Trismus in head and neck cancer patients

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The use of stretching devices for treatment of trismus in head and neck cancer patients: a randomized controlled trial

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ABSTRACT

Purpose: To compare the effects of two stretching devices, the TheraBite® Jaw Motion Rehabilitation System™ and the Dynasplint Trismus System®, on trismus in head and neck cancer patients

Methods: Patients were randomly assigned to one of two exercise groups: the TheraBite® Jaw Motion Rehabilitation System™ group or the Dynasplint Trismus System® group. Patients performed stretching exercises for three months. During the three study visits, maximal mouth opening was measured and the patients completed questionnaires on mandibular function and quality of life.

Results: In our study population (n=27), five patients did not start the exercise protocol, eight patients discontinued exercises and two patients were lost to follow-up. No significant differences between the stretching devices on maximal mouth opening, mandibular function, and patients' perception of difficulties opening the mouth were found. Patients had an increase in MMO of 3.0 mm (IQR -2.0; 4.0) using the TheraBite® Jaw Motion Rehabilitation System™ and 1.5 mm (IQR 1.0; 3.0) using the Dynasplint Trismus System®. Exercising with either stretching device was challenging for the patients due to the intensive exercise protocol, pain during the exercises, fitting problems with the stretching device and overall deterioration of their medical condition.

Conclusions: The increase in mouth opening between the two stretching devices did not differ significantly in our study population. The factors described, influencing the progression of stretching exercises, need to be taken into account when prescribing similar stretching regimen for trismus in head and neck cancer patients.

INTRODUCTION

Trismus, a severely restricted mouth opening, is a common problem in head and neck cancer patients.[1] Trismus reduces mandibular function and quality of life.[2-5] Trismus can impair speech, oral hygiene, dental treatment, airway clearance and oncological follow-up[2,6,7], resulting in problems for patients, their dentists and oncological professionals.

To increase mouth opening, a variety of exercise therapies are used.[8] Exercise therapy with stretching devices such as the TheraBite® Jaw Motion Rehabilitation System™ (TheraBite) and the Dynasplint Trismus System® (DTS) have been reported to increase mouth opening up to 14 mm.[9-11] However the effects of these two devices have not been compared side-by-side. In a randomized controlled trial, we therefore compared the effects of the TheraBite and the DTS on mouth opening in head and neck cancer patients with trismus. We also compared the effects of the TheraBite and DTS on mandibular function and the patients' perception of difficulties opening the mouth.

MATERIALS AND METHODS

This parallel group Randomized Controlled Trial (RCT) is reported according to the CONSORT statement 2010. The trial was registered on 5 December 2015, NTR (Dutch Trial Register) 5589. The study was approved by the Medical Ethical Committee of the University Medical Center Groningen (METC number 2015.468).

Study Population

Patients were recruited from March 2016 till December 2017 at the Department of Oral and Maxillofacial Surgery at the University Medical Center Groningen (UMCG). Patients were eligible for inclusion in the study if they were at least 18 years old, if they were treated for head and neck cancer (including surgery, radiotherapy, or chemotherapy), and had a maximal mouth opening (MMO) of 35 millimetres or less. The patients were assessed for eligibility by a surgeon, nurse practitioner, dentist or resident, all specialized in Head and Neck Oncology.

Patients were checked for eligibility when they visited the Department of Oral and Maxillofacial Surgery during the recruitment period and a restricted mouth opening was observed or reported in the patient file during previous visits. Patients were also assessed for eligibility after responding to a recruitment poster in the waiting area.

Patients were excluded from the study if they were not diagnosed with head and neck cancer, were unable to provide informed consent, were diagnosed with osteoporosis, osteo(radio)necrosis, had severe periodontitis or mobility of teeth, had an oral abscess or other infectious process in the head and neck region, or had a tumour recurrence, metastasis or a new primary tumour in the head and neck region.

Patients who met the inclusion criteria were informed about the study, and their informed consent was obtained prior to enrolment.

Sample size calculation

A MMO difference of 5 millimetres between the two stretching devices was considered clinically relevant. We assumed a within group standard deviation of 6 mm.[12] With an alpha of 0.05 and a power of 80%, we calculated the sample size using the PS Power and Sample Size Calculations, Version 3.0. In total, 24 subjects per group were needed. To compensate for drop- outs, we aimed to include 30 patients per group.

Randomization

The randomization occurred on the basis of two strata, with blocks of four with an allocation ratio of one. One stratum included patients who received cancer treatment less than 36 months ago and the other included patients who received cancer treatment 36 months ago or longer. Per block, two sheets containing the word "TheraBite" and two sheets containing the word "DTS", were placed separately into opaque envelopes. The envelopes were then shuffled and provided with the letter of the stratum and a consecutive number.

After informed consent was obtained, the researcher (JG) enrolled the patients in the study. JG provided the necessary information for randomization (name, date of birth, interval between last cancer treatment and exercise protocol) to a secretary at the department of Rehabilitation. The secretary recorded the data, opened an opaque envelope (concealed) containing the assigned stretching device, and recorded the assigned stretching device on a log sheet. The secretary then scheduled appointments for the patients for the assigned intervention.

Blinding

The researcher (JG) was initially blinded for the stretching devices. The patient and therapists (physical therapist or dentist) could not be blinded due to logistic reasons.

The exercise program

The TheraBite exercise program consisted of two options: 20 stretches per session, 6 times a day, 30 seconds per stretch, or 30 stretches per session, 4 times a day, 30 seconds per stretch. The DTS exercise program consisted of 1 stretch per session, 3 times a day, 30 minutes per stretch.

Patients performed the exercises for 3 months. During the first visit (T1), the stretching device and a diary were provided by the therapists. The diary was meant for registration of exercise compliance, pain before, during and after exercises (using the VAS score), intake of pain medication, and pain relief in the form of heat or cold application. The TheraBite exercise program was provided by a physical therapist and the DTS exercise program was provided by a dentist. The patients filled in questionnaires (Mandibular Functional Impairment Questionnaire (MFIQ)[13], European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Cancer module (EORTC QLQ-C30),

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Head & Neck cancer modules (EORTC QLQ-H&N35) [14-16]) and their MMO was measured.

To evaluate stretching exercises and to answer questions, the patients visited the therapists after 3 and 6 weeks. Due to the high burden of the program for patients, the visits after 3 and 6 weeks were replaced by telephone consultations. During the second visit (T2), 12 weeks after T1, the stretching device and diary were handed in. The patients filled in questionnaires (MFIQ, EORTC QLQ-C30, EORTC QLQ-H&N35 and the Dutch version of the Quebec User Evaluation of Satisfaction with Assistive Technology questionnaire 2.0 (D-Quest 2.0) [17]) and MMO was measured. During the third visit (T3), 26 weeks after T1, the patients filled in questionnaires (MFIQ, EORTC QLQ-C30 and EORTC QLQ-H&N35) and MMO was measured again.

During the visits, JG had an interview with the patients about their experiences with the stretching devices and exercise protocol.

Data collection

Additional patient data was retrieved from the patient files in the hospital information system: gender, date of birth, tumour localization (maxilla or mandible, tongue, cheek, pharynx, salivary glands, others), cT classification based on the Union for International Cancer Control (UICC) TNM classification 2009 (T1-2, T3-4, no classification available), date of last cancer treatment, surgery (yes, no), neck dissection (yes, no), reconstruction after surgery (skin graft, soft tissue flap, bony tissue flap), radiotherapy (yes, no), total dose of radiotherapy (Gy), and chemotherapy (yes, no).

For the primary outcome, MMO was measured by JG using a sliding calliper. Patient ID, MMO and dental status were recorded on a separate form. Patients were classified as dentate when they had frontal dentition or wore prosthesis. The incisal edges of the upper central incisor 11 and the lower central incisor 41 were used as measurement points. Patients were classified as edentulous if they had no frontal dentition and wore no prosthesis. The top of the alveolar ridge at the former location of the 11 and 41 were used as measurement points. Patients were classified as partially edentulous if they had a frontal dentition or wore prosthesis in one jaw (upper or lower jaw) and had no dentition or wore no prosthesis on the other jaw (upper or lower jaw).

For the secondary outcomes, the questionnaires and the diary were collected. The primary focus was on the results of the mandibular function and the "Opening the mouth" score of the EORTC QLQ-H&N35, as those are most likely related to the MMO.

Statistical analysis

Due to the small sample sizes and skewed data, non- parametric analyses were performed. MMO measurements and the scores of the domains of the questionnaires were described using the median and interquartile range.

The differences between the groups (TheraBite and DTS) and the differences in changes over time between the groups regarding MMO, MFIQ and quality of life were analysed using the Mann-Whitney U test.

P-values less than 0.05 were considered statistically significant. Analyses were performed using IBM SPSS Statistics Program version 23.0.

RESULTS

Recruitment

In total, 166 patients were assessed for eligibility, of which 86 did not meet the inclusion criteria, 35 declined to participate, and18 did not participate due to other reasons (Figure 1). In most cases, patients declined to participate because they thought the protocol was too intensive or because they had no desire to receive therapy for their restricted mouth opening. Other reasons for non-participation were overall poor health, old age (≥80 years), or because using the stretching device was not possible due to previous extensive treatment for head and neck cancer (such as hemi-mandibulectomy or large cheek resections).

Blinding

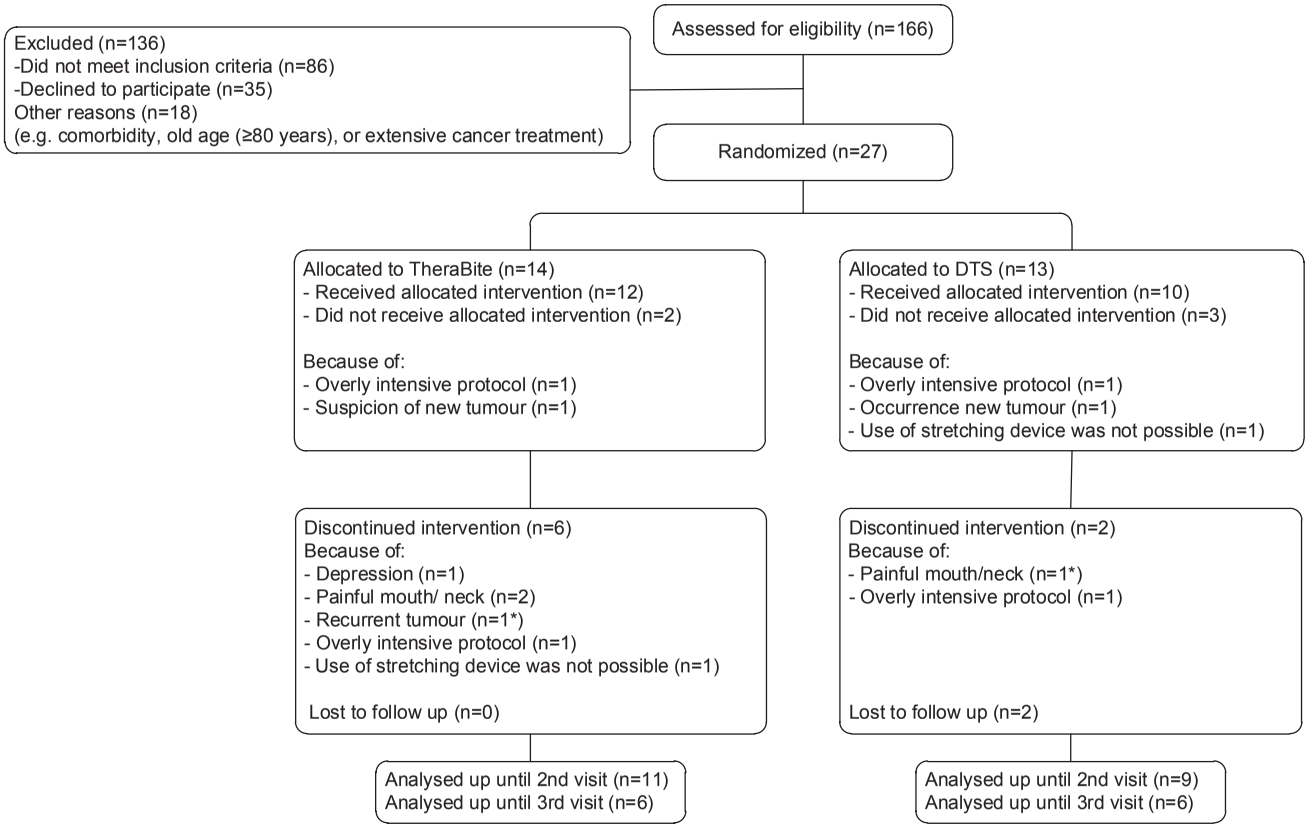
In order to answer questions of patients and refer them to the right department (dental or rehabilitation department), blinding of JG could not be maintained.

The exercise program

In total, 27 patients were enrolled in the study (Figure 1). Five patients did not start the exercise program due to reconsideration of the exercise program (n=2; too intensive, too much comorbidity), occurrence or suspicion of new tumour (n=2), and because use of a stretching device was not possible (n=1; insufficient support of lower plate as the patient could not wear a lower prosthesis due to sensitivity of the lower jaw).

Of the 22 patients who started the protocol, eight discontinued exercises due to additional depression/suicide attempt (n=1), painful mouth/neck (n=3), recurrent tumour (n=1), overly intensive protocol (n=2), use of stretching device was not possible (n=1) (mouth opening of approximately 7mm). Two patients were lost to follow up.

Figure 1. Flow diagram of patient randomization and analysis.



*no data available

Adverse events

Eleven adverse events occurred. One patient suffered from extreme migraine attacks and vision difficulties during the exercise program. This patient was familiar with a history of migraine attacks and vision difficulties before the exercise program began. In consultation with an ophthalmologist, it was determined that the migraines and vision difficulties were not triggered by the stretching exercises. Two patients had ulcers related to wearing dental prosthesis. If an ulcer was observed, the prosthesis was adjusted. Three patients had sores in the corner of their mouths; petroleum jelly was advised and was in most cases a sufficient treatment. Two patients reported problems with tenderness of the masticatory muscles, which was related to the exercises. Patients used pain medication, hot or cold application, reduced force of stretching device, or reduced intensity of exercise protocol. One patient had an uncomplicated fracture of a molar. The sharp edges were removed. Another patient had jaw spasms during and after stretching, due to incorrect use of the stretching device. Together with the physical therapist, the use of the stretching device was modified. One patient experienced pain while stretching. A depression developed and exercises were stopped.

Serious adverse events

Four serious adverse events were reported but were unrelated to the stretching device. These adverse advents consisted of metastasis (n=1), recurrent tumour growth (n=2), and new primary tumour (n=1). One of these patients did not receive therapy (DTS). One patient discontinued therapy (TheraBite). The exercise program was modified for the other two patients (both received therapy with the DTS). This modified program included a temporary cessation of exercises; after cancer treatment, exercises were resumed based on what the patient thought was achievable.

Premature stop

The study was stopped prematurely due to the low inclusion rate and high attrition rate of patients.

Patient population

Patient, tumour and treatment characteristics of those who received the TheraBite were not significantly different from those who received the DTS (Table 1). Of the patients who dropped out of the study, significantly more had received radiotherapy as treatment (or part of treatment). Slightly more females than males dropped out of the study, but this difference was not significant.

Table 1. Patient, tumour and treatment characteristics of patients receiving TheraBite versus DTS and patients who discontinued the study versus those who completed the study.

	TheraBite (n=14)	DTS (n=13)		Discontinued (n=15)	Complete (n=12)	
	n (%)	n (%)	*p*	n (%)	n (%)	*p*
Patient characteristics						
Male	7(50)	8(62)	*0.547*	6(40)	9(75)	*0.069*[c]
Age at baseline (years); Med (IQR)	67.8(63.6;73.9)	64.7(56.3;69.1)	*0.140*[a]	68.0(62.4;75.3)	64.0(57.9;68.5)	*0.166*[a]
MMO; Med(IQR)	27.0(18.0;29.0)	22.0(19.0;25.0)	*0.663*[a]	(21.5(14.5;28.0)	(24.0(20.5;28.5)	*0.235*[a]
Dental status[d]			*0.825*			*0.385*
Dentate	10(77)	8(73)		8(67)	10(83)	
Partially edentulous	2(15)	1(9)		1(8)	2(17)	
Edentulous	1(8)	2(18)		3(25)	0(0)	
Group ≤36 months[e]	6 (43)	5 (39)		6(43)	6(46)	
MMO; Med(IQR)	16.0 (8.1;16.7)	9.7 (7.2;12.6)	*0.418*[a]	9.3 (8.3;11.2)	15.0 (8.1;16.1)	*0.556*[a]
Group >36 months[e]						
MMO; Med(IQR)	98.4 (54.2;132.7)	53.2 (41.0;157.0)	*0.439*[a]	119.3 (54.2;132.7)	65.3 (42.5;157.0)	*0.606*[a]
Tumour characteristic						
Multiple primary tumours	2(14)	4(31)	*0.385*	4(27)	2(17)	*0.662*
Tumour localization			*0.840*			*0.558*
Maxilla or Mandible	4(29)	2(15)		2(13)	4(33)	
Tongue	1(7)	3(23)		3(20)	1(8)	
Cheek	1(7)	2(15)		1(7)	2(17)	
Pharynx	5(36)	3(23)		4(27)	4(33)	
Salivary glands	1(7)	1(8)		2(13)	0(0)	
Others	2(14)	2(15)		3(20)	1(8)	
cT-stage[d]			*0.188*			*1.000*
T1,2	5(36)	3(23)		4(27)	4(33)	
T3,4	9(64)	7(54)		9(60)	7(58)	
Treatment characteristics						
Surgery	10(71)	10(77)	*1.000*	11(73)	9(75)	*1.000*
Neck dissection	8(57)	7(54)	*1.000*	7(50)	8(67)	*0.391*
Reconstruction			*0.571*			*0.267*
Skin graft	1(20)	3(60)		2(100)	2(25)	
Soft tissue flap	2(40)	1(20)		0(0)	3(38)	
Bony tissue flap	2(40)	1(20)		0(0)	3(38)	
Radiotherapy	6(43)	5(39)	*1.000*	9(60)	2(17)	***0.047***[b]
Total dose (Gy)	70.0(60.0;70.0)	68.0(66.0;70.0)	*0.739*[a]	70.0(59.0;70.0)	68.0(66.0;70.0)	*0.970*[a]
Chemotherapy	4(29)	5(39)	*0.695*	3(20)	6(50)	*0.217*

Table 1. (Continued)

	TheraBite (n=14)	DTS (n=13)	*p*	Discontinued (n=15)	Complete (n=12)	*p*
TheraBite				8(53)	6(50)	*0.863*
DTS				7(47)	6(50)	
Heat or cold application	3(21)	2(15)	*1.000*	3(20)	2(17)	*1.000*
Intake pain medication	3(21)	1(8)	*0.596*	2(13)	2(17)	*1.000*
Continue exercising after 3 months	2(33)	3(38)	*1.000*	1(50)	4(33)	*1.000*

Data is presented in numbers (%) or median (25th;75th percentile)
P-values are the result of the Chi-Square test.
a: p-values are the result of the Mann-Whitney U test.
b: p-values <0.05
c: p-values near significance level (<0.05)
d: Dental status: data of three patients are missing, these patients dropped out of the study before measurement could take place.
e: Interval between last tumour treatment and start exercise protocol (months)
MMO: Maximal mouth opening at baseline (millimetres)
cT-classification: data of three patients are missing, as information could not be retrieved from the patient files in the hospital information system.

Primary outcome

No significant differences in MMO between the two devices were found (Table 2). Patients who exercised with the TheraBite gained 3.0 mm (median) and those who exercised with the DTS gained 1.5 mm (median) (Table 3). Between T1 and T3, the MMO of one patient who exercised with the DTS decreased by 13 mm. This patient developed a tumour during the trial. When this patient was excluded from the analyses, no substantial changes between T1 and T3 were found when comparing the outcomes of this study. Patients who started exercises 36 months or less after cancer treatment began with a larger MMO of 23.0 mm (IQR 21.0; 29.0), and gained 2.5 mm (IQR 1.0; 3.0) at the end of the study protocol, while patients who started more than 36 months after cancer treatment had a median MMO of 20.0 mm (IQR 18.0; 27.0), and gained 2.0 mm (IQR -2.0; 4.0). No significant difference in gain in median MMO was found between the group who started early after cancer treatment and the group who started later after cancer treatment (p=0.936).

One patient recovered from trismus. This patient, who received the TheraBite, had an MMO of 33 mm on T1 and 38 mm on T2 and T3.

Secondary outcomes

Although not significant, patients receiving the TheraBite scored slightly worse on mandibular function, perception of difficulties opening the mouth than patients receiving the DTS. Of the other domains of the EORTC QLQ-C30 and EORTC QLQ-H&N35, patients who received the TheraBite scored worse than patients who received the DTS, especially on the following domains: constipation, senses problems, dry mouth and sticky saliva (Table 2 and 3).

Patient satisfaction regarding the stretching device, assessed with the D-Quest 2.0, did not differ significantly between the TheraBite (2.6, IQR 2.4;3.0) and the DTS (2.8, IQR 2.4;3.8), U=37.5, p=0.540.

Patient compliance with completing the diaries was poor. Data concerning exercise compliance and pain before, during or after exercises could not be reliably extracted or assessed.

During the interview, five patients stated that they experienced a gain in mouth opening immediately after doing the exercises, but the mouth opening declined soon thereafter. Two patients reported a gain in mouth opening during the first weeks (approximately four weeks), but no further gain thereafter. Three patients reported no effect even though they complied with the protocol regimen. Besides gain in mouth opening, one patient reported more saliva flow in the front part of the mouth, four patients reported improved suppleness of the mouth (which led to improvements in speaking and eating), one patient reported improved smell and taste, but was in doubt whether it was related to the stretching exercises.

Two patients who received the TheraBite reported difficulties with using the device because the rotation angle of the TheraBite was not the same as the rotation angle of the lower jaw and because grip was difficult as the plates became slippery. One patient who received the DTS reported difficulty applying enough force, as the upper denture tilted when force was applied.

Table 2. Differences between groups (TheraBite versus DTS) at T1,T2, and T3.

	TheraBite	DTS	T1	TheraBite	DTS	T2	TheraBite	DTS	T3
	Med (IQR)	Med (IQR)	*p*	Med (IQR)	Med (IQR)	*p*	Med (IQR)	Med (IQR)	*p*
Maximal mouth opening (millimetres)	27.0 (18.0;29.0)	22.0 (19.0;25.0)	*0.663*	25.0 (16.0;32.0)	26.0 (22.0;28.0)	*0.849*	29.0 (25.0;32.0)	24.5 (17.0;30.0)	*0.261*
MFIQ	34.0 (26.3;38.6)	28.0 (13.0;37.0)	*0.185*	31.0 (27.0;42.0)	15.5 (9.0;36.0)	*0.200*	31.5 (27.5;37.0)	8.3 (5.0;17.0)	*0.065*[a]
EORTC QLQ c30									
Global quality of life	83.3 (75.0;83.3)	83.3 (75.0;100.0)	*0.276*	83.3 (66.7;91.7)	91.7 (75.0;100.0)	*0.456*	66.7 (58.3;83.3)	87.5 (75.0;100.0)	*0.197*
Physical Functioning	90.0 (73.3;100.0)	86.7 (80.0;100.0)	*0.750*	80.0 (66.7;93.3)	86.7 (60.0;100.0)	*0.560*	90.0 (66.7;100.0)	96.7 (86.7;100.0)	*0.616*
Role Functioning	83.3 (58.3;100.0)	100.0 (83.3;100.0)	*0.101*	83.3 (50.0;100.0)	100.0 (100.0;100.0)	*0.315*	83.3 (66.7;100.0)	100.0 (100.0;100.0)	*0.209*
Emotional Functioning	100.0 (83.3;100.0)	91.7 (58.3;100.0)	*0.153*	95.8 (83.3;100.0)	100.0 (75.0;100.0)	*0.820*	83.3 (75.0;100.0)	100.0 (91.7;100.0)	*0.231*
Cognitive Functioning	91.7 (66.7;100.0)	100.0 (83.3;100.0)	*0.713*	100.0 (66.7;100.0)	100.0 (83.3;100.0)	*0.777*	91.7 (83.3;100.0)	100.0 (100.00;100.00)	*0.293*
Social Functioning	100.0 (91.7;100.0)	100.0 (66.7;100.0)	*0.495*	100.0 (66.7;100.0)	100.0 (100.0;100.0)	*0.916*	75.0 (66.7;83.3)	100.0 (100.0;100.0)	*0.072*
Fatigue	11.1 (0.0;38.9)	16.7 (0.0;55.6)	*0.801*	22.2 (0.0;33.3)	11.1 (0.0;11.1)	*0.443*	33.3 (22.2;44.4)	5.6 (0.0;11.1)	*0.140*
Nausea and vomiting	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.563*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.909*	0.0 (0.0;33.3)	0.0 (0.0;16.7)	*0.924*
Pain	0.0 (0.0;16.7)	0.0 (0.0;33.3)	*0.744*	8.3 (0.0;33.3)	0.0 (0.0;50.0)	*0.785*	16.7 (0.0;33.3)	0.0 (0.0;16.7)	*0.388*
Dyspnea	0.0 (0.0;33.3)	0.0 (0.0;0.0)	*0.183*	0.0 (0.0;33.3)	0.0 (0.0;0.0)	*0.426*	16.7 (0.0;33.3)	0.0 (0.0;0.0)	*0.211*

Table 2. (Continued)

	TheraBite Med (IQR)	DTS Med (IQR)	T1 *p*	TheraBite Med (IQR)	DTS Med (IQR)	T2 *p*	TheraBite Med (IQR)	DTS Med (IQR)	T3 *p*
Insomnia	0.0 (0.0;16.7)	0.0 (0.0;33.3)	*0.904*	0.0 (0.0;33.3)	0.0 (0.0;33.3)	*0.849*	33.3 (0.0;33.3)	0.0 (0.0;0.0)	*0.083*
Appetite loss	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.922*	0.0 (0.0;0.0)	0.0 (0.0;33.3)	*0.398*	16.7 (0.0;33.3)	0.0 (0.0;0.0)	*0.386*
Constipation	0.0 (0.0;16.7)	0.0 (0.0;66.7)	*0.245*	0.0 (0.0;33.3)	0.0 (0.0;0.0)	***0.039****	0.0 (0.0;33.3)	0.0 (0.0;0.0)	*0.673*
Diarrhea	0.0 (0.0;16.7)	0.0 (0.0;0.0)	*0.325*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.699*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*1.0000*
Financial difficulties	0.0 (0.0;0.0)	0.0 (0.0;33.3)	*0.225*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.818*	0.0 (0.0;0.0)	0.0 (0.0;33.3)	*0.673*
EORTC QLQ H&N35									
Pain	20.8 (16.7;33.3)	25.0 (8.3;41.7)	*0.803*	29.2 (22.5;33.3)	25.0 (0.0;33.3)	*0.708*	29.2 (16.7;41.7)	16.7 (0.0;25.0)	*0.294*
Swallowing	16.7 (8.3;25.0)	8.3 (0.0;16.7)	*0.056*[a]	16.7 (0.0;25.0)	8.3 (0.0;8.33)	*0.446*	20.8 (8.3;41.7)	0.0 (0.0;8.3)	*0.081*
Problems with senses	25.0 (0.0;33.3)	0.0 (0.0;0.0)	***0.009****	16.7 (0.0;50.0)	0.0 (0.0;0.0)	*0.055*[a]	33.3 (33.3;33.3)	0.0 (0.0;0.0)	***0.034****
Problems with speech	11.1 (0.0;38.9)	0.0 (0.0;11.1)	*0.341*	0.0 (0.0;55.6)	0.0 (0.0;11.1)	*0.706*	16.7 (11.1;33.3)	0.0 (0.0;11.1)	*0.132*
Trouble with social eating	33.3 (12.5;37.5)	8.3 (0.0;50.0)	*0.289*	33.3 (16.7;50.0)	8.3 (0.0;58.3)	*0.284*	20.8 (16.7;41.7)	4.2 (0.0;8.3)	*0.051*[a]
Trouble with social contact	6.7 (0.0;18.3)	0.0 (0.0;6.7)	*0.405*	0.0 (0.0;13.33)	0.0 (0.0;13.3)	*0.925*	6.7 (6.7;13.3)	0.0 (0.0;0.0)	*0.101*
Less sexuality	25.0 (0.0;33.3)	0.0 (0.0;66.7)	*0.647*	25.0 (0.0;58.3)	0.0 (0.0;100.0)	*0.821*	41.7 (33.3;66.7)	0.0 (0.0;0.0)	*0.067*[a]

Table 2. (Continued)

	TheraBite Med (IQR)	**DTS** Med (IQR)	**T1** *p*	**TheraBite** Med (IQR)	**DTS** Med (IQR)	**T2** *p*	**TheraBite** Med (IQR)	**DTS** Med (IQR)	**T3** *p*
Teeth	33.3 (16.7;50.00)	33.3 (0.0;33.3)	*0.204*	16.7 (0.0;100.0)	33.3 (0.0;33.0)	*0.693*	16.7 (0.0;66.7)	0.0(0.0;33.3)	*0.367*
Opening mouth	83.3 (50.0;100.0)	33.3 (33.3;100.0)	*0.327*	66.7 (33.3;100.0)	33.3 (0.0;66.7)	*0.083*	66.7 (33.3;66.7)	33.3 (33.3;66.7)	*0.309*
Dry mouth	75.0 (50.0;100.0)	33.3 (0.0;33.3)	***0.011****	83.3 (33.3;100.0)	0.0 (0.0;33.3)	***0.009****	50.0 (33.3;100.0)	16.7 (0.0;33.3)	*0.053*[a]
Sticky saliva	66.7 (33.3;83.3)	0.0 (0.0;33.3)	***0.006****	66.7 (33.3;100.0)	0.0 (0.0;33.3)	***0.047****	33.3 (33.3;33.3)	0.0 (0.0;33.3)	*0.227*
Coughing	0.0 (0.0;33.3)	0.0 (0.0;33.3)	*0.944*	16.7 (0.0;33.3)	0.0 (0.0;66.7)	*0.788*	16.7 (0.0;33.3)	0.0 (0.0;33.3)	*0.465*
Felt ill	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.950*	0.0 (0.0;0.0)	0.0 (0.0;33.3)	*0.673*	50.0 (0.0;66.7)	0.0 (0.0;0.0)	*0.105*
Pain killers	0.0 (0.0;100.0)	0.0 (0.0;100.0)	*0.561*	100.0 (0.0;100.0)	0.0 (0.0;100.0)	*0.509*	50.0 (0.0;100.0)	50.0 (0.0;100.0)	*1.000*
Nutritional supplements	0.0 (0.0;100.0)	0.0 (0.0;100.0)	*0.672*	0.0 (0.0;100.0)	0.0 (0.0;100.0)	*1.000*	0.0 (0.0;100.0)	0.0 (0.0;0.0)	*0.523*
Feeding tube	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.925*	0.0 (0.0;100.0)	0.0 (0.0;0.0)	*0.081*	0.0 (0.0;100.0)	0.0 (0.0;0.0)	*0.138*
Weight loss	0.0 (0.0;0.0)	0.0 (0.0;100.0)	*0.547*	0.0 (0.0;100.0)	0.0 (0.0;0.0)	*0.331*	0.0 (0.0;100.0)	0.0 (0.0;0.0)	*0.523*
Weight gain	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.166*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.292*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.317*
Weight gain	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.166*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.292*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.317*

Table 3. Differences between time points and between groups (TheraBite versus DTS).

	TheraBite	DTS	T2-T1	TheraBite	DTS	T3-T1
	Med (IQR)	Med (IQR)	*p*	Med (IQR)	Med (IQR)	*p*
Maximal mouth opening (millimetres)	2.0 (0.0;4.0)	2.0 (1.0;4.0)	*0.618*	3.0 (-2.0;4.0)	1.5 (1.0;3.0)	*0.628*
MFIQ	3.8 (-2.5;7.8)	-1.0 (-4.0;1.5)	*0.500*	1.5 (-3.5;5.0)	-1.7 (-7.0;3.0)	*0.470*
EORTC QLQ c30						
Global quality of life	0.0 (0.0;12.5)	0.0 (-8.3;0.0)	*0.272*	2.1 (-16.7;4.2)	0.0 (-8.3;0.0)	*0.870*
Physical Functioning	0.0 (-6.7;0.0)	0.0 (-13.3;0.0)	*0.880*	-3.3 (-6.7;0.0)	0.0 (-6.7;0.0)	*1.000*
Role Functioning	0.0 (0.0;16.7)	0.0 (0.0;0.0	*0.091*	8.3 (-16.7;33.3)	0.0 (0.0;0.0)	*0.346*
Emotional Functioning	0.0 (0.0;0.0)	0.0 (0.0;8.3)	*0.705*	-8.3 (-16.7;8.3)	0.0 (0.0;0.0)	*0.591*
Cognitive Functioning	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.875*	0.0 (-16.7;0.0)	0.0 (0.0;0.0)	*0.652*
Social Functioning	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.330*	-16.7 (-33.3;0.0)	0.0 (0.0;0.0)	*0.071*
Fatigue	0.0 (0.0;11.1)	0.0 (-11.1;11.1)	*0.752*	5.6 (-11.1;22.2)	-5.6 (-16.7;11.1)	*0.332*
Nausea and vomiting	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.317*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.902*
Pain	0.0 (-16.7;0.0)	0.0 (0.0;16.7)	*0.207*	0.0 (-16.7;16.7)	0.0 (0.0;16.7)	*0.605*
Dyspnea	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.586*	0.0 (0.0;33.3)	0.0 (0.0;0.0)	*0.138*

Table 3. **(Continued)**

	TheraBite	DTS	T2-T1	TheraBite	DTS	T3-T1
	Med (IQR)	Med (IQR)	*p*	Med (IQR)	Med (IQR)	*p*
Insomnia	0.0 (0.0;0.0)	0.0 (0.0'0.0)	*0.903*	0.0 (0.0;33.3)	0.0 (-33.3;0.0)	*0.056*[a]
Appetite loss	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.096*	0.0 (0.0;33.3)	0.0 (0.0;.0)	*0.830*
Constipation	0.0 (0.0;0.0)	0.0 (-33.3;0.0)	*0.197*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.317*
Diarrhea	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.169*	0.0 (-33.3;0.0)	0.0 (0.0;0.0)	*0.138*
Financial difficulties	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.586*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.674*
EORTC QLQ H&N35						
Pain	-8.3 (-16.7;5.8)	0.0 (-8.3;25.0)	*0.195*	12.5 (0.0;16.7)	0.0 (0.0;0.0)	*0.244*
Swallowing	-8.3 (-16.7;-4.2)	0.0 (0.0;8.3)	*0.054*[a]	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.562*
Problems with senses	0.0 (0.0;16.7)	0.0 (0.0;0.0)	*0.427*	16.7 (0.0;33.3)	0.0 (0.0;0.0)	*0.209*
Problems with speech	0.0 (-11.1;0.0)	0.0 (0.0;0.0)	*0.119*	0.0 (0.0;11.1)	0.0 (0.0;11.1)	*0.857*
Trouble with social eating	0.0 (-8.3;8.3)	0.0 (-8.3;8.3)	*0.892*	8.3 (0.0;16.7)	0.0 (-8.3;11.1)	*0.055*[a]
Trouble with social contact	0.0 (-3.3;0.0)	0.0 (0.0;13.3)	*0.070*[a]	0.0 (-3.3;6.7)	0.0 (0.0;0.0)	*0.864*
Less sexuality	0.0 (-8.3;0.0)	0.0 (0.0;16.7)	*0.432*	8.3 (0.0;33.3)	0.0 (16.7;0.0)	*0.126*

Table 3. **(Continued)**

	TheraBite	DTS	T2-T1	TheraBite	DTS	T3-T1
	Med (IQR)	Med (IQR)	*p*	Med (IQR)	Med (IQR)	*p*
Teeth	0.0 (-33.3;0.0)	0.0 (0.0;0.0)	*0.527*	0.0 (-33.3;33.3)	0.0 (0.0;0.0)	*0.788*
Opening mouth	0.0 (-33.3;0.0)	-33.3 (-33.3;0.0)	*0.571*	0.0 (-33.3;0.0)	0.0 (-33.3;0.0)	*0.857*
Dry mouth	0.0 (-33.3;0.0)	0.0 (0.0;0.0)	*0.874*	0.0 (-50.0;33.3)	0.0 (0.0;0.0)	*0.863*
Sticky saliva	0.0 (0.0;0.0)	0.0 (0.0;33.3)	*0.102*	-33.3 (-33.3;0.0)	0.0 (0.0;33.3)	*0.054*[a]
Coughing	0.0 (0.0;0.0)	0.0 (0.0;33.3)	*0.667*	0.0 (0.0;33.3)	0.0 (0.0;0.0)	*0.336*
Felt ill	0.00 (0.0;0.0)	0.0 (0.0;33.3)	*0.197*	50.0 (0.0;66.7)	0.0 (0.0;0.0)	*0.105*
Pain killers	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.317*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*1.000*
Nutritional supplements	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*1.000*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*1.000*
Feeding tube	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.317*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.317*
Weight loss	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.562*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*1.000*
Weight gain	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.317*	0.0 (0.0;0.0)	0.0 (0.0;0.0)	*0.317*

P-values are the result of the Mann-Whitney U test.
*: P-values <0.05
a: P-values near significance level (<0.05)

DISCUSSION

Key results

No significant differences between the two stretching devices were found regarding maximal mouth opening in this head and neck cancer population with trismus.

Attrition rate

A relatively high percentage of patients dropped-out of our study (56%). Drop-out rates ranging from 11% to 42% were found in similar studies.[18-23] High drop-out rates in exercise studies among head and neck cancer patients seem common, as an intensive protocol was prescribed for patients who were already burdened. The reasons for drop-out in these similar studies were related to stretching problems, such as pain during exercises[20,22,23], no perceived improvement[19], and fitting issues of stretching device.[18,22]. The reasons were also related to other patient factors, such as early mortality[18-21,24], tumour progression (recurrent tumour or metastasis)[18,20,24] or lack of need for therapy.[18] Some of these studies did not report a drop-out rate.[9,10] In one study, only patients who completed the stretching protocol were analysed.[10]

Maximal mouth opening

No significant improvement in MMO was found in our study. The median increase in MMO using the TheraBite (3.0 mm) and the DTS (1.5 mm) was very small in our study compared to other studies. Greater improvements of 5.4 mm, SD 5.7 using the TheraBite[25] or 6.2mm, SD 3.4 using the DTS[19] have been reported, but both of these studies were retrospective in design. Their study design might have led to selection bias and an overestimation of the effect. Additionally, both of these studies had a higher frequency of follow-up appointments at shorter intervals, during which patients were informed, guided, and motivated, which might have led to improved compliance and better execution of exercises.[19,25] Due to the incomplete diaries in our study, compliance could not be determined reliably and could not be compared with other studies. Another study with a prospective design reported a median increase of 9.7 mm (Range 1-21) using the TheraBite.[26] Exercises were introduced to prevent trismus. The patients included in that study had a larger mean baseline mouth opening of 30 mm (range 24-38 mm) and might not have been at risk for trismus. Additionally, the exercises started early, within 6 weeks postoperatively.[26] The earlier patients start exercising, the more likely the exercises will result in a gain of MMO.[25] However, the additional benefit of starting exercises early could not be confirmed in our study.

Patients' perception

No significant differences regarding mandibular function and patients' perception of difficulties opening the mouth were found. The domains that were found to be significantly different: constipation, problems with senses, dry mouth and sticky saliva, were less likely to be influence by the stretching devices used.

Although not significant, patients who received the TheraBite had a slightly worse baseline status than the DTS; they had a longer interval between cancer treatment and exercise, had a larger tumour (higher T-classification), and received radiotherapy more frequently (Table 1), which could explain these slightly worse domain scores.

Study limitations and strengths

A limitation of this study was that blinding of the patient and therapist was not possible and blinding of the researcher JG could not be maintained. To reduce the risk of bias as much as possible, the measurement tool was standardized using a spring with a standard stretching force (1.7 Newton). Additionally, during measurement, patients were encouraged only once to open the mouth as wide as possible and MMO was rounded up to the higher value in case of doubt. Another limitation was the high drop-out rate. Additionally, not all patients who completed the protocol, completed their patient diary or questionnaires, leading to missing data. As a result, we had limited statistical power for data analyses.

However, the results of this study provide information on what to expect when performing similar studies or using similar exercise protocols.

Conclusion

No differences in effects on MMO between the TheraBite, and DTS were found. High attrition rates and stretching problems are common when prescribing an intensive stretching protocol on head and neck cancer patients.

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