into institutional care significantly (Rockwood K *et al*., 2005). The CFS was simple and practical for physicians in assessing related risks of frailty. Using the CFS to predict the length of stay for elderly in otolaryngology unit was also feasible(Tung WK, Hung HC, Tung WC *et.al.* 2019). If CFS was 5 or more, the patient was frail.

Study of Osteoporotic Fractures (SOF) Criteria for Frailty (Ensrud KE, Ewing SK, Cawthon PM, *et al*., 2009) with the components of weight loss, inability to rise from a chair 5 times without using arms, and reduced energy level was a practical index for assessing frailty. The simple SOF index predicted risk of falls, disability, fracture, and death as well as the more complex index derived from the Cardiovascular Health Study (CHS index) and provided a useful definition of frailty to identify older women at risk of adverse health outcomes in clinical practice (Ensrud, KE., *et al*., 2008). The SOF Criteria for Frailty was the screening tool for frailty in the 10-year long-term-care 2.0 plan in Taiwan. If summed SOF score was 2 or 3, the patient was frail.

Vocal fold atrophy(VFA) with bowing of vocal folds could result from aging, atrophy or idiopathic causes, such as an inappropriate vocal cord surgery (Koo, Y.C. *et al*., 2012, Gartner-Schmidt, J. *et al*., 2011). Bowing of the vocal folds resulted in dysphonia and shortening of MPT due to inadequate approximation of the vocal cords. The aerodynamic manifestation of VFA could be evaluated by measures of air volume, air flow and subglottal air pressure, and MPT. The MPT was a practical examination that did not require any instrument and could be used to evaluate the respiratory and phonatory function in clinical practice. In general, 10 seconds or less was abnormal, and 5 seconds or less interfered with daily living (Omori K, 2011). Disorders which shorten MPT include recurrent nerve paralysis and vocal fold atrophy (Omori K, 2011).

The CFS was a practical and efficient tool for assessing frailty; however, its correlation with the MPT of VFA had not been well studied. The MPT could vary with participant's age (Maslan J, Leng X, Rees C, Blalock D, Butler SG., 2011), CCI, CFS, demographics, disease-related factors, and the length of exercise. One of the purposes of this investigation was to find out the association of AGE, GENDER, CCI, CFS, SOF, SDW and MPT in pa-

tients with NVF and VFA.

Materials And Methods

Study Design and Participants

The Antae Tian-Sheng Memorial Hospital institutional review board reviewed and approved the study prior to its initiation (TSMH IRB No./ Protocol No.: 19-047-B). The institutional review board of the Antai Tian-Sheng Memorial Hospital agreed to waive the informed consents of the study participants because all the participant data were protected and deidentified.

A retrospective medical chart review of all patients who were diagnosed with NVF and VFA from January 2014 to November 2018 was performed in Kaohsiung Municipal United Hospital, Taiwan. The selection criteria were: (1) >65 years of age; (2) experiencing hoarseness / dysphonia caused by glottal incompetence or inadequate approximation of the vocal cords; (3) normal vocal fold mobility with bowed, atrophic vocal folds demonstrated by flexible fiber optic laryngoscope or videostroboscopy with photo- documentation.; (4) patients with normal vocal folds as controlled groups. The exclusion criteria were: (1) patients preference for surgical treatment; (2) congenital laryngeal palsy; (3) acute inflammation, sulcus, cyst, polyp, benign tumors, malignancies, granuloma, or nodules of the vocal cords.; (4) traumatic causes of vocal paralysis, such as complications of thyroidectomy or surgery for patent duct arteriosus.

212 elderly patients 65 years or older were enrolled. There were 112 patients (Group 1 with 60 male, Group 2 with 52 female) with VFA which was diagnosed by experienced otolaryngologist. There were 100 elderly patients (Group3 with 50 males, Group 4 with 50 females) were with NVF.

Data Collection

All the patients were recorded with MPT, GENDER, AGE, CFS, SOF, CCI, and SDW. The SDW were counted if over-30-minute exercise each time per day was reached. The exercise referred to any kind of physical activities using muscles unrelated to intrinsic laryngeal muscles. Three times of MPT with production of vowel/i/ were recorded for each patient and the longest one was selected. The patient was diagnosed with frailty by a qualified family physician if CFS was greater or equal to 5 or if SOF was greater or equal to 2.

Statistical Analysis

Statistical analyses by IBM SPSS

Statistics version 20 and Excel were performed. Homogeneity of variance was compared by F-test. Independent sample t-test for variables' difference between different groups was used. One-way ANOVA was used to assess different groups' variables. Stepwise regression and R.O.C. (receiver operating characteristic) curve were used to find the predictive factors for MPT. Pearson's product moment correlation coefficient, partial correlation and semi-partial correlation were used to assess the correlation of independent variables and dependent variables.

Research Framework

There were four hypotheses in this research to explore: 1. The MPT in each group. 2. The correlation between CFS, SOF and MPT. 3. The predictive factors for MPT in VFA and NVF. 4. The difference of SDW between the VFA groups and NVF groups; the association between SDW and MPT in both of VFA and NVF.

H1. The MPT of the 4 groups was equal.

H2a. There were no relationship between the CFS1, SOF1 and MPT1 (elderly male patients with VFA).

H2b. There were no relationship between the CFS2, SOF2 and MPT2 (elderly female patients with VFA).

H2c. There were no relationship between the CFS3, SOF3 and MPT3 (elderly male patients with NVF).

H2d. There were no relationship between the CFS4, SOF4 and MPT4 (elderly female patients with NVF).

H3a. AGE, GENDER, CCI, CFS, SOF, SDW were not the predictive factors for MPT in VFA.

H3b. AGE, GENDER, CCI, CFS, SOF, SDW were not the predictive factors for MPT in NVF.

H4a. The patients' SDWs in VFA groups and NVF groups were equal.

H4b. There were no correlation between SDW12 and MPT12; there were no correlation between SDW34 and MPT34.

Results

A total of 212 elderly patients 65 years or older were eligible and included in the data analyses. As shown in Table.1, 112 patients (Group 1 with 60 males, Group 2 with 52 females) had vocal fold atrophy. One hundred patients (Group 3 with 50 males, Group 4 with 50 females) had normal vocal folds. The average age of participants was 76.48 years (SD = 8.64, range = 65-96) for Group 1, 75.71 years (SD = 8.94, range = 65-96) for Group 2, 73.94 years (SD = 6.88, range = 65-89) for

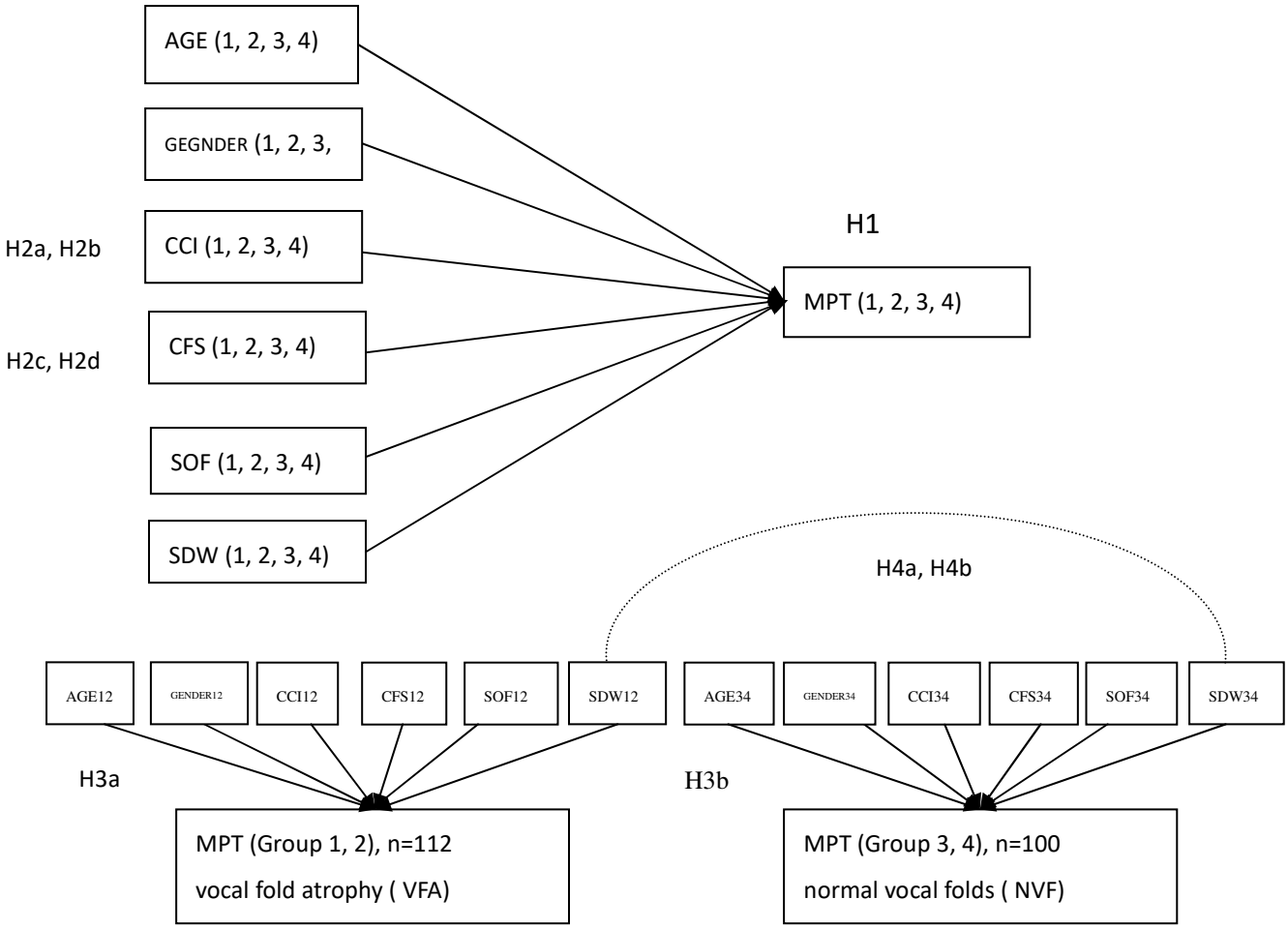

Figure 1. Research Framework

Table 1.Descriptive Statistics

	num-ber	*rang e*	*Min.*	*Max.*	*Mea n*	*S.D .*	*Vari-ance*	*Skewness*		*Kurtosis*	
	Stat.	*Stat.*	*Stat.*	*Stat.*	*Stat.*	*Stat .*	*Stat.*	*Stat.*	*S.E.*	*Stat.*	*S.E.*
MPT1 (male, VFA)[a]	60	20.10	.50	20.6	5.54	3.84	14.76	1.416	.309	3.323	.608
AGE 1	60	31.00	65.00	96.00	76.48	8.64	74.66	0.227	.309	-1.178	.608
CCI 1	60	5.00	2.00	7.00	4.23	1.52	2.32	-0.022	.309	-0.757	.608
CFS1	60	5.00	1.00	8.00	3.97	2.07	4.24	0.444	.309	-0.923	.608
SOF1	60	3.00	.00	3.00	1.65	1.09	1.18	-0.154	.309	-1.259	.608
SDW1	60	7.00	.00	7.00	3.05	2.74	7.51	0.019	.309	-1.513	.608

MPT2 (female, VFA)[b]	52	23.6	0.50	24.10	6.62	4.54	20.61	1.350	.330	3.420	.650
AGE 2	52	31.00	65.00	96.00	75.71	8.94	79.86	0.520	.330	-0.883	.650
CCI 2	52	7.00	2.00	9.00	4.27	2.26	5.10	0.511	.330	-1.074	.650
CFS2	52	7.00	1.00	8.00	4.08	2.19	4.82	0.292	.330	-1.110	.650
SOF2	52	3.00	.00	3.00	1.50	1.28	1.63	-0.029	.330	-1.700	.650
SDW2	52	7.00	.00	7.00	2.06	1.95	3.82	0.572	.330	-0.684	.650
MPT3 (male, NVF)[c]	50	20.7	1.00	21.7	10.07	5.45	29.68	0.473	.337	-0.612	.662
AGE 3	50	24.0	65.00	89.00	73.94	6.88	47.28	0.493	.337	-0.718	.662
CCI3	50	3.00	2.00	5.00	2.98	0.87	0.76	0.623	.337	-1.78	.662
CFS3	50	4.00	1.00	5.00	2.38	0.88	0.77	1.419	.337	2.028	.662
SOF3	50	3.00	.00	3.00	.420	0.70	0.49	1.768	.337	3.004	.662
SDW3	50	7.00	.00	7.00	4.42	2.32	5.39	-0.475	.337	-0.941	.662
MPT4 (female, NVF)[d]	50	19.3	1.00	20.3	10.51	5.52	30.49	0.392	.337	-1.029	.662
AGE 4	50	24.00	65.00	89.00	73.68	7.18	51.57	0.405	.337	-1.019	.662
CCI4	50	3.00	2.00	5.00	2.92	0.92	0.85	0.651	.337	-0.512	.662
CFS4	50	5.00	1.00	6.00	2.58	1.18	1.39	1.277	.337	1.251	.662
SOF4	50	2.00	.00	2.00	0.56	0.61	0.37	0.599	.337	-0.522	.662
SDW4	50	7.00	.00	7.00	3.98	2.11	4.47	-0.108	.337	-1.004	.662

Abbreviation: CCI, Charlson Comorbidity Index, CFS: Clinical Frailty Scale, SOF: Study of Osteoporotic Fracture Criteria for Frailty, SDW (Sports-Days per Week), VFA: vocal fold atrophy, NVF: normal vocal folds

[a]Group1. Male patients with vocal fold atrophy (VFA), [b]Group2. Female patients with vocal fold atrophy (VFA)

[c]Group3. Male patients with normal vocal fold (NVF), [d]Group4. Female patients with normal vocal fold (NVF)

Group 3, and 73.68 years (SD = 7.18, range = 65-89) for Group 4.As presented in Table 2, one-way ANOVA and Tamhane's T2 test showed that the MPTs for patients in Group 1 (M = 5.54, SD = 3.84) and Group 2 (M = 6.62, SD = 4.54) with vocal fold atrophy were significantly shorter than those of patients in Group 3 (M =10.04, SD = 5.45) and Group 4 (M =10.51, SD = 5.52) with normal vocal folds ($p < 0.05$).

Levene's test of MPT1 and MPT2 showed equal variances assumed was valid (p=0.492). Independent sample t-test of MPT1 and MPT2 were equal (difference between the groups, 1.08; 95%CI, -2.65 to 0.48). Levene's test of MPT3 and MPT4 showed equal variances assumed was valid (p=0.616). Independent sample t-test of MPT3 and MPT4 were equal (difference between the groups, 0.47; 95%CI, -2.65 to 1.70).

Brown-Forsythe test of MPT1、MPT2, MPT3 and MPT4 were significant (p=0.000). Tamhane's T2 test showed the mean of MPT1 was shorter than that of MPT3 (difference between the groups, -4.50; 95%CI, -6.96 to -0.74). Similarly, the mean of MPT2 is shorter than that of MPT4 (difference between the groups, -3.89; 95%CI, -6.59 to -1.20). (MPT1≒MPT2< MPT3≒ MPT4).

Table 2. MPT of all groups

	number	*mean*	*S.D.*	*S.E.*	*95% C.I.*		*Min.*	*Max.*	*Shpiro-Wilk Test of Normality (p)*
					Lower Limit	*Upper Limit*			
MPT1 (group1)	60	5.5367	3.841	.49593	4.5443	6.5290	0.50	20.6	0.000***
MPT2 (group2)	52	6.6212	4.540	.62955	5.3573	7.8850	0.50	24.10	0.000***
MPT12 (gr1+2)	112	6.0402	4.196	0.39650	5.2976	6.9144	0.5	23.6	0.000***
MPT3 (group3)	50	10.0380	5.448	.77049	8.4897	11.5863	1.00	20.70	0.096
MPT4 (group4)	50	10.5120	5.522	.78089	8.9427	12.0813	1.00	19.3	0.895
MPT34 (gr3+4)	100	10.2750	5.462	0.54625	9.2171	11.2988	1.0	20.7	0.306
MPT1234 (all)	212	8.0377	5.268	0.36182	9.1593	11.4139	0.5	23.6	0.000***

Table 3 listed the incidence rate of frailty among four groups. The incidence rate of frailty was 55.00% for males with vocal fold atrophy (Group 1) and 51.92% for female with vocal fold atrophy (Group 2). The incidence rate of frailty was 8.00% for males with normal vocal folds (Group 3) and 6.00% for females with normal vocal folds (Group 4). The incidence rate of frailty (53.67%) was higher in all patients with vocal fold atrophy than that (7.00%) in all patients with normal vocal folds (χ^2 test: $p<0.005$).

As shown in Table 4, MPT1 in elderly male patients with vocal fold atrophy was moderately negatively correlated with CFS1(Pearson's r=-0.641***, p=.000) and SOF1 (Pearson's r=

Table 3. Incidence rate of frailty in each group (χ^2 test: p<0.000)

Incidence rate of frailty	
Group1: male patients with vocal fold atrophy	33/60 (55.00%)
Group2: female patients with vocal fold atrophy	27/52 (51.92%)
Group12: all patients with vocal fold atrophy	60/112 (53.67%)
Group3: male patients with normal vocal folds	4/50 (8.00%)
Group4: female patients with normal vocal folds	3/50 (6.00%)
Group34: all patients with normal vocal folds	7/100 (7.00%)

-0.662 * * *, p=.000). In elderly female patients with vocal fold atrophy, MPT2 was highly negatively correlated with CFS2 (Pearson's r= -0.700 * * *, p=.000) and SOF2 (Pearson's r= -0.709 * * *, p=.000). In elderly male patients with normal vocal fold , MPT3 was modestly negatively correlated with CFS3 (Pearson's r=-0.389 * *, p=.001) and was moderately negatively correlated with SOF3 (Pearson's r= -0.557 * * *, p=.000). In elderly female patients with normal vocal fold , MPT4 was modestly negatively correlated with CFS4 (Pearson's r=-0.389 * *, p=.001) and was moderately correlated with SOF4 (Pearson's r= -0.460 * * *, p=.000). In all patients with vocal fold atrophy, MPT was moderately negatively correlated with CCI. In all patients with normal vocal fold, MPT was modestly negatively correlated with CCI.

Table 4. the Correlation of CFS, SOF, CCI and MPT

Pearson's *r*	*CFS*	*SOF*	*CCI*	
MPT1 n=60	r= -0.641 * * * p=.000	r= -0.662 * * * p=.000	r= -0.608 * * * p=.000	elderly male patients with vocal fold atrophy (Group1)
MPT2 n=52	r= -0.700 * * * p=.000	r=-0.709 * * * p=.000	r= -0.628 * * * p=.000	elderly female patients with vocal fold atrophy (Group2)

MPT3	r= -0.389 * *	r= -0.557 * *	r= -0.294 * * *	elderly male patients with normal
n=50	p=.001	* p=.000	p=.038	vocal fold (Group3)
MPT4	r= -0.389 * *	r= -0.460 * *	r= -0.320 * * *	elderly female patients with normal
n=50	p=.001	* p=.000	p=.024	vocal fold (Group4)

For all the patients with vocal fold atrophy, stepwise regression was used to assess the predictive factors (GENDER12, AGE12, CCI12, CFS12, SOF12, SDW12) for the dependent variable MPT12 (Table 5). This model was significant (p=.001) and had an adjusted R^2=0.552. The significant predictive factors for MPT12 were SOF12, SDW12, GENDER12, AGE12, and CFS12 (Table 5). The SDW12 (AUC:0.85) and CFS12 (AUC:0.84) had comparably excellent performances in ROC analyses, which was better than the performance of SOF12 (AUC:0.71)and AGE12 (AUC:0.78). The GENDER12 (AUC=0.53) was excluded due to its weak discrimination in ROC analyses.

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Table 5. Stepwise Regression of MPT12 on AGE12, GENDER12, CCI12, CFS12, SOF12, SDW12 (all patients with vocal fold atrophy) and ROC analyses

The Standardized regression equation is MPT12[ab] = -6.755-1.319 SOF12 +0.519SDW12+1.628GENDER12 +0.195AGE12 -0.919CFS12						*ROC analyses*
Predictor	*B Coef*	*SE Coef*	*Beta*	*T*	*p*	*AUC*
Constant	-6.755	3.926		-1.721	0.088	
SOF12 * *	-1.319	0.457	-0.369	-2.883	0.005	0.71 (p=0.116)
SDW12 * *	0.519	0.169	-0.303	3.074	0.003	0.85 (p=0.009)
GENDER12 * *	1.628	0.571	0.194	2.850	0.005	0.53 (p=0.800)
AGE12 * * *	0.195	0.054	0.406	3.618	0.000	0.78 (p=0.038)
CFS12 * *	-0.919	0.277	-0.463	-3.318	0.001	0.84 (p=0.010)
S=0.001	R-Sq =0.572	R-Sq (adj)=0.55				

[a]MPT12:the MPT of total patients (n=112) with vocal fold atrophy

[b]Shapiro-Wilk test of Normality: p=0.000

For all the patients with normal vocal folds, stepwise regression was used to assess the predictive factors (GENDER34, AGE34, CCI34, CFS34, SOF34, SDW34) for the dependent variable MPT34 (Table 6). This model was significant (p=.017) and had an adjusted $R^2$0.345. The significantly

predictive factors for MPT34 were SOF34, SDW34 and CFS34. In ROC analyses, SOF34 (AUC:0.867) and CFS34 (AUC:0.883) revealed comparably excellent performances which was better than that of SDW34 (AUC:0.628).

Table 6. Stepwise regression of MPT34 on AGE34, GENDER34, CCI34, CFS34, SOF34, SDW34 (all patients with normal vocal folds) and ROC analyses

The Stepwise regression equation is MPT34[a] =12.439 -2.750 SOF34 +0.550 SDW34-1.261CFS34						*ROC analyses*
Predictor	B Coef	SE Coef	Beta	T	*p*	*AUC*
Constant * * *	12.439	1.568		7.935	0.000	
SOF34 * * *	-2.750	0.832	-0.332	-3.307	0.000	0.867 (*p*=0.089)
SDW34 * * *	0.550	0.207	0.224	2.661	0.000	0.628 (*p*=0.538)
CFS34 *	-1.261	0.520	-0.240	-2.426	0.013	0.883 (*p*=0.065)
S=0.017	R-Sq =0.365	R-Sq (adj)=0.345				

[a]MPT34: the MPT of all patients (n=100) with normal vocal cords.

As presented as table 7, the SDW12 of vocal cord atrophy was less than SDW34 of normal vocal folds (difference: -1.61; 95%CI. -2.246 to-0.975; *p*=0.000). Besides, in elderly patients with vocal cord atrophy, MPT12 is highly correlated with SDW12 (Pearson's *r*= 0.733 * *, *p*=.000). In elderly patients with normal vocal folds, MPT34 is moderately correlated with SDW34 (Pearson's *r* = 0.409 * *, *p*=.000).

Table 7. the SDW in group12 (Vocal fold atrophy) and group34 (Normal vocal fold)

Variable	*Group*	*N*	*Mean*	*SD*	*SE of Mean*	*p value*
SDW12	Vocal fold atrophy (Group12)	112	2.589	2.448	0.23	0.000
SDW34	Normal vocal fold (Group34)	100	4.200	2.220	0.22	

Discussion

Since April 2018, Taiwan officially announced its entry into the aged soci-

ety which meant that the elderly accounted for 14% of total population. More and more geriatric syndrome, such as sarcopenia and frailty, demonstrated impact on phonation which was confronted by ENT physicians in voice clinic. The CFS index and SOF index were convenient and quick tools to assess how frail the patients were. Their ability to predict outcomes were with acceptable discrimination at least in our study which had not been well studied within the vocal fold atrophy

The implementation of MPT needed cooperation of nucleus solitarius, nucleus ambiguus, intrinsic muscles of larynx, recurrent laryngeal nerve and still available cardiopulmonary functions. The MPTs of the elderly equal to 65 or more were seldom reported in Asia in these years. The MPTs/i/ of our report were shorter than the previous study (Maslan J, Leng X, Rees C, Blalock D, Butler SG., 2011). A study showed the maximum phonation time (MPT) had been proven to be a highly reliable measure in voice assessment. Only MPT was sufficient to provide highly reliable measurements (Speyer R, Bogaardt H, Lima Passos V, *et al*., 2010).Because the use of MPT was practical, non-invasive, quick and inexpensive , it was widely used in evaluation of maximum vocal capabilities in a variety of diseases (Izawa KP, Kasahara Y, Hirano Y, Watanabe S., 2017).

There were many aerodynamic parameters of phonatory mechanism, such as MPT, mean expiratory airflow (MEAF), mean peak air pressure (MPAP), aerodynamic resistance (ARES), aerodynamic efficiency (AEFF), and the airflow regression slope (ARS).The MPT was the aerodynamic parameter that did not need instrument in clinic. When the patients with some disease causing them immobile, such as polio, arthritis or fracture of lower extremities, were not convenient to rate SOF or CFS, the MPT was another good tool to estimate their physical condition because they were modestly to highly negatively correlated in our samples.

The incidence rate of frailty was higher in patients with vocal fold atrophy than patients with normal vocal folds, no matter in male or female. In our study, the frailty was correlated with vocal fold atrophy (χ^2test, $p<0.005$). This result hinted that in patients with vocal cord atrophy, we should pay more attention to prevent the occurrence of frailty.

In our study, the sports-day per week (SDW) of patients with vocal cord atrophy was less than that of pa-

tients with normal vocal folds. This meant that more exercise can reduce the risk of vocal fold atrophy. There was a law about muscles:"Use it or lose it". If physical exercise was active, muscle cells would become hypertrophic. But as soon as you stopped using a muscle, it began to break it down and shrink. The muscle became atrophic in size as well as weak in strength. Evidence was clear and firm that periods of unloading of skeletal muscle also caused reductions in muscle cross- sectional area (mCSA), volume, mass, and strength in both young and older populations (Bodine SC, 2013; Coker *et al*., 2015; Deschenes *et al*., 2008; Hvid *et al*., 2010; Kortebein *et al*., 2007; Rejc *et al*., 2015; Suetta *et al*., 2009; Wall *et al*., 2013).

Our results showed that MPT12 was highly correlated with SDW12 in elderly patients with vocal cord atrophy. Likewise, MPT34 was also moderately correlated with SDW34 in elderly patients with normal vocal folds. In other words, there were near linear correlations between the MPT and SDW, no matter in the patients of vocal cord atrophy or normal vocal cord. ROC analyses of the vocal fold atrophy groups revealed SDW12 was a predictor for MPT12 with excellent discrimination (AUC, 0.85, p=0.009). The more the exercise, the longer the MPT was. These were corresponding to step- reduction model proposed by researchers such as Breen et al., 2013, Krogh-Madsen *et al*., 2010 and Devries *et al.,* 2015. The status of skeletal muscle, including muscle power and muscle mass, was correlated to physical exercise. Exercise training represented an intervention that can attenuate or even reverse the process of muscle wasting, by exerting anti-inflammatory and anti-oxidative effects that were able to attenuate signalling pathways associated with protein degradation and activate molecules associated with protein synthesis (T. Scott Bowen, Gerhard Schuler & Volker Adams., 2015). Besides, exercise can strengthen the role of IGF-1, PGC-1α4, PGC-1α, and satellite cell which represented the major source of muscle regeneration (Husmann I *et al*., 1996, Cassano M *et al.*, 2009, Sacheck JM *et al*., 2004, Chrysis D *et al*., 1999, Hong D *et al*., 1994, Bowen TS. *et al*., 2015, Wenz T *et al*., 2009). The SDW34 (M =4.20, SD = 2.22) of the NVF group was more than the SDW12 (M =2.59, SD =2.45) of the VFA group. The MPT34 (M =10.28, SD =5.46) of the NVF group was more than the MPT12 (M =6.04, SD=4.20) of the VFA group. The incidence rate of frailty (7.00%) was lower in all patients with NVF than that (53.67%) in all patients with VFA (χ^2 test: p<0.005). In conclusion, the NVF group had more

SDW, longer MPT, lower incidence rate of frailty than those of VFA group.

Because the restraints of gathering more samples, we were looking forward to having more precise results in the future in case we have more samples.

Conclusion

The MPT of vocal fold atrophy was shorter than that of normal vocal fold. The incidence rate of frailty was higher in patients of both genders with vocal fold atrophy than those with normal vocal folds. In elderly patients of both genders with vocal fold atrophy, the MPT was moderately to highly negatively correlated with CFS, SOF and CCI. In elderly patients of both genders with normal vocal fold, MPT was modestly to moderately negatively correlated with CFS, SOF and CCI.

In elderly patients of both genders with vocal fold atrophy, SOF, SDW, AGE, CFS were predictive factors for the MPT. Exercise using muscles unrelated to intrinsic laryngeal muscles played an important role on the MPT of patients with vocal fold atrophy.

In all elderly patients with normal vocal folds, SOF, SDW, and CFS were predictive factors for the MPT. The amount of exercise also played an important role on the MPT of patients with normal vocal fold.

Finally, it could be found by our study that more exercise (SDW34), although which exerted muscles unrelated to the intrinsic laryngeal muscles, would be correlated with longer MPT34 and lower incidence rate of frailty in normal vocal folds groups. Besides, less amount of exercise (SDW12) would be correlated with shorter MPT12 and higher incidence rate of frailty in vocal fold atrophy groups.

Acknowledgements

This research program was supported by grants from the department of Otolaryngology and Medical Education Committee of Kaohsiung Municipal United Hospital, Taiwan. We were grateful to the Antai Medical Care Cooperation Antai-Tian-Sheng memorial Hospital Institutional Review Board reviewed for the approval of this research.

Availability Of Data And Material

All of the data and materials were available.

Conflict Of Interest Disclosures

The authors declared that no conflicts of interest existed.

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