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ORIGINAL ARTICLE

Prevalence and prediction of trismus in patients with head and neck cancer: A cross-sectional study

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Abstract

Background: Trismus occurs frequently in patients with head and neck cancer. Determining the prevalence and associated factors of trismus would enable prediction of the risk of trismus for future patients.

Methods: Based on maximal mouth opening measurements, we determined the prevalence of trismus in 730 patients with head and neck cancer. Associated factors for trismus were analyzed using univariate analyses and multivariate logistic regression analyses. Based on the regression model, a calculation tool to predict trismus was made.

Results: Prevalence of trismus was 23.6%. Factors associated with trismus were: advanced age; partial or full dentition; tumors located at the maxilla; mandible; cheek; major salivary glands; oropharynx; an unknown primary; a free soft tissue transfer after surgery; reirradiation; and chemotherapy.

Conclusion: About one-fourth of patients with head and neck cancer develop trismus. Based on prevalence and associated factors of trismus, a simple calculation tool predicts the risk of trismus in these patients.

KEYWORDS

head and neck neoplasms, mouth neoplasms, oral, risk factors, surgery, trismus

1 | INTRODUCTION

Trismus, also referred to as a restricted mouth opening, is a common problem in patients with head and neck cancer.[1] Patients with trismus often experience difficulties in performing activities of daily living, such as eating, drinking, laughing, and kissing.[2–5] These difficulties adversely affect their quality of life.[2–7] Moreover, as the access to the oral cavity is restricted, intubation, dental treatment, and oncologic follow-up may become more complicated.[2,6,7]

A wide variety in prevalence of trismus (ranging from 5% to 65%) and factors associated with trismus have been found due to narrow inclusion criteria, a single tumor localization,[5,8,9] one treatment modality,[4,5,8–11] small sample sizes,[8,9] and different cutoff points for trismus.[8,11,12]

Due to this wide variety and lack of clarity about the prevalence of trismus and the associated factors, clinicians are uncertain about when to take precautionary measures to prevent trismus. If patients at risk for trismus could be identified early, they could potentially benefit from preventive measures. In this study, based on a large study population

(n = 730) with a variety of tumor and treatment characteristics, we, therefore, determined the prevalence of trismus and identified associated factors for trismus in patients with head and neck cancer.

2 | MATERIALS AND METHODS

2.1 | Patients

In this cross-sectional study, patients with head and neck cancer were included who visited the Department of Oral and Maxillofacial Surgery of the University Medical Center Groningen (Netherlands) between November 2012 and January 2015. Their maximal mouth opening was measured as part of routine care. Patients were included if they had a tumor located in the upper aerodigestive tract, unknown primaries with metastases in the head and neck region, or a major salivary gland tumor. Patients were excluded if they visited the Oral and Maxillofacial Surgery Department for a consultation but were not diagnosed with head and neck cancer or had a rare type of tumor, were younger than 18 years, or had missing data regarding maximal mouth opening (MMO) measurements. Our study was carried out according to the regulations of our institute. The Medical Ethical Committee of the University Medical Center Groningen concluded that our research was not subject to the Medical Research (Human Subject) Act (METc number 2016.692).

2.2 | Maximal mouth opening measurement and dental status

The MMO was measured and recorded on a registration form by one of the oral and maxillofacial surgeons, nurse practitioners, or residents, using the OraStretch Range-of-Motion Scale (Craniomandibular Rehab, Denver, CO) during a visit at the department of Oral and Maxillofacial Surgery. This visit could have taken place before or after head and neck cancer treatment. The OraStretch Range-of-Motion Scale is a disposable paper measurement tool, which measures MMO in millimeters (mm), with a scale range from 3 to 52 mm. Because OraStretch Range-of-Motion Scale is limited to 52 mm, patients with a MMO of 52 mm or more were measured using a sliding caliper (in mm).

Additionally, the dental status was recorded. Patients were recorded as "dentate" in cases in which they had frontal dentition or wore prosthesis.

The incisal edge of the right upper central incisor and the right lower central incisor was used as the measurement points. Patients were recorded as "edentulous" if they had no frontal dentition and wore no prosthesis.

The top of the alveolar ridge at the former location of the right upper and lower central incisor were used as measurement points. Patients were recorded 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).

2.3 | Data

The following data were recorded on the registration form: patient identification number; date of birth; sex; dental status (dentate, partially edentulous, and edentulous); MMO measurement (in mm); and date of measurement. Additional data were retrieved from the patient file in the hospital information system: cT classification based on the Union for International Cancer Control TNM classification 2009 (TX, T1-2, T3-4, and unknown); tumor localization (tongue, floor of mouth, maxilla, mandible, cheek, major salivary glands, oropharynx, hypopharynx and larynx, lip, unknown primary, and others); squamous cell carcinoma (yes or no); surgery (no surgery, surgery, or multiple surgical procedures); neck dissection (yes or no); reconstruction after surgery (no reconstruction, skin graft, soft tissue flap, plates, or bony tissue flap); radiotherapy (no radiotherapy, radiotherapy, or reirradiation); chemotherapy (yes or no); and trismus treatment (yes or no).

To classify the extension of the primary tumor, the cT classification was used instead of the pT classification because the cT classification had least missing data. Not every tumor was treated surgically, so pathologic staging was often not available.

No reconstruction was recorded in case of primary wound closure or in case no surgery was performed. A soft tissue flap was recorded in case of a pectoralis major flap, nasolabial flap, or radial forearm flap. A bony tissue flap was recorded in case of a fibula osteocutaneous flap. Because the soft tissue flaps involve different procedures and are harvested from different locations we have chosen to combine these flaps in the univariate and multivariate analyses in order to enable sufficient numbers in each group for analyses and preserve as much data as possible. Specified information about the soft tissue flaps are displayed in the descriptive table (Table 1).

2.4 | Statistics

Prevalence of trismus was calculated using the cutoff point of an MMO of 35 mm or less. The chi-square test and *t* test for independent samples were used to analyze the differences between patients with and without trismus in age, sex, dental status, cT classification, tumor localization, surgery, reconstruction after surgery, radiotherapy, and chemotherapy. Based on statistical significance ($P < .10$), variables were entered in the multivariable logistic regression analyses. A *P* value of .10 was chosen in order to prevent missing potential associated factors. Thereafter, variables with a *P* value of $> .05$ were removed stepwise. If the model fit improved significantly (based on the Omnibus Tests of Model Coefficients), the variables remained in the model. Interaction effects were explored as well. In the final model, the variable "age" was standardized to improve clinical

TABLE 1 Patient, tumor, and treatment characteristics of total study population (n = 730)

Characteristics	No. of patients (%)
Male	388 (53.2)
Deceased	63 (8.6)
Age, years, mean (SD)	63.6 (13.5)
Dental status	
Fully dentulous	575 (79.4)
Fully edentulous	104 (14.4)
Partially edentulous	45 (6.2)
cT classification	
T1, T2	450 (74.4)
T3, T4	155 (25.6)
Tongue	164 (25.4)
Floor of mouth	92 (14.2)
Maxilla	36 (5.6)
Mandible	51 (7.9)
Cheek	21 (3.3)
Major salivary glands	73 (11.3)
Oropharynx	111 (17.2)
Lip	54 (8.4)
Unknown primary	12 (1.9)
Hypopharynx and larynx	32 (5.0)
Squamous cell carcinoma	510 (69.9)
Surgery	
Surgery	444 (60.8)
Multiple surgical procedures	62 (8.5)
Neck dissection	
Neck dissection	251 (34.4)
Multiple neck dissections	25 (3.4)
Reconstruction after surgery	
Skin graft	118 (16.2)
Soft tissue flap	31 (4.2)
Radial forearm flap	28 (3.8)
Nasolabial flap	2 (0.3)
Pectoralis major flap	1 (0.1)
Plates	11 (1.5)
Solitary plate	4 (0.5)
Radial forearm flap and plate	2 (0.3)
Nasolabial flap and plate	1 (0.1)
Pectoralis major flap and plate	4 (0.5)
Bony tissue flap	46 (6.3)
Radiotherapy	
Radiotherapy	236 (32.3)
Reirradiation	22 (3.0)
Chemotherapy	95 (13.0)
Exercise therapy	47 (6.5)

Missing values (no. of patients; %): dental status (6; 0.8), cT classification (125; 17.1), tumor localization (84; 11.5), squamous cell carcinoma (84; 11.5), neck dissection (1; 0.1), and reconstruction (32; 4.4).

interpretation; the individual age was subtracted from the mean age of the study population. The validity of our final model was tested based on the assessment of discrimination (using the area under the curve) and calibration (using the Hosmer-Lemeshow test).

A risk score for trismus was calculated as the sum of the regression coefficients of our final logistic regression model. The reference categories were given a value of zero for their regression coefficients.

For the variable "standardized age," the mean age was subtracted from the age of the patient. The standardized age was multiplied by the regression coefficient for the variable "standardized age." For the interaction effect "standardized age*radiotherapy," the standardized age is multiplied by the corresponding regression coefficient. The regression coefficient of the "constant" was always added to the calculation. We calculated a range of probabilities (P) based on the formula "ln (P/1-P) = risk score for trismus." Using the calculated risk score for trismus, the risk for trismus for future patients can be estimated.

Our study population consisted of all included patients who had head and neck cancer. Of this study population, some patients had multiple tumors receiving multiple treatments. To verify the final logistic regression model, we also studied a population that only had one primary tumor.

Analyses were performed using IBM SPSS Statistics Program version 23.0 (IBM, Armonk, NY).

3 | RESULTS

3.1 | Study population

The MMO of 839 patients was recorded during visits at the department of Oral and Maxillofacial Surgery. In total, 109 patients were excluded because 78 patients were not diagnosed with head and neck cancer; 29 patients had rare types of tumors, and 2 patients had missing data regarding MMO measurement. Of the 138 patients who had an MMO of 52 mm or larger, 112 patients were measured with a sliding caliper and 26 patients were recorded as having an MMO of 52 mm, because a sliding caliper was unavailable at that time. Ultimately, the total study population consisted of 730 patients (87.0%; Table 1).

The results of the total study population are reported. The results of the study population with only primary tumors are reported in the Supporting Information Tables S1-S3.

The univariate analysis of the study population with only primary tumors differs from the univariate analysis of the total study population, as the variables dental status and surgery are not significantly associated with trismus (Table 2 and Supporting Information Table S2). However, for the multivariate logistic regressions model, the same variables are inserted into the model to analyze which variables contribute significantly to the equation. The multivariate logistic regression model of the study population with only primary tumors shows that dental status contributes significantly to the equation. The interaction

TABLE 2 Comparison between patients with and without trismus

	No. of patients without trismus (n = 558)		No. of patients with trismus (n = 172)				
	No.	**%**	**No.**	**%**	**Chi-square**	**DF**	***P* value**
Male sex	304	54.5	84	48.8	1.681	1	.195
Dental status					6.650	2	.036
Dentate	437	79.0	138	80.7			
Partially edentulous	29	5.2	16	9.4			
Edentulous	87	15.7	17	9.9			
cT classification					23.059	2	< .001
T1, T2	360	79.3	90	59.6			
T3, T4	94	20.7	61	40.4			
Tumor localization					42.683	9	< .001
Tongue	134	27.6	30	18.6			
Floor of mouth	76	15.7	16	9.9			
Maxilla	21	4.3	15	9.3			
Mandible	30	6.2	21	13.0			
Cheek	10	2.1	11	6.8			
Major salivary glands	55	11.3	18	11.2			
Oropharynx	74	15.3	37	23.0			
Lip	50	10	4	2.5			
Unknown primary	8	1.6	4	2.5			
Hypopharynx and larynx	27	5.6	5	3.1			
Surgery							
Surgery	348	62.4	96	55.8	10.677	2	.005
Multiple surgical procedures	37	6.6	25	14.5			
Neck dissection							
Neck dissection	173	31.1	78	45.3	15.791	2	< .001
Multiple neck dissections	16	2.9	9	5.2			
Reconstruction after surgery					25.083	4	< .001
Skin graft	85	16.0	33	19.8			
Soft tissue flap	16	3.0	15	9.0			
Plates	7	1.3	4	2.4			
Bony tissue flap	27	5.1	19	11.4			
No reconstruction	396	74.6	96	57.5			
Radiotherapy							
Radiotherapy	163	29.2	73	42.4	13.926	2	.001
Reirradiation	14	2.5	8	4.7			
Chemotherapy	59	10.6	36	20.9	12.458	1	< .001
	Mean	**SD**	**Mean**	**SD**	**DM**	**95% CI**	***P* value**
Age, years	62.9	13.6	65.9	12.9	-3.0	-5.3; -0.7	.011[a]

Abbreviations: CI, confidence interval; DF, degrees of freedom; DM, difference in means.
[a] The *t* test was used for independent samples.

"standardized age*radiotherapy" did not contribute significantly to the equation (Table 3 and Supporting Information Table S3).

3.2 | Prevalence

In our study, 23.6% of the patients had trismus (n = 172). Compared to patients without trismus, patients with trismus were older, were partially edentulous or dentate more frequently, had advanced tumors (T3 or T4) more frequently, had tumors located near the maxilla, mandible, cheek, oropharynx, or had an unknown primary more frequently, underwent multiple surgical procedures, neck dissections, and/or reconstruction after surgery more frequently, and received radiotherapy, reirradiation, or chemotherapy more frequently (Table 2).

3.3 | Selecting potential factors

In the univariate analysis, the following variables were significantly associated with trismus: age ($P = .011$), dental status ($P = .036$), tumor size ($P < .001$), tumor localization

TABLE 3 Results of multivariate logistic regression analysis to identify the contribution of associated factors of trismus

			95% CI		
	β	OR	Lower	Upper	*P* value
Age, years[a]	0.030	1.031	1.006	1.055	.013
Dental status					.002
Dentate	1.186	3.274	1.679	6.382	.000
Partially edentulous	1.254	3.504	1.346	9.123	.010
Edentulous, RC[†]	0.000	1.000			
Tumor localization					.000
Tongue	0.702	2.018	0.680	5.985	.206
Floor of mouth	0.286	1.331	0.405	4.374	.637
Maxilla	1.736	5.673	1.610	19.991	.007
Mandible	1.586	4.883	1.407	16.941	.012
Cheek	2.062	7.858	1.854	33.299	.005
Major salivary glands	1.166	3.208	0.994	10.355	.051
Oropharynx	1.154	3.171	1.079	9.323	.036
Lip	-0.311	0.733	0.171	3.138	.675
Unknown primary	1.685	5.392	1.054	27.577	.043
Hypopharynx and larynx, RC[b]	0.000	1.000			
Reconstruction after surgery					.010
Skin graft	0.492	1.636	0.921	2.908	.093
Soft tissue flap	1.403	4.067	1.739	9.511	.001
Plates	0.596	1.816	0.411	8.017	.431
Bony tissue flap	0.844	2.326	1.036	5.223	.041
No reconstruction, RC[b]	0.000	1.000			
Radiotherapy					.000
Radiotherapy	0.974	2.648	1.622	4.324	.000
Reirradiation	1.756	5.789	1.757	19.070	.004
No radiotherapy, RC[b]	0.000	1.000			
Chemotherapy	1.418	4.129	2.210	7.715	.000
Age[a] × radiotherapy[c]					.039
Age[a] × radiotherapy[c]	-0.001	0.999	0.966	1.034	.968
Age[a] × reirradiation[c]	-0.137	0.872	0.784	0.970	.011
Constant	-3.999	0.018			.000

Abbreviations: CI, confidence interval; OR, odds ratio; RC, reference category.
[a] Age is standardized; the mean age of 63.6 years will be subtracted from the individual age.
[b] Reference category (variable): edentulous (dental status); hypopharynx and larynx (tumor localization); no reconstruction (reconstruction); no radiotherapy (radiotherapy).
[c] Interaction effect of standardized age and radiotherapy.

($P < .001$), surgery ($P = .005$), neck dissection ($P < .001$), reconstruction after surgery ($P < .001$), radiotherapy ($P = .001$), and chemotherapy ($P < .001$; Table 2). These potential factors were entered in the logistic regression model.

3.4 | Logistic regression analyses

Our final regression model (Nagelkerke's R^2 0.233, percentage correctly predicted 78.1%) contained the variables: standardized age, dental status, tumor localization, reconstruction after surgery, radiotherapy, chemotherapy, and interaction effect "standardized age*radiotherapy" (Table 3). Other interaction effects among standardized age, dental status, tumor localization, reconstruction after surgery, radiotherapy, and chemotherapy were explored as well but did not contribute significantly to the regression equation.

The area under the curve was 0.764 (95% confidence interval [CI] 0.720-0.807; $P < .001$), indicating that the model classifies the groups significantly better than by chance. The Hosmer and Lemeshow test was not significant ($P = .865$), indicating that there was no disagreement between the predicted and observed values.

3.5 | Risk score trismus

Based on our model, the risk score for trismus for a hypothetical patient can be calculated as follows using arbitrarily chosen characteristics. A patient is 68 years old, is partially edentulous, and has a tumor located near the oropharynx.

TABLE 4 Clinical calculation tool to predict trismus

Risk score	Probability
Risk score ≤ -2.197	≤ 0.10
-2.197 < Risk score ≤ -1.386	0.11–0.20
-1.386 < Risk score ≤ -0.847	0.21–0.30
-0.847 < Risk score ≤ -0.405	0.31–0.40
-0.405 < Risk score ≤ 0.000	0.41–0.50
0.000 < Risk score ≤ 0.405	0.51–0.60
0.405 < Risk score ≤ 0.847	0.61–0.70
0.847 < Risk score ≤ 0.386	0.71–0.80
1.386 < Risk score ≤ 2.197	0.81–0.90
> 2.197	> 0.9

This clinical tool can be used to predict the risk of trismus for individual patients. The risk score calculation is the sum of the regression coefficients from the logistic regression model of Table 3.

The patient will receive radiotherapy. To calculate this patients' risk score, the regression coefficients of our final regression model are filled in for this patient (Table 3): (68-63.6 years; age - mean age) * 0.030 + 1.254 (partially edentulous) + 1.154 (tumor localization oropharynx) + 0.000 (no reconstruction) + 0.974 (radiotherapy) + 0.000 (no chemotherapy) + (68-63.6) * −0.001 ((age − mean age)*radiotherapy)) - 3.999 (constant) = −0.489.

In Table 4, it is shown that that the calculated risk score (regression coefficient sum score) of −0.489 lies between −0.405 and −0.847. This means that the hypothetical patient has a risk of developing trismus between 31% and 40%.

4 | DISCUSSION

In our study population of patients with head and neck cancer, the prevalence of trismus is 23.6%. We identified the following characteristics as associated factors for trismus: older patient age, dentate or partially edentulous dentition, tumors located near the maxilla, mandible, cheek, major salivary glands, oropharynx, or an unknown primary, a free soft tissue transfer after surgery, reirradiation, and chemotherapy.

In comparison to the prevalence found in this study, higher prevalence was reported in study populations that received radiotherapy predominantly or solely (range 35%-41%).[11,13,14] A lower prevalence (8%) was reported in a study population including patients treated with surgery solely. A similar prevalence (28.3%) was reported in patients who received surgery, radiotherapy, or chemotherapy.[12] The higher prevalence of trismus among patients who received radiotherapy with or without chemotherapy, compared with patients who had surgery, is generally the result of a larger and more extensive field of fibrosis due to prolonged inflammatory responses, angiogenesis, and extended and increased expression of extracellular matrix components.[15–17]

The differences in prevalence are not only related to study populations with different treatment characteristics but also to different patient and tumor characteristics.

Our found association between age and trismus could not be confirmed by other studies.[2,4,13] This could be explained by the difference in mean age of the study population. The mean age in our study population (66.0; SD 12.8 in trismus group and 62.9; SD 13.9 in no trismus group) was higher than the mean age in another study population (56.4; SD 7.5 in trismus group and 54.4; SD 13.1 in no trismus group).[4] As the patient gets older, the range of motion diminishes due to the micro and macro changes of joints and ligaments, which might also involve the temporomandibular joint.[18]

Patients also become frailer as they age, resulting in increased vulnerability, decreased adaptive capacity, and longer recovery periods after treatment, enhancing the risk of trismus even further.[19,20] Compared with other studies, we have a large dataset, therefore, we were able to detect small effects. As the risk of trismus only increases with 0.030 per year, the enhanced risk per year contributed by age is small but present. Additionally, a small interaction effect between age and radiotherapy has been found. We cannot explain this effect in a plausible biological way. Clinically, this interaction effect suggests that clinicians should not be too reluctant to choose for reirradiation as cancer treatment on the basis of the patients' older age.

Tumor size could have an effect on the development of trismus. However, in contrast with other studies,[13,21] we could not find an association between tumor size, based on the cT classification, and trismus in our study. Nonetheless, it seems that a greater extension of the tumor increases the risk of trismus. We found that dental status and type of reconstruction were associated with trismus, which could have been an indirect effect of tumor size. Large tumors most likely lead to large resections, commonly involving partial jaw removal, and, therefore, resulting in patients becoming partially edentulous. Large tumors might also lead to large reconstructions, leading to a greater field of fibrosis. One study reported that of 15 patients who had developed trismus, 14 patients had received a free flap reconstruction, suggesting that receiving a reconstruction might increase the risk of trismus.[9] However, 13 of the 15 patients received radiotherapy as well. Therefore, no direct association between reconstructions and the development of trismus could be made on the basis of that study.

Due to different tumor localization categorization, no definite tumor localization can be appointed that increases the risk of developing trismus. A variety of localizations, such as the oropharynx, nasopharynx, maxilla, mandible, maxillary sinus, pterygoid muscles, and masseter muscle, are mentioned to increase the risk of developing trismus.[3,10,13,22,23] In general, it can be stated that tumors located near the temporomandibular joint and masticatory muscles will most likely increase the risk of developing trismus. In our study, this statement is confirmed as the maxilla, mandible, cheek, major salivary glands, and oropharynx are

near the temporomandibular joint and the masticatory muscles.

Tumor infiltration and/or fibrosis near these structures make it difficult to open the mouth adequately and may also lead to trismus.[22–24]

Our large study population consisted of patients with a variety of tumor and treatment characteristics. Therefore, our findings can be generalized to patients with head and neck cancer with different patient, tumor, and treatment characteristics. However, all patients included in this study were recruited at the department of Oral and Maxillofacial Surgery, resulting in a predominance of patients with tumors who were treated with surgery as part of their treatment strategy. As the risk of trismus might be higher among patients treated with radiotherapy in comparison to surgery, the recruitment might have resulted into an underestimation of prevalence of trismus compared to the total head and neck cancer population.

Another possible limitation of our study is that MMO was measured by different assessors, which could have introduced a measurement error. However, a previous study reported that measurement differences between assessors are minimal.[25]

We were not able to measure all patients with an MMO of 52 mm or more, because the sliding caliper was unavailable. Therefore, 26 patients were recorded to have an MMO of 52 mm. This might have led to some inaccuracy in our database. However, it was certain that these patients did not have a trismus. As we have dichotomized trismus, this inaccuracy has minor influence on our results.

In this study, we developed a simple calculation tool to predict the risk of trismus for future patients. No complex calculations are needed. The tool should be seen as a guideline or relative prediction tool when used in other populations. No absolute risk scores for other populations can be made on the basis of this tool.

The recognition of factors associated with trismus and the simple calculation tool will enable clinicians to take precautionary measures as soon as possible, if needed.[26–28] In future studies, the associated factors for trismus can be taken into account when recruiting patients to study the effectiveness of preventive exercise trismus therapy.

5 | CONCLUSION

About one-fourth of patients with head and neck cancer develop trismus. We provide a simple calculation tool to predict the risk of trismus in patients with head and neck cancer.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest with the contents of this article.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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