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Effects of a mouth-opening intervention with remote support on adherence, the maximum interincisal opening, and mandibular function of postoperative oral cancer patients: A randomized clinical trial

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ABSTRACT

Purpose: The purpose of the study was to investigate the effects of a mouth-opening intervention for postoperative trismus and remote support provided via telephone following hospital discharge for intervention adherence in patients with oral cancer.

Methods: The study is a parallel randomized trial. Patients admitted at a general hospital for oral cancer surgery were recruited and randomly assigned to either the experimental or the active control group. Both groups underwent a 12-week intervention program, including warm compress, masticatory muscle massage, and jaw exercise. Subjects in the experimental group received additional support via telephone following hospital discharge. Data on intervention adherence maximum interincisal opening and mandibular function impairment were collected at baseline, week 4, and week 12.

Results: Sixty subjects (30 in each group) that completed the study were included in the analysis. At week 12, the intervention practice time in the experimental group was 299.67 min (95% CI: 223.44–357.89) more than that of the active control group. From baseline to week 12, the change in maximum interincisal opening was 10.30 mm (95% CI: 8.22–12.37) greater in the experimental than in the active control group. The change in mandibular function impairment score was −0.36 (95% CI: −0.44 to −0.28) greater in the experimental than in the active control group.

Conclusions: The study results support the effect of remote support via telephone for enhancing adherence to the intervention protocol, and the effect of the intervention program for alleviating trismus and mandibular function impairments in patients who receive curative surgery for oral cancer.

1. Introduction

Trismus, a restricted mouth opening, is one of the most troublesome sequela of oral cancer and its treatments (Agarwal et al., 2016; Wetzels et al., 2014). It affects various aspects of everyday life, including speaking, laughing, chewing, swallowing, and retaining oral hygiene (Gellrich et al., 2015; Peisker et al., 2016). The maximum interincisal opening (MIO) < 35 mm is a well-accepted criterion for trismus (Dijkstra et al., 2006; Kamstra et al., 2017). Studies found trismus occurred in 4%–50% of oral cancer patients at the time of diagnosis, in 44%–86% of patients shortly after surgery and radiotherapy, and in 31%–65% of oral cancer patients six months after treatments (Agarwal et al., 2016; Scott et al., 2011; Wetzels et al., 2014).

Currently, there is no clinical guideline for treating oncologic therapy related trismus. A number of stretching techniques and jaw mobilizing strategies exist, but their effects for oral cancer related trismus are inconclusive. In a systemic review including four studies (n = 240), Scherpenhuizen et al. (2015) concluded that exercise therapy with a jaw-mobilizing device versus no exercise produces better therapeutic effects for radiotherapy-induced trismus in head and neck cancer (HNC) patients. The improvements of MIO in the intervention groups ranged from 4.4 to 13.6 mm. However, generalizability of the

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findings are limited by the small sample sizes or the use of non-experimental designs. In a more recent systemic review (n = 691), Kamstra et al. (2017) concluded that jaw exercise interventions were effective for the treatment of trismus, but were ineffective for the prevention of trismus in patients receiving radiotherapy (RT) or combined chemoradiotherapy (CCRT) for HNC. Two RCTs, one prospective study, five chart reviews, and four case studies were included in the review for exercise effects on treating trismus. It also included the four studies reviewed in the Scherpenhuizen et al. (2015) article. Exercise interventions in these studies usually started 3–6 months after RT/CCRT and when trismus had already developed. Three RCTs and five prospective studies were included in the review for exercise effects on preventing trismus. Exercise interventions in these studies usually started at the beginning of RT/CCRT and before trismus occurred (Kamstra et al., 2017). All exercise interventions included active jaw movements and passive stretching with a jaw mobilizing device, such as a dynamic bite opener, the TheraBite®, the Engstrom Jaw mobilizing device, the Dynasplint® Trismus System (DTS), wooden tongue blades, and rubber plugs. Exercises were performed 2 to 10 times a day with 3–40 repetitions each time for 2 weeks to 12 months.

In recent years, several other studies have been published on the effects of exercise for trismus. In a prospective study (n = 15), Montalvo et al. (2017) found that structural exercise with the TheraBite device significantly improved MIO and trismus-related symptoms in patients with trismus resulting from head and neck cancer. The MIO significantly improved by 4.7 mm at six-month follow-up. On the other hand, in a randomized clinical trial (n = 100), Høgdal et al. (2015) found that early preventive exercises versus usual care did not decrease trismus in patients treated with radiotherapy for oral cancer. Current evidence supports the potential beneficial effects of mouth-opening exercises for radiotherapy induced trismus in HNC populations, but not for preventing trismus. No evidence has supported that one type of mouth-opening exercise is superior to others (Kamstra et al., 2017; Lee et al., 2018). However, most of these previous studies were small sample size RCTs, prospective studies, or single case studies, and varied in study design, stretching techniques, exercise frequency, and duration (Montalvo et al., 2017; Kamstra et al., 2017; Scherpenhuizen et al., 2015). In addition, most of these studies were conducted on patients during or after RT/CCRT (Høgdal et al., 2015; Kamstra et al., 2017; Lee et al., 2018; Scherpenhuizen et al., 2015). Few studies have investigated the effects of mouth-opening exercises for fresh post-operative oral cancer patients.

Warm compress and massage may provide additional benefits for relieving trismus. Results of an integrative literature review showed that warm compresses were effective for reducing pain, relieving muscle tension, and increasing mouth opening in patients with temporomandibular joint and muscle disorders (Furlan et al., 2015). Gomes et al. (2014) found that 4 weeks of masticatory muscle massage significantly increased the average MIO in patients with temporomandibular disorders, suggesting that massage may be helpful for improving trismus. The potential effect of warm compress and masticatory muscle massage for relieving trismus in oral cancer patients has not yet been investigated.

Furthermore, the effectiveness of mouth-opening exercise is associated with its adherence rate (Kamstra et al., 2017; Pauli et al., 2015, 2016; Scherpenhuizen et al., 2015). In general, adherence to mouth-opening exercise regimens is poor (Lee et al., 2018). Factors such as pain, anxiety, motivation, perceived effect, and exercise goals were found to affect adherence to mouth-opening exercise (Melchers et al., 2009). Training upon discharge alone, without follow-up reminders and continuous support, may lead to failure in the execution of correct and routine mouth-opening exercises at home. Additional support and reminders through follow-up phone calls has shown to be effective for improving rehabilitation exercise adherence in total knee arthroplasty patients after discharge from the hospital (Chen et al., 2016; Clari et al., 2015; Li et al., 2014). This strategy may also be helpful for enhancing mouth-opening exercise adherence and then reduce trismus in post-operative oral cancer patients. However, to the best of our knowledge, no previous study has been reported on the effect of combining discharge mouth opening training and remote support provided via telephone for reduction of trismus in oral cancer patients.

Therefore, the purpose of the study was to investigate the effects of combining warm compress, masticatory muscle massage, and jaw exercise for postoperative trismus as well as remote support provided via telephone following hospital discharge for intervention adherence in patients with oral cancer. The specific aims were to test the intervention effects on enhancing mouth-opening exercise practice, MIO, and mandibular function. We hypothesized that the experimental group would show 1) better adherence to the intervention protocol, 2) greater MIO, and 3) better mandibular function over time, compared to the active control group.

2. Methods

2.1. Study design and subject recruitment

The study is a parallel randomized trial with 1:1 allocation ratio. Patents admitted to the hospital for curative oral cancer surgeries were recruited from surgical units of a regional teaching hospital in southern Taiwan. Potential subjects were referred by physicians and then screened by one of the researchers to determine their eligibility. Patients who met the following inclusion criteria were solicited: (a) aged 18 years or older, (b) diagnosed with oral cancer, (c) scheduled for a primary curative oral cancer surgery, (d) able to communicate in Mandarin or Taiwanese, and (e) obtained medical clearance from the patient's attending physician to participate in the study. The exclusion criteria were: (a) diagnosed with lip or tongue cancers which were less relevant to trismus or (b) had central incisors extracted during the surgery. The study was approved by the Yuan's General Hospital Institutional Review Boards (IRB No. YGH20110818B).

2.2. Randomization, allocation concealment, and blinding

The study used one block randomization with a 1:1 allocation ratio. An independent researcher generated the random allocation sequence with the Random Allocation Software (Saghaei, 2004). The sequence was concealed from the investigators and subjects in sequentially numbered, opaque, and sealed envelopes. The investigator who enrolled the subjects opened the corresponding envelopes and assigned them to interventions after completing their baseline assessment. Subjects, care providers, and the outcome assessor were blinded after assignment to interventions.

2.3. Data collection

A blinded outcome assessor measured subjects' maximum interincisal opening (MIO) and collected self-report data on intervention adherence and mandibular function impairments prior to surgery (T1), one month (T2) after discharge from the hospital, and three months (T3) after discharge. Data collection took place in a quiet room at the outpatient clinics during the patients' visits to the clinics. At T1, each subject was also asked to complete a self-report demographics questionnaire. Data on disease variables, including tumor location, cancer stage, and type of surgery, were collected from the subjects' charts.

2.4. Interventions

To avoid potential contamination and ethical issues associated with the no intervention control group, an active control group was used. The experimental and active control groups both underwent a 12-week intervention program, differing in the level of remote support provided to them via telephone following hospital discharge. The focus of the intervention was on the flexibility of mastication muscles and temporomandibular joints (TMJ), which have commonly been found to be stiff and cramping in postoperative oral cancer patients (Agarwal et al., 2016; Wetzels et al., 2014). The subjects were instructed to practice the intervention 3 times a day. The training began at the discharge day and continued for three months after discharge. The intervention protocol was designed as follows: (1) warm compresses on the cheeks for 15 min and masseter muscles massage for 5 min, (2) jaw active range of motion and stretching exercises for 5 min, and (3) passive stretching using wooden tongue depressors for 15 min. First, warm compresses and masseter muscles massage were used to improve circulation and relax mastication muscles. The subjects were instructed to soak a clean cloth in water at the temperature right between warm and comfortably hot and then apply the warm cloth on their cheeks for 15 min, followed by massaging his/her cheek bones and surrounding tissues with the index and middle fingers in a circular direction for 5 min. Second, jaw active range of motion and stretching exercises were used to stretch mastication muscles and increase TMJ range of motion. The subjects were instructed to open their mouth as wide as possible and then hold the stretch for 10 s, followed by moving their jaws to the left and hold for 3 s, and then moving to the right and hold for another 3 s. These movements were repeated ten times. Finally, wooden tongue depressors were used to do passive stretching. The subjects placed a stack of wooden tongue depressors between their upper and lower incisors, and then pushed the last piece of tongue depressor from the middle, using the force to open their mouths more. The tongue depressors were kept in one's mouth for 15 min. The number of tongue depressors was gradually increased to passively stretch the jaw and push open the subject's mouth.

The intervention protocol was developed by our team and validated by a panel of experts that included a HNC oncologist, an oral and maxillofacial surgeon, an oncologist, a rehabilitation physician, and a physical therapist. A pilot study was conducted on five oral cancer patients to evaluate intervention feasibility and safety. These patients were followed over 1 month to observe any potential adverse responses. There was no wound dehiscence or other adverse responses.

The interventionist, a nurse practitioner, gave each subject two 30-min sessions of individualized instructions on the intervention. The first instruction session was given to a subject on the day before surgery. The focuses of the instruction were to provide an overview of the intervention program and to discuss the purposes and basic principles of jaw exercises. The second set of instructions was given to the subject on the hospital discharge day. The focuses of these instructions were to discuss the protocols of the intervention and the detail steps of each component, including warm compresses, masseter muscles massage, active jaw range of motion and stretching exercises, and passive jaw motion rehabilitation. A pamphlet with illustrations of the detailed steps developed by the research team was used for the instructions and then given to the subjects for their reference. Each subject was also given opportunities to practice these mouth-opening exercises during the instruction.

Subjects in the experimental group received additional support via telephone following hospital discharge. The interventionist called each experimental subject at week 1, 2, 3, 4, 8 and 12 to monitor training progress, enhance adherence, and resolve any questions and concerns. During each phone call, the interventionist first explained the purposes of the call and assessed the subject's adherence to the intervention by asking his/her weekly practice in mouth-opening exercises; including the content, intensity, duration, and frequency. The interventionist then provided appropriate feedback to the subject according to this assessment. Second, the potential barriers to the intervention, including problems with pain, drooling, inconvenience, not knowing how to use tongue depressors, and lack of motivation, were explored and feasible plans to solve these problems were provided. Third, the importance of continuous practice was emphasized and the subject was encouraged to follow the intervention protocol. Finally, the subject was invited to ask questions and express his/her concerns.

2.5. Instruments

The primary outcome measure was the MIO, which was the maximal vertical distance between the edges of the incisors of the maxilla and the mandible. The TheraBite Range-of-Motion Scale was used to measure MIO with the subject in an upright position. Subjects with MIO < 35 mm were considered to have trismus (Dijkstra et al., 2006; Kamstra et al., 2017).

The secondary outcome measures included intervention adherence and mandibular function impairment. Intervention adherence was assessed by a self-reported questionnaire. The subjects were also asked to indicate how many weeks a month, how many days a week, how many times a day, and for how long (minutes) each time that they had practiced the intervention over the last month. The average time of practicing mouth-opening exercises each week was calculated by the multiplication of these four numbers.

The Mandibular Function Impairment Questionnaire (MFIQ) (Stegenga et al., 1993) was used to measure the extent of subjects' mandibular function impairment. The questionnaire consists of 17 items, each of which targets a specific oral function impairment; including difficulties in social activity, speech, taking a large bite, chewing hard food, chewing soft food, work and/or daily activities, drinking, laughing, chewing resistant food, yawning, kissing, and eating different types of food. The subjects were asked to indicate how much difficulty they had with each activity or with eating each type of food using a 5-point Likert scale (0 = no difficulty, 4 = very difficult or impossible without help). The total score of the 17 items divided by 68 provides the scale score, with a possible range of 0–1. A higher score indicates greater severity of the mandibular function impairment. A score ≤ 0.3, between 0.3 and 0.6, and > 0.6 indicates mild, moderate, and severe mandibular function impairment, respectively. This scale has demonstrated good test-retest reliability ($r = 0.80$) and internal consistency (Cronbach's α between 0.63 and 0.95) when used with 95 patients with temporomandibular joint disorders (Stegenga et al., 1993). The scale was translated into Chinese and then back-translated into English. Discrepancies between the back-translated and original versions were resolved by discussion and reiteration of the translation procedure. The final version of the Chinese scale reached satisfactory semantic equivalence with the original scale. Five content experts rated the item relevance of the scale, the item content validity index (iCVI) was greater than 0.8 for all items. The Cronbach's α coefficient was 0.96 in our study.

2.6. Sample size determination

The required sample size was calculated before recruitment by using the G-Power software (version 3.1.2) (Faul et al., 2009). A sample size of 31 in each group was needed to have an 80% statistical power for testing a moderate intervention effect ($f^2 = 0.30$) at a 0.05 significance level. A moderate effect of mouth opening exercise for reducing trismus reported in the Kamstra et al. (2017) systemic review was used to estimate the desired sample size. The study was approved by the institutional review board of the hospital where the subjects were recruited.

2.7. Statistical analysis

All statistical analyses were executed using the Statistical Package for the Social Sciences (SPSS), version 20 (IBM Corp, NY, USA). Descriptive statistics were used to summarize characteristics of the subjects. Chi-squared tests or Fisher's exact tests and two independent samples *t*-tests were used to examine group baseline equivalency. Value changes of study outcomes (MIO and mandibular function impairment) and mouth-opening exercises performed from T1, T2, to T3 were expressed in two study groups. A general linear model was used to model these outcomes as a function of main group effect and main time effect. An interaction term (group difference by time) was added into each model to investigate the synergistic effect of the intervention with time. Both the stability analysis and the analysis of repeated relationships were performed by generalized estimation equations (GEE).

3. Results

3.1. Subjects' characteristics and baseline equivalence

One hundred forty-six patients were screened for eligibility; 72 of them did not meet the eligibility criteria and were excluded. Of these 72 patients, 37 were not scheduled for a primary curative oral cancer surgery, and 35 were diagnosed with lip or tongue cancers. The 74 potentially eligible patients were approached; six of them refused to participate due to not having mouth opening difficulties. Sixty-eight patients consented to participate and were randomly assigned to either the experimental (n = 34) or active control group (n = 34). All subjects provided signed informed consent. During the study, four subjects in the experimental group were excluded due to having central incisors extracted during the surgery (n = 3) and surgical wound bleeding after discharge (n = 1); four subjects in the comparison group were excluded due to having central incisors extracted during the surgery (n = 1) and not returning to the clinics for postoperative follow-ups (n = 3). This left 60 valid cases, with 30 cases in each group (Fig. 1). For each group, 30 subjects included in each analysis and the analysis was by original assigned groups.

The average age of the subjects was 55.98 years (*SD* = 11.73; range: 30–82). Subjects were mainly men (90.0%, *n* = 54), married (83.3%,

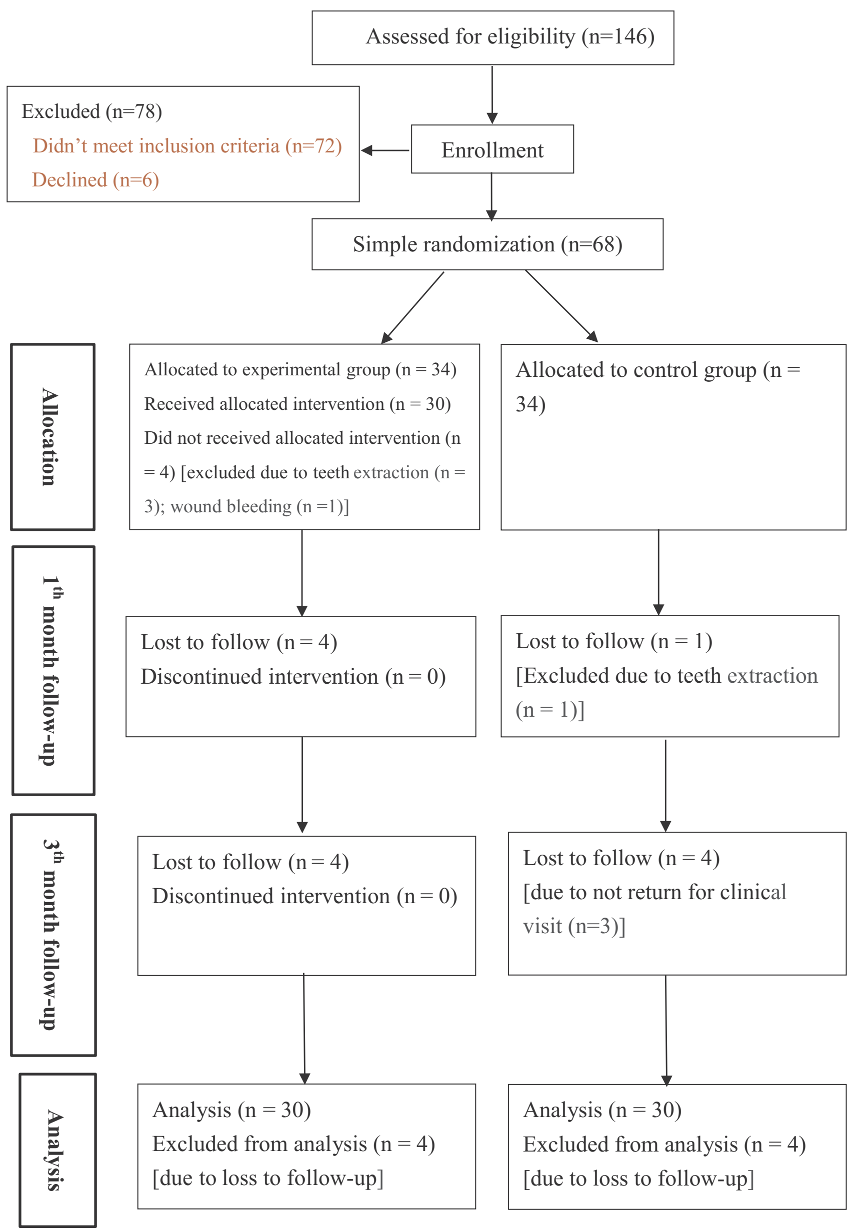

Fig. 1. Flow diagram of the progress of the study (enrollment, intervention allocation, follow-up, and data analysis).

Table 1
Demographics and Baseline sample characteristics (n = 60).

Variables	Total	Intervention	Control	Between Group	
	f (%)	*f (%)*	*f (%)*	X^2/t	*p*
Age [mean (SD)]	55.98 (11.73)	54.27 (11.68)	57.7 (11.73)	−1.13[b]	0.799
Gender				0.74[a]	0.671
Male	54 (90.0)	28 (93.3)	26 (86.7)		
Female	6 (10.0)	2 (6.7)	4 (13.3)		
Education				0.16	0.984
Primary school	15 (25.0)	7 (23.3)	8 (26.7)		
Junior high school	22 (36.7)	11 (36.7)	11 (36.7)		
Senior high school	11 (18.3)	6 (20.0)	5 (16.7)		
College and above	12 (20.0)	6 (20.0)	6 (20.0)		
Marital status				0.00[a]	1.000
Married	50 (83.3)	25 (83.3)	25 (83.3)		
Single	10 (16.6)	5 (16.7)	5 (16.7)		
Employment status				0.60[a]	0.438
Unemployed	32 (53.3)	14 (46.7)	18 (60.0)		
Employed	28 (46.7)	16 (53.3)	12 (40.0)		
Cancer location				1.27	0.529
Buccal mucosa	54 (90.0)	26 (86.7)	28 (93.3)		
Gingival	5 (8.3)	3 (10.0)	2 (6.7)		
Hard palate	1 (1.7)	1 (3.3)	0 (0)		
Cancer stage				0.590	0.899
Stage I	29 (48.3)	14 (46.7)	15 (50.0)		
Stage II	18 (30.0)	10 (33.3)	8 (26.7)		
Stage III	3 (5.0)	1 (3.3)	2 (6.7)		
Stage IV	10 (16.7)	5 (16.7)	5 (16.7)		
Adjuvant therapy				1.287	0.525
NO	46 (76.7)	24 (80.0)	22 (73.3)		
RT	9 (15.0)	3 (10.0)	6 (20.0)		
CCRT	5 (8.3)	3 (10.0)	2 (6.7)		
Tumor resection & reconstructive surgery				0.48[a]	0.731
With neck dissection	10 (16.7)	6 (20.0)	4 (13.3)		
Without neck dissection	50 (83.3)	24 (80.0)	26 (86.7)		

Note. RT radiotherapy, CCRT concurrent chemoradiation therapy, [a] Fisher's exact test, [b] Student's t –test, $^*p < 0.05$.

n = 50), and unemployed (53.3%, n = 32); with an education level of junior high school or below (61.7%, n = 37). Majority of them had stage I (48.3%, n = 29) or stage II (30.0%, n = 18) buccal mucosa carcinomas (90.0%, n = 54). All subjects had tumor resection and reconstructive surgeries; fourteen of them also received adjuvant therapies. The demographics and disease characteristics were balanced between the groups (Table 1). At baseline, there was no difference in mean (SD) MIO between the experimental (27.43 (10.71) mm) and active control (26.57 (10.53) mm) groups. In addition, there was no difference in mean (SD) MFIQ scores between the groups (0.16 (0.21) vs 0.17 (0.20)) (Table 3).

3.2. Effects on adherence to the intervention protocol

At T2, 90.0% of the subjects in the experimental group were still practicing the intervention, but only 26.7% of the subjects in the active control subjects were (X^2 = 22.21, $p < 0.001$). The weekly intervention practice time of the intervention group was 377 min [95% confidence interval (CI): 272.56–481.44] more than it of the active control group. At T3, 93.3% of the subjects in the experimental group were still practicing the intervention, compared to only 16.7% of the subjects in the active control group were (X^2 = 32.59, $p < 0.001$). The weekly intervention practice time of the experimental group was 299.67 min (95% CI: 223.44–357.89) more than it of the active control group (Table 2). Both the number of subjects continuously practicing the intervention and the subjects' average weekly practicing time were significantly higher in the experimental group than they were in the active control group. These results support the first hypothesis that the experimental group shows better adherence to the intervention protocol than the active control group does.

3.3. Effects on MIO

Results of GEE showed a statistically significant group-by-time interaction in MIO (Wald X^2 = 96.79, $p < 0.001$). The parameter of the slope (ß) revealed the change in MIO from T1 to T3, which was 10.30 mm [95% CI: 8.22–12.37] greater in the experimental than in the active control group. The change in MIO from T1 to T2 was 3.73 mm (95% CI: 1.65–5.81) greater in the experimental group than in the active control group (Table 4). In the experimental group, the mean (SD) MIO was 27.43 (10.71) mm, 22.13 (9.38) mm, and 27.33 (9.73) mm, at T1, T2, and T3, respectively. In the active control group, the mean (SD) MIO was 26.57 (10.53) mm, 17.53 (8.12) mm, and 16.17 (8.01) mm, at T1, T2, and T3, respectively (Table 3). As showed in a linear graph (Fig. 2), the MIO of the experimental group declined from T1 to T2 then substantially increased from T2 to T3. In contrast, the MIO of the active control group continued to decrease over time.

Using MIO < 35 mm as the cut-off point for trismus, at T1, 20 (66.7%) subjects in the experimental group and 22 (73.3%) subjects in the active control group had trismus. There was no significant between group difference. At T2, 29 (96.7%) subjects in the experimental group and 30 (100%) subjects in the active control group had trismus, with no significant between group difference. However, at T3, 21 (70%) subjects in the experimental group had trismus, which was significantly less than the 30 (100%) subjects in the active control group with trismus (X^2 = 8.36, p = 0.002) (Table 3). These results support the second hypothesis that there is a greater improvement of MIO over time for subjects in the experimental group than in the active control group.

3.4. Effects on mandibular function impairment (MFI)

Results of the GEE showed a statistically significant group-by-time interaction in mandibular function impairment (Wald X^2 = 88.39, $p < 0.001$). The parameter of the slope (ß) revealed the change in MFIQ score from T1 to T3, which was −0.36 (95% CI: −0.44 to −0.28) greater in the experimental than in the active control group. The change in MFIQ score from T1 to T2 was −0.13 (95% CI: −0.21 to −0.06) greater in the experimental group than in the active control group (Table 4). In the experimental group, the mean (SD) scores of the

Table 2
Between group comparisons on mouth opening exercise performed at different time points (n = 60).

Variables	Time	Intervention		Control		Between group	
		n	%	*n*	%	OR	[95%CI]
Continuing exercise	T2	27	90	8	26.7	24.75	[5.56, 104.61]
	T3	28	93.3	5	16.7	70	[12.46, 393.36]
Exercise time per week (minutes)		Mean	*SD*	Mean	*SD*	Mean difference	[95%CI]
	T2	470.2	256.7	93.2	119.9	377.00	[272.56, 481.44]
	T3	303.3	204.0	3.7	7.8	299.67	[223.44, 375.89]

Note. T2 at the first month post-surgery, T3 at the third month post-surgery, OR Odds ratio, CI confidence interval.

Table 3
Between Group Comparisons on Maximum Interincisal Opening and Mandibular Function Impairment at Different Time Points (n = 60).

Variables	Time		Intervention		Control		Between group	
			Mean	*SD*	Mean	*SD*	Mean difference	[95%CI]
Maximum interincisal opening, MIO (mm)	T1		27.43	10.71	26.57	10.53	.87	[-4.63, 6.36]
	T2		22.13	9.38	17.53	8.12	2.27	[.07, 9.14]
	T3		27.33	9.73	16.17	8.01	2.30	[6.56, 15.78]
Mandibular function impairment (MFI)	T1		0.16	0.21	0.17	0.20	-.00	[-.12, .11]
	T2		0.36	0.27	0.50	0.24	-.14	[-.28, −.01]
	T3		0.18	0.23	0.55	0.30	-.37	[-.51, −.23]
			n	%	n	%	X^2	*p*
Trismus (MIO < 35 mm)	T1		20	66.7	22	73.3	0.317[a]	0.779
	T2		29	96.7	30	100	1.017[a]	1.000
	T3		21	70	30	100	10.59[a]	0.002**
Severity of MFI	T1	Low	24	86	23	76.7	0.22	0.895
		Medium	4	13.3	4	13.3		
		High	2	6.7	3	10.0		
	T2	Low	16	53.3	6	20.0	7.20	0.027*
		Medium	9	30.0	16	53.3		
		High	5	16.7	8	26.7		
	T3	Low	25	83.3	7	23.3	22.25	< 0.001***
		Medium	1	3.3	10	33.3		
		High	4	13.3	13	43.3		

Table 4
Parameters of the generalized linear model for the effect of mouth opening exercise on MIO and mandibular function impairment.

Variables	*ß*	*SE*	95% CI	Wald X^2	*p*
Maximum interincisal opening (MIO)					
Intervention VS. control	0.86	2.44	−3.92–5.66	0.12	0.723
Intervention (T3-T1) VS. control (T3-T1)	10.30	1.06	8.22–12.37	94.40	< 0.001***
Intervention (T2-T1) VS. control (T2-T1)	3.73	1.06	1.65–5.81	12.40	< 0.001***
Mandibular function impairment					
Intervention VS. control	−0.00	0.06	−0.13–0.12	0.00	0.940
Intervention (T3-T1) VS. control (T3-T1)	−0.36	0.03	−0.44 ~ −0.28	86.67	< 0.001***
Intervention (T2-T1) VS. control (T2-T1)	−0.13	0.03	−0.21 ~ −0.06	12.39	< 0.001***

Note. Using generalized estimation equations for repeated measurements and an exchangeable correlation structure. MIO maximum interincisal opening, *$p < 0.01$, **$p < 0.001$.

MFIQ were 0.16 (0.21), 0.36 (0.27), and 0.18 (0.23), at T1, T2, and T3, respectively. In the active control group, the mean (SD) scores of the MFIQ were 0.17 (0.20), 0.50 (0.24), and 0.55 (0.30) at T1, T2, and T3, respectively (Table 3). As showed in a linear graph (Fig. 3), the mandibular function impairment of the experimental group increased from T1 to T2 then substantially decreased from T2 to T3. In contrast, the mandibular function impairment of the active control group continued to increase over time.

The MFIQ ≤0.3, between 0.3 and 0.6, and > 0.6 were used as the cut-off point for mild, moderate, and severe mandibular function impairment, respectively. At T1, there were 24, 4, and 2 subjects in the experimental group and 23, 5, and 2 subjects in the active control group that had mild, moderate, and severe impairment, respectively. There was no between group difference in the number of subjects at different levels of mandibular function impairment. At T2, there were 16, 9, and 5 subjects in the experimental group and 6, 16, and 8 subjects in the active control group that had mild, moderate, and severe impairment, respectively. At T3, there were 25, 2, and 3 subjects in the experimental group and 7, 11, and 12 subjects in the active control group that had mild, moderate, and severe impairment, respectively. Both at T2 and T3, the number of subjects at different levels of mandibular function impairment were significantly different between groups (Table 3). There were more subjects with moderate or severe mandibular function impairment in the active control group than in the experimental group. These results support the third hypothesis that there is a greater improvement of mandibular function over time for subjects in the experimental group than in the active control group.

3.5. Ancillary analyses

Additionally, the subjects' weekly intervention practicing time was significantly correlated with both their MIOs and MFIQ scores. At T2, the correlations were 0.549 ($p < 0.01$) and −0.554 ($p < 0.01$) respectively; at T3 the correlations were 0.589 ($p < 0.01$) and −0.519 ($p < 0.01$), respectively.

3.6. Adverse events

Subjects in both groups were instructed to call the investigator for reporting any concerns, adverse events, or increasing discomfort from practicing the intervention during the study. No unintended effects or harms have been reported.

4. Discussion

This is the first known report of the effect of remote support provided to patients via telephone following hospital discharge for alleviating postoperative trismus in patients with oral cancer. Consistent with findings of previous research (Chen et al., 2016; Clari et al., 2015; Dijkstra et al., 2006), we found that remote support provided to patients via telephone following hospital discharge are effective for enhancing adherence to home-based rehabilitation exercises. In the experimental group, 20 subjects (66%) had trismus pre-surgery, 29 (97%) had trismus four weeks after discharge, and 21 subjects (70%) had trismus at three months after discharge. The exercise treatment effect

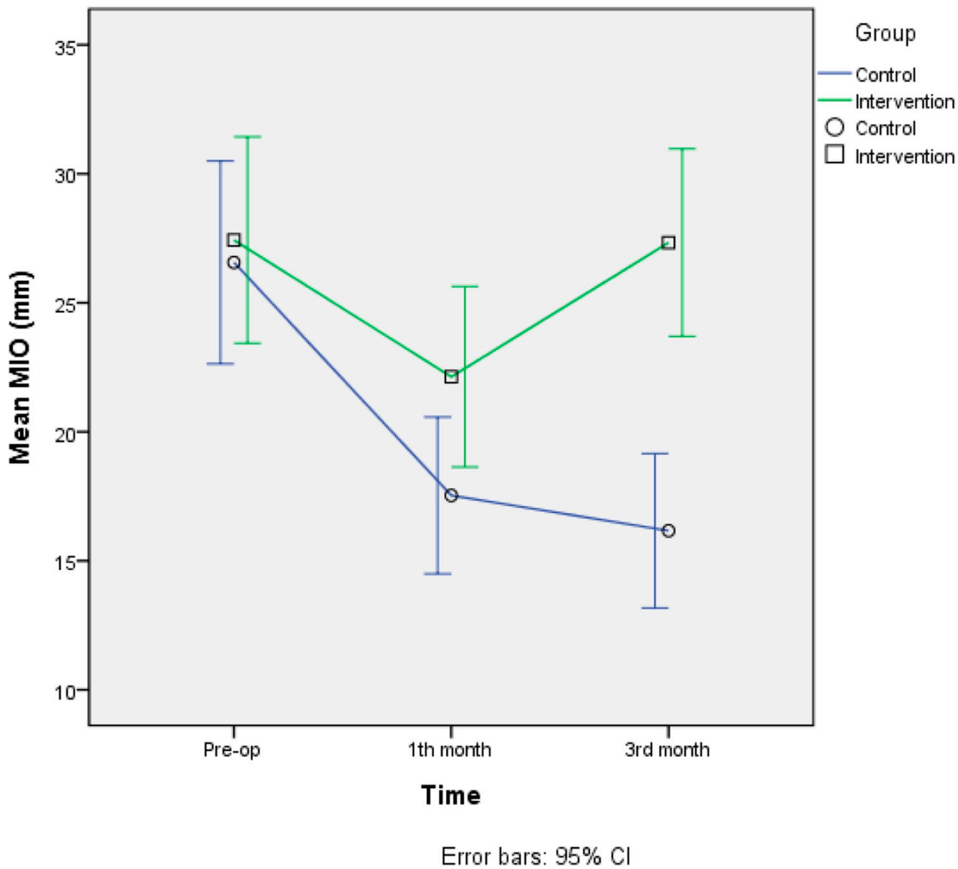

Fig. 2. Changes in the distance of maximum interincisal opening over time at pre-operation, 1th month follow-up, and 3rd month follow-up. The data are shown as mean ± 95% confidence interval (error bars).

resulted in an increased MIO and reduced the number of subjects with trismus between four weeks and three months after discharge. The change in MIO from pre-surgery to three-month follow up was 10.30 mm greater in the experimental group than in the active control group. This small beneficial effect can be considered as clinically relevant as it is greater than 5 mm, the smallest detectable difference (Jager-Wittenaar et al., 2009). The average MIO of the experimental subjects was increased by 5.2 mm from one-month to three-month follow-up. The size of the change is comparable with previous findings in patients with head and neck cancers: 5.4 mm in Kamstra et al. (2013) study (n = 69), 6.4 mm in the Pauli et al. (2014) study (n = 50), and 7.2 mm (n = 25) and 5.5 mm (n = 25) in the Pauli et al. (2015) study. Different from these previous studies, we used a stack of wooden tongue depressors instead of the commercial made Therabite ® or the Engstrom jaw mobilizing device for passive stretching and found similar effects. Although the intervention significantly improved MIO, 70% of subjects in the experimental group still had trismus at three-month follow-up. This suggests that a longer program may be needed.

We also found that the study intervention was effective for improving mandibular function, a patient reported outcome. In the experimental group, 14 (46.7%) subjects reported medium or high mandibular function impairments four weeks after discharge and only 5 (16.6%) subjects reported medium or high mandibular function impairments three months after discharge. The size of the change in mandibular function from pre-surgery to three-month follow up in the experimental group (0.36) reflected a significantly greater improvement in mandibular function versus the active control group.

Our study results also support the finding in a systemic review that starting training early and adherence to exercises is vital for good results (Kamstra et al., 2017). However, not all our subjects were interested in the intervention or able to learn it with two 30-min individual training sessions. Some subjects felt that they did not need to learn the intervention because they did not have a problem with mouth opening. Some subjects were not interested and unwilling to practice the intervention at home. Others were not motivated and often forgot to perform the intervention. During the telephone follow-up, subjects often expressed their frustration at not seeing improvements and wanting to quite. The interventionist worked with them to overcome the challenges and motivated them to continue the intervention by sharing successful cases. Notably, we found that all subjects except one had trismus four weeks after discharge; therefore, it is wise to advise month opening interventions to all oral cancer surgical patients. The remote support provided to patients via telephone following hospital discharge can be used to enhance intervention adherence.

The study had several limitations. First, the subjects were recruited from surgical units of a regional teaching hospital and might be different from those seen in other clinical settings. Second, there may have been a selection bias because we excluded people who were diagnosed with lip or tongue cancers or had central incisors extracted during the surgery, as they were less relevant to trismus. Third, the study was also limited by its small sample size and might not be generalized to other oral cancer populations. Fourth, it is difficult to evaluate the net effect of the intervention because both study groups underwent similar intervention program and only differed in the level of remote support. Fifth, in addition to jaw exercises, we also included warm compresses and massages in the intervention. However, it is not possible to know whether adding these components offers any additional beneficial effects for alleviating trimus with our study design. Lastly, we only assessed the intervention effects up to three months, precluding the evaluation of long-term effects.

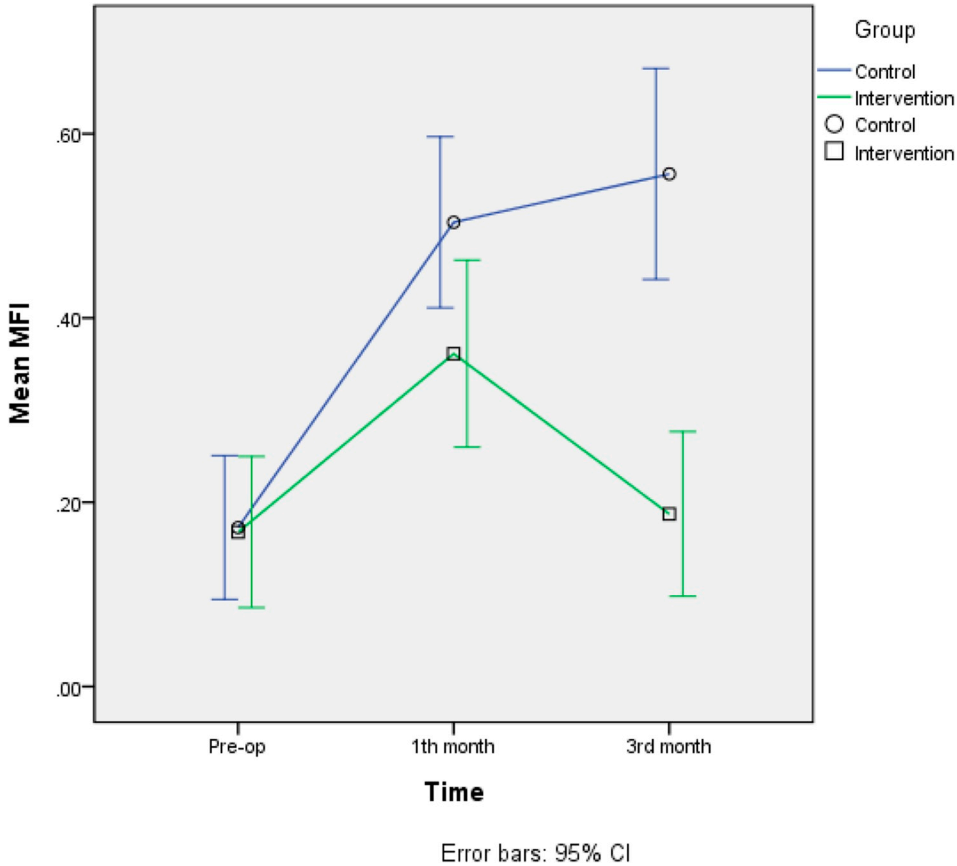

Fig. 3. Changes in the mandibular function impairment score over time at pre-operation, 1th month follow-up, and 3rd month follow-up. The data are shown as mean ± 95% confidence interval (error bars).

5. Conclusion

The study results support the effect of remote support via telephone for enhancing adherence to the intervention protocol, and the effect of the intervention program for alleviating trismus and mandibular function impairments in patients who receive curative surgery for oral cancer. Two sessions of in person training with six follow-up telephone calls significantly increased patients' mouth-opening practicing time, maximum mouth opening, and mandibular function. No adverse reaction to the intervention was observed. Additional randomized controlled trials with longitudinal designs and larger sample sizes are needed to better define the role of the intervention in the treatment protocol for oral cancer associated trismus. Replicating this study in other settings is also recommended. Although further research is called for, this study is a promising step in investigating the beneficial effect of the intervention for trismus and mandibular function impairments.

6. Clinical implications

Trismus is a prevalent condition in patients after surgeries for oral cancer. Treating trismus can be a discouraging effort and remains a great challenge for clinicians. Once trismus happens, it is difficult to alleviate; therefore, it is wise to deal with it as soon as possible. Home-based mouth-opening exercises can be considered as a feasible option for lessening the restrictions of mandibular movement and function. However, the benefits of exercise take time and consistent practice to become apparent. Patients should be inspired to maintain regular exercise and to keep realistic expectations. Being discharged from the hospital after oral cancer surgery is an inherently stressful time. The results of the study showed that in person training before hospital discharge was not sufficient enough for patients to consistently perform the intervention at home. Remote support provided to patients via telephone following hospital discharge was effective in enhancing intervention adherence, and thereafter alleviated trismus and mandibular function impairment. Follow-up phone calls not only can provide additional support to the patients, but can also give them the opportunity to ask questions and motivate them to do oral exercise and self-care tasks. These strategies may be included as part of the post-operative care and post discharge case management for patients with oral cancer.

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Trial registration

ClinicalTrials.gov NCT03875118.

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