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Trismus in head and neck cancer patients

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

This chapter is an edited version of:
van der Geer SJ, van Rijn PV, Kamstra JI, Langendijk JA, van der Laan BFAM, Roodenburg JLN, Dijkstra PU. Prevalence and prediction of trismus in patients with head and neck cancer: A cross-sectional study. Head Neck. *2019;41(1):64-71.*

ABSTRACT

Purpose: Trismus occurs frequently in head and neck cancer patients. 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 head and neck cancer patients. Associated factors for trismus were analysed 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, tumours located at the maxilla, mandible, cheek, major salivary glands, or oropharynx, an unknown primary, a free soft tissue transfer after surgery, re-irradiation, and chemotherapy.

Conclusions: About one quarter of head and neck cancer patients develops trismus. Based on prevalence and associated factors of trismus, a simple calculation tool predicts the risk of trismus in these patients.

INTRODUCTION

Trismus, also referred to as a restricted mouth opening, is a common problem in head and neck cancer patients.[1] Patients with trismus often perceive 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 oncological 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 (such as one single tumour localization[5,8,9] or one treatment modality[4,5,8-11]), small sample sizes[8,9], and different cut-off 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 tumour and treatment characteristics, we therefore (1) determined the prevalence of trismus and (2) identified associated factors for trismus in head and neck cancer patients.

MATERIALS AND METHODS

Patients

In this cross- sectional study, head and neck cancer patients 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 tumour located in the upper aero-digestive tract, unknown primaries with metastases in the head and neck region, or a major salivary gland tumour. 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 tumour, 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).

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, Inc., Denver, USA) 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 millimetres (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 calliper (in mm).

Additionally, the dental status was recorded. Patients were recorded as “dentate”, when 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 measurement point. 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).

Data

The following data were recorded on the registration form: patient ID number, date of birth, gender, dental status (dentate, partially edentulous, and edentulous), MMO measurement (mm), and date of measurement. Additional data was retrieved from the patient file in the hospital information system: tumour localization (tongue, floor of mouth, maxilla, mandible, cheek, major salivary glands, oropharynx, hypopharynx and larynx, lip, unknown primary, others), clinical T classification based on the Union for International Cancer Control (UICC) TNM classification 2009 (TX, T1-2, T3-4, unknown), squamous cell carcinoma (yes, no), surgery (no surgery, surgery, multiple surgical procedures), neck dissection (yes, no), reconstruction after surgery (no reconstruction, skin graft, soft tissue flap, plates, bony tissue flap), radiotherapy (no radiotherapy, radiotherapy, re-irradiation), chemotherapy (yes, no), and trismus therapy (yes, no). To classify the extension of the primary tumour, the clinical T (cT) classification was used instead of the pathological T (pT) classification, because the cT classification had least missing data. Not every tumour was treated surgically, so pT 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 fibular osteocutaneous flap. Although 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 will be displayed in the descriptive table (Table 1).

Statistics

Prevalence of trismus was calculated using the cut-off point of a MMO of 35 mm or less. Chi-Square test and t-test for independent samples were used to analyse the differences between patients with and without trismus in age, gender, dental status, cT classification, tumour localization, surgery, reconstruction after surgery, radiotherapy, and chemotherapy. Based on statistical significance ($p<0.10$), variables were entered in the multivariable logistic regression analyses. A p-value of 0.10 was chosen in order to prevent missing potential associated factors. Thereafter, variables with a p-value of >0.05 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 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 patients who had had head and neck cancer. Of this study population, some patients had multiple tumours receiving multiple treatments. To verify the final logistic regression model, we also studied a population that only had one primary tumour.

Analyses were performed using IBM SPSS Statistics Program version 23.0.

RESULTS

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 tumours, and 2 patients had missing data regarding MMO measurement. Of the 138 patients who had a MMO of 52 mm or larger, 112 patients were measured with a sliding calliper and 26 patients were recorded as having a MMO of 52 mm, because a sliding calliper 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 tumours are reported in the supplementary tables and figures.

The univariate analysis of the study population with only primary tumours 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 Supplementary Table 2). For the multivariate logistic regressions model the same variables are inserted into the model, to analyse which variables contribute significantly to the equation. The multivariate logistic regression model of the study population with only primary tumours shows that dental status contributes significantly to the equation. The interaction 'standardized age*radiotherapy' did not contribute significantly to the equation. (Table 3 and Supplementary Table 3).

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 tumours located near the maxilla, mandible, cheek, oropharynx or had an unknown primary more frequently, had advanced tumours (T3, T4) more frequently, underwent multiple surgical procedures, neck dissections, and/or reconstruction after surgery more frequently, and received radiotherapy, re-irradiation, or chemotherapy more frequently (Table 2).

Table 1. Patient, tumour and treatment characteristics of total study population (n=730).

Characteristics	Number of patients
	n (%)
Patient characteristics	
Male	388 (53.2)
Deceased	63 (8.6)
Age (years), Mean (SD)	63.6 (13.5)
Dental status	
Dentate	575 (79.4)
Partially edentulous	45 (6.2)
Edentulous	104 (14.4)
Tumour characteristics	
Tumour localization	
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)
cT classification	
T1,T2	450 (74.4)
T3,T4	155 (25.6)
Squamous cell carcinoma	510 (69.9)
Treatment characteristics	
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)
Soft tissue flap and reconstruction plate	11 (1.5)
Bony tissue flap	46 (6.3)
Radiotherapy	
Radiotherapy	236 (32.3)
Re-irradiation	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), tumour localization (84; 11.5), squamous cell carcinoma (84; 11.5), neck dissection (1; 0.1), reconstruction (32; 4.4).

Table 2. Comparison between patients with and without trismus.

	Number of patients without trismus (n=558)		Number of patients with trismus (n=172)				
	n	%	n	%	χ^2	DF	*p*
Patient characteristics							
Male gender	304	54.5	84	48.8	1.681	1	0.195
Age	62.9[a]	13.6[b]	65.9[a]	12.9[b]	-3.0[c]	-5.3; -0.7[d]	0.011*
Dental status					6.650	2	0.036
Dentate	437	79.0	138	80.7			
Partially edentulous	29	5.2	16	9.4			
Edentulous	87	15.7	17	9.9			
Tumour characteristics							
Tumour localization					42.683	9	<0.001
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			
***c*T classification**					23.059	2	<0.001
T1, T2	360	79.3	90	59.6			
T3, T4	94	20.7	61	40.4			
Treatment characteristics							
Surgery							
Surgery	348	62.4	96	55.8	10.677	2	0.005
Multiple surgical procedures	37	6.6	25	14.5			
Neck dissection							
Neck dissection	173	31.1	78	45.3	15.791	2	<0.001
Multiple neck dissections	16	2.9	9	5.2			
Reconstruction after surgery					25.083	4	<0.001
Skin graft	85	16.0	33	19.8			
Soft tissue flap	16	3.0	15	9.0			
Soft tissue flap and reconstruction plate	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	0.001
Re-irradiation	14	2.5	8	4.7			
Chemotherapy	59	10.6	36	20.9	12.458	1	<0.001

%: column percentage, χ^2: Results of Chi-Square test, DF: Degrees of freedom, a: mean, b: standard deviation, c: difference in means, d: 95% confidence interval, *: t- test for independent samples.

Table 3. Results of multivariate logistic regression analysis to identify the contribution of factors associated with trismus.

	β	OR	95% Confidence Interval		Sig.
			Lower	Upper	
Patient characteristics					
Age *	0.030	1.031	1.006	1.055	0.013
Dental status					0.002
Dentate	1.186	3.274	1.679	6.382	0.000
Partially edentulous	1.254	3.504	1.346	9.123	0.010
Edentulous [RC†]	0.000	1.000			
Tumour characteristics					
Tumour localization					0.000
Tongue	0.702	2.018	0.680	5.985	0.206
Floor of mouth	0.286	1.331	0.405	4.374	0.637
Maxilla	1.736	5.673	1.610	19.991	0.007
Mandible	1.586	4.883	1.407	16.941	0.012
Cheek	2.062	7.858	1.854	33.299	0.005
Major salivary glands	1.166	3.208	0.994	10.355	0.051
Oropharynx	1.154	3.171	1.079	9.323	0.036
Lip	-0.311	0.733	0.171	3.138	0.675
Unknown primary	1.685	5.392	1.054	27.577	0.043
Hypopharynx and Larynx [RC†]	0.000	1.000			
Treatment characteristics					
Reconstruction after surgery					0.010
Skin graft	0.492	1.636	0.921	2.908	0.093
Soft tissue flap	1.403	4.067	1.739	9.511	0.001
Plates	0.596	1.816	0.411	8.017	0.431
Bony tissue flap	0.844	2.326	1.036	5.223	0.041
No reconstruction [RC†]	0.000	1.000			
Radiotherapy					0.000
Radiotherapy	0.974	2.648	1.622	4.324	0.000
Re-irradiation	1.756	5.789	1.757	19.070	0.004
No radiotherapy [RC†]	0.000	1.000			
Chemotherapy	1.418	4.129	2.210	7.715	0.000
Interaction effect					
Age * x Radiotherapy [‡]					0.039
Age * x Radiotherapy [‡]	-0.001	0.999	0.966	1.034	0.968
Age * x Re-irradiation [‡]	-0.137	0.872	0.784	0.970	0.011
Constant					
Constant	-3.999	0.018			0.000

* age is standardized; the mean age of 63.6 will be subtracted from the individual age.
†RC: Reference category (variable): edentulous (dental status); hypopharynx and larynx (tumour localization); no reconstruction (reconstruction); no radiotherapy (radiotherapy). ‡: interaction effect of standardized age and radiotherapy.

Selecting potential factors

In the univariate analysis, the following variables were significantly associated with trismus: age (p=0.011), dental status (p=0.036), tumour localization (p<0.001), tumour size (p<0.001), surgery (p=0.005), neck dissection (p<0.001), reconstruction after surgery (p<0.001), radiotherapy (p=0.001), and chemotherapy (p<0.001) (Table 2). These potential factors were entered in the logistic regression model.

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, tumour localization, reconstruction after surgery, radiotherapy, chemotherapy, and interaction effect 'standardized age*radiotherapy' (Table 3).

Other interaction effects between standardized age, dental status, tumour localization, reconstruction after surgery, radiotherapy and chemotherapy were explored as well, but did not contribute significantly to the regression equation.

The AUC was 0.764 (95% CI: 0.720-0.807, p<0.001), indicating that the model classifies the groups significantly better than by chance. The Hosmer-Lemeshow test was not significant (p=0.0.865), indicating that there was no disagreement between the predicted and observed values.

Risk score trismus

Based on the final regression model, a risk score for trismus can be calculated. Using arbitrarily chosen characteristics for a hypothetical patient (68 years old, partially edentulous, tumour located near the oropharynx, radiotherapy treatment), the risk score for trismus can be calculated as follows (Table 3): (68 - 63.6) (age - mean age) * 0.030 + 1.254 (partially edentulous) + 1.154 (tumour 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 the 31 and 40 per cent.

Table 4. Clinical calculation tool for 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
Risk score > 2.197	>0.9

This clinical tool can be used to calculate the possible 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.

DISCUSSION

Key results

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

Interpretation

In comparison to the prevalence found in this study, higher prevalences were 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 to 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 tumour 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 to 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 re-irradiation as cancer treatment based on patients' older age.

Due to different tumour localization categorization, no definite tumour 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 trismus.[3,10,13,22,23] In general, it can be stated that tumours 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. Tumour infiltration and/ or fibrosis near these structures make it difficult to open the mouth adequately and may also lead to trismus.[22-24]

Tumour size could influence the development of trismus. However, in contrast with other studies[13,21], we could not find an association between tumour size, based on the cT classification, and trismus in our study. Nonetheless, it seems that a greater extension of the tumour 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 tumour size.

Large tumours most likely lead to large resections, commonly involving partial jaw removal, and therefore resulting into patients becoming partially edentulous. Large tumours might also lead to large reconstructions, leading to a greater field of fibrosis. One study reported that out of 15 patients that 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 out 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.

Study limitations and strengths

Our large study population consisted of patients with a variety of tumour and treatment characteristics. Therefore, our findings can be generalized to head and neck cancer patients with different patient-, tumour-, 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 tumours that 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 a MMO of 52 mm or more, because the sliding calliper was unavailable. Therefore, 26 patients were recorded to have a 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.

We have 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 using 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.

Conclusion

About one quarter of head and neck cancer patients develops trismus. We provide a simple calculation tool to predict the risk of trismus in head and neck cancer patients.

Supplementary Table 1. Patient, tumour and treatment characteristics of study population with only one primary tumour (n=653).

Characteristics	Number of patients
	n (%)
Patient characteristics	
Male	350 (53.6)
Deceased	51 (7.8)
Age (years). Mean (SD)	63.3 (13.4)
Dental status	
Dentate	522 (80.6)
Partially edentulous	37 (5.7)
Edentulous	89 (13.7
Tumour characteristics	
Tumour localization	
Tongue	138 (24.3)
Floor of mouth	81 (14.2)
Maxilla	30 (5.3)
Mandible	40 (7.0)
Cheek	16 (2.8)
Major salivary glands	69 (12.1)
Oropharynx	104 (18.3)
Lip	50 (8.8)
Unknown primary	11 (1.9)
Hypopharynx and larynx	30 (5.3)
cT classification	
T1,T2	394 (73.5)
T3,T4	142 (26.5)
Squamous cell carcinoma	442 (67.7)
Treatment characteristics	
Surgery	433 (66.3)
Neck dissection	224 (34.4)
Reconstruction after surgery	
Skin graft	100 (15.3)
Soft tissue flap	24 (3.7)
Soft tissue flap and reconstruction plate	9 (1.4)
Bony tissue flap	39 (6.0)
Radiotherapy	214 (32.8)
Chemotherapy	82 (12.6)
Exercise therapy	41 (6.3)

Missing values (no. of patients ;%): dental status (5; 0.8). cT classification (117; 17.9). tumour localization (84; 12.9). squamous cell carcinoma (84; 12.9). neck dissection (1; 0.2). reconstruction (23; 3.5).

Supplementary Table 2. Comparison between patients with and without trismus of study population with only one primary tumour.

	Number of patients without trismus (n=508)		Number of patients with trismus (n=145)				
	n	%	n	%	χ^2	DF	p
Patient characteristics							
Male gender	277	54.5	73	50.3	0.794	1	0.373
Age	62.7[a]	13.6[b]	65.5[a]	12.2[b]	-2.9[c]	-5.3; -0.4[d]	0.023*
Dental status					3.476	2	0.176
Dentate	403	80.0	119	82.6			
Partially edentulous	26	5.2	11	7.6			
Edentulous	75	14.9	14	9.7			
Tumour characteristics							
Tumour localization					25.545	9	0.002
Tongue	113	26.0	25	18.7			
Floor of mouth	67	15.4	14	10.4			
Maxilla	20	4.6	10	7.5			
Mandible	26	6.0	14	10.4			
Cheek	9	2.1	7	5.2			
Major salivary glands	52	12.0	17	12.7			
Oropharynx	70	16.1	34	25.4			
Lip	46	10.6	4	3.0			
Unknown primary	7	1.6	4	3.0			
Hypopharynx and Larynx	25	5.7	5	3.7			
cT classification					24.902	1	<0.001
T1,T2	323	78.8	71	56.3			
T3,T4	87	21.2	55	43.7			
Treatment characteristics							
Surgery	338	66.5	95	65.5	0.052	1	0.819
Neck dissection	159	31.4	65	44.8	9.067	1	0.003
Reconstruction after surgery					21.093	4	<0.001
Skin graft	75	15.4	25	17.5			
Soft tissue flap	13	2.7	11	7.7			
Soft tissue flap and reconstruction plates	5	1.0	4	2.8			
Bony flap	23	4.7	16	11.2			
Radiotherapy	149	29.3	65	44.8	12.296	1	<0.001
Chemotherapy	51	10.0	31	21.4	13.210	1	<0.001

%: column percentage, χ^2: Results of Chi-Square test, DF: Degrees of freedom, a: mean, b: standard deviation, c: difference in means, d: 95% confidence interval, *: t- test for independent samples.

Supplementary Table 3. Results of logistic regression analyses to identify the contribution of factors associated with trismus in a study population with only one primary tumour.

	β	OR	95% Confidence Interval		Sig.
			Lower	Upper	
Patient characteristics					
Age *	0.031	1.031	1.012	1.051	0.002
Dental status					0.023
Dentate	0.957	2.605	1.308	5.187	0.006
Partially Edentulous	0.945	2.572	0.896	7.386	0.079
Edentulous [RC†]	0.000	1.000			
Tumour characteristics					
Tumour localization					0.033
Tongue	0.748	2.114	0.694	6.436	0.188
Floor of mouth	0.308	1.361	0.404	4.583	0.619
Maxilla	1.311	3.708	0.987	13.938	0.052
Mandible	1.212	3.362	0.885	12.769	0.075
Cheek	1.733	5.656	1.233	25.947	0.026
Major salivary glands	0.193	3.298	1.002	10.855	0.050
Oropharynx	1.049	2.855	0.960	8.492	0.059
Lip	-0.269	0.764	0.176	3.325	0.720
Unknown primary	1.758	5.802	1.101	30.582	0.038
Hypopharynx and Larynx [RC†]	0.000	1.000			
Treatment characteristics					
Reconstruction					0.011
Skin graft	0.553	1.738	0.916	3.297	0.091
Soft tissue flap	1. 419	4.133	1.614	10.579	0.003
Plates	1.080	2.946	0.593	14.623	0.186
Bony tissue flap	0.909	2.481	1.026	6.004	0.044
No reconstruction [RC†]	0.000	1.000			
Radiotherapy	1.040	2.830	1.696	4.724	<0.001
Chemotherapy	1.547	4.696	2.386	9.241	<0.001
Constant					
Constant	-3.814	0.022			<0.001

*: Age is standardized; the mean age of 63.3 was subtracted from the individual age.
†RC: Reference category (variable): edentulous (dental status); hypopharynx and larynx (tumour localization); no reconstruction (reconstruction). Nagelkerke's R^2: 0.207; percentage correctly predicted: 77.6%; Area Under the Curve: 0.752 (95% CI: 0.704-0.799, p<0.001); Hosmer and Lemeshow test: p=0.634.

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