Quality of Voice after Surgical Treatment for Thyroid Cancer

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Quality of Voice after Surgical Treatment for Thyroid Cancer

甲状腺癌摘出術後の音声の評価

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Key words: thyroid cancer, thyroidectomy, neck dissection, quality of voice, F0, MPT, MFR, jitter, shimmer, NHR

Quality of Voice after Surgical Treatment for Thyroid Cancer

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ABSTRACT

Background. Thyroidectomy is a standard treatment for thyroid cancers. Hoarseness due to the paralysis of the recurrent laryngeal nerve is one of the most common postoperative complications and has been studied by many investigators. However, the quality of voice after thyroidectomy in the patients in whom recurrent laryngeal nerves were preserved and vocal cord morbidity was endoscopically normal has not been well studied. To further understand the quality of voice after thyroidectomy, we conducted the time-course analysis of the voice quality in the patients who had thyroidectomy with normal cord morbidity by various measures.

Methods. We evaluated voice parameters including the voice handicap index-10 (VHI-10), the alternating current/direct current ratio (AC/DC), the fundamental frequency (F0), the maximum phonation time (MPT), the mean air flow rate (MFR), jitter, shimmer and the noise-to-harmonics ratio (NHR) before and after total thyroidectomy (TT) or lobectomy (LO) for thyroid cancers in 110 patients in whom the recurrent laryngeal nerves were preserved without apparent injury and normal vocal cord mobility was confirmed by endoscopic examination. Thirteen patients who underwent parotidectomy were enrolled as controls.

Results. Immediately after the surgery, a significant decrease of the MPT (P=0.003) and a significant increase of jitters, shimmers and the NHR (P=0.0002, 0.02, 0.03) were observed in the patients who had TT. In comparison with the controls, jitters and NHR were significantly higher in the patients who had TT (P=0.03, 0.04). MFR was significantly higher in the patients who had LO than in the controls (P=0.02). As compared with the patients who had LO, MPT was significantly shorter, and MFR and NHR were significantly higher in the patients with TT (P=0.0004, 0.004, 0.03). In the patients who had TT, the MPT immediately after the surgery was significantly longer in the patients who had simultaneously neck dissection (ND) in comparison with the patients who did not have ND. However, All these differences gradually decreased and were not significant at one month after the surgery.

Conclusions. Our results suggested that thyroidectomy and neck dissection have distinct impact on quality of voice after the surgical treatment for thyroid cancer, probably due to slight and transient nerve conduction disorders induced by the manipulation around recurrent laryngeal nerves and/or laryngeal edema induced by the disturbance of venous and lymphatic drainages. However, these changes appear to be temporary, lasting only a few weeks.

INTRODUCTION

Vocal dysfunction is one of the most important complications after thyroidectomy and is closely related to a patient's quality of life. Although some vocal changes are transient and become normal again in a few days or months, others remain long term. A typical cause of vocal dysfunction is injury of therecurrent laryngeal nerve (RLN)(1-3), which results in the disturbance of mobility and atrophy of vocal cords (4), decrease of phonation time and increase of perturbation parameters (5). Also, injury to the external branch of the superior laryngeal nerve (EBSLN) causes paralysis of the cricothyroid muscle, which makes a lower pitched, husky voice that is easily fatigued and has a reduced range (5-7).

To date, a number of studies have been reported on the voice dysfunction after thyroidectomy in patients without apparent paralysis of the RLN or EBSLN (5, 8-12). In these papers, many factors are proposed as possible causes of voice alternation, in particular: (a) transient neural conduction disorder of the RLN; (b) transient neural conduction disorder of the EBSLN; (c) movement disturbance of the cricothyroid muscle; (d) temporary malfunction of the strap muscles(5), resulting from the surgical approach; (e) laryngotracheal fixation by scar-impairing vertical movement(5); (f) mucosal damage, hematoma, inflammation, consolidation of vocal folds(10, 11); and (g) laryngeal edema induced by the disturbance of venous and/or lymphatic drainages. Furthermore, gender (12); emotional and behavioral conditions(13); and mental stress (14) have been pointed out as potentially influential factors.

However, most of the studies did not demonstrate the impact of these factors mentioned above on the quality of voice in patients without injury of the RLN or EBSLN. Several studies (9, 12, 15, 16) have failed to demonstrate the significant impact of surgical procedures for thyroid cancer

on the postoperative voice, and most of these studies had a small sample size. To clarify the mechanism of the voice dysfunction in the patients who had surgical treatment for thyroid cancer without injury to the RLN or EBSLN we evaluated the voice of the patients who had surgical treatment for thyroid cancer by means of mental, acoustic, and aerodynamic analysis.

MATERIALS AND METHODS

Subjects

One hundred ten patients who underwent surgical treatment for thyroid cancer at Kuma Hospital from July 2009 to February 2010 were enrolled in this study. In all patients, the RLN and the EBSLN were anatomically preserved without injury and no apparent vocal fold palsy was observed on the postoperative endoscopic examination. Age ranged from 19 to 85 years with the mean age of 53 years old. Nineteen patients were men and 91 patients were women. Thirteen patients who underwent parotidectomy at Kobe University Hospital from November 2010 to June 2011 were used as controls as we considered these surgeries would not influence the voice. All subjects had no history of voice disease or previous neck surgery. Total thyroidectomy (TT) and lobectomy (LO) were performed on 55 patients and 55 patients, respectively. Lateral neck lymph nodes were simultaneously dissected on 17 patients with TT. No patient with LO had lateral neck dissection (ND). Assessment of voice was performed preoperatively and again immediately after surgery and again at 1 and 3 months after surgery.

Surgical Technique

Kuma Hospital is a specialized hospital for thyroid diseases, and surgeons are well trained in thyroid surgery. The RLNs were routinely identified and preserved if these are not involved by cancers. The EBSLNs were necessarily not identified, but surgery was carefully performed so as not to damage these nerves and cricothyroid muscles. The sternohyoid muscles were preserved in most cases. The sternothyroid muscles were dissected in the case where there was an enlarged thyroid gland (estimated weight was over 200 grams), or invasion. Modified lateral neck dissection was performed in cases where there was lymph node metastases.

Pre and Post-Operative Voice Assessment

For Acoustic Voice Analysis the patients' voices were recorded using a 24-bit WAVE/MP-3 recorder (Edirol R-09, Roland, Tokyo). The sampling frequency was set at 44.1 kHz. A microphone was set at a distance of approximately 20 cm from the mouth. The patients were asked to pronounce the sustain vowel "a" at their self-selected comfortable pitch and intensity. All samples wererecorded in a sound-proof room. Praat (17) was used for acoustic voice analysis. A middle stationary segment with a length of 2.5 seconds was chosen for analysis of fundamental frequency (F0), the lowest vibration rate of vocal folds, jitter, shimmer, noise-to-harmonics ratio (NHR). Maximum phonation time (MPT) and mean air flow rate (MFR) were obtained by the sustained vowel "a" at a comfortable pitch and intensity as long as possible, and the alternating current/direct current (AC/DC) ratio (18), that is, the vocal efficacy index, was obtained by a middle stationary segment of each sustained vowel production using Phonation Analyzer PA-1000 (MINATO Medical Science Co., LTD, OSAKA, Japan).

The Voice handicap index-10 (VHI-10), a mental assessment battery published by Rosen et al. (19), was used as mental assessment. The VHI-10 consists of 10 questions which are rated according to a five-point ordinal scale: never [0], almost never [1], sometimes [2], almost always [3], and always [4]. The total score ranges from 0 (no problem perceived) to 40 (maximum perceived disability due to voice difficulties).

Statistical Analysis

The values of each parameter, except VHI-10, were divided by their own preoperative value to demonstrate the time-related change from baseline. JMP version 8.0 (SAS Institute, Cary, NC, USA) was used for the statistical analysis. For comparison of the preoperative data with the postoperative data,Dunnett's multiple comparison test was applied. Tukey-Kramer multiple comparison test was used to compare the values among the groups at the same period. $P<0.05$ was determined as significant.

This study was approved by the ethical committees of Kuma Hospital and Kobe University Graduate School of Medicine. Informed consent was obtained from all the participants of this study.

RESULTS

Impact of Thyroidectomy on the Quality of Voice

To investigate the impact of thyroidectomy and neck dissection on the quality of voice, we first analyzed the quality of voice of the patients who had TT (n=38) or LO (n=55), who did not have ND, measuring the following parameters: VHI-10, AC/DC, F0, MPT, MFR, jitter, shimmer, and NHR.

Despite the significant changes in the several objective parameters (see below), the values of VHI-10 were not significantly different among the patients who had TT or LO, or the controls at any postoperative period. Also, no significant difference was observed in each group before and at any postoperative period (Fig. 1-a). Values of AC/DC and F0 were not significantly different among the patients with TT, LO, and control at any postoperative period. Also, no significant difference was observed in each group before and at any postoperative period (Fig. 1-b, 1-c). Immediately after surgery, a significant decrease of the MPT (P=0.003, Fig.1-d) was observed in comparison with the preoperative values in the patients who had TT. In comparison with the patients who had LO, immediately after surgery the MPT was significantly shorter (P=0.0004, Fig.1-d), whereas the MFR (P=0.004, Fig.1-e) was significantly higher in the patients who had TT. Comparing the control group with the patients who had TT or LO, the MFR of patients having LO was significantly lower than that of the control group (P=0.02, Fig.1-e). These differences gradually decreased and were not present at one month after the surgery.

Immediately after the surgery, significant increases of jitter (P=0.0002, Fig.1-f) andshimmer (P=0.02, Fig.1-g) were observed in comparison with the preoperative values in the patients who had TT. Comparing the control group with the patients who had TT or LO, jitter (P=0.03, Fig.1-f) in the patients who had TT was significantly higher than in control patients. Similarly, immediately after the surgery, significant increases of the NHR (P=0.001, Fig.1-h) were observed in comparison with the preoperative values in the patients who had TT. In comparison with patients who had LO, the NHR values (P=0.03, Fig.1-h) were significantly higher in the patients who had TT. Comparing the control group with the patients having TT or LO, the NHR values (P=0.04, Fig.1-h) of the patients

with TT were significantly higher than those of control patients. These differences gradually decreased and were not present one month after surgery.

Impact of Neck Dissection on the Quality of Voice

To evaluate the impact of neck dissection on the postoperative quality of voice, we compared the patients who had ND (n=17) to the patients who did not have ND (n=38). All patients in this analysis had total thyroidectomy. Immediately after the surgery, the MPT was significantly longer in the patients who had simultaneously ND in comparison with the patients who did not have ND (P=0.004, Fig. 2-d). This difference gradually decreased and was not present one month after surgery. No other significant differences were observed between the patients who had ND and the patients who did not have ND.

Impact of Intubation on Quality of Voice

The average intubation time of the patients who had TT was significantly longer than that of the patients who had LO (TT: 110.1 min.; LO: 76.5 min.; t-test; P=0.0009). The average intubation time of the subjects in the control group was even longer than that of the patients who had TT and ND (226 min. vs 192.4 min., not significant). Despite the significant longer intubation time of control patient (Tukey-Kramer multiple comparison test, TT vs control: P<0.0001; LO vs control: P<0.0001), the values for F0, MPT, jitter, shimmer, and NHR of the control patients were better than those of the patients who had TT or LO (Fig. 1).

DISCUSSION

The main goal of this study was to clarify the mechanism of the voice dysfunction in patients who had surgical treatment for thyroid cancer without apparent injury of the RLN or EBSLN. For this purpose, we analyzed the quality of voice of the patients who had surgical treatment for thyroid cancer according to the types of surgical treatment for thyroid and cervical lymph nodes. The major findings were: (a) several voice parameters in the patients who had TT deteriorated significantly immediately after thyroid surgery; (b) these changes recovered within 1 month; and (c) neck dissection might interfere with the decrease of the

MPT in the patients who had TT.

Several researchers investigated the impact of thyroidectomy on the quality of voice (9) (12) (15) (16) and concluded that there was no significant difference in the quality of voice according to the types of surgical procedure for thyroid cancer. The most probable reason for the difference between these studies and our study might be the sample size, because the number of patients in most of these studies was limited. The difference between Stojadinovic's study (16) and ours might come from the statistical procedures. We used the values of postoperative data divided by their own preoperative data for analysis in order to eliminate the effect of differences among individuals.

The VHI-10 is a mental assessment battery published by Rosen et al. (19), which is a shortened version of the Voice Handicap Index (VHI) published by Jacobson (20). Irrespective of the diagnosis, the correlation between the VHI and the VHI-10 was greater than 0.90 (P=0.01) (19). In the present study, despite the significant changes in the several objective parameters, values of the VHI-10 were not significantly different among the patients who had TT or LO, or during the postoperative periods of each patient group. These results indicate that subjective changes in voice after thyroidectomy were so minimal that the patients did not recognize the differences, as long as the RLN and the EBSLN were anatomically preserved by the well-experienced surgeons and no apparent recurrent palsy or subjective changes in the vocal cord were observed on the postoperative endoscopic examination.

In the present series, the F0 values were also not significantly different among the patients who had TT, LO, or the controls, or during the postoperative periods of each patient group or between the patients who had or who did not haven ND. The F0 is the lowest vibration rate of vocal folds and is influenced by the length, size, and tension of the vocal folds. Movement disorder of the cricothyroid muscle and laryngotracheal fixation by scar-impairing vertical movement lead to a decrease of F0 (5). Thus, no significant change of F0 in this series indicated that the EBSLN and cricothyroid muscles were not damaged during the surgical treatment for thyroid cancer in all subjects in this series.

The AC/DC (alternating current/direct current) ratio (18) is the vocal efficacy index reflecting the difference between modulated AC flow

and unmodulated DC flow (21). In cases of glottal closure insufficiency, AC/DC is considerably reduced due to the decrease of modulated AC flow (22). The MPT is a measure of the ability to regulate ventilator and laryngeal systems for voice production independent of a frequency or intensity target (16). The MFR is the average flow rate of air through the vocal folds and is measured in liters/second. In cases of vocal dysfunction or laryngeal pathology, a decrease of MPT and an increase of MFR are predicted. In the present study, the MPT was significantly lower and the MFR was significantly higher in the patients who had TT immediately after the surgery, comparing with the preoperative status of the patients having LO or the control patients. Although no significant differences were observed in AC/DC ratios, these results suggest insufficient glottic closure, especially in the patients who had TT.

A possible explanation for these changes are (a) slight and transient damage of the RLN, EBSLN, and/or cricothyroid muscle, or (b) vocal cord stiffness due to inflammation and edema (10, 11, 23). Indeed, total thyroidectomy has a higher potential to affect these nerves and muscles than thyroid lobectomy. Because the F0 was not significantly different in all the patients in the present study as mentioned above, the possibilities of injury to the EBSLN and/or the cricothyroid muscles were considered minimal. While noapparent vocal fold palsy was observed on the postoperative endoscopic examination in the present series, partial RLN dysfunction may be missed by standard endoscopic examination. Thus, the greater changes in the MPT and the MFR in the patients who had TT suggest that total surgical thyroidectomy has a possibility to induce slight and transient nerve conduction disorders which might result in a slight glottal closure insufficiency. However, postoperative cricothyroid muscle EMG should be performed to draw a definitive conclusion since cricothyroid muscle EMG is the only method to provide objective information as to the functioning of the external branch of the superior laryngeal nerve (24).

Vocal cord stiffness due to inflammation and edema after surgery might be also responsible for these results. The surgical area in patients who had TT is obviously wider than in patients who had LO. Thus, immediately after surgery, venous return and/or lymphatic drainage should be damaged more severely, and greater vocal cord stiffness might tend to

occur, in patients who had TT than in patients who had LO. Rigid vocal cords might shorten the glottal closure time and demand redundant air flows during phonation, causing irregular variation of frequency and peak amplitude.

Jitter is the pitch perturbation quotient and shimmer is the amplitude perturbation quotient. The NHR is calculated as the ratio of noise and harmonics components. Simply speaking, jitter, shimmer, and the NHR indicate irregular frequency, irregular amplitude, and increasing noise component of voice, respectively (25). Thus, a significant deterioration of these parameters in the patients who had TT compared with patients who had LO, as shown above, also suggest that thyroidectomy spontaneously causes mucosal stiffness of the vocal cord.

Few studies discuss the influence of neck dissection on voice after thyroidectomy. Van Lierde et al. (9) reported the possibility that slight modifications of the vascular supply and/or disturbance of venous drainage of the larynx promote postoperative voice alteration. Storper (26) reported severe laryngeal edema secondary to a circulation disturbance. Based on these reports, we assumed that neck dissection during thyroidectomy might influence postoperative voice parameters. In the present study there was a significant difference in the MPT between patients having ND and those not having ND. As expected, the MPT immediately after surgery of patients who had ND was significantly longer than that of patients who did not have ND. The difference gradually decreased in the month after surgery. Laryngeal edema, due to disturbance in venous and lymphatic drainage after neck dissection, might fill in a slight glottal closure insufficiency caused by the subclinical transient recurrent laryngeal nerve conduction disorders related to total thyroidectomy.

Another explanation for the deteriorated subjective parameters of voice of the patients with TT and ND is the influence of longer endotracheal intubation. However, despite the significantly longer intubation time of the control group, the values of F0, MPT, jitter, shimmer and NHR of the control were better than those of the patients who had TT or LO. Peppard et al. (10) reported that 30 (6.3%) of 475 patients following general endotracheal anesthesia were found to have traumatic lesions of the larynx or hypopharynx, and 20 of 30 patients (66.7%) complained of hoarseness, but no correlation could be drawn between the injured and

uninjured groups with respect to length of intubation. Hamdan et al. (23) performed an acoustic analysis of the 35 patients who admitted for non-ear, nose and throat surgery. In this study, the MPT was increasing and the F0 became higher 24 hours after surgery, but other indexes (jitter, shimmer, NHR, and so on) did differ significantly. Beckford et al. (27) reported the voice changes of 10 gynecological patients and concluded that, although jitter increased postoperatively, no consistent difference was observed in the F0 and laryngeal endoscopy, stroboscopic laryngoscopy and EGG. On the basis of these reports and our present results, glottic contribution to postintubation vocal changes is rather minimal, and other extralaryngeal factors may be responsible.

In conclusion, we investigated the voice changes after thyroidectomy using the following parameters: VHI-10, AC/DC, F0, MPT, MFR, jitter, shimmer, and NHR.

The major findings were: (a) several voice parameters in the patients who had total thyroidectomy deteriorated significantly immediately after the surgery; (b) these changes recovered within 1 month; and (c) neck dissection might interfere with the decrease of the MPT resulting from total thyroidectomy. These voice changes might be due to slight and transient damages of the RLN, and from mucosal stiffness of the vocal cords following laryngeal edema. Laryngeal edema due to the disturbance of venous and lymphatic drainages after neck dissection might improve the decrease of MPT induced by total thyroidectomy. In our series EBSLNs and cricothyroid muscles were not considered to be damaged by surgical treatment for thyroid cancer.

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Disclosure Statement

No competing financial interests exist.

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Figure Legends

Fig 1 Time-dependent change of subjective and objective parameters of the patients with TT or LO, and control.
(a) VHI-10; (b) AC/DC; (c) F0; (d) MPT; (e) MFR; (f) jitter; (g) shimmer; (h) NHR.
TT: total thyroidectomy; LO: lobectomy; Post 1: immediate postoperation; Post 2: one-month postoperation; Post 3: three-month postoperation.
Significance level: *P<.05; **P<.01; ***P<.001.

Fig 2 Time-dependent change of subjective and objective parameters of the patients with or without neck dissection, and control.
(a) VHI-10; (b) AC/DC; (c) F0; (d) MPT; (e) MFR; (f) jitter; (g) shimmer; (h) NHR.
ND+: with neck dissection; ND-: without neck dissection; Post 1: immediate postoperation; Post 2: one-month postoperation; Post 3: three-month postoperation.
Significance level: *P<.05; **P<.01; ***P<.001.

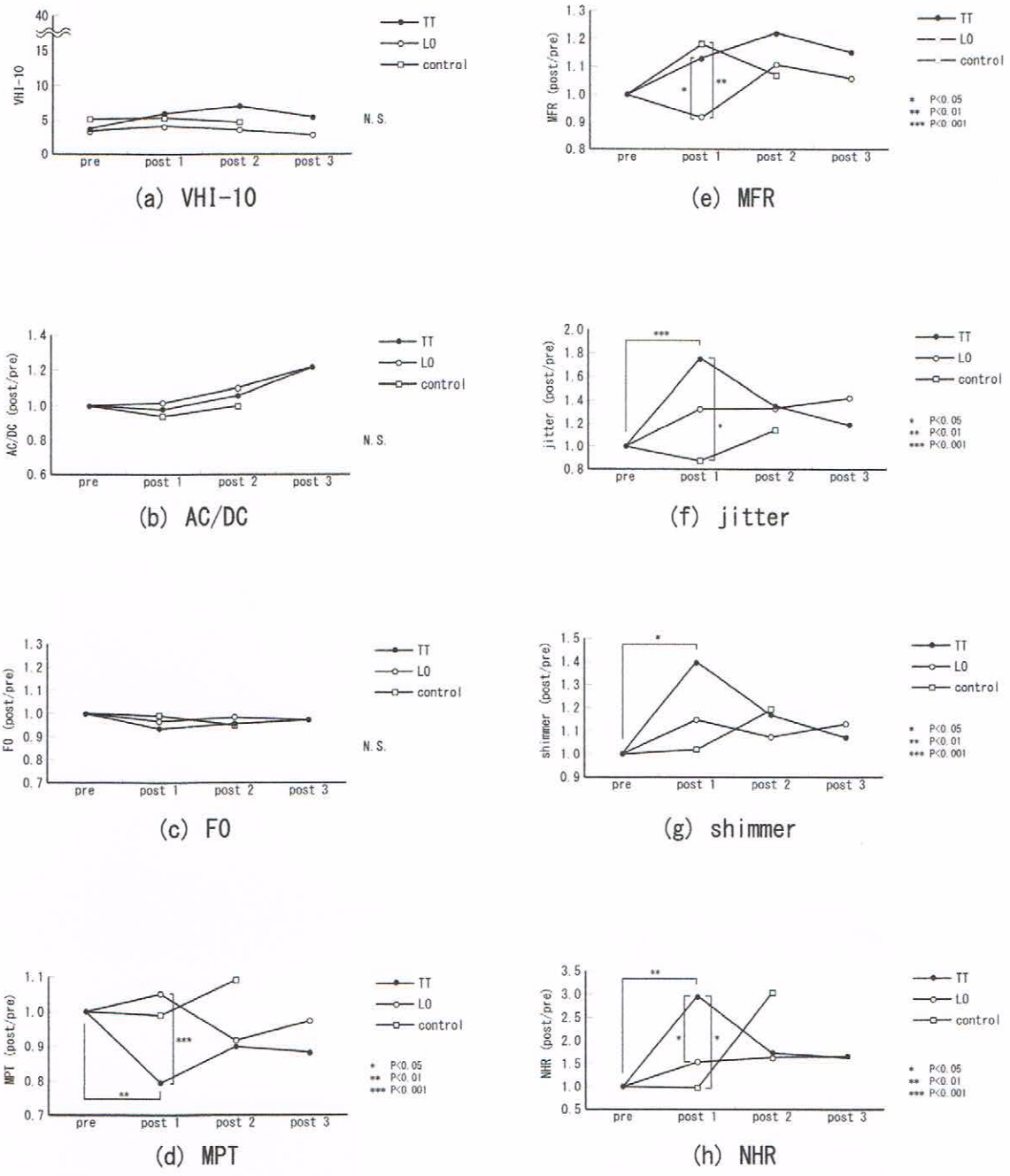
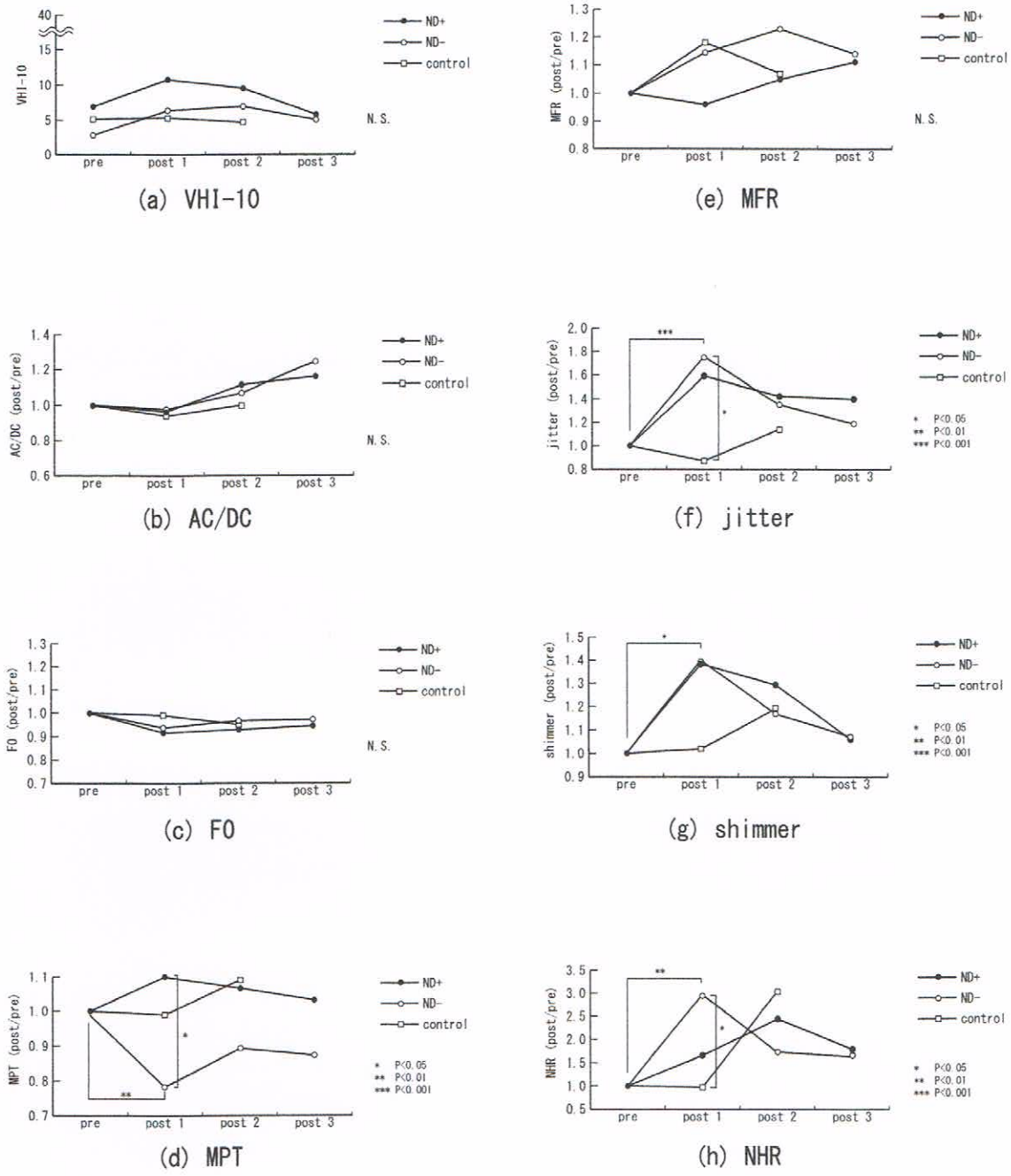


Fig 1 Time-dependent change of subjective and objective parameters of the patients with TT or LO, and control.



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