TURKISH JOURNAL of ONCOLOGY

Turk J Oncol 2024;39(2):191–199
doi: 10.5505/tjo.2024.4231

ORIGINAL ARTICLE

The Importance of Self-Rehabilitation in Irradiated Head and Neck Cancer Patients

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OBJECTIVE

Restricted mouth opening (trismus) is a common late effect of radiotherapy (RT) in patients (pts) with head and neck cancer. This study aims to reveal whether self-rehabilitation therapy, without any apparatus utilized after RT, has any therapeutic impact on trismus and mouth opening distance (MOD) in head and neck cancer pts.

METHODS

Fifty-three consecutive pts with squamous cell carcinoma of the head and neck treated with RT ± chemotherapy (ChT) were included in the study. An MOD of less than 35mm was accepted as trismus. Self-rehabilitation exercises were started 3 months after RT and continued for 3 months. The risk factors for trismus and MOD in relation to exercises were determined using univariate and multivariate statistics.

RESULTS

The median age was 59 years (range: 31-84). Trismus was present in 41.5% of the group as a whole (22 of 53 pts). The MOD for the entire group prior to physiotherapy was 37.33±7.83mm, and it was 38.75±7.66mm after physiotherapy (p=0.035). In multivariate analysis, concomitant ChT (OR=5.648, 95% CI: 1.043–30.596) and time passed after RT of more than 36 months (OR=8.238, 95% CI: 1.410–48.136) were found to significantly increase the risk of trismus. However, when physiotherapy is used, these risk factors lose their significance.

CONCLUSION

Self-rehabilitation without the use of any apparatus was discovered to be an effective treatment for trismus after RT for the first time. We also discovered that self-rehabilitation improves the MOD values of the entire patient population.

Keywords: Chemotherapy; exercise; head and neck cancer; radiotherapy; physiotherapy; self-rehabilitation; trismus.

This study was presented in part at the ASTRO's 57th Annual Meeting (October 18–21, 2015, San Antonio, Texas, United States of America).

Received: November 16, 2023
Accepted: February 18, 2024
Online: February 29, 2024

Accessible online at:
www.onkder.org

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Turk J Oncol 2024;39(2):191–199
doi: 10.5505/tjo.2024.4231

INTRODUCTION

Head and neck radiotherapy (RT) is a highly effective therapeutic intervention in the treatment of head and neck cancer. Side effects of RT, such as cutaneous reactions, xerostomia, and mucositis, can have a negative impact on function and quality of life. However, the effects of RT or chemoradiotherapy (ChRT) on mastication are less well understood. Trismus, or restricted mouth opening, is a significant late effect of head and neck tumor irradiation that can cause difficulties with everyday activities such as chewing, swallowing, eating, breathing, and speaking.[1,2] Pain, loss of weight, and poor oral hygiene can all complicate the clinical scene. The disruption of the temporomandibular joint, tumor invasion into masticator muscles and mouth-closing muscles, and the presence of additional treatments such as surgery and chemotherapy can all increase the risk of trismus. The severity of trismus is affected by the patient's tolerance as well as several treatment-related factors such as the size of RT fields, the total dose of RT, and concurrent chemotherapy.[3–5] The restriction of mouth opening usually begins 2.5–3 months after the completion of RT and progresses over time. A 35mm cut-off value is widely accepted as the criterion for trismus.[4,6]

Patients at risk of trismus should begin trismus prevention exercises as soon as possible to maintain maximum mouth opening and jaw mobility. Once trismus has developed, it requires a rigorous exercise regimen, which may be supplemented with physiotherapy if necessary.[2] Patients with trismus can benefit from prosthetic appliances (dynamic bite openers) with springs and bands that stretch their muscles.[7] Compliance with trismus exercises by patients is critical to the success of preventative and treatment regimens. The aim of the current study is to identify the risk factors for trismus in patients with irradiated head and neck cancer whose disease has not spread to the temporomandibular joint, as well as to determine whether self-rehabilitation exercises used after RT have an effective therapeutic impact on mouth opening distances.

MATERIALS AND METHODS

The study included 53 patients with squamous cell carcinoma of the head and neck who were receiving RT at Trakya University, Department of Radiation Oncology. The study protocol was approved by the University's Medical-Ethical Review Board. The patients were evaluated in a multidisciplinary clinic, where they received evaluations and treatment recommendations from a physical therapist and radiation oncologists. The measurements were always taken by the same examiner. The patients were instructed to completely open their mouths, and the mouth opening distances (MOD) were measured in millimeters using a Boley gauge. When the maximal interincisal distance between the upper and lower alveolus is less than 35 mm, it is considered trismus, according to Dijkstra et al.[6].

Radiotherapy: Megavoltage beams were used to deliver RT using either a linear accelerator (6 MV) or a Cobalt-60 treatment unit. The patients were treated using either conventional (two lateral opposed and supraclavicular fields) or 3D conformal irradiation techniques. Patients were given a 66 Gy dose for T1–2 tumors and a 70 Gy dose for T3–4 tumors or persistent lymphadenopathy. To treat subclinical disease, a radiation dose of 50 (50–60) Gy was used.

Chemotherapy: Depending on the patients' overall medical condition, three cycles of concurrent cisplatin (CDDP) were administered, either every three weeks at 100 mg/m^2 or at weekly intervals at 40 mg/m^2.

Rehabilitation Program

Three months after RT, the patients were seen by the physiotherapist, the first mouth opening distance measurements were taken, and the rehabilitation program was initiated. The patients did self-rehabilitation exercises for three months. The second set of measurements was taken six months after RT. The exercises listed below are geared toward patients.[8] The exercises were performed three times a day, after breakfast, lunch, and dinner:

- Opening the mouth completely, counting to 3 seconds with the mouth open, and then closing the mouth – 5 times.
- Counting to 3 seconds with the chin on the right, then returning to the normal position – 5 times.
- Counting to 3 seconds with the chin on the left, then returning to the normal position – 5 times.
- Counting to 3 seconds with the chin forward, then returning to the normal position - 5 times.

Patients chewed two sticks of gum (Trident sugarless) for 15 minutes immediately following the exercises. For three months, they repeated these exercises on a daily basis.

Statistical Analysis

The normality assumption was checked using the Shapiro-Wilk test. The Student's t-test or Mann-Whitney U tests were used to compare two independent groups based on the normal distribution. The Wilcoxon signed-rank test was used to compare dependent groups. Pearson chi-square and Fisher's exact tests were used to

Table 1 Patient characteristics based on trismus before physiotherapy exercises

Variable	Trismus Before physiotherapy exercises				p
	Yes (n=22)		No (n=31)		
	n	%	n	%	
Gender					
Male	15	35.7	27	64.3	0.198
Female	7	63.6	4	36.4	
Age (year)	57.6±12.3		61±12.8		0.335
Primary tumour site					
Nasopharynx	5	83.3	1	16.7	0.006*
Larynx	8	25.0	24	75.0	
Other	9	60.0	6	40.0	
Concomitant ChT					
Yes	18	50.0	18	50.0	0.068
No	4	23.5	13	76.5	
Tumour stage					
Early (T1-T2)	8	38.1	13	61.9	0.634
Late (T3-T4)	13	44.8	16	55.2	
Nodal stage					
N0-1	8	36.4	14	63.6	0.474
N2-3	13	46.4	15	53.6	
Primary treatment					
RT	12	46.2	14	53.8	0.501
RT+S	10	37.0	17	63.0	
Time after RT					
≤36 months	11	32.4	23	67.6	0.025*
>36 months	10	66.7	5	33.3	
RT dose					
≤50	1	20.0	4	80.0	0.389
>50	21	43.8	27	56.2	

Descriptives expressed as mean±standard deviation and frequency (percentage). *: Statistically significant at p<0.05.
ChT: chemotheraphy; RT: Radiotherapy; S: Surgery

investigate relationships between categorical variables. Multivariate logistic regression models were used to detect independent risk factors for trismus before and after physiotherapy. Descriptives were expressed as mean and standard deviation or median and interquartile range for numerical variables, and as frequency and percentages for categorical variables. A p-value of less than 0.05 was considered statistically significant. All analyses were performed using R software version 4.0.3.

RESULTS

In this study, 53 patients were examined. The average age was 59 years (range: 31–84). Men made up 42 of the 53 patients (79%). The larynx was the most common primary tumor site (32 pts, 60.3%). Prior to RT, no patients had tumor invasion of the temporomandibular joint.

T3–4 disease was staged in 29 (54.2%) of the patients, while N2–3 disease was staged in 28 (52.8%). Adjuvant RT was given to 27 patients (51%) after initial surgery. Seventeen (32.1%) of these 27 patients received concomitant ChRT, whereas 10 (18.9%) received only RT. There were 26 patients who had definitive RT (49%). Seventeen (32.1%) of the 26 patients received concomitant ChRT. Only RT was applied to 9 (17%) of the patients. Concomitant ChRT was administered to 34 (64.1%) of the 53 patients, while RT alone was administered to 19 (35.9%). The average dose of RT was 63.1 Gy (range: 30–72 Gy). Table 1 summarizes the patients' characteristics based on trismus prior to treatment.

For the whole group, the rate of trismus was 41.5% (22 of 53 pts). Although there was no statistically significant difference between genders, trismus before physiotherapy was found to be higher in females

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doi: 10.5505/tjo.2024.4231

Table 2 Relations between time after radiotherapy, concomitant chemoradiotherapy, and primary tumor site with physiotherapy in regard to mouth opening distance (MOD)

	MOD before phisyothreapy (mm)	MOD after phisyothreapy (mm)	p
Time after RT			
≤36 months	40 (25–62)	40 (25–62)	0.242
>36 months	35 (8–48)	40 (10–50)	<0.001*
p	0.182	0.791	
Concomitant ChT			
Yes	35.83±7.51	36.77±7.35	0.313
No	40.52±7.56	42.94±6.71	<0.001*
p	0.040*	0.005*	
Primary tumour site			
Nasopharynx	30.00±11.30	31.67±12.51	0.329
Larynx	39.78±7.12	40.5±7.10	0.479
Other	36.07±5.26	37.87±4.56	<0.001
p	0.006*	0.027*	

Descriptives expressed as median (25^{th} –75^{th} percentile) and mean±standard deviation. *: Statistically significant at p<0.05.

than in males (63.6% vs. 35.7%; p=0.198). There was no statistically significant difference in the mean ages of the trismus and non-trismus groups (57.6±12.3 vs. 61±12.8; p=0.335). The primary tumor site was found to be a significant factor for trismus, as the prevalence of trismus was found to be higher in the nasopharynx compared to the larynx (83.3% vs. 25.0%; p=0.006). Trismus before therapy was more prevalent in patients who had concomitant chemotherapy (50.0% vs. 23.5%; p=0.068). Time after RT was another significant factor that affected trismus before physiotherapy. Trismus prevalence was found to be higher in patients with more than 36 months past after RT compared to less than 36 months (66.7% vs. 32.4%; p=0.025). There were no statistically significant differences in tumor stage (early: 38.1% vs. late: 44.8%; p=0.634), nodal stage (N0–1: 36.4% vs. N2–3: 46.4%; p=0.474), primary treatment (RT: 28.6%, RT+S: 43.5%; p=0.686), or RT doses (≤50 Gy: 20.0% vs. >50 Gy: 43.8%; p=0.389).

Before physiotherapy, the mean mouth opening distance (MOD) for the entire group was 37.33±7.83 mm. After physiotherapy, this value was found to be 38.75±7.66 mm, and the difference was statistically significant (p = 0.035). Time after RT, concurrent ChRT, and primary tumor localization were statistically significant factors in univariate analysis that could affect MOD in terms of physiotherapy. In patients with more than 36 months past after RT, the median MOD was 35 mm (8–48) before physiotherapy. Although patients with fewer than 36 months past after RT had a greater MOD [40 mm (25–62)] than those with more than 36 months [35 mm (8–48)], the difference was not statistically significant (p = 0.182). However, the median MOD values in these two groups converged after physiotherapy (40 mm (25–62) vs 40 mm (10–50); p = 0.791). In patients more than 36 months following RT, physiotherapy resulted in a substantial improvement in median MOD values (35 mm (8–48) vs. 40 mm (10–50), p<0.001). In patients with less than 36 months since RT, there was no significant difference in MOD values before and after physiotherapy (p=0.242). (Table 2).

Another risk factor for MOD was concurrent chemotherapy. Patients who received concurrent chemotherapy had significantly lower mean MOD values (35.83±7.51 mm and 36.77±7.35 mm) before and after physiotherapy than patients who did not receive concurrent chemotherapy (40.52±7.56 mm and 42.94±6.71 mm; p=0.04 and 0.005, respectively). Although physiotherapy improved mean MOD values somewhat in individuals receiving concurrent chemotherapy, the change was not significant (35.83±7.51 mm vs 36.77±7.35 mm; p=0.313). In patients who did not receive concurrent chemotherapy, however, physiotherapy resulted in a statistically significant improvement in mean MOD values (40.52±7.56 mm vs 42.94±6.71 mm; p<0.001) (Table 2).

Similarly, there were significant differences in MOD values among primary tumor sites before and after physiotherapy (p=0.006 and 0.027, respectively). Pa-

Table 3 Multivariate logistic regression results for independent risk factors of trismus before and after physiotherapy

	Model 1			Model 2		
	b	OR (95% CI)	p	b	OR (95% CI)	p
Gender (female)	–0.696	0.499 (0.049–5.076)	0.557	0.255	1.290 (0.149–11.174)	0.817
Primary tumour site						
Nasopharynx (reference)	–	–	–	–	–	–
Larynx	–2.416	0.089 (0.003–2.547)	0.158	–1.375	0.253 (0.015–4.333)	0.343
Other	–0.043	0.958 (0.047–19.427)	0.978	–1.136	0.321 (0.026–3.913)	0.373
Concomitant ChT (yes)	1.731	5.648 (1.043–30.596)	0.045	1.230	3.420 (0.614–19.056)	0.161
Time after RT (>36 months)	2.109	8.238 (1.410–48.136)	0.019	0.114	1.121 (0.232–5.404)	0.887

Model 1: Dependent variable is trismus before physiotherapy (trismus: n=22, non-trismus: n=31); Model 2: Dependent variable is trismus after physiotherapy (trismus: n=15, non-trismus: n=38). OR: Odds ratio; CI: Confidence interval

tients with tumors located in the nasopharynx had the lowest mean MOD values compared to those in the larynx and other locations before and after physiotherapy (30.00±11.30 mm and 31.67±12.51 mm, respectively). Although physiotherapy improved mean MOD values slightly, differences were not significant for nasopharynx and larynx localizations (p=0.329 and 0.479, respectively), but significant for other localizations (36.07±5.26 mm vs 37.87±4.56 mm; p<0.001) (Table 2).

Two multivariate logistic regression models were built to evaluate the risk factors for trismus before and after physiotherapy (Table 3). The variables with p-values less than 0.20 in Table 1 were included in the models as independent risk factors. In Model 1, where the dependent variable was trismus before physiotherapy, concomitant chemotherapy (OR=5.648, 95% CI: 1.043–30.596) and time passed after RT of more than 36 months (OR=8.238, 95% CI: 1.410–48.136) were found to significantly increase the risk of trismus. However, no significant independent risk factor was found in Model 2, where the dependent variable was trismus after physiotherapy. This result suggests that physiotherapy might be effective against trismus. The multivariate logistic regression results are visualized in Figure 1.

DISCUSSION

In this study, we aimed to determine whether self-rehabilitation therapy, used after RT, has an effective therapeutic impact on trismus in patients with irradiated head and neck cancer, for the first time. We discovered that the time elapsed after RT has a significant impact on MOD, with the longer the time elapsed after RT resulting in less MOD. Furthermore, there was a significant correlation in trismus incidence between concurrent ChRT and tumor localization. It was also discovered that self-rehabilitation exercises have a positive impact on MOD values in patients with more than 36 months of follow-up after RT, in patients who did not receive concurrent ChRT, and in patients whose tumors were not located in the nasopharynx or larynx.

The prevalence of trismus in patients with head and neck cancer ranges from 8% to 62%.[1,4,5,9–11] One reason for this variation is the lack of uniform criteria for defining trismus. Nguyen et al.[10] used 40 mm or less of MOD for trismus, whereas Chua et al.[12] used 25 mm or less. In this patient population, a MOD of 35 mm or less has been accepted as a cut-off level for trismus. The mouth opening was 35 mm or less in 22 of 53 patients (41.5%) in our study group, which is similar to the study of Johnson et al.,[13] which found trismus (35 mm) in 42% (29 of 69) of the patients.

Although trismus is an important RT-related side effect, there have been only a few prospective randomized studies comparing the rehabilitation programs.[12,14–18] Additionally, the best rehabilitation approach is still unclear.[15] The common and traditional approach to treating patients with RT-induced trismus is to treat them based on their needs in the event of loss of function in the symptomatic period.[19] Another approach is to integrate preventive rehabilitation into the existing

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doi: 10.5505/tjo.2024.4231

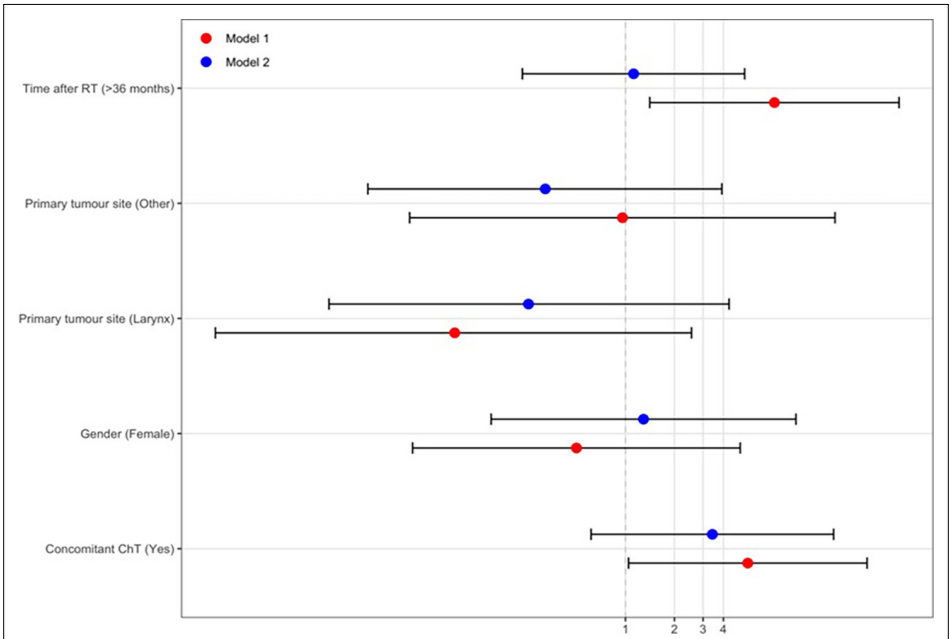

Fig. 1. Error bars for multivariate logistic regression models. The bars represent odds ratios and corresponding 95% confidence intervals.
Model 1: Dependent variable is trismus before physiotherapy (trismus: n=22, non-trismus: n=31);
Model 2: Dependent variable is trismus after physiotherapy (trismus: n=15, non-trismus: n=38).

clinical routines for all patients with or without trismus. However, the effectiveness of this approach is controversial. Some studies state that preventive exercises do not yield any improvement in MOD.[20] Ahlberg et al.[21] were not able to show any positive effect of early self-care preventive rehabilitation. In a recent meta-analysis, the authors found no significant difference between the standard of care and exercise therapy.[7]

Physiotherapy was applied with various apparatus in almost all studies to treat or prevent trismus.[7] Those apparatuses are used as incentives to improve exercise compliance or therapeutic effectiveness. Rubber plugs, wooden tongue blades, TheraBite exercisers, and dynamic bite openers are among the devices used.[1,4,22,23] So far, two studies have employed physiotherapy exercises without any apparatus for the prevention of trismus, but as with other prevention studies, no benefit has been found with this practice.[15,24] Grandi et al.[15] compared two different physiotherapy exercise methods, including the method described by Santos et al.,[8] to prevent trismus in irradiated patients. Although there were no statistically significant differences between the two methods, the authors stated that there was a trend toward better clinical results in patients who were given the exercises described by Santos et al. In another study, Hogdal et al.[24] looked at the effectiveness of early guided exercises combined with self-care treatment on trismus in 100 individuals undergoing head and neck irradiation. When compared to standard treatment, the authors discovered that an early exercise regimen did not appear to provide any additional benefits. Unlike previous studies, in the current study, the motion exercises without using any apparatus described by Santos et al.[8] were used for the treatment of trismus for the first time, and improvements in MOD values were obtained. It's possible that patients' compliance in conducting the exercises is higher once the problem occurs, which explains why exercises are more effective in treating than preventing trismus.

Because trismus is a late effect of RT, which causes fibrosis in the masticatory muscles and soft tissue of the cheek, its occurrence and severity worsen over time. According to studies, the restriction in MOD occurs quickly in the first year and continues for the next four years. Wang and colleagues investigated the long-term effects of RT on trismus after nasopharyngeal carcinoma and discovered that the MOD decreased significantly between one and nine months after RT, with an overall reduction of 32% in MOD within four years.[25] Furthermore, these findings were supported by a systematic review, which revealed that patients have a reduced MOD of 18% between 6 and 12 months after RT.[1] In

our study, time was also a prominent factor for trismus in multivariate analysis (p=0.019). Patients with more than 36 months past RT have less MOD than those with less than 36 months. Self-rehabilitation had a positive impact on MOD values in this patient group (p<0.001).

Another negative factor for trismus is applying chemotherapy concomitantly to RT. This approach is more intensive and leads to more fibrosis and hence more trismus. In a study by Jeremic et al.,[26] the most independently significant factor was concurrent chemotherapy in the multivariate analysis (p=0.0181) for moderate to severe trismus. Bensadoun et al.[27] discovered a 30.7% prevalence of trismus in 12 studies of concurrent ChRT in a systematic review. Similarly, in our study, patients who had concomitant chemotherapy had significantly lower mean MOD values than those who did not have concomitant chemotherapy, both before and after physiotherapy, and the application of physiotherapy made a slight improvement, which was not statistically significant in mean MOD values in patients who had concomitant chemotherapy (p=0.313). Furthermore, we discovered in multivariate analysis that concomitant ChT, one of the risk factors for trismus, lost significance with the application of self-rehabilitation exercises. However, as Payakachat et al.[28] illustrate, there has been other research with contradictory results. When comparing the surgery and RT groups to the ChRT group, the authors discovered that the median score differences on the open mouth item were considerably higher in the surgery and RT groups. Additionally, survivors in the ChRT group had more problems with swallowing, sticky saliva, feeding tubes, and weight gain, while survivors in the surgery and postoperative radiation therapy groups had more problems with trismus.

Tumor localization is one of the other risk factors for trismus. Tumors in the nasopharynx, oral cavity, and oropharynx involving the muscles of mastication have been linked to trismus due to the necessity of using a wider range of RT fields and irradiation of the temporomandibular joint.[13,26,29] Similarly, in our study, it was observed that patients with tumors located in the nasopharynx had the lowest mean MOD values compared to those in the larynx and other locations before and after physiotherapy. Moreover, physiotherapy did not make a significant improvement in MOD values in patients whose tumors were located in the nasopharynx and larynx.

Some other additional risk factors, such as gender, age, RT dose, and nodal status, have been found to contribute to the development of trismus in several studies.[14,30,31] However, their effectiveness has yet to be proven in the majority of other studies.[13,26,29] In our study, none of these risk factors was found to be significantly related to trismus.

Our research has some limitations. The first is that our study was not a randomized controlled trial. Furthermore, self-rehabilitation exercises were used in our study, and it is clear that it is impossible to determine the patient's compliance with these exercises and the extent to which the patients did these exercises as instructed. As a result, we believe it is prudent to approach our findings with caution. Furthermore, no apparatus was used in the exercises. It should be noted, however, that we discovered a significant contribution to MOD in our entire patient group with exercises performed on their own.

CONCLUSION

In conclusion, for the first time, the self-rehabilitation method used in this study, which did not include any apparatus, was found to be an effective method for treating trismus in irradiated patients with head and neck cancer. We also discovered that self-rehabilitation improves the MOD values of the entire patient group, especially in patients who have had more than 36 months of follow-up after RT, in patients who did not receive concurrent ChRT, and in patients whose tumors were not in the nasopharynx or larynx. These findings were obtained following a three-month period of exercise. We believe that long-term exercises would be more beneficial to MOD. Future randomized and multicenter studies are needed to characterize the associated risk factors for trismus and to determine the best treatment or prevention method.

Ethics Committee Approval: The study was approved by the Trakya University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (no: 19/20, date: 19/09/2012).

Authorship contributions: Concept – V.Y.Ç., F.Ö.; Design – V.Y.Ç., F.Ö., S.Y., M.Ç.; Supervision – V.Y.Ç., M.Ç.; Funding – V.Y.Ç., F.Ö., M.Ç.; Materials – V.Y.Ç., F.Ö., S.Y., G.T.; Data collection and/or processing – V.Y.Ç., F.Ö., S.Y., G.T.; Data analysis and/or interpretation – S.K., M.Ç.; Literature search – V.Y.Ç., M.Ç.; Writing –V.Y.Ç., M.Ç.; Critical review – M.Ç.

Conflict of Interest: All authors declared no conflict of interest.

Use of AI for Writing Assistance: Not declared.

Financial Support: None declared.

Peer-review: Externally peer-reviewed.

Turk J Oncol 2024;39(2):191–199
doi: 10.5505/tjo.2024.4231

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