Speech Evaluation in Patients Treated for Oral Cancer: a 5-year Prospective Study

Part of Quality of Oral Function (QuOFu) Study

Madelon J. Joosten
Studentnumber 4152069
Utrecht University, Clinical Language, Speech and Hearing Sciences,
master Clinical Health Sciences, Faculty of Medicine, Utrecht University, the Netherlands.

Date:	30-06-2016
Version:	Final version
Course:	Afstudeeronderzoek
Coursenumber:	KGWL06014
Course lecturer:	R. Zwitserlood, PhD / I. Cnossen, PhD
Course supervisor:	C. Speksnijder, PhD
Course examinator:	Professor E. Gerrits
Intended journal:	Oral Oncology
Maximum words intended journal:	250 words (abstract), 3500 words (total)
Maximum words UMC Utrecht	300 words (abstract), 3800 words (total)
Referencestyle:	Vancouver Reference Style Guide
Reporting guidelines:	STROBE for cohort studies
Number of words in total:	3707
Number of words English abstract:	297
Number of words Dutch abstract:	298

SAMENVATTING

Achtergrond: Spraakproblemen worden bij 34% tot 65% van de patiënten met mondkanker gezien, waarbij een perceptuele beoordeling van deze problemen door logopedisten zeer gebruikelijk is. Een longitudinale studie waarbij de spraak van patiënten met mondkanker wordt beoordeeld met behulp van een gevalideerde schaal, mist.

Doel: Het eerste doel is meer inzicht krijgen in het verloop van de spraakkwaliteit van patiënten met mondkanker tot vijf jaar na oncologische behandeling. Daarnaast worden klinische factoren die van invloed zijn op spraak bij patiënten met mondkanker gedurende vijf jaar geïdentificeerd. Tot slot wordt de betrouwbaarheid van de parameter 'grade' van de London Speech Evaluation (LSE) schaal onderzocht.

Methode: Een perceptuele beoordeling van de spraak middels de parameter 'grade' is 4-6 weken voorafgaand aan de behandeling, 4-6 weken postoperatief en/of 4-6 weken na radiotherapie en 6,12 en 60 maanden na behandeling uitgevoerd. Een generalized linear mixed backward stepwise model voor de parameter 'grade' is geconstrueerd. Daarnaast zijn gewogen Kappa's berekend om de intra- en interrater mate van overeenstemming te bepalen.

Resultaten: De spraakkwaliteit verslechterde significant na behandeling en verbeterde significant tussen de metingen gedaan na 6 en 12 maanden. Het meetmoment, de leeftijd bij aanvang van de behandeling, tumorlocatie, tumorgrootte, wijze van reconstructie en dentale status hadden een significant effect op de parameter 'grade'. De interrater mate van overeenstemming varieerde van redelijk tot voldoende/goed en de intrarater mate van overeenstemming van redelijk tot bijna perfect.

Conclusie en implicaties: Het verloop van de spraakkwaliteit bij patiënten met mondkanker is vastgesteld. De spraakkwaliteit wordt beïnvloed door het meetmoment, de leeftijd bij aanvang van de oncologische behandeling, tumorlocatie, tumorgrootte, wijze van reconstructie en dentale status. De parameter 'grade' van de LSE is een valide manier om de spraakkwaliteit te beoordelen. Deze parameter kan door logopedisten worden gebruikt om het effect van hun interventie te beoordelen.

Kernwoorden: mondkanker, spraakproblemen, London Speech Evaluation schaal, spraakkwaliteit, orale functie.

ABSTRACT

Background: Speech difficulties are found in 34% to 65% of patients with oral cancer and perceptual assessment of these difficulties is common practice among speech and language therapists (SLTs). A longitudinal study using a validated assessment tool regarding speech quality in patients with oral cancer is missing.

Aim: Firstly to obtain insight in the development over time regarding speech quality up to five years after oral oncological treatment. Secondly to identify the clinical factors during a 5-year period that are of influence on speech quality in patients treated for oral cancer. Finally to determine the reliability of the parameter 'grade' of the London Speech Evaluation (LSE).

Methods: Perceptual assessment of speech using the parameter 'grade' of the LSE was carried out 4-6 weeks before treatment, 4-6 weeks after surgery and/or 4-6 weeks after radiotherapy, and 6, 12, and 60 months after treatment. A generalized linear mixed backward stepwise model for 'grade' was constructed. To determine intra- and interrater level of agreement weighted Kappa's were calculated.

Results: Speech quality decreased significantly after intervention and increased significantly between the 6 and 12 months assessments. Assessment period, age shortly before oncological intervention, tumour location, tumour size, reconstruction method and dental status had a significant effect on the parameter 'grade'. Interrater level of agreement ranged from moderate to substantial, intrarater agreement ranged from moderate to almost perfect.

Conclusion and implications: The development over time in patients with oral cancer has been obtained. Quality of speech is influenced by the effect of assessment period, age shortly before the oncological intervention, location of the tumour, tumour size, reconstruction method, and dental status. The parameter 'grade' of the LSE has proven to be a valid manner to assess speech quality. This parameter can be used by SLTs to monitor effects of their intervention.

Key words: oral cancer, speech difficulties, London Speech Evaluation scale, speech quality, oral function.

Introduction

Worldwide, oral cancer is among the ten most common types of cancer. Cancer of the lip and oral cavity accounts for 2.1% of the total cancer incidence (1). Oral cancer is mostly seen between the ages of 55 and 75 (2). Numerous risk factors are described having a correlation with oral cancer. The major and most described factors are tobacco, which includes smoking and chewing, chewing betel quid, and excessive alcohol abuse (1,3-5). Other risk factors are the human papillomavirus (HPV), syphilis, viruses, low social economic status, oro-dental factors, dietary deficiencies and chronic candidiasis (1,3-5). The five-year survival rate of oral cancer is approximately 50% to 60% (1,3,6).

More enhanced surgical techniques and more effective chemo-radiotherapy treatment protocols have resulted in increased survival rates. However, as a result of these survival rates more and more patients experience long-term negative side effects (7,8). Survivors of oral cancer are frequently confronted with difficulties in oral functioning. Problems with eating and drinking, dental state, bite force, maximum mouth opening and swallowing occur regularly (8-11). More importantly, speech is often negatively affected (8,9,12-14). Speech difficulties are found in 34% to 65% of patients with oral cancer (15,16). A decrease in oral function and deviant speech is found to have a dependency with a decrease in health-related quality of life (HRQoL) (8,9,12,17).

Speech difficulties can be assessed in different ways: questionnaire evaluation, perceptual evaluation and acoustic evaluation are most common (12). Studies evaluating these speech difficulties are rather scarce. A decrease in speech quality was found in a 1-year prospective study done in 2005 (13). However, in this study, a non-validated perceptual speech test was used. To assess speech quality more systematically, the London Speech Evaluation (LSE) scale has been developed recently. The LSE is a validated speech perception scale to analyse speech quality in patients with oral cancer in a valid way (17). To our knowledge a long-term prospective study regarding the perceptual assessment of patients receiving oral oncological treatment using a validated tool is missing. A more accurate prediction of clinical factors influencing speech enhances insight in expectations and results in better patient education.

Aim

The aim of this prospective cohort study is to obtain insight in the development over time regarding speech quality up to five years after oral oncological treatment. Secondly to identify the clinical factors during a 5-year period that are of influence on speech quality in patients treated for oral cancer. Finally to determine the reliability of the parameter ‘grade’ of the LSE scale, which gives an overall judgement of speech quality.

Methods

Patients

This multicentre prospective cohort study included patients who received oral oncological treatment. Patients were recruited between 2007 and 2009 from two University Hospitals in the Netherlands; the University Medical Center Utrecht (UMC Utrecht) and the Radboud university medical centre (Radboudumc) of Nijmegen. The criteria below are in accordance with the QuOFu-study and have been published before (11).

In order to be eligible to participate in the study, a patient had to suffer a primary malignant tumour involving the oral cavity and the tumour had to be treated with surgery, a combination of surgery and radiotherapy or only radiotherapy. A potential subject who met any of the following criteria was excluded from participation: a previous and/or current malignancy, visual and/or cognitive impairment and/or inability to understand and read Dutch. Patients could leave the study at any time without reason. If applicable, radiotherapy was applied 4-6 weeks after surgery as stated in the guidelines of the Dutch Head and Neck Oncology Group. The dosage (adjuvant or primary) was 54-70 Gy. This study was conducted according to the principles of Helsinki (18). The study was approved by the Ethics Committees of UMC Utrecht and Radboudumc.

Gender, age, tumour location, tumour size (T of TNM) (19), treatment modality, resection site and reconstruction details were derived from the medical status. The amount of tobacco use and amount of alcohol consumption were collected at the pre-treatment session. A distinction was made between patients who smoked irregularly or did not smoke and those who smoked daily. As to the alcohol consumption two groups were made, patients who drank one or more alcoholic beverage a day and those who drank less than this amount of alcohol.

Patients in this study were assigned to 3 anatomic groups based on their tumour location; a tumour in the mandible, maxilla and tongue and/or floor of the mouth (TFM). Tumour locations included codes C00, C02 to C06, and C31 of the World Health Organization International Classification of Diseases Oncology (20). Maxillary tumours included the upper alveolar process, tuber maxillae, palate and maxillary sinus (C03.0, C05, and C31.0). Mandible tumours included the lower alveolar process, the retromolar trigone, the buccal mucosa, and the lower lip (C00.4, C03.1, C06.0, C06.1, and C06.2). TFM tumours included the tongue and the anterior floor of the mouth (C02 and C04) (11).

Measurements

Assessment of dental status, presence of an obturator prosthesis and performing a reading task out loud were carried out 4-6 weeks before treatment, 4-6 weeks after surgery and/or 4-6 weeks after radiotherapy, and 6, 12, and 60 months after treatment.

Dental status

Dental status was divided into the following groups. 0) edentate, 1) full denture in upper- and lower jaw, 2) full denture in upper or lower jaw and full denture with implant retention in upper or lower jaw, 3) full denture in upper or lower jaw and dentate upper or lower jaw, 4) full denture with implant retention in upper and lower jaw, 5) full denture with implant retention in upper or lower jaw and dentate upper or lower jaw, 6) dentate upper and lower jaw. Partially dentate jaws were classified as 'dentate'.

Obturator prosthesis

For patients who underwent maxillectomy, a temporary obturator was fabricated based on preoperative assessments and dental casts. This obturator was fitted preoperatively using a soft reline material (Viscogel, art. 61605001, York, PA, USA). This obturator was immediately inserted after tumour resection and remained in situ for the following 4-6 weeks to prevent shrinkage of the maxillectomy cavity. Two to three months post-surgery an interim obturator was fabricated and after approximately 1 year the patient was provided with the definite obturator, made of acrylic resin based on Beumer's method (21). This obturator protocol remained unchanged during the whole study period. Having an obturator prosthesis was scored using a nominal scale. The possible scores were: 0) no obturator prosthesis and 1) obturator prosthesis.

Speech evaluation

All patients have performed a standard Dutch reading task out loud ('Loos alarm op het strand') from the test for Dysarthria and Apraxia of Speech (Appendix A) (22). This test was common practice in 2007 and its reading task was considered to be the best way to evaluate connected speech at the start of the study. Data were recorded using a Logitech USB Desktop Microphone (Logitech® A-0186A, Newark, CA, USA). The microphone was placed in front of each subject with a thirty centimetre mouth-to-microphone distance.

The samples of all patients were anonymised and randomised before they were assessed. The assessors were blinded for any patient characteristics. They only knew that these patients were treated for oral oncology. The reading task (connected speech) was assessed for quality of speech using the parameter 'grade' of the LSE scale. Assessment was done by three trained speech and language therapists (SLTs). Before assessment a dozen samples were assessed and discussed and parameters were defined until consensus was reached.

The parameter ‘grade’ is an overall score of the severity of the impairment regarding speech quality. The parameter was scored using a four-point scale ranging from 0 (no impairment) to 4 (severe impairment). A higher score on the parameter ‘grade’ implicates more deviant speech quality.

Statistical analysis

A chi-square goodness-of-fit test was used to analyse any differences in patient characteristics regarding tumour location. ANalysis Of VAriance (ANOVA) was used to analyse differences in age (mean and standard deviation) regarding tumour location. A Kruskal Wallis Test was used to determine any differences in the scores of the parameter ‘grade’ of the LSE (ordinal outcome) among the three groups at baseline. A Wilcoxon Signed Rank Test was used regarding the parameter ‘grade’ (ordinal outcome) in patients treated with surgery and radiotherapy to analyse differences between the measurements 4-6 weeks after surgery and the measurements 4-6 weeks after radiotherapy. No statistical significance differences were found between these two ‘grade’ measurements in time. Therefore, the outcomes of the measurements directly after surgery were not used for further analysis, in patients treated for both surgery and radiotherapy. A Wilcoxon Signed Rank Test was executed to compare the assessment periods regarding the parameter ‘grade’ (ordinal outcome).

A generalized linear mixed backward stepwise model for the parameter ‘grade’ was constructed to assess both the changes over time at each assessment period and the effect of clinical factors and patient characteristics. The assessment period, gender, age, tumour size, treatment modality, surgical reconstruction, the presence of an obturator prosthesis, dental status, smoking, alcohol usage as well as interactions regarding assessment period were added as fixed effects. If an interaction with the assessment period was in the model, then the main effects were also in the model. Next, the fixed effects that were not significant at a .05 level were then removed backwardly, beginning with the interactions, to build a parsimonious model with sufficient good fit keeping a hierarchical structure. A Mann-Witney *U* Test was then used to conduct pairwise-comparisons regarding tumour locations and tumour sizes.

A weighted Kappa was performed to determine the intra- and interrater level of agreement. No imputation of missing values was performed. All statistical analyses were executed 2-sided and were considered statistically significant if $p \leq .05$. All statistical analyses were done using SPSS version 21 (IBM SPSS Statistics) except the linear mixed backward stepwise model which was conducted using SAS version 9.2 (SAS Institute, Cary, NC).

Sample size calculation

Since this study is part of the QuOFu Study, a sample size calculation was already done. The appropriate sample size was deducted from other studies. Earlier research regarding oral function was done in patients with myasthenia gravis, a neuromuscular disease (23). In patients with different dental status this function was investigated (24). Research regarding oral function tests (for example swallowing and chewing ability) showed a significant difference is found in groups larger than 20 participants (23,24). In the QuOFu Study a drastic decrease in oral function was expected. It is known that mortality of cancer in the oral cavity is 50% to 60% in five years (1,3,6). As mentioned before, 3 anatomic groups were distinguished. Due to the high mortality rate, groups of 20 patients will not be sufficient to find a significant difference between groups in time. Therefore each group was multiplied by two, resulting in 3 groups each consisting of approximately 40 patients.

Results

Patient characteristics

In total 142 patients participated in this study. Table 1 shows baseline patient characteristics. Thirty-four patients suffered a tumour in the maxilla, 53 patients had a tumour in the mandible and 55 patients had a TFM tumour. In 59 patients treatment consisted of primary surgery (surgery group), 20 patients were treated with primary radiotherapy (radiotherapy group) and 64 patients were treated with surgery as well as radiotherapy (surgery-radiotherapy group). Statistical significant outcome at baseline were found regarding age, tumour size and surgical reconstruction. No statistical significant differences were found among the three anatomic groups at baseline regarding the parameter 'grade'. After 1 year one patient was excluded because of a recurrence of the tumour. After five years 71 of 142 patients were still enrolled in the study. Thirty-nine patients died and 32 patients stopped participating. Five measurements were not collected because of scheduling conflicts or time constraints (Figure 1).

Development of speech quality over time

Speech quality significantly decreased shortly after the oral oncological treatment related to the speech quality measured shortly before the oncological treatment ($p \leq .000$). No statistical difference was found between the assessment period shortly after treatment and at the 6 months assessment ($p = .986$). Comparing the 6 months assessment to the 12 months assessment showed a significant increase in speech quality ($p = .004$). Between the 12 months assessment and the 60 months assessment no significant difference was found regarding speech quality ($p = .354$).

Clinical factors predicting 'grade'

The assessment period, age shortly before oncological intervention, tumour location, tumour size, reconstruction method and dental status all had a significant effect on influencing the overall parameter 'grade'. Furthermore there was a significant interaction between the assessment period and tumour location, between the assessment period and tumour size and between the assessment period and reconstruction method.

Tumour location had a significant interaction with the assessment period meaning that the parameter 'grade' differed between tumour location at each assessment (Table 2, Figure 2), which means that in time the speech quality of the maxillary tumour group decreased significantly more than the mandibular and TFM group. There was a statistically significant difference between maxillary and mandibular tumours at baseline assessment ($p = .033$). The TFM tumour group showed no significant differences with the other tumour groups at baseline.

Maxillary and mandibular tumours also differed significantly direct after intervention ($p \leq .000$) and at the 12 months assessment ($p = .002$). There were no statistically significant differences regarding all assessment periods between patients with mandibular and patients with a tumour in TFM. Comparing patients with maxillary tumours to patients with TFM tumours showed significant differences directly after treatment ($p \leq .000$), 6 months after treatment ($p = .019$) and 12 months after treatment ($p = .001$).

Assessment period also had a significant interaction with tumour size (T of TNM) (Table 3, Figure 3), which means that there is a different speech quality course for the tumour sizes in time. At the baseline assessment there were no statistic significant differences between tumour sizes. Patients with a T1 and T2 tumour performed better overall, there was a significant difference between these groups at the 6-months assessment ($p = .001$). Between patients with T1 and T3 tumour statistic significant differences were found from the 6-months assessment until the 60-months assessment. The same statistical results were seen comparing patients with T2 tumours to patients with T3 or T4 tumours. Comparing patients with T1 to T4 tumours showed statistical significant differences from the assessment directly after intervention until the 60-months assessment. Patients with T3 tumours had a statistically significant poorer score at the 60-months assessment in comparison to patients with T4 tumours ($p = .011$). Furthermore assessment period had a significant interaction with reconstruction method, which means that the course in time differed per reconstruction method.

Finally aging accounted for a decrease in speech quality. Edentulous patients or patients with (partial) dental implants achieved a more deviant score on the parameter ‘grade’.

Reliability of ‘grade’

The scores of the three experts were analysed to determine the intra- and interrater level of agreement of the overall parameter ‘grade’ of the LSE. The interrater scores were done using in 685 speech samples of all 142 patients having a substantial agreement. The scores varied from 0.62 (rater 1 versus rater 2) and 0.74 (rater 1 versus rater 3 and rater 2 versus rater 3). The intrarater scores were done using a random selection of 360 speech samples and had a substantial to almost perfect agreement, respectively 0.73 (rater 1), 0.89 (rater 2) and 0.81 (rater 3).

Discussion

Key findings

Although speech can be assessed in many different ways, perceptual evaluation of speech is common practice (25). The present study shows the results of the development over time regarding speech quality in 142 patients suffering oral cancer who received oral oncological intervention. Statistical significant differences were found between the assessment shortly after intervention and before intervention and between the assessments at 6 and 12 months. Clinical factors that have an influence on this parameter are the assessment period, age before intervention, tumour location and tumour size, reconstruction method and dental status. Speech quality was measured using the parameter 'grade' of the LSE scale, which gives an overall judgement of speech quality.

Speech quality

Speech quality was examined using the overall parameter 'grade' of the validated LSE scale (17). In our study, cancer of the oral cavity and its treatment is found to have a deteriorating effect on speech quality, as is confirmed by multiple studies (13,26-29).

The assessment period accounted for a significant decrease in speech quality directly after treatment compared to the pre-treatment assessment. In another cohort study the same trend regarding the parameters 'communicative suitability' and 'intelligibility' was found (13). In our study a significant decrease was found between the 6 and 12 months assessment. These findings are in contradiction with the results regarding the two parameters in the cohort study mentioned before (13). A possible explanation is that the parameter 'grade' used in our study embodies more than only 'communicative suitability' and 'intelligibility'.

In a survey done among SLTs, clinical factors were searched which were thought to predict functional recovery in patients suffering oral cancer. The age before oral oncological intervention was found to be a large factor of influence according to SLTs (25). Our study confirms this perceptual view of the SLT group, showing aging was a risk factor in developing speech difficulties. Dental status was also thought to be a factor of influence among the SLTs (25), our study confirms the findings found in the survey.

Tumour location was of influence in speech quality in our study and more deviant speech quality is seen in patients with maxillary tumours. Other studies found more deviant speech in patients suffering TFM tumours (13,27). A factor of influence can be the role of deviant nasality, which is expected to be more affected in patients suffering maxillary tumours. Maybe in our study this has a large effect in scoring the quality of speech. Another possible explanation of these different findings is that in our study the group of patients with TFM tumours have the smallest tumours while the group of patients with maxillary tumours have the

largest tumours. Thereby, tumour size was found a significant risk factor in our study. Larger tumours cause more deviant speech quality. These results are confirmed in other studies, showing patients are more at risk when suffering larger tumours (13,25,29).

Reconstruction method is a factor of influence in our model. As result of a prospective study a model containing factors influencing speech intelligibility was developed. Although reconstruction method was included, a significant relation to speech intelligibility was not found (29). In another prospective cohort study no statistical significant differences regarding speech rehabilitation between the different reconstruction methods were found (27). A possible explanation of these contradictive findings is that our study has higher power due to the larger amount of participants. Furthermore these two studies included patients with smaller tumours than in our study. Larger tumours probably need a more extensive reconstruction and therefore have a more deviant effect on speech quality.

Although in other studies treatment modality (e.g. surgery, radiotherapy or a combination of these) is correlated with speech difficulties (29,30), in our model treatment modality has not been found a factor of influence. A recent study showed no statistical significant outcomes for treatment modality, regarding health related quality of life (31).

Strengths and limitations

Several studies exist, investigating speech quality in a perceptual way in patients treated for oral cancer (13,17,26,32,33). To our knowledge this study is the only study having a 5-year prospective design. This study is strengthened by the large amount of patients and the distinction in anatomic groups based on tumour location. Furthermore this study uses the first and only validated speech-specific scale, which is developed for perceptual evaluation of patients treated for head and neck cancer (17). The reading task ‘Loos alarm op het Strand’ was common practice among SLTs to assess speech at the start of the study (22).

As stated this study uses a validated speech assessment tool. This validation was done using English data instead of Dutch. Therefore intra- and interrater level of agreement regarding the Dutch speech samples were calculated. With Kappa’s of at least a substantial agreement, this parameter appears to be a valid manner to perceptually assess speech in patients with oral cancer. Assessment was done based on connected speech. Possibly, a more accurate evaluation of speech quality could have been done by adding a repetition task of specific (non)words or a verbal diadochokinesis task.

If necessary, patients were redirected to a speech and language therapist. Unfortunately, the number of patients who have had speech and language therapy prior or during the course of the study, has not been monitored systematically. The resected tumour

volume is shown to be a risk factor in other studies. This factor was not included in this study, although tumour size is highly related to the resected tissue (29,30).

Clinical implications and future research

Whether or not speech therapy is of influence in patients with different tumour locations of oral cancer still remains unknown. It was already demonstrated that speech therapy has a positive effect in patients undergoing glossectomy (34). In our study the parameter 'grade' of the LSE scale has proven to be a reliable way for SLTs to assess speech quality in patients with oral cancer. Since perceptual assessment is common practice, SLTs now have a reliable tool to monitor effects of their intervention regarding speech therapy in patients with oral cancer.

Since the clinical factors which have an effect on speech quality have been set, a next step should be to examine the effects of speech and language therapy on speech quality in patients suffering from oral cancer who are at risk of developing speech difficulties.

Further research should be directed at pinpointing which clinical factors play a role in the other parameters of the LSE scale and therefore establish which category of patients with oral cancer are at risk.

Conclusion

Speech quality decreased significantly shortly after intervention and increased significantly between the 6 and 12 months assessment. The quality of speech in patients with cancer of the oral cavity was influenced by the effect of assessment period, age shortly before the oncological intervention, location of the tumour, tumour size, reconstruction method, and dental status. The used parameter ‘grade’ of the LSE-scale has proven to be a valid manner to assess speech quality for research as well as for SLTs.

Acknowledgements

The authors thank the three speech and language experts K. de Boer, J. Lufueni and L. Scheperman, for their effort in scoring the samples used in this study. Furthermore the authors thank drs. T. de Haan for his contribution regarding the generalized linear mixed backwise stepward model which was constructed for this study.

References

(1) Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136(5):E359-86.

(2) Sarini J, Fournier C, Lefebvre JL, Bonafos G, Van JT, Coche Dequéant B. Head and neck squamous cell carcinoma in elderly patients: a long-term retrospective review of 273 cases. Arch Otolaryngol Head Neck Surg 2001;127(9):1089-92.

(3) Johnson N, Warnakulasuriya S, Gupta P, Dimba E, Chindia M, Otoh E, et al. Global oral health inequalities in incidence and outcomes for oral cancer: causes and solutions. Adv Dent Res 2011;23(2):237-46.

(4) Ram H, Sarkar J, Kumar H, Konwar R, Bhatt M, Mohammad S. Oral cancer: risk factors and molecular pathogenesis. J Maxillofac Oral Surg 2011;10(2):132-7.

(5) Cerrati E, Nguyen S, Farrar J, Lentsch E. The efficacy of photodynamic therapy in the treatment of oral squamous cell carcinoma: a meta-analysis. Ear Nose Throat J 2015;94(2):72-9.

(6) Integraal Kankercentrum Nederland. Available at: https://www.iknl.nl/cijfers/over-cijfers. Accessed November 28, 2015.

(7) van der Molen L, van Rossum M, Burkhead L, Smeele L, Hilgers F. Functional outcomes and rehabilitation strategies in patients treated with chemoradiotherapy for advanced head and neck cancer: a systematic review. Eur Arch Otorhinolaryngol 2009;266(6):889-900.

(8) Rogers S, Lowe D, Fisher S, Brown JV,ED. Health-related quality of life and clinical function after primary surgery for oral cancer. Br J Oral Maxillofac Surg 2002;40(1):11-8.

(9) Vartanian J, Carvalho A, Yueh B, Priante A, de Melo R, Correia L, et al. Long-term quality-of-life evaluation after head and neck cancer treatment in a developing country. Arch Otolaryngol Head Neck Surg 2004;130(10):1209-13.

(10) Speksnijder C, van der Bilt A, Abbink J, Merkx M, Koole R. Mastication in patients treated for malignancies in tongue and/or floor of mouth: A 1-year prospective study. Head Neck 2011;33(7):1013-20.

(11) Wetzels JGH, Merkx MAW, de Haan, Anton F J, Koole R, Speksnijder C. Maximum mouth opening and trismus in 143 patients treated for oral cancer: a 1-year prospective study. Head Neck 2014;36(12):1754-62.

(12) Dwivedi R, Kazi R, Agrawal N, Nutting C, Clarke P, Kerawala C, et al. Evaluation of speech outcomes following treatment of oral and oropharyngeal cancers. Cancer Treat Rev 2009;35(5):417-24.

(13) Borggreven P, Verdonck-de Leeuw I, Langendijk J, Doornaert P, Koster M, de Bree R, et al. Speech outcome after surgical treatment for oral and oropharyngeal cancer: a longitudinal assessment of patients reconstructed by a microvascular flap. Head Neck 2005;27(9):785-93.

(14) van der Molen L, van Rossum M, Jacobi I, van Son R, Smeele L, Rasch C, et al. Pre- and posttreatment voice and speech outcomes in patients with advanced head and neck cancer treated with chemoradiotherapy: expert listeners' and patient's perception. J Voice 2012;26(5):664-33.

(15) Rinkel R, Verdonck-de Leeuw I, van Reij E, Aaronson N, Leemans C. Speech Handicap Index in patients with oral and pharyngeal cancer: better understanding of patients' complaints. Head Neck 2008;30(7):868-74.

(16) Thomas L, Jones TM, Tandon S, Carding P, Lowe D, Rogers S. Speech and voice outcomes in oropharyngeal cancer and evaluation of the University of Washington Quality of Life speech domain. Clin Otolaryngol 2009;34(1):34-42.

(17) Dwivedi R, St Rose S, Chisholm E, Kerawala C, Clarke P, Nutting C, et al. Development and validation of first-ever speech-specific perceptual speech evaluation tool for patients with head and neck cancer: the London speech evaluation (LSE) scale. Head Neck 2012;34(1):94-103.

(18) World Medical Association Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects. JAMA 2013;310(20):2191-2194.

(19) Patel S, Shah J. TNM staging of cancers of the head and neck: striving for uniformity among diversity. CA Cancer J Clin 2005;55(4):242-58; quiz 261.

(20) WHO. The International Classification of Diseases for Oncology. 3rd ed. Geneva, Switzerland: World Health Organization; 2000.

(21) Beumer, J. Curtis, TA. Marunick, MT. Maxillofacial rehabilitation; prosthodontic and surgical considerations. St Louis/ Tokyo: Ishiyaku EuroAmerica 1996:240-324.

(22) Dharmaperwira-Prins R. Dysartrie en Verbale Apraxie. Lisse: Zwets; 1998.

(23) Weijnen F. Quantitative and qualitative evaluation of bulbar symptoms in patients with myasthenia gravis. Proefschrift UMC Utrecht 2000.

(24) van Kampen F. Implant-supported overdentures; a clinical and functional comparison of magnet, bar-clip and ball-socket retained mandibular overdentures. Proefschrift UMC Utrecht 2006.

(25) Husaini H, Krisciunas G, Langmore S, Mojica J, Urken M, Jacobson A, et al. A survey of variables used by speech-language pathologists to assess function and predict functional recovery in oral cancer patients. Dysphagia 2014;29(3):376-386.

(26) Nicoletti G, Soutar D, Jackson M, Wrench A, Robertson G, Robertson C. Objective assessment of speech after surgical treatment for oral cancer: experience from 196 selected cases. Plast Reconstr Surg 2004;113(1):114-125.

(27) Riemann M, Knipfer C, Rohde M, Adler W, Schuster M, Noeth E, et al. Oral squamous cell carcinoma of the tongue: Prospective and objective speech evaluation of patients undergoing surgical therapy. Head Neck 2014.

(28) Schuster M, Stelzle F. Outcome measurements after oral cancer treatment: speech and speech-related aspects--an overview. Oral Maxillofac Surg 2012;16(3):291-298.

(29) Stelzle F, Knipfer C, Schuster M, Bocklet T, Nöth E, Adler W, et al. Factors influencing relative speech intelligibility in patients with oral squamous cell carcinoma: a prospective study using automatic, computer-based speech analysis. Int J Oral Maxillofac Surg 2013;42(11):1377-1384.

(30) Pauloski BR, Rademaker AW, Logemann JA, Colangelo LA. Speech and swallowing in irradiated and nonirradiated postsurgical oral cancer patients. Otolaryngol Head Neck Surg 1998;118(5):616-624.

(31) Crombie A, Farah C, Batstone M. Health-related quality of life of patients treated with primary chemoradiotherapy for oral cavity squamous cell carcinoma: a comparison with surgery. Br J Oral Maxillofac Surg 2014;52(2):111-117.

(32) Bundgaard T, Tandrup O, Elbrønd O. A functional evaluation of patients treated for oral cancer. A prospective study. Int J Oral Maxillofac Surg 1993;22(1):28-34.

(33) Colangelo LA, Logemann JA, Rademaker AW. Tumor size and pretreatment speech and swallowing in patients with resectable tumors. Otolaryngol Head Neck Surg 2000;122(5):653-661.

(34) Furia CL, Kowalski LP, Latorre MR, Angelis EC, Martins NM, Barros AP, et al. Speech intelligibility after glossectomy and speech rehabilitation. Arch Otolaryngol Head Neck Surg 2001;127(7):877-883.

Tables and figures

Table 1 Baseline patient characteristics

Table 1. Baseline demographics and clinical characteristics for the patient groups based on tumour location.

	maxilla (n = 34)		mandible (n = 53)		TFM (n = 55)		p-value
gender (n, %)							.607
male	17	50	28	53	33	60	
female	17	50	25	47	22	40	
age, years (mean, SD)	68.4 (12.2)		67.2 (12.6)		62.3 (12.9)		.046*
smoking, daily (n, %)							.767
yes	11	32	20	38	22	40	
no	23	68	33	62	33	60	
alcohol usage, > 1 daily (n, %)							.095
yes	8	24	15	28	24	44	
no	26	76	38	72	31	56	
tumour size, T of TNM (n, %)							.014*
T1	5	15	17	32	23	42	
T2	11	32	13	25	17	31	
T3	1	3	3	6	6	11	
T4	17	50	20	38	9	16	
treatment (n, %)							.666
surgery	12	35	24	45	23	42	
surgery & radiotherapy	18	53	23	43	22	40	
radiotherapy	4	12	6	11	10	18	
surgical reconstruction (n, %)							.000*
no surgery	4	12	6	11	10	18	
primary closure	17	50	15	28	23	42	
local flap	2	6	2	4	0	0	
myocutaneous or free flap	11	32	12	23	19	35	
bone graft/flap	0	0	18	34	3	5	

Continued Table 1. Baseline demographics and clinical characteristics for the patient groups based on tumour location.

	maxilla (n = 34)		mandible (n = 53)		TFM (n = 55)		p-value
measurement at baseline (n, %)	34	100	53	100	55	100	
parameter grade (median, SD)	1	(.59)	1	(.62)	1	(.61)	.444

Abbreviations: TFM, tongue and/or floor of the mouth; SD, standard deviation.
The Chi-square test was used to analyse the differences between the three patient groups.
Analysis of variance (ANOVA) was used to analyse the age differences. Kruskal Wallis was used to analyse differences regarding speech outcome (parameter 'grade' of LSE) of the three patient groups.
* $p < .05$

Table 2 ρ-values of the analyses per assessment period between tumour locations

Table 2. ρ-values of the analyses of the assessment period between tumour locations on 'grade'					
	T0	T1	T2	T3	T5
maxilla - mandible	.033*	.000*	.059	.002*	.131
mandible - TFM	.952	.656	.966	.928	.498
maxilla - TFM	.051	.000*	.019*	.001*	.146

Abbreviations: TFM, tongue and/or floor of the mouth; SD, standard deviation; T0, before intervention; T1, after intervention; T2, 6 months after intervention; T3, 12 months after intervention; T5, 60 months after intervention.

The Mann-Witney *U* Test was used to analyse differences between tumour locations at each assessment.

* $p < .05$

Table 3 ρ-values of the analyses per assessment period between tumour sizes

Table 3. ρ-values of the analyses per assessment period between tumour sizes on 'grade'

	T0	T1	T2	T3	T5
T1 - T2 (T of TNM)	.620	.153	.001*	.563	.102
T2 - T3 (T of TNM)	.908	.634	.001*	.007*	.000*
T3 - T4 (T of TNM)	.967	.075	1.000	.447	.011*
T1 - T3 (T of TNM)	.894	.403	.000*	.015*	.000
T1 - T4 (T of TNM)	.897	.007*	.000*	.000*	.000*
T2 - T4 (T of TNM)	.733	.150	.001*	.000*	.000*

Abbreviations: TFM, tongue and/or floor of the mouth; SD, standard deviation; T0, before intervention; T1, after intervention; T2, 6 months after intervention; T3, 12 months after intervention; T5, 60 months after intervention.

The Mann-Witney *U* Test was used to analyse differences between tumour sizes at each assessment.

* $\rho < .05$

Figure 1 Flowchart

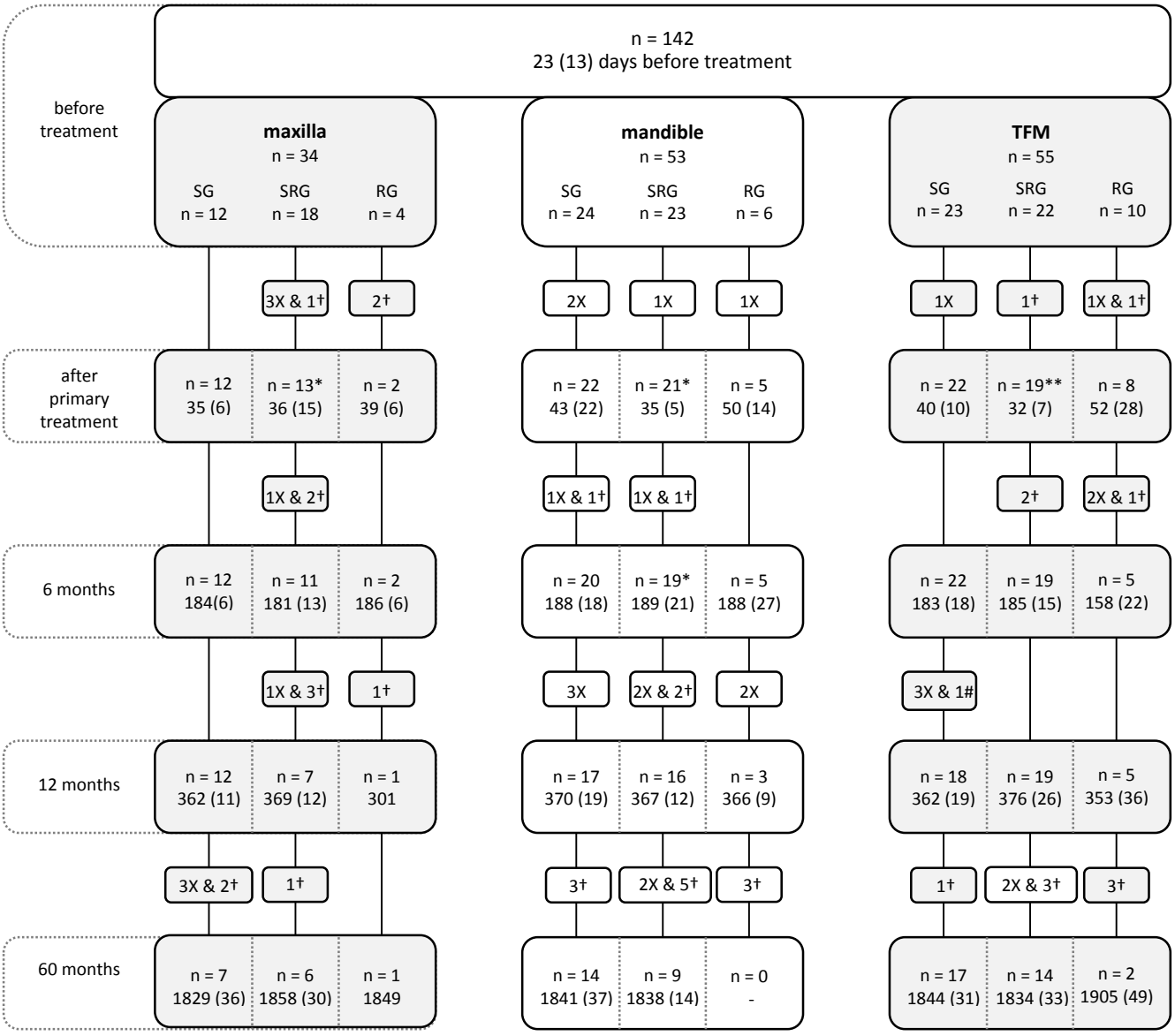

Figure 1. Flowchart showing the number of patients (n) at each assessment and the average time in days (SD) since the primary oncological treatment. Abbreviations: TFM, tongue and/or floor of the mouth; SG, surgery group; SRG, surgery-radiotherapy group; RG, radiotherapy group; X, patient(s) stopped participating; †, patient(s) died; *, missing measurement(s); #, patient excluded because of recurrence of the tumour.

Figure 2 Graph estimates of 'grade' per tumour location

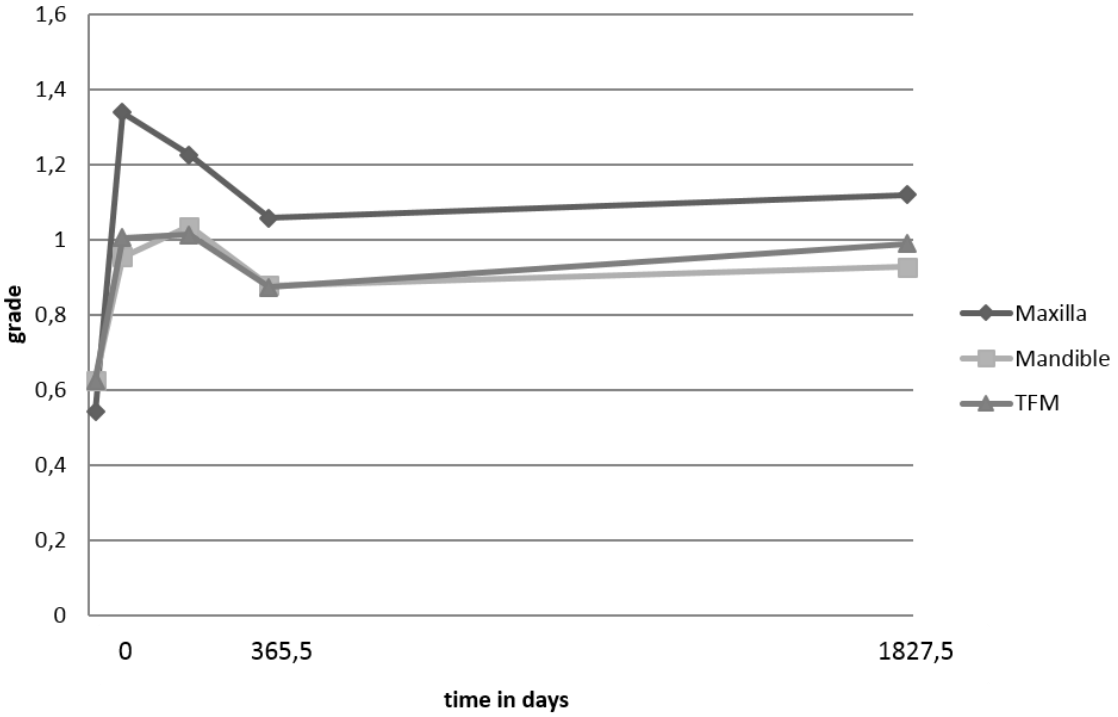

Figure 2. Graph showing estimates of 'grade' for the indicated tumour locations at every assessment against the time in days from baseline measurement. Abbreviations: TFM, tongue and/or floor of the mouth.

Figure 3 Graph estimates of 'grade' per tumour size (T of TNM)

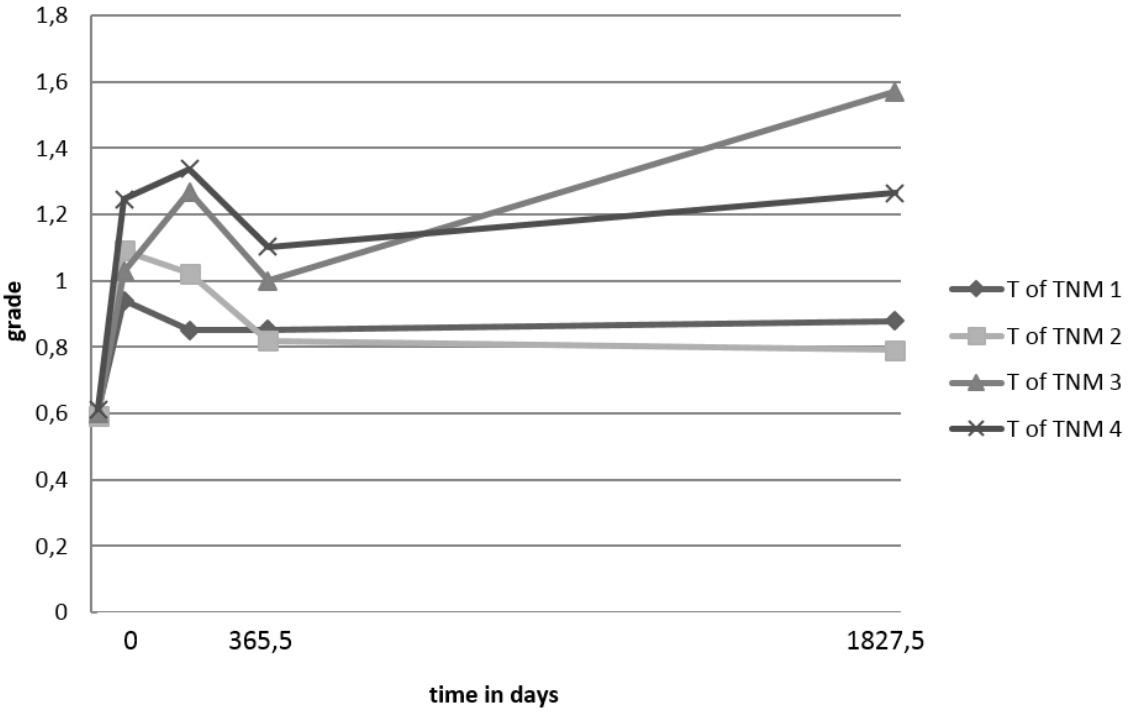

Figure 3. Graph showing estimates of 'grade' for the indicated tumour size (T of TNM) at every assessment against the time in days from baseline measurement.

Appendix

Appendix A Reading text 'Loos alarm op het strand'

Loos alarm op het strand

Groot alarm, afgelopen donderdag op het strand van Zandvoort. De kustwacht was gewaarschuwd dat er een persoon, die zich in het water had begeven, vermist was. Hij was tegelijk met nog twee andere personen de zee ingegaan, en nu waren die twee personen komen vertellen dat ze hem misten. Ze waren er zeker van dat hij niet terug gegaan was naar het strand. De reddingsbrigades van Zantvoort en IJmuiden werden daarom ingeschakeld om deze ene persoon te zoeken. Ook werd er een helikopter ingezet. Een ziekenauto werd in gereedheid gebracht. Het alarm dat was geslagen bleek loos te zijn, want er bleken niet drie maar twee personen in het water te zijn geweest. Tot groot paniek leidde het alarm onder de badgasten echter niet. De meesten bleven kalm en sloegen het een en ander met belangstelling gade.

From: Dharmaperwira-Prins R. Dysartrie en Verbale Apraxie. Lisse: Zwets; 1998.