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ORIGINAL ARTICLE

Radiation dose to the masseter and medial pterygoid muscle in relation to trismus after chemoradiotherapy for advanced head and neck cancer

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Abstract

Background: We studied the relationship between trismus (maximum interincisor opening [MIO] ≤35 mm) and the dose to the ipsilateral masseter muscle (iMM) and ipsilateral medial pterygoid muscle (iMPM).

Methods: Pretreatment and post-treatment measurement of MIO at 13 weeks revealed 17% of trismus cases in 83 patients treated with chemoradiation and intensity-modulated radiation therapy. Logistic regression models were fitted with dose parameters of the iMM and iMPM and baseline MIO (bMIO). A risk classification tree was generated to obtain optimal cut-off values and risk groups.

Results: Dose levels of iMM and iMPM were highly correlated due to proximity. Both iMPM and iMM dose parameters were predictive for trismus, especially mean dose and intermediate dose volume parameters. Adding bMIO, significantly improved Normal Tissue Complication Probability (NTCP) models. Optimal cut-offs were 58 Gy (mean dose iMPM), 22 Gy (mean dose iMM) and 46 mm (bMIO).

Conclusions: Both iMPM and iMM doses, as well as bMIO, are clinically relevant parameters for trismus prediction.

KEYWORDS

dose effect, head and neck cancer, NTCP, radiotherapy, trismus

1 | INTRODUCTION

Trismus, a restricted mouth opening, has been considered one of the most burdensome side effects of radiation treatment for advanced head and neck cancer (HNC).[1–3] It impairs eating, speech, and oral hygiene, and it is often persisting and difficult to manage, affecting quality of life.[2–4] Trismus is usually defined as a maximum interincisor opening (MIO) of 35 mm or less,[5] which is regarded as the critical minimal mouth opening for normal functioning. Studies reporting on the incidence of trismus following radiation treatment present incidence rates ranging from 5% to 55%, depending on the radiation technique used, the applied definition of the chosen endpoint, and the follow-up time.[4–8] Trismus usually starts at the end of treatment, up to 6 months after treatment, but can also occur gradually during subsequent years, as radiotherapy effects can be progressive over time.[6,7]

The etiology of trismus in HNC is multifactorial. Especially radiation-induced fibrosis of the masticatory system seems to result in trismus, when the muscles of mastication are within the field of radiation.[6,9–11] Furthermore, mouth opening function before start of treatment seems relevant for the risk of trismus development. A study from Johnson et al[12] showed that MIO values at baseline were significantly different between patients who developed trismus and those who did not.

Recent literature investigating dose-effect relationships between radiation dose to the masticatory muscles and trismus revealed the ipsilateral masseter muscle (iMM) and ipsilateral medial pterygoid muscle (iMPM) as main risk structures for developing trismus.[7,8,13–15] With improved radiation techniques such as intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT), the radiation fields can be modeled around the target volume, resulting in more conformal dose distributions, which offer possibilities to reduce radiation dose to these muscles critical for mouth opening.

In current clinical practice, dose constraints to limit dose to the masticatory muscles are often not included in treatment optimization. Although several studies have identified the iMM and iMPM as potential organs at risk (OARs), it is unclear whether these muscles should be regarded as a joined OAR or separately, how to take baseline mouth opening into account, and which dose parameters to use for constraints or trismus prediction models. Therefore, the aim of the current study was to calculate and compare separate dose-effect relationships between trismus and radiation dose to (1) the iMM and (2) the iMPM, in patient with HNC population treated with IMRT-VMAT, taking into account the baseline MIO (bMIO).

2 | PATIENTS AND METHODS

Study design is a retrospective cohort study evaluating prospectively collected mouth opening data collected at the Netherlands Cancer Institute.

2.1 | Patients

Over time, mouth opening data of 98 patients who were treated with chemoradiotherapy (CRT) for advanced squamous cell carcinoma in the head and neck region between 2008 and 2014 were systematically measured and collected. In order to estimate true dose-effect relationships, inclusion criteria were no trismus at baseline and no gross tumor infiltration of the iMM or iMPM on the planning CT images. All patients participated in a preventive exercise program during and after treatment to preserve oral function and gave informed consent for study participation, which was approved by the Medical Ethical Committee.[16,17]

2.2 | Treatment

Patients received concomitant CRT. Radiotherapy consisted of 70 Gy in 35 fractions to the primary tumor and involved nodes with IMRT and VMAT. Typically, the treatment setup consisted of a five-angle coplanar setup and a caudal oblique irradiation field for IMRT and a full dual arc for VMAT. Elective nodal regions were treated either sequential (46 Gy in 23 fractions) or with a simultaneous integrated boost. The OARs delineated for treatment plan optimization were the spinal cord, parotid glands, submandibular glands, oral cavity, larynx, and pharyngeal constrictor muscles. Cisplatin infusion (100 mg/m^2) was administered concurrently on days 1, 22, and 43. Patients were included if they had received at least two cycles of cisplatin.

2.3 | Delineation and dose parameters

The original treatment plan was used for retrospective bilateral delineation and calculation of the dose to the masseter muscle (MM) and medial pterygoid muscle (MPM). The MM and MPM nearest to the gross tumor volume were considered as ipsilateral. Supporting Information File S1 illustrates the delineation of the MM and MPM. The following dose parameters were analyzed (absolute and relative dose parameters): mean dose, V40, V50, V60, V65, and V70, wherein Vx indicates the volume of the muscles receiving at least the specified dose.

2.4 | Maximum mouth opening

Upon commencing treatment and at 3-months after the start of radiation therapy (RT), MIO was measured in millimeter in upright position using the disposable TheraBite range of motion scale (Atos Medical, Hörby, Sweden). Each measurement was performed twice, and the highest measurement was registered. If (partially) edentate patients wore prosthetics before treatment but not afterward, a correction of 5 mm was made after registration. If patients wore prosthetics both before and after treatment, no correction was made. Trismus was defined as a MIO of $\leq$35 mm.[5] Dijkstra et al[5] did not find a clear cut-off point for the subgroups dentate, partially dentate, and edentulous; therefore, a mouth opening of 35 mm or less was regarded as the cut-off point for trismus of the total group.

2.5 | Statistical analysis

Statistical analyses were performed in IBM SPSS version 23.0 (IBM Corporation, Armonk, New York). Binary logistic regression with bootstrapping was applied (2000 samples) to obtain robust estimates of the confidence intervals. Mean dose and dose-volume parameters of iMM and iMPM (calculated in cm^3 and as % of volume) were tested. The estimated parameter Exp(B) was interpreted as odds ratio (OR). A Chi-square-based risk classification tree was generated to identify risk groups based on the identified significant prognostic factors with logistic regression models. This method uses algorithms to create subgroups and cutoffs based on maximal distances.

3 | RESULTS

Initially, data of 98 patients who had undergone CRT between 2008 and 2014 for advanced HNC were collected.

Patients with trismus at baseline were excluded (n = 2), as were patients with gross tumor infiltration of the iMM or iMPM on their planning CT (n = 9). Additionally, four patients were excluded because the original treatment plan could not be retrieved digitally. Therefore, sufficient data for meaningful analyses could be retrieved for 83 patients.

3.1 | Descriptive data

Baseline characteristics are summarized in Table 1. The majority of patients were men (72.3%). Most frequent tumor site was oropharynx (40%) and hypopharynx (31%). All patients had received primary CRT, planned as either IMRT (n = 53) or VMAT (n = 30), with either two (25%) or three (75%) concurrent cisplatin cycles. Delineated mean volumes of the iMPM and iMM were 10.2 cm^3 ± 2.6 1SD and 18.9 cm^3 ± 5.0 1SD, respectively. The delivered dose to the iMPM was on average higher compared to the iMM (mean dose 53.3 Gy ± 17.8 1SD and 30.3 Gy ±13.5 1SD, respectively). The difference in mean dose between the contralateral and ipsilateral MM and MPM was on average (median) 7.9 and 11.1 Gy, respectively. The mean dose to the iMPM and iMM were highly correlated (Figure 1), with a Pearson correlation coefficient of 0.83 ($P < .001$).

TABLE 1 Baseline characteristics (N = 83)

Characteristics	Number of patients	%
Patient characteristics		
Age, y		
Median (range)	59	(22-74)
Sex		
Men	60	72
Women	23	28
Dentition		
(Partially) dentate	56	67
Edentulous	27	33
Tumor characteristics		
Tumor site		
Oral cavity	4	5
Oropharynx	33	40
Hypopharynx	26	31
Nasopharynx	11	13
Larynx	2	2
Unknown primary	4	5
Other	3	4
T classification		
T1	9	11
T2	27	33
T3	19	23
T4	24	29
Tx	4	5
N classification		
N0	18	22
N1	7	8
N2	47	57
N3	11	13
Treatment characteristics		
Radiotherapy		
IMRT	53	64
VMAT	30	36

Abbreviations: IMRT, intensity-modulated radiation therapy; VMAT, volumetric arc therapy.

3.2 | Mouth opening and trismus

The median time between pretreatment and post-treatment MIO measurements was 13 weeks. bMIO ranged from 36 to 69 mm with a median of 46 mm and a mean of 48.3 mm (7.1 mm 1SD). Post-treatment, the range was 21-65 mm, with a mean of 44.3 mm (8.8 1SD) and median of 43 mm. Figure 1 shows all MIO measurements in a scatterplot, with trismus cases in red (n = 14; 17%). The mean relative decrease of maximum mouth opening was 8.3%. The minimal MIO observed post-treatment was 21 mm (1 case). The majority of the patients were measured with their own teeth or prostheses, but in six patients, measurements were done without teeth (all measurements in the range of 45-55 mm with no reduction in MIO for five patients, and one patient with a MIO reduction from 49 to 45 mm). A correction factor of 5 mm was done for two patients who did not wear prosthesis at the second measurement (one trismus case and one case with a post-treatment MIO of 56 mm). This correction factor for one missing prosthesis was based on the average difference in MIO in our data set between patients with and without teeth/prosthesis, as no clear guideline on this issue was found in literature. In addition, trismus classification in these two cases was insensitive for alternative correction factors in the range of 5-10 mm.

3.3 | Predictive clinical factors

bMIO was a significant predictor for trismus at univariable analysis ($P = .05$, OR = 0.854 per mm increase). The optimal cut-off value was 46 mm ($P = .06$, OR = 17.9 for ≤46 mm vs >46 mm). Women more often had a bMIO ≤46 mm (74%) as compared to men (42%; $P < .01$), and women had a higher risk of trismus (30% vs 12%, respectively; $P = .04$). Adjusting for bMIO, the variable sex was not associated with trismus risk anymore. Trismus was most frequently observed for oropharyngeal tumors (9 of 24; 27%), oral cavity tumors (1 of 4; 25%), and nasopharynx tumors (2 of 9; 18%), and less frequent for other sites (2 of 30; 7%). However, tumor site as a categorical variable was not a significant predictor in this study. Moreover, tumor site is associated with the level of dose exposure to the mastication structures, and therefore not a relevant additional factor in dose-effect models. Furthermore, tumor volume, T and N classification, and age were not predictive at univariable analysis.

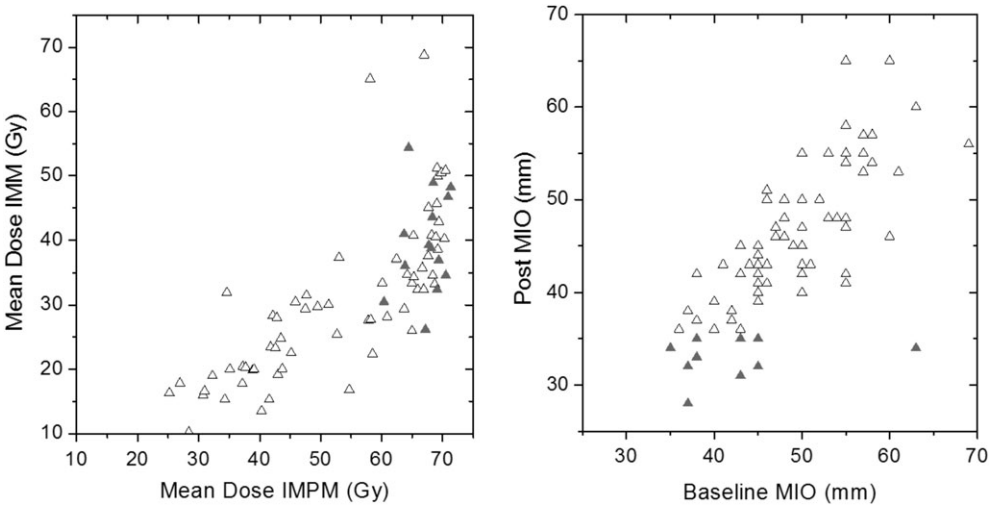

FIGURE 1 Scatterplots (gray triangles are trismus cases; maximum interincisor opening ≤35 mm). Left, Correlation between mean dose ipsilateral medial pterygoid muscle and ipsilateral masseter muscle. Right, Maximum mouth opening measurements before versus at 3-months after start of treatment

3.4 | NTCP modeling

In general, relative dose parameters were more predictive than absolute dose parameters. For iMPM, mean dose and all tested dose volume parameters in the intermediate to high range (V40-V70) were significant predictors for trismus (Table 2). For iMM, mean dose and V40 (%) were significant, and V50 (%) was close to significance. Dose to the contralateral muscles (ciMM and ciMPM) was associated with trismus as well, but less significant compared to the ipsilateral muscles of interest (OR = 1.07, $P = .03$ for mean dose to ciMM and OR = 1.05, $P = .03$ for mean dose to ciMPM). Adding bMIO to the logistic regression models significantly improved univariable dose parameter models ($P < .01$ for nested models). Table 2 shows the results for all obtained two-parameter models with $P < .2$. The best models with iMPM (ie, lowest −2 log likelihoods) was with mean dose (OR = 1.1785, $P = .001$) and for the relative volume receiving ≥50 Gy (OR = 1.082, $P = .001$). For iMM, the dose parameters, mean dose (OR = 1.084, $P = .05$) and the relative volume receiving ≥40 Gy (OR = 1.039, $P = .002$), showed best fits. In general, the models with iMPM showed superior fits (lowest −2 log likelihoods, lowest P values, better goodness-of-fit statistics) compared to the iMM models, although the differences were not statistically significant. A three parameter model with bMIO and iMPM dose and iMM dose was not possible because of the collinearity between iMPM and iMM dose parameters. Figure 2 shows the corresponding NTCP models for trismus as function of mean iMM and mean iMPM dose, respectively, for subgroups of patients with a bMIO of ≤46 mm and >46 mm. The actual incidence of trismus is indicated as well within three dose bins; they show a fair agreement with the obtained model.

TABLE 2 Results of logistic regression models with bootstrapping[a]

Dose volume parameter	-2LLH	Exp(B) per unit	95% CI[b]	*P* value[b]
Ipsilateral-medial pterygoid muscle				
Mean dose	44.0	1.18	1.11-1.45	.001
Vol > 40 Gy %	44.7	1.14	1.07-1.87	.01
Vol > 40 Gy cm^3	58.6	1.18	1.02-1.43	.03
Vol > 50 Gy %	43.4	1.08	1.05-1.19	.003
Vol > 50 Gy cm^3	54.8	1.26	1.10-1.63	.001
Vol > 60 Gy %	46.7	1.05	1.03-1.10	.001
Vol > 60 Gy cm^3	57.0	1.20	1.04-1.52	.03
Vol > 65 Gy %	46.0	1.05	1.03-1.11	.001
Vol > 65 Gy cm^3	52.9	1.33	1.16-1.86	<.001
Vol > 70%	48.6	1.05	1.03-1.09	<.001
Vol > 70 cm^3	52.5	1.53	1.22-2.61	.001
Ipsilateral masseter muscle				
Mean dose	53.2	1.08	1.03-1.21	.01
Vol > 40 Gy %	53.2	1.04	1.01-1.09	.002
Vol > 50 Gy %	57.2	1.03	1.00-2.62	.10

Abbreviations: CI, confidence interval; Gy, gray; LLH, likelihood; Vol, Volume.
[a] All dose volume parameters were evaluated in a two-parameter model with baseline maximum interincisor opening (≤46 mm vs >46 mm) as a covariate.
[b] p value and 95% CI as result of bootstrapping with 2000 samples.

3.5 | Risk classification tree

Figure 3 shows the results of the classification tree procedure. The results showed that mean dose iMPM was selected with an optimal cutoff of 58 Gy, and an optimal cutoff of 46 mm for the bMIO, identifying three subgroups with statistically significant trismus risks: iMPM dose ≤58 Gy (41 cases, 0% trismus), iMPM dose >58.2 Gy and bMIO >46 mm (19 cases, 5% trismus), and iMPM dose >58 Gy and bMIO ≤46 mm (23 cases, 57% trismus). A risk classification model with iMM and bMIO (not shown) showed an optimal cutoff of 22 Gy for mean dose to the iMM in cases with bMIO ≤46 mm (n = 42), with 0 of 10 and 19 of 32 trismus cases, respectively, for bMIO ≤46 mm and iMM ≤22 Gy and bMIO ≤46 mm and iMM >22 Gy (the remaining group bMIO >46 mm: 1 of 41 trismus cases).

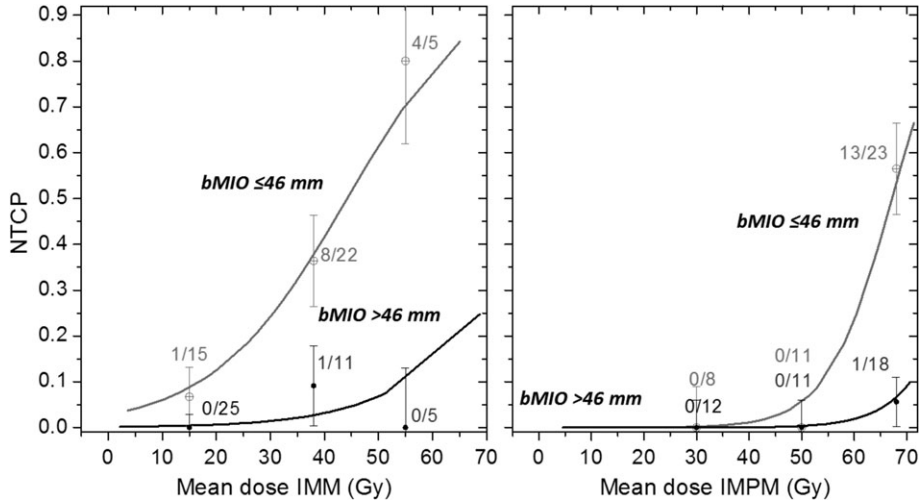

FIGURE 2 Calculated NTCP models for trismus as a function of mean dose (gray) ipsilateral masseter muscle and mean dose (gray) ipsilateral medial pterygoid muscle. Both for patients with baseline maximum mouth opening ≤46 mm and >46 mm. The actual incidences with 1SE within three dose bins are shown as well

4 | DISCUSSION

The aim of the present study was to evaluate the relationship between trismus (MIO ≤35 mm) and the dose to iMM and iMPM, respectively, in patient with HNC population treated with CRT and modern RT techniques, taking into account the bMIO. After an average interval of 3 months after treatment start (ie, 6 weeks after the last fraction), we observed an incidence of 17% (14 of 81) of objectively measured trismus. The bMIO was a significant predictor for development of trismus with an optimal cutoff of 46 mm. With regards to dose-effect relationships, results of this study showed that in general, radiation dose to the iMPM provided the best fit parameters, showing a typical steep inverse dose-effect relationship with trismus. The observed correlation between the mean radiation dose to the iMM and trismus was predictive as well. It is, however, difficult to conclude on the impact of each structure separately because of high correlations. In addition, because of high correlations between the calculated dose parameters, it is difficult to conclude whether the mean dose or the observed significant dose volume parameters (V40 and V50) are most relevant, based on the current study. However, the mean dose has been reported by several other authors as the most relevant parameter.[7,8,18]

4.1 | Timing of measurement

Most reports on trismus after RT concern data 6-36 months post-RT when chronic trismus typically is presented in clinical practice, whereas we evaluated data of MIO 3 months post-RT. Lindblom et al[7] retrieved longitudinal patient-reported data on limited mouth opening and showed that the incidence of trismus had a peak around the end of RT and then decreased and stabilized after 3 months follow-up. Therefore, the currently presented data are suitable for estimating dose-effect relationships although they do not reflect the chronic cases and neither cases that develop complaints after a longer follow-up period. However, our results are indeed in line with other studies in which trismus was assessed at later endpoints as well,[7,8,18] which strengthens the validity of our observations.

4.2 | Baseline maximum interincisor opening

In the current study, bMIO was a highly significant predictor for trismus at 3-months post-treatment. Likewise, in the prospective studies of Pauli et al and Kamstra et al, results from regression analysis revealed that a low MIO at baseline is predictive for trismus.[2,19] Because mouth opening reflects both mobility of the temporomandibular joints (TMJ) and mandibular length,[20] this might implicate that some patients, especially women, already at treatment onset, are at higher risk for developing trismus.

4.3 | NTCP models

A number of studies constructed NTCP models for trismus in various settings: (1) prospectively or retrospectively collected data on mouth opening, (2) radiation only or CRT, (3) objectively measured MIO or assigned toxicity grades (without measurement) based on physician- or patient-reported limited mouth opening, (4) modern intensity-modulated radiation techniques (IMRT) or three-dimensional conformal radiotherapy (3DCRT), (5) with variations in the delineated and evaluated mastication structures, (6) with variations in the evaluated (absolute and/or relative) dose parameters, and (7) with variations in the evaluated follow-up period.[7,8,18] Furthermore, most studies reported only physical dose levels without adjustment for fractionation effects, and all studies retrospectively delineated the structures, as these had not been part of prospective treatment optimization in any study.

Rao et al[8] analyzed retrospectively obtained data, evaluating grade ≥1 trismus (maximum score) according the

Common Terminology Criteria for Adverse Events (CTCAE) scoring system in 421 patients treated with CRT and with IMRT, which is similar to our study population with a median follow-up of 33 months. The best dose-effect relationships were found at univariable analysis for the mean dose to iMM and iMPM. Their dose response curves showed a steep rise after 40 Gy (mean dose) for iMM, whereas in our study, it rises earlier around 20 Gy for patients with a baseline MMO ≤46 Gy and also around 60 Gy for >46Gy. For iMPM the NTCP curve rises after 60 Gy which is very similar to the shape of the NTCP model we obtained. The level of the complication probability is higher in our NTCP model since we had 17% of trismus cases vs 11% in the population of Rao et al. This is probably related to the retrospective nature of their study and the difference in trismus definition and timing.

Gebre-Medhin et al[18] studied trismus (MIO ≤35 mm) in 131 patients mainly treated with IMRT and radiotherapy only, measured after a median follow-up of 16 months with a large range (3-66 months) and no baseline measures. Both mean dose to the iMM and iMPM was predictive at univariable analysis and only iMM remained in the model in a stepwise multivariable analysis. The obtained dose response curves for iMM and iMPM were shallower with a more gradual effect compared to our NTCP curves that show a relatively steep rise for higher dose levels.

Lindblom et al[7] studied trismus and defined as (1) MIO ≤35 mm and (2) patient-reported limitations in mouth opening, using prospective data from a randomized trial. Study patients (n = 124) received radiotherapy only, mainly delivered with 3DCRT. bMIO was not obtained. They observed the best fit for the iMM and a somewhat steeper NTCP curve for MIO ≤35 mm compared to patient-reported trismus.

In summary, the current results are in general agreement with other studies. Our observation of bMIO being a significant predictor was not evaluated in the aforementioned studies but has been reported as a prognostic factor in other studies without dose evaluation.[2,12,19] In our study, iMPM was most predictive, whereas other studies reported iMM as the most important OAR. The close proximity of the two muscles, and therefore the high correlation in dose levels, makes it difficult to draw definite conclusions about the exact role of each individual structure. Different shapes of the dose-response curves of both muscles were suggested in several studies including our study, implying that the muscles should possibly be regarded as separate OARs.

4.4 | Structures involved in trismus development

Previous studies evaluating the dose-effect relationship between various mastication structures and trismus evaluated not only the iMM and iMPM but also contralateral structures, the lateral pterygoid muscles, the temporalis muscle, and/or the TMJ.[7,8,15,18] The iMM and/or iMPM was reported in all these studies as the dominant structure with respect to dose-effect relationships. However, radiation damage to the other mastication structures is likely to have an impact on trismus as well.[7,21] Therefore, in treatment plan optimization, limiting dose to the iMM and iMPM only might not be optimal. In the current study, we aimed at developing an NTCP model for the iMM and iMPM, which was found to be of most importance according to the existing literature. In additional studies, we will consider other mastication structures as well, in a larger data set with more follow-up in which we can also study long-term trismus as a result of progressive late effects such as osteonecrosis of the mandible and TMJ.[21,22]

4.5 | Clinical factors associated with trismus

Previous studies evaluating prognostic baseline factors for trismus have reported significant relationships of trismus with: tumor location, tumor invasion of mastication structures, tumor volume/T classification, baseline mouth opening, sex, age, poor physical function, use of alcohol, CRT, prescribed dose, and surgical procedures.[1,2,4,12,19,21–24] In our homogeneous study population, all patients had CRT, a prescribed dose of 70 Gy, no surgery, and no tumor invasion of mastication structures. In line with literature, we identified baseline mouth opening as a prognostic factor in a multivariable model together with iMM/iMPM dose, whereas sex was only significant in the univariable model and not in the multivariable model because of the relationship with bMIO. Age, T classification, and tumor volume were not associated with trismus in our study.

4.6 | Strengths and weaknesses of the study

The current study is one of the few that systematically measured the MIO preradiotherapy and postradiotherapy in a study group of patients with HNC. Data were collected in patients treated with modern techniques and according to common treatment protocols (including an exercise program), which strengthens the external validity of the study results with respect to current clinical practice. Measuring the mouth opening has a large objective component and is therefore a suitable endpoint for exploring dose-effect relationships. A limitation of the study is the lack of repeated measurements and the lack of data after a longer follow-up period. Also the lack of patient-reported problems with their mouth opening is a limiting factor. The study did not include patient- or physician-reported trismus, which might be a more clinically relevant endpoint, although its subjective component might lead to obtaining less accurate dose-effect relationships. Finally, the obtained results might in part be the results of overfitting and should be tested in a future patient cohort with baseline and follow-up MIO measurements.

4.7 | Clinical relevance

Despite the use of advanced radiation techniques, trismus remains a clinical relevant complication, especially for

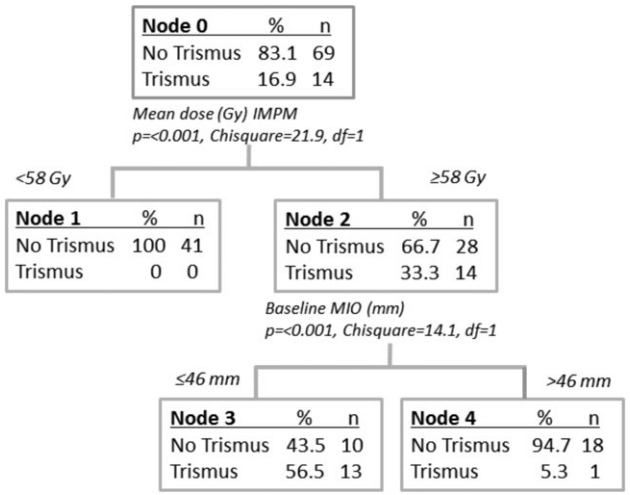

FIGURE 3 Obtained risk classification tree for postchemoradiation trismus

patients with a limited bMIO. Based on the results of the current study and other studies, iMPM and iMM are the most important OARs, and dose levels should be limited during treatment plan optimization. However, as shown in Figure 1, high mean dose levels around 70 Gy for iMPM were present for a considerable number of patients, implying that this structure was likely to be situated for a large part in the planning target volume. Therefore, sparing this OAR by keeping mean dose levels below thresholds may not always be possible. In the current study, *all* events (14 of 14) concerned patients with a mean dose ≥58 Gy to the iMPM: 13 cases with a bMIO ≤46 mm and 1 case with a bMIO >46 mm (Figure 3), strongly suggesting this might be an optimal dose constraint. Also, with respect to the iMM, keeping the mean dose below a certain threshold (eg, <22 Gy) could be advocated to keep trismus risks limited, especially for patients with a limited MIO at baseline.

5 | CONCLUSIONS

We conclude that both the iMPM and the iMM dose are predictive for trismus. Furthermore, we conclude that the strong correlation between the iMPM and iMM is caused by close proximity of the two muscles and therefore it is difficult to establish the impact of each mastication structure separately. Investigated dose parameters were highly correlated as well. However, taking into account reports from literature, the mean dose to both iMPM and iMM seems to be most importance. Furthermore, we conclude that bMIO is highly predictive and clinically relevant information that should be taken into account in trismus models.

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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 section at the end of the article.

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