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ORIGINAL ARTICLE

# Effects of Low-Frequency Repetitive Transcranial Magnetic Stimulation on Swallowing Function and Quality of Life of Post-stroke Patients

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## Abstract

Repetitive transcranial magnetic stimulation (rTMS) is one of the non-invasive techniques, which is used to modulate cortical regions in patients with stroke. The aim of this single blind, controlled study was to investigate the effect of rTMS on swallowing function and quality of life of mono-hemispheric post-stroke patients with dysphagia. Twenty-eight patients were randomized and split between study and control group. Each group received conventional dysphagia rehabilitation 3 days a week for 4 weeks, and study group also received 1 Hz rTMS to unaffected hemisphere in the final week. The descriptive information was noted. The clinical and radiological swallowing evaluation and quality of life assessment have been performed at four different times including before and after the treatment, 1 month and 3 months after the treatment. At baseline, no significant differences were observed between groups in terms of demographic and clinical features ($p > 0.05$). Swallowing function and quality of life of the patients were statistically improved in both groups towards the third month ($p < 0.05$). Swallowing function was comparable between two groups. However, a significant improvement was observed on appetite, fear of eating, and mental health parameters of quality of life assessment in the study group compared to the control group ($p < 0.05$). In conclusion, despite positive changes in some aspects of quality of life, rTMS did not enhance the swallowing function when compared conventional dysphagia rehabilitation. Therefore, the application of 1 Hz rTMS should be reconsidered to improve swallowing function in the chronic period.

**Keywords** Stroke · Deglutition · Repetitive transcranial magnetic stimulation · Deglutition disorders · Quality of life

## Introduction

Oropharyngeal dysphagia is a common finding in patients with stroke. Dysphagia rehabilitation after stroke is patient specific, including oropharyngeal exercises, expiratory muscle training, sensory stimulation techniques, and compensatory strategies [1]. Recent studies have been conducted about enhancing swallowing function by increasing the cortical neuroplasticity through neurostimulation techniques [2]. Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive technique used to modulate the cortical regions in patients with hemispheric lesions [2]. Discrepancies exist regarding the effectiveness of rTMS on dysphagia improvement following stroke. One potential reason for this discrepancy might relate to the lack of a standard rTMS protocol regarding dysphagia rehabilitation. One of the important rTMS parameters is frequency. It has been reported that low-frequency rTMS applied to the unaffected hemisphere reduces the interhemispheric imbalance [3–5] after stroke, while high-frequency rTMS increases the motor

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excitability [6]. For example, Kim et al. [7] reported that greater improvement in swallowing function was gained in the low-frequency rTMS application to the unaffected hemisphere than high-frequency rTMS application to the affected hemisphere. Khedr et al. [8] reported that bilateral stimulation of the cortical swallowing motor area led to a greater improvement in swallowing compared to the sham group. Although all studies found significant clinical recovery from dysphagia, there is no consensus on which hemisphere should be applied, or which modulation is more effective, or optimal timing of the application after stroke [9, 10]. Namely, the use of rTMS in the treatment of dysphagia remains uncertain due to no certain treatment protocol related to the application method and its efficacy.

This study was based on the hypothesis that patients with unilateral brain damage may have an imbalance between the hemispheres, which may lead to functional neurological impairment [11]. This interhemispheric imbalance is considered to arise from altered transcallosal inhibition, and an abnormal increase in excitability of the unaffected hemisphere exerts an inhibitory effect on the affected hemisphere [12]. Low-frequency rTMS produces lasting cortical excitability inhibition when applied to the hemisphere [13]. This suggests that a reduction in inhibition facilitates the induction of plasticity via rTMS [14]. Consequently, 1 Hz rTMS was used in the current study to restore the interhemispheric balance to improve swallowing function.

The aim of this study was to identify whether applying low-frequency rTMS can enhance the effect of conventional swallowing treatment and quality of life of chronic (2–6 months) stroke patients suffering from dysphagia.

## Materials and Methods

### Subjects

This study was conducted in cooperation with Hacettepe University Faculty of Health Sciences, Physiotherapy and Rehabilitation and Hacettepe University Faculty of Medicine, Department of Neurology in Turkey. Stroke patients with dysphagia were included. The inclusion criteria were as follows: confirmed diagnosis of unilateral hemispheric stroke, oropharyngeal dysphagia continuing 2–6 months after the stroke, and no prior dysphagia rehabilitation and/or cortical stimulation therapy. The exclusion criteria were as follows: having dysphagia before the stroke, history of any other neurogenic disease, epilepsy, tumor, radiotherapy in the head and neck prior to the stroke, unstable medical condition, severe cognitive impairment, severe aphasia, contraindication to magnetic or electrical stimulation, and treatment with any cortical stimulation techniques before participating in this study. Written informed consent was obtained from all the subjects prior to inclusion, and this study was approved by the Hacettepe University Ethics Boards and Commissions. This research was performed in accordance with the Declaration of Helsinki (Protocol Number: GO13/270).

A total of 40 post-stroke dysphagic patients were assessed for eligibility, of which 30 patients matching with the inclusion/exclusion criteria were included. Thirty patients were equally randomized into two groups. Two patients in the control group gave up the treatment due to transportation problems. Therefore, the study was completed with 15 patients in the study group and 13 patients in the control group. Figure 1 shows the flow diagram of the participants.

### Experimental Design

This study was designed as a single-blind, randomized, controlled trial. The patients were divided into two groups by random sequence numbering using sealed opaque envelopes that were opened only at the time of enrollment: rTMS group (study group) and conventional dysphagia rehabilitation group (control group).

All patients received conventional dysphagia rehabilitation. Conventional dysphagia rehabilitation included oropharyngeal muscle strengthening exercises, thermal tactile stimulation, Masako and Mendelson maneuvers, vocal cord exercises, Shaker exercises, and tongue retraction exercises for 4 weeks. These exercises were performed actively under the control of a trained physical therapist 3 days per week. In addition, a home program was implemented 2 days per week. The conventional dysphagia rehabilitation took 30–45 min in the control group. All exercises were done by same physical therapist (N.Ö.Ü.). At the same time, the study group also received 1 Hz rTMS applied to the unaffected hemisphere during the final week (Fig. 2). Home program was followed using a chart in both groups.

### rTMS Application

Before performing the rTMS, the cortical motor representation area related to swallowing was determined. Thus, the potentials in the mylohyoid muscle (representing the oral swallowing musculature) were recorded using silver–silver chloride surface electrodes [15]. A Keypoint electromyography device was used for recording (Medtronic A/S, Copenhagen, Denmark). The figure eight coil (MMC-140, 33 kT/s) was first placed at the vertex of the cranium, then it was positioned 2–4 cm anteriorly and 4–6 cm laterally, and then it was moved around in this region using the MagPro stimulator (Medtronic A/S) to obtain the highest motor-evoked potential recording to locate the mylohyoid cortical area of the hemisphere. This site was marked on the scalp as the "hot spot," and we delivered the magnetic

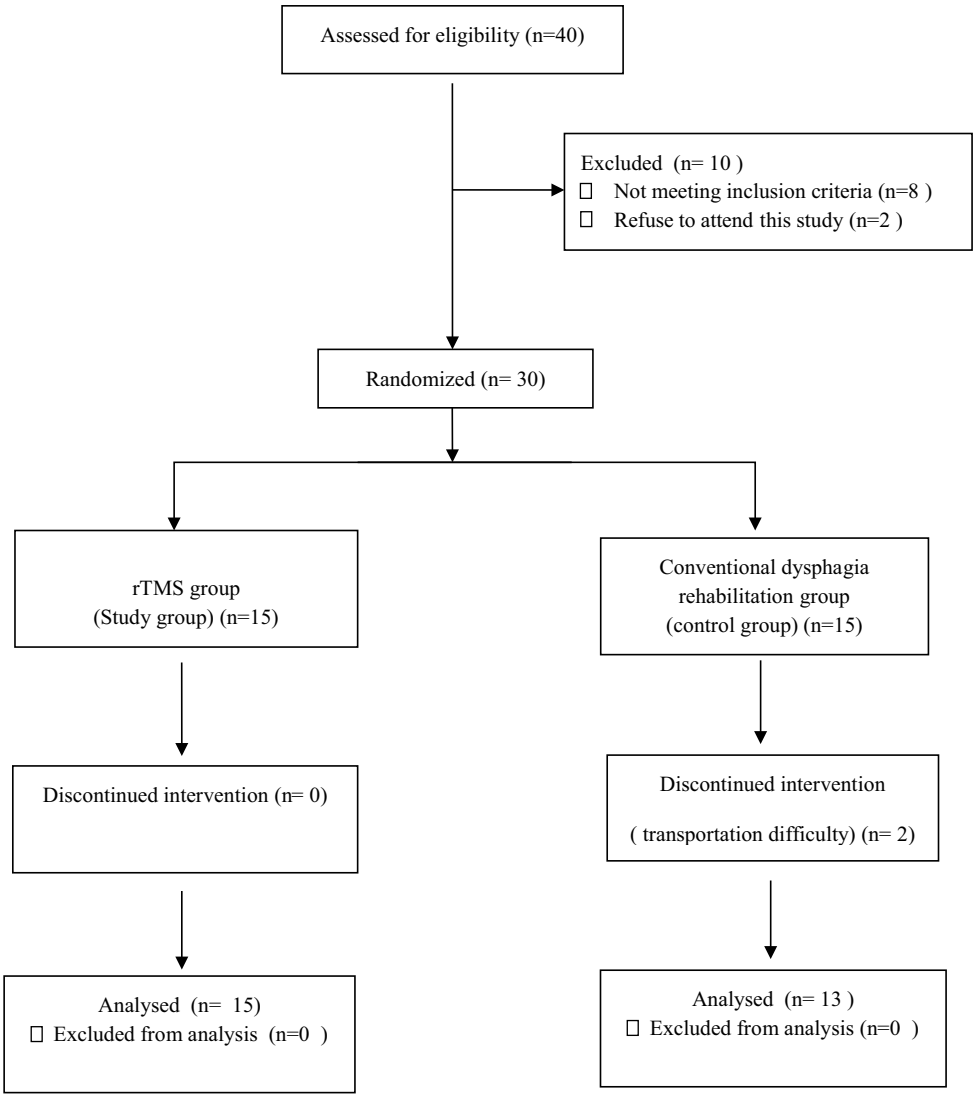


**Fig. 1** Participants' flow diagram

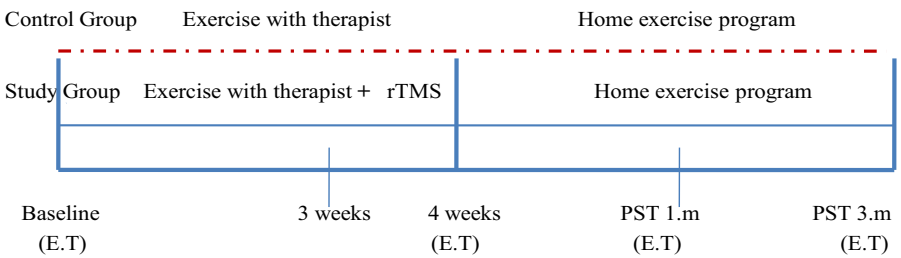


**Fig. 2** Intervention design

PST: post-treatment; ET: evaluation time; m: month; rTMS: Repetitive transcranial magnetic stimulation

stimulation to that point. Then, a single-pulse TMS was delivered to the hot spot. After induction was detected at this site, the resting motor threshold was determined as the minimal stimulus intensity creating a response > 100 μV [16]. For the treatment, each patient received 1 Hz at 90% of the resting motor threshold intensity at the hot spot for 20 min daily for five consecutive days (for a total of 1200 pulses each day). The rTMS application was done by the same neurologist at the Hacettepe University Faculty of Medicine, Neurology Department.

## Patient Safety

The patients were asked about any potential adverse events due to the magnetic stimulation, such as headaches, decreased hearing ability, convulsions, nausea, and visual and neurological changes. One patient complained of dizziness and another complained of nose bleeding. However, none of the other patients complained of any other adverse events.

## Clinical Assessment

The demographic information, including age, height, weight, comorbid diseases, time from stroke onset, and treatments were recorded from the patient files. Additionally, patients were asked about the presence of any previous pulmonary infections or weight loss. The site and type of stroke were identified in all patients before using computed tomography or magnetic resonance imaging. Observational assessments of the facial asymmetry and speech were conducted. The information about the comorbid diseases was obtained from the patients' file or a face to face interview.

The National Institutes of Health Stroke Scale (NIHSS) was used to assess the stroke severity [17]. In addition, all participants were assessed using the Turkish Barthel Index (T-BI) [18] and modified Rankin Scale (mRS) [19] prior to the interventions to compare the patients' functional abilities at the baseline in each group.

Immediately before each video fluoroscopic swallowing study (VFSS), a physical therapist who was blinded to the group allocations performed assessments of nutritional status and quality of life. All assessments were conducted by physical therapists who were blinded to the group distributions.

### Nutritional Status Assessment

The nutritional status of each patient was evaluated and noted as oral feeding, modified oral feeding, non-oral feeding, and modified enteral feeding. Total oral intake included those patients with no restrictions, modified oral feeding indicated patients requiring special preparation (i.e., thickened liquids), and non-oral feeding indicated no oral intake (i.e., percutaneous endoscopic gastrostomy or nasogastric tube feeding) [20]. Modified enteral feeding represented gradual oral feeding while the patient was still being fed enterally.

### Quality of Life Assessment

The Swallowing Quality of Life (SWAL-QOL) questionnaire was used to evaluate the quality of life of dysphagic patients. The SWAL-QOL was developed by McHorney et al. [21], and the Turkish version of the SWAL-QOL (T-SWAL-QOL) was shown to be valid and reliable in a dysphagic Turkish population [22]. The T-SWAL-QOL contains ten subscales including burden, eating duration, eating desire, food selection, communication, fear, mental health, social functioning, fatigue, and sleep. Each parameter is scored using a 5-point Likert scale. All subscales range from 0 to 100, and higher scores indicate a better quality of life with regard to dysphagia [21].

### Swallowing Function Assessments

The Swallowing Ability and Function Evaluation (SAFE) was used to quantify the clinical severity of dysphagia [23]. Immediately before each VFSS, a physical therapist who was blinded to the group allocations performed a physical examination to score the SAFE assessment.

The SAFE is used to provide a standardized, efficient, systematic, and comprehensive format for clinical evaluation of swallowing [23]. The SAFE consists of three subscales including physical examination of the oropharyngeal mechanism, and oral and pharyngeal phases of swallowing function. The parameters included in each subscale are scored from 0 to 3 (0 = severe impairment, 1 = moderate impairment, 2 = mild impairment, and 3 = within functional limits), and as the total points accumulated by a patient in a subtest. The SAFE scores can be converted to stanines and percentiles using an appendix. The severity levels were determined from the stanines, and they indicated the degree of the swallowing function problem in each subscale. Based on the score, the stanines were graded from 1 to 9. Stanines of 8 or 9 indicated that the individual was within normal limits. Stanines of 6 or 7 indicated that the individual had a mild problem. Stanines 3–5 indicated that the individual had a moderate problem. Stanines of 1 or 2 indicated that the individual had a severe problem.

## VFSS

A VFSS was performed to evaluate the swallowing function of each patient. The VFSS is the gold standard for evaluating swallowing physiology [24], and it is commonly utilized in clinical settings [25]. In this study, the VFSS were performed in all subjects in the fluoroscopic laboratory using the same protocol. While the patient was seated comfortably in a chair, the VFSS was performed to obtain lateral images of the oral cavity, pharynx, larynx, and upper esophagus during deglutition. These images were obtained following the oral administration of 1, 3, 5, 10, and 20 ml for the liquid barium test, 3, 5, and 10 ml for the semisolid barium test, and a biscuit for the solid barium test. All consistencies and materials were standardized. The capture rate was 30 frames per second. The recorded images were analyzed during and

after the test by individuals who were blinded to the patient groups. In our statistical analysis, 5 ml of the liquid and semisolid was used as a reference quantity, which was the optimal amount for monitoring the physiological events that occur during swallowing. In addition, the position of the bolus in the mouth could easily be seen in 5 ml bolus. All the procedures were recorded on a digital video file. Based on the VFSS findings, the Penetration–Aspiration Scale (PAS), and the oral parameters, including the tongue retraction, hyolaryngeal elevation, delayed swallowing reflex, and residue, were scored according to the average values by the agreement of two-blinded physical therapists who took the worst score of all the swallows.

The PAS is used to define the penetration and aspiration severity. It is an 8-point clinical scale used for rating penetration and aspiration, conveying the depth of the airway invasion, and determining whether the material entering the airway is expelled. One point indicates no penetration or aspiration, 2–5 points indicate penetration, and 6–8 points indicate aspiration [26, 27].

Several oral parameters, including tongue retraction, hyolaryngeal elevation, delayed swallowing reflex, and residue (oral cavity, vallecula, pharyngeal wall, and pyriform sinus) after swallowing were also evaluated. These parameters were scored between 0 and 3 according to the VFSS images. A score of 0 demonstrates normal function, 1 indicates a mild problem, 2 indicates a moderate problem, and 3 indicates a severe problem. For residue scores, 0 means no residue, 1 means mild residue (1–5%), 2 means moderate residue (5–10%), and 3 means severe residue (10% or more) [28].

### Follow-Up and Outcome Measures

All participants were evaluated at four different times: before and after the treatment, and 1 month and 3 months after the treatment. The primary outcome was the PAS score, while the secondary outcomes included the other dysphagia rating scales, as well as the nutritional status and quality of life assessment.

### Statistical Analysis

Power analysis was estimated that at least 11 individuals for each group had to be included in this study for 80% power with 5% type I error level to detect a minimum clinically significant difference of 2 point for PAS score, when the average value of PAS in experimental group is 3.41, with a standard deviation of 2.32 mm [29].

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA). The data were assessed using descriptive statistics, and they were shown as the mean ± standard deviation for the numerical measurements and numbers. Percentages were used for the qualitative measurements. The variables were evaluated using the Shapiro–Wilk test to determine whether or not they were normally distributed. As a result of the test, the data were not normally distributed. The differences through time were evaluated using the nonparametric Friedman test for the comparisons among the pretreatment, immediate post-treatment, post-treatment 1st month, and post-treatment 3rd month values in the study and control groups. The assessment times, which were significantly different, were determined using the Dunn's multiple comparison tests, after obtaining the Friedman test results. At the same time, the Mann–Whitney *U* test was performed in each category between the groups for every assessment period. A $p$ value $< 0.05$ was considered to be significant.

## Results

The mean age of the study group was $67.80 \pm 11.88$ years (nine males and six females), and the mean age of the control group was $69.31 \pm 12.89$ years (seven males and six females). At baseline, there were no significant differences between groups in terms of the demographic and clinical characteristics, including age, sex, stroke type, affected hemisphere, facial asymmetry, duration of stroke onset, T-BI score, mRS score, NIHSS score, PAS score, and T-SWAL-QOL score (Table 1).

The nutritional status of the patients is shown in Table 2. No difference was found between groups in terms of the pretreatment nutritional status ($p = 0.138$). The nutritional statuses of the patients changed to oral feeding in both groups during the 3rd month after treatment, and no differences were observed between groups ($p = 0.999$).

The SAFE sub-parameters, including physical oromotor function, and oral and pharyngeal phase scores, showed statistically significant improvements in both groups ($p = 0.000$). The improvements were statistically significant in both groups from baseline to 1 month after the treatment and from baseline to 3 months after the treatment. However, when the SAFE outcomes were compared between groups at each evaluation time, no statistically significant differences were found ($p > 0.05$) (Table 3).

### VFSS Outcomes

The PAS scores of the liquid and semisolid swallowing decreased beginning from post-treatment to 1 month in both groups ($p < 0.05$). No significant differences were found between groups with regard to the post-treatment, and 1-month and 3-month after treatment scores ($p > 0.05$) (Table 3).

**Table 1** Demographic and clinical characteristics of patients

| | Study group | | Control group | | *p* |
|---|---|---|---|---|---|
| | *N* | % | *N* | % | |
| Sex | | | | | |
| Female | 6 | 40 | 6 | 46 | 0.743 |
| Male | 9 | 60 | 7 | 54 | |
| Type of stroke | | | | | |
| Hemorrhage | 1 | 7 | 1 | 8 | 0.916 |
| Ischemia | 14 | 93 | 12 | 92 | |
| Affected hemisphere | | | | | |
| Right | 8 | 53 | 6 | 46 | 0.705 |
| Left | 7 | 47 | 7 | 54 | |
| Facial asymmetry | | | | | |
| Right | 3 | 20 | 3 | 23 | 0.743 |
| Left | 3 | 20 | 1 | 28 | |
| History of pulmonary infection | | | | | |
| Present | 6 | 40 | 6 | 46 | 0.743 |
| Speech assessment | | | | | |
| Normal | 11 | 73 | 6 | 46 | 0.080 |
| Aphasia | 4 | 27 | 3 | 23 | |
| Dysarthria | 0 | 0 | 4 | 31 | |
| | $X \pm SD$ | | $X \pm SD$ | | *p* |
| Age (years) | $67.80 \pm 11.88$ | | $69.31 \pm 12.89$ | | 0.892 |
| NIHSS | $7.80 \pm 3.18$ | | $7.69 \pm 3.32$ | | 0.999 |
| Duration of onset of stroke (days) | $105.93 \pm 49.02$ | | $101.38 \pm 42.06$ | | 0.982 |
| Weight loss post stroke dysphagia (kg) | $9.47 \pm 6.18$ | | $6.85 \pm 4.20$ | | 0.467 |
| Barthel Index | $54.53 \pm 30.69$ | | $58.08 \pm 28.77$ | | 0.751 |
| PAS (baseline) liquid | $6.87 \pm 1.45$ | | $7.15 \pm 1.34$ | | 0.650 |
| PAS (baseline) semi-solid | $3.27 \pm 2.84$ | | $4.54 \pm 3.15$ | | 0.294 |
| | Median (min–max) | | Median (min–max) | | *p* |
| mRS | 3(1–4) | | 3(1–4) | | 0.856 |

*PAS* penetration-aspiration Scale, *kg* kilogram

$p < 0.05$

**Table 2** Nutritional status of patients

| Patients' dietary patterns | Study group | | | | | Control group | | | | | *p* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Oral | NG | PEG | ME | MO | Oral | NG | PEG | ME | MO | |
| Pre-T (*n*/%) | 0/0 | 2/13 | 5/33 | 1/7 | 7/47 | 3/23 | 1/8 | 2/15 | 3/23 | 4/31 | 0.138 |
| Post-T(*n*/%) | 6/40 | 1/7 | 3/20 | 2/13 | 3/20 | 6/46 | 1/8 | 1/8 | 4/30 | 1/8 | 0.271 |
| 1 Month (*n*/%) | 9/60 | 0/0 | 2/13 | 1/7 | 3/20 | 9/69 | 0/0 | 1/8 | 2/15 | 1/8 | 0.758 |
| 3 Month (*n*/%) | 10/67 | 0/0 | 1/7 | 2/13 | 2/13 | 9/68 | 0/0 | 0/0 | 2/16 | 2/16 | 0.999 |

*M.E* modified enteral, *M.O* modified oral, *Pre-T* pre-treatment, *Post-T* post-treatment

$p < 0.05$

Improvements in the triggering of the swallowing reflex and residue after swallowing were obtained during the post-treatment evaluation in the study group, while these improvements were obtained during the post-treatment 1 month evaluation in the control group. There were significant differences in the hyolaryngeal elevation and tongue

**Table 3** Clinical and instrumental swallowing results of patients

| Variables | Pre-treatment | Post treatment | Post treatment 1 month | Post treatment 3 month | Overall | Pairwise comparisons of the time points | | |
|---|---|---|---|---|---|---|---|---|
| | $X \pm SD$ | $X \pm SD$ | $X \pm SD$ | $X \pm SD$ | Intra groups | (Pretrt–posttrt) | (Pretrt–posttr1 m) | (Pretrt–posttrt3 m) |
| Study | | | | | | | | |
| Safe | | | | | | | | |
| PE | 5.20 ± 1.14 | 6.27 ± 1.58 | 7.20 ± 1.52 | 7.53 ± 1.88 | 0.000* | 0.463 | 0.001* | 0.000* |
| OP | 5.53 ± 2.03 | 7.00 ± 2.33 | 7.60 ± 1.68 | 8.20 ± 1.20 | 0.000* | 0.097 | 0.004* | 0.000* |
| PP | 3.47 ± 1.68 | 4.93 ± 1.71 | 6.20 ± 2.27 | 6.73 ± 2.31 | 0.000* | 0.463 | 0.001* | 0.000* |
| VFSS | | | | | | | | |
| PAS liquid | 6.87 ± 1.45 | 4.00 ± 2.92 | 3.53 ± 3.18 | 3.60 ± 3.24 | 0.001* | 0.142 | **0.035*** | 0.053 |
| PAS semi-solid | 3.27 ± 2.84 | 2.60 ± 2.84 | 2.00 ± 2.26 | 1.73 ± 1.58 | 0.000* | 0.099 | 0.286 | 0.097 |
| Tongue Retraction | 1.07 ± 1.03 | 0.47 ± 0.64 | 0.20 ± 0.41 | 0.13 ± 0.35 | 0.000* | 0.623 | 0.053 | 0.028* |
| Delayed Swallowing Reflex | 2.00 ± 0.75 | 0.93 ± 0.79 | 0.80 ± 0.86 | 0.40 ± 0.63 | 0.000* | 0.028* | 0.007* | 0.000* |
| Hyolaryngeal elevation | 1.80 ± 1.14 | 1.13 ± 1.12 | 0.80 ± 0.94 | 0.60 ± 0.82 | 0.000* | 0.538 | 0.022 | 0.002* |
| Residue | 4.47 ± 1.80 | 2.20 ± 2.27 | 1.53 ± 1.76 | 1.33 ± 1.75 | 0.000* | 0.011* | 0.001* | 0.000* |
| Control group | | | | | | | | |
| Safe | | | | | | | | |
| PE | 3.85 ± 2.11 | 5.85 ± 2.26 | 6.92 ± 2.17 | 7.15 ± 2.03 | 0.000* | 0.201 | 0.000* | **0.000*** |
| OP | 4.31 ± 2.92 | 6.23 ± 2.35 | 7.46 ± 2.10 | 7.46 ± 2.06 | 0.000* | 0.410 | 0.000* | 0.000* |
| PP | 3.15 ± 1.67 | 5.23 ± 1.69 | 6.69 ± 1.65 | 6.69 ± 1.35 | 0.000* | 0.201 | 0.000* | 0.000* |
| VFSS | | | | | | | | |
| PAS liquid | 7.15 ± 1.34 | 4.77 ± 2.89 | 3.69 ± 2.84 | 3.62 ± 2.90 | 0.000* | 0.090 | 0.001* | 0.000* |
| PAS semi-solid | 4.54 ± 3.15 | 2.23 ± 2.20 | 1.69 ± 1.31 | 1.54 ± 1.12 | 0.000* | 0.242 | 0.037* | 0.030* |
| Tongue Retraction | 1.46 ± 1.05 | 0.92 ± 1.03 | 0.46 ± 0.77 | 0.38 ± 0.65 | 0.000* | 0.999 | 0.047* | 0.018* |
| Delayed swallowing Reflex | 2.31 ± 0.75 | 1.31 ± 1.03 | 1.00 ± 0.91 | 0.54 ± 0.66 | 0.000* | 0.059 | 0.004* | 0.000* |
| Hyolaryngeal elevation | 2.08 ± 0.64 | 1.08 ± 0.86 | 1.00 ± 0.91 | 0.77 ± 0.83 | 0.000* | 0.073 | 0.037* | 0.002* |
| Residue | 5.92 ± 4.05 | 3.46 ± 3.73 | 2.54 ± 2.33 | 1.85 ± 2.23 | 0.000* | 0.242 | 0.023* | 0.001* |

| Pre-treatment | Post treatment | Post treatment | Post treatment 1 month | Post treatment 3 month |
|---|---|---|---|---|
| PE | 0.079 | 0.856 | 0.999 | 0.555 |
| OP | 0.338 | 0.316 | 0.820 | 0.316 |
| PP | 0.650 | 0.683 | 0.856 | 0.617 |
| PAS liquid | 0.650 | 0.683 | 0.999 | 0.963 |
| PAS semi-solid | 0.294 | 0.891 | 0.891 | 0.856 |
| Tongue retraction | 0.362 | 0.316 | 0.555 | 0.413 |
| Delayed swallowing reflex | 0.316 | 0.338 | 0.586 | 0.586 |
| Hyolaryngeal elevation | 0.617 | 0.999 | 0.551 | 0.586 |
| Residue | 0.316 | 0.751 | 0.273 | 0.650 |

*SAFE* swallowing ability and function evaluation test, *VFSS* videoflouroscopy Swallowing Study, *SD* standard deviation, *PE* physical examination, *OP* oral phases, *PP* pharyngeal phases, *pretrt* pre-treatment, *posttrt* post-treatment, *m* month, *PAS* Penetration-Aspiration Scale

*$p < 0.05$

retraction 1 month after treatment in the control group, while they were shown 3 months after treatment in the study group. Nevertheless, no significant differences were found between groups in terms of all the parameters at each evaluation time ($p > 0.05$) (Table 3).

### T-SWAL-QOL Outcomes

Significant differences were determined in general burden, eating duration, eating desire, fear of eating, mental health, and social function parameters in the study group ($p = 0.001$, $p = 0.001$, $p = 0.021$, $p = 0.004$, $p = 0.000$, and $p = 0.042$, respectively) towards the 3rd month. In addition, significant differences were determined in the burden and fear of eating parameters between pretreatment and the post-treatment 3rd month ($p = 0.035$, Table 4a), and in the mental health parameter between pretreatment and the post-treatment 3rd month ($p = 0.009$) and between post-treatment and the post-treatment 3rd month ($p = 0.002$, Table 4a, b). In the control group, significant differences were only found in the burden and mental health parameters ($p = 0.03$ and $p = 0.05$, respectively) towards the 3rd month. Moreover, when the quality of life outcomes were compared at each evaluation time between both groups, significant differences were found in the eating desire and fear of eating parameters in the post-treatment 1st month assessment ($p = 0.006$ and $p = 0.012$, respectively) and in the mental health parameter in the post-treatment 3rd month assessment ($p = 0.007$). These differences were determined based on the study group.

## Discussion

This study was designed to investigate the effects of 1 Hz rTMS on the swallowing function and swallowing-related quality of life in stroke patients with dysphagia. Our study revealed that rTMS combined with swallowing exercises did not create any differences in the swallowing function when compared to the swallowing exercises alone. However, the quality of life was improved in the group undergoing rTMS combined with the swallowing exercises.

There was no difference between the effects of swallowing exercises and 1 Hz rTMS combined swallowing exercises on swallowing function in 2–6 months after stroke. Our results were not in agreement with previous studies that have reported positive effects of 1 Hz rTMS on swallowing function in different time from post-stroke [7, 10, 30, 31]. However, differently from our study, most of these studies included dysphagic patients in both acute and subacute stages. Swallowing function in these patients might also have improved because of spontaneous recovery [7, 30, 31]. Only one study [10] involved patients with chronic phase, but there was no sham and control group in this study. Due to inconsistency in the results, it is not clear that adding low-frequency rTMS has beneficial effects of the swallowing function in chronic stage.

In our study, all evaluations of swallowing function determined that there were significant improvements in each groups, but there were no differences between groups. The most significant considerable effects of the 1 Hz rTMS application on the swallowing function showed that delayed swallowing reflex and residue scores improved immediately after the treatment. In the control group, significant improvement was ensured at the 1st month after the treatment with the same parameters. This situation indicates the positive effects of rTMS in the early period. Verin and Leroi [10] indicated that there was a reduction in the residue score after a 1 Hz rTMS application in their pilot study of dysphagia in chronic-phase post-stroke patients. Park et al. [29] indicated that a 5 Hz rTMS application in patients with dysphagia that persisted over 1 month after a stroke did not create any differences in the swallowing reflex and the pharyngeal transit time; however, there were reductions in the PAS and residue scores. No alterations in any of the parameters were indicated in the sham group. Although the application methods varied in the other studies, we believe that the rTMS application reduced the residue score and, thereby had a positive effect on the dysphagia treatment.

In our study, the changes in swallowing function were evaluated using the PAS during the VFSS. Two different viscosities (liquid and semisolid) were used for the VFSS. With regard to the PAS scores for liquids in both groups, significant improvement was seen in the first month after treatment; however, there were no differences between groups. In the literature, there is no research similar to the present study. There were studies comparing 1 Hz rTMS with other treatment modalities [30] or 3 Hz rTMS [31], and there was one study that investigated the effects of 1 Hz rTMS on swallowing function [10]. For these reasons, the results of these previous studies could not be simply compared. In their study, Verin and Leroi [10] applied 1 Hz rTMS in seven individuals who had dysphagia for more than 6 months. They suggested that liquid aspiration score decreased significantly; however, there was no sham or control group, and they could not explain whether this recovery arose from the cortical stimulation or whether there was an effect of the placebo stimulation. In the current study, we could not demonstrate the superiority of the transcallosal inhibition effect of applying 1 Hz rTMS to the unaffected hemisphere in chronic post-stroke patients (2–6 months) due to the fact that there were no significant correlations between swallowing function and clinical and instrumental evaluations. The small number of patients in this study could be the reason for these inconsistent results.

Few studies have compared the effects of high-frequency- versus low-frequency stimulation on post-stroke dysphagic

**Table 4** Life quality assessment of patients in pre-treatment, post treatment, post treatment 1st month, post treatment 3rd month

| T-SWAL-QOL | Study group | Control group | Inter groups | |
|---|---|---|---|---|
| | $X \pm SD$ | $X \pm SD$ | $z$ | $p$ |
| General burden | | | | |
| Pre-treatment | 27.53 ± 32.18 | 32.92 ± 30.92 | 0.640 | 0.555 |
| Post-treatment | 29.40 ± 31.07 | 38.54 ± 24.75 | 0.962 | 0.362 |
| Post-treatment 1st month | 46.87 ± 31.61 | 44.31 ± 28.82 | − 0.281 | 0.785 |
| Post-treatment 3rd month | 50.13 ± 35.38[a] | 49.15 ± 30.41 | − 0.093 | 0.927 |
| Intra-groups $p$ value | 0.001* | 0.030* | | |
| Food selection | | | | |
| Pre-treatment | 61.80 ± 31.80 | 45.31 ± 36.99 | − 1.292 | 0.217 |
| Post-treatment | 79.27 ± 33.60 | 55.85 ± 35.23 | − 1.875 | 0.072 |
| Post-treatment 1st month | 74.27 ± 38.07 | 54.92 ± 30.02 | − 1.764 | 0.088 |
| Post-treatment 3rd month | 77.60 ± 31.57 | 58.77 ± 34.80 | − 1.694 | 0.107 |
| Intra-groups $p$ value | 0.299 | 0.201 | | |
| Eating duration | | | | |
| Pre-treatment | 51.73 ± 36.29 | 35.62 ± 29.69 | − 1.286 | 0.217 |
| Post-treatment | 54.27 ± 32.24 | 44.31 ± 38.69 | − 0.841 | 0.413 |
| Post-treatment 1st month | 74.27 ± 38.07 | 54.92 ± 30.02 | − 1.764 | 0.088 |
| Post-treatment 3rd month | 77.60 ± 31.57 | 58.77 ± 34.80 | − 1.694 | 0.107 |
| Intra-groups $p$ value | 0.001* | 0.108 | | |
| Eating desire | | | | |
| Pre-treatment | 55.60 ± 36.56 | 43.54 ± 30.47 | − 0.841 | 0.413 |
| Post-treatment | 66.73 ± 30.00 | 53.92 ± 31.78 | − 1.228 | 0.235 |
| Post-treatment 1st month | 84.53 ± 23.78 | 56.46 ± 31.11 | − 2.738 | 0.006* |
| Post-Treatment 3rd month | 80.53 ± 25.19 | 62.85 ± 30.85 | − 1.832 | 0.072 |
| Intra-groups $p$ value | 0.021* | 0.580 | | |
| Fear of eating | | | | |
| Pre-treatment | 61.40 ± 28.72 | 52.00 ± 36.20 | − 0.603 | 0.551 |
| Post-treatment | 58.27 ± 31.11 | 60.15 ± 33.39 | 0.185 | 0.856 |
| Post-treatment 1st month | 80.47 ± 25.64 | 50.46 ± 32.88 | − 2.476 | 0.012* |
| Post-treatment 3rd month | 80.53 ± 25.19[a] | 62.85 ± 30.85 | − 1.832 | 0.072 |
| Intra-groups $p$ value | 0.004* | 0.727 | | |
| Sleep | | | | |
| Pre-treatment | 41.67 ± 37.40 | 33.77 ± 34.74 | − 0.447 | 0.683 |
| Post-treatment | 45.07 ± 31.98 | 48.23 ± 26.86 | 0.328 | 0.751 |
| Post-treatment 1st month | 52.60 ± 33.11 | 52.00 ± 34.92 | − 0.141 | 0.891 |
| Post-treatment 3rd month | 53.40 ± 32.22 | 54.00 ± 32.81 | 0.000 | 0.999 |
| Intra-groups $p$ value | 0.778 | 0.185 | | |
| Fatigue | | | | |
| Pre-treatment | 40.07 ± 31.02 | 40.38 ± 30.42 | − 0.023 | 0.999 |
| Post-treatment | 53.93 ± 30.53 | 61.54 ± 25.05 | 0.464 | 0.650 |
| Post-treatment 1st month | 57.20 ± 25.97 | 63.46 ± 25.34 | 0.464 | 0.650 |
| Post-treatment 3rd month | 60.53 ± 28.22 | 58.92 ± 29.96 | − 0.209 | 0.856 |
| Intra-groups $p$ value | 0.096 | 0.257 | | |
| Communication | | | | |
| Pre-treatment | 47.67 ± 32.80 | 44.38 ± 27.37 | − 0.210 | 0.856 |
| Post-treatment | 51.07 ± 40.43 | 42.46 ± 29.63 | − 0.675 | 0.525 |
| Post-treatment 1st month | 50.93 ± 41.54 | 46.31 ± 26.76 | − 0.351 | 0.751 |
| Post-treatment 3rd month | 50.20 ± 38.71 | 57.85 ± 33.69 | 0.511 | 0.617 |
| Intra-groups $p$ value | 0.455 | 0.099 | | |

**Table 4** (continued)

| T-SWAL-QOL | Study group | Control group | Inter groups | |
|---|---|---|---|---|
| | $X \pm SD$ | $X \pm SD$ | $z$ | $p$ |
| Mental health | | | | |
| Pre-treatment | 41.33 ± 33.19 | 25.00 ± 30.61 | − 1.442 | 0.155 |
| Post-treatment | 32.00 ± 34.83 | 44.62 ± 37.88 | 0.939 | 0.362 |
| Post-treatment 1st month | 62.00 ± 40.87 | 46.15 ± 37.86 | -1.125 | 0.273 |
| Post-treatment 3rd month | 86.00 ± 26.80[a,b] | 53.08 ± 35.62 | − 2.735 | 0.007* |
| Intra-groups $p$ value | 0.000* | 0.050* | | |
| Social function | | | | |
| Pre-treatment | 41.00 ± 36.11 | 40.77 ± 34.14 | − 0.069 | 0.963 |
| Post-treatment | 38.67 ± 31.36 | 55.00 ± 32.40 | 1.411 | 0.169 |
| Post-treatment 1st month | 62.67 ± 34.94 | 49.62 ± 33.19 | − 0.810 | 0.439 |
| Post-treatment 3rd month | 70.33 ± 40.42 | 62.69 ± 33.26 | − 0.833 | 0.439 |
| Intra-groups $p$ value | 0.042* | 0.084 | | |

*SWAL-QOL* swallowing quality of life

*$p < 0.05$

[a]Different from pre-treatment $p < 0.05$

[b]Different from post treatment $p < 0.05$

patients in acute terms. Kim et al. [7] showed that only low-frequency rTMS improved dysphagia in the patients when compared to the high-frequency rTMS and sham groups. However, Du et al. [31] showed that both low frequency and high frequency rTMS applied over the swallowing motor cortex could significantly promote dysphagia recovery when compared to a sham stimulation in patients with dysphagia within 2 months after a stroke. We followed the 3-month results, as Du et al. [31], but in the study by Du et al. [31], the recovery of swallowing function was not evaluated using instrumental techniques, suggesting that their results were more subjective than ours. Lim et al. [30] followed up patients with subacute unilateral cerebral infarctions and hemorrhage in their study for comparing 1 Hz rTMS, neuromuscular electrical stimulation (NMES), and a conventional treatment group. They revealed that there was rapid improvement in the first 2 weeks in the rTMS and NMES groups; however, there were no significant differences in the changes from the initial to the 4th week evaluation among groups. They showed that changes in the functional dysphagia scale and PAS scores of the rTMS and NMES groups exhibited statistically significant differences when compared to the conventional group for 2 weeks after the baseline evaluation, but differences between the rTMS and NMES group were not statistically significant. This suggests that conventional exercises exhibited a greater treatment effect over a longer period of time than the rTMS or NMES.

The quality of life describes the general wellbeing of an individual based on daily experiences. Therefore, after a stroke, careful evaluations by dysphagia team (and creating a joint treatment plan) are significant parameters. The quality of life of individuals with dysphagia is often hampered by discomfort and anxiety while eating, and by the need for special mealtime arrangements, which may hinder social interactions during mealtimes [32]. In the literature, the effects of various rTMS applications on swallowing physiology have been investigated [33], but there are limited studies available that have investigated the effects of rTMS on the quality of life in post-stroke dysphagia [34]. This signifies the difference between this study and others that have evaluated the quality of life. Only Cheng et al. [34] found no significant treatment effects of 5 Hz rTMS on the swallowing function, tongue strength, or swallowing-related quality of life in patients with chronic post-stroke dysphagia. In our study, when dysphagia specific quality of life was evaluated separately, the eating desire, fear of eating, and mental health parameters were more significant in the study group than the control group. The differences seen in the study group suggest that the magnetic area creates a positive effect on the mood, thereby diffusing through the prefrontal cortex during the rTMS application. Moreover, in the pre-treatment assessment of the study group, there were no patients feeding orally with food consistency alterations, but one patient continued feeding enterally at the 3rd month post-treatment assessment. Therefore, we believe that the patient's dietary pattern may be a factor that can change the quality of life. We also considered the fact that although 1 Hz rTMS did not alter swallowing function, it affected the quality of life positively, and many patients prefer stimulation approaches (unlike exercise treatment), so it may have created a placebo effect. However, more

detailed studies are required to examine how these differences in the quality of life are created by rTMS. In summary, the patient's life quality may change due to multiple conditions after stroke, but it is important to evaluate the changes using a specific assessment of swallowing disorders because therapies can create alterations in the quality of life of these patients. When rTMS and conventional rehabilitation used together were compared with conventional treatment methods alone, there were no differences in terms of swallowing assessment. However, the differences created in the quality of life suggest that alternative treatment approaches should be included in the treatment protocols.

Our study did have some limitations. First, our sample size was small. Larger randomized controlled studies using rTMS in dysphagia will hopefully help to answer these questions in the literature. Most patients recover from dysphagia within a few weeks after a stroke, but there are wide discrepancies in the reported frequencies, with a dysphagia prevalence of 47% 2 to 3 weeks after the stroke onset, and a prevalence of 17% at the 2 to 4-month follow-ups [35]. While we were designating the inclusion criteria for our study, we decided to integrate those individuals with dysphagia 2–6 months after a stroke to eliminate, as far as possible, spontaneous recovery. Future studies should also investigate for which subtypes or severity of stroke this treatment is effective as well as the timing of treatment initiation from onset because there has been no standard treatment protocol for applying rTMS. In addition, for ethical reasons, we could not apply rTMS without conventional rehabilitation; therefore, we could not evaluate the effectiveness of rTMS alone or investigate the effects of rTMS on the swallowing function when only using 1 Hz. When determining the effect of rTMS on the swallowing function, study designs should include the investigation of different rTMS frequencies. Furthermore, a major limitation of the current study was that the study design did not include a sham stimulation group for rTMS, and conventional rehabilitation was used as the control group, which led to incomplete blinding. In the literature, more studies performed with sham groups are needed. Not having a sham group in our study means that we could not indicate the positive effect of rTMS. The improvement in the quality of life in the study group was more significant than in the control group, which suggests that rTMS may be included in the conventional rehabilitation approaches. However, we propose to increase the number of studies evaluating the quality of life regarding application of rTMS on swallowing function. Finally, the swallowing function at 3 months after the baseline was evaluated, but a long-term follow-up was not performed while considering the aforementioned limitations. Additional studies should be conducted in the future to supplement the results of this study.

## Conclusion

In this study, no differences were found between the combination of rTMS and conventional treatment and conventional treatment only in the swallowing function, despite the differences in the quality of life changes. These results suggest that applying 1 Hz rTMS to the unaffected hemisphere was not superior to the use of conventional therapy alone in these dysphagic patients. Therefore, in the chronic period, the application of 1 Hz rTMS should be reconsidered to improve the swallowing function.

### Compliance with Ethical Standards

**Conflict of interest** The authors declare that they have no conflicts of interest with regard to this research.

**Ethical Approval** All the procedures performed in the studies involving human participants were conducted in accordance with the ethical standards of the institutional research committee, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

**Informed Consent** Informed consent was obtained from all the individual participants included in this study.

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