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Factors influencing intelligibility and severity of chronic speech disorders of patients treated for oral or oropharyngeal cancer

Mathieu Balaguer^{1,2}, Aline Boisguerin¹, Anaïs Galtier¹, Nadège Gaillard¹, Puech Michèle^{1,3}, Virginie Woisard^{1,3,4}

(1) CHU Larrey, Toulouse, France

(2) IRIT, CNRS, University of Toulouse, France

(3) Oncopole, Toulouse, France

(4) Octogone-Lordat Interdisciplinary Research Unit (EA 4156), University of Toulouse II-Jean Jaurès, Toulouse, France

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Informed consent: Informed consent was obtained from all individual participants included in the study.

ABSTRACT

Purpose: Oral or oropharyngeal tumors degrade patients' speech quality because of their location. The treatment of these cancers also affects the functional outcomes, depending on type (surgery, radiotherapy, chemotherapy), volume resection (according the size of the tumor) or on the anatomical area treated, and the post-treatment delay. The aim of this work is to determine the factors influencing the chronic speech disorders (in terms of intelligibility and severity) of patients treated for an oral or oropharyngeal cancer.

Methods: Speech perceptive assessment was led by a panel of six expert speech therapists, on a task of a description of a picture, presented to 87 patients. Clinical and treatment data were gathered by examining medical files.

Results: Intelligibility and severity scores in our population were 6.06 (interquartile range 4.2-8) and 7.61 (interquartile range 6.8-9.5) on a maximum of 10. After adjusting for age and anatomical region involved, multivariate analysis showed a principal impact of surgery on both intelligibility and severity, while the size of the tumor significantly affected the intelligibility score (-1.43; 95% CI [-2.21, -0.65]). These results are consistent with the definitions of intelligibility and severity of speech disorders.

Conclusions: The lack of information on the impact of tumor location, however, requires more work to contribute to reducing impact on the quality of life of patients.

Keywords: Head and Neck cancer, Oropharyngeal cancer, Oral cavity cancer, speech disorders, intelligibility

1. INTRODUCTION

Among tumor pathologies, upper aerodigestive tract cancers are those with the greatest effect on the patients' communication abilities.

Referring to the International Classification of Functioning, Disability and Health Classification (ICF) proposed by the WHO in 2001, oral and/or pharyngeal tumors can affect all levels of this classification. Functional impact corresponds at the communication level because of sensorimotor consequences from tumor site in the anatomical areas involved in speech articulation [1]. This often led to major consequences for the patient's quality of life [2,3].

Although tumors affect the patients' speech, several studies have shown that the treatment offered to these patients is not without consequences on communication abilities.

The size of the tumor determines the anatomical volume treated (whether by surgical resection or radiotherapy), which is a critical factor in post-treatment speech quality [2,4,5]. Speech outcomes also depend on the therapy conducted on the tumor mass, where surgery combined with radiotherapy is more harmful than radiotherapy alone [6]. Finally, tumor location affects speech performances: tumors in the oral cavity adversely affect speech more than those in the oropharynx [3], since the anatomical structures involved in speech production are concerned in a greater way in the oral cavity. Finally, age can also affect post-treatment speech competences [7].

Then, it seems crucial to assess all components of speech in terms of both intelligibility and comprehensibility, in a communicational perspective.

Intelligibility is defined as the functional deficit of speech reducing the capacity to interact with others [8], in other words the "proportion of speech understood" [9]. The concept of comprehensibility is intimately linked to intelligibility because it includes the listener's capacity to understand the overall sense of the message, taking contextual or non-verbal aspects into account that may improve or palliate a deficient message [10]. Finally, the notion of severity [11] combines those of intelligibility and comprehensibility, and associates them with other speech signal parameters, such as temporal and/or prosodic features [12].

The aim of our study is to determine which factors influence the intelligibility and severity of chronic speech disorders in patients treated for an oral or oropharyngeal cancer.

2. MATERIAL AND METHODS

2.1- Subjects description

The data of this study came from the C2SI project (Carcinologic Speech Severity Index), granted by the INCa (Institut National du Cancer). The aim of the C2SI study was to measure the impact of treatments of upper aerodigestive tract cancers (oral cavity and pharynx) on speech production by the use of perceptive methods and also by automatic speech processing. Our study is then a part of this whole project.

The corpus was composed of patients coming for a follow-up consultation at the Toulouse "Institut Universitaire du Cancer Oncopole", after treatment of an oral or oropharyngeal cancer between 2015 and 2016.

To be included, patients must have finished the therapeutic protocol six months beforehand and had to be in clinical remission so that their speech disorder (whether or not audible to measure the slightest deficits) was the most stable possible. These aspects enabled patients to be in a context of chronicity.

Exclusion criteria were patients with a speech disorder potentially related to another pathology, i.e. after a cerebrovascular accident or a fluence-type of disorder such as stuttering.

The following data were gathered for included patients from their medical files: age, sex, anatomical area involved by the tumor, T (size of the tumor) and N criteria (presence or absence of regional lymph nodes) of the TNM classification, post-treatment delay, and therapeutic protocol (tumor and/or lymph node surgery, and/or radiotherapy and/or chemotherapy, reconstruction on local site).

2.2- Recording speech

After a medical consultation, patients were then asked to proceed a recording of their speech in an anechoic room located in the oncorehabilitation unit of the Toulouse Institut Universitaire du Cancer Oncopole. The patients were seated in front of a microphone with a pop shield filter and audio files sampled in 16 kHz were recorded with a digital recorder to get highest possible quality and to avoid biases by expert evaluations. Several tasks were recorded in the framework of the C2SI project [13]. Only the picture description test was

analyzed (considered as an assessment of semi-spontaneous speech) in our study because of its greater reliability [14].

Patients randomly selected one picture among several, each showing a seaside scene with one or several boats. They were then asked to describe the image so that a listener could imagine the scene according to their instructions without seeing it. The description was required to last for at least one minute so that the listeners could have enough auditive cues to evaluate the description.

2.3- Perceptive evaluation of severity by a jury of experts

The recordings were analyzed by a jury composed of six speech therapists, experts in speech disorders evaluation or care. After anonymization, the samples were provided to each expert, who had to hear the recording with headphones and in a quiet environment.

The experts were told that they would hear recordings by subjects describing a picture showing some sort of ocean scene. Once they listened to the audio file, they were asked to assess intelligibility and severity on a scale from 0 to 10 (the lower the score, the more severe the disorder was perceived) using a form to fill in. The instructions given to the experts included the definition of the two terms: "*Intelligibility is defined as the comprehensibility of the message sent by the signal, while severity is defined as the degree of overall deterioration of the audible signal*". Thus, the intelligibility and severity scores of speech were on a scale from 0 to 10 (discrete variable).

2.4- Statistical analyses

All analyses were conducted with the software Stata 14.2.

We first carried out univariate descriptive analyses of each variable. For quantitative variables (interval since the end of treatment, severity of speech disorder, intelligibility), a normal distribution test was also run (Shapiro-Wilk test) that enabled the choice of using non-parametric tests for bivariate analyses.

These bivariate analyses between each variable and the mean of intelligibility score in an initial analysis, then of severity in a second analysis, were used to determine which parameters were potentially linked, and to be included in a multivariate analysis (the variables with p-values less than or equal to 0.20 in the bivariate test were kept). Non-parametric tests were used (Mann-Whitney U test for binary variables, Kruskal-Wallis test for variables with several categories) because of the non-normal distributions of quantitative variables.

Finally, an analysis of covariance was conducted to determine which factors were associated with intelligibility and severity of the speech disorder, as well as the impact that each could have on their mean scores.

3. RESULTS

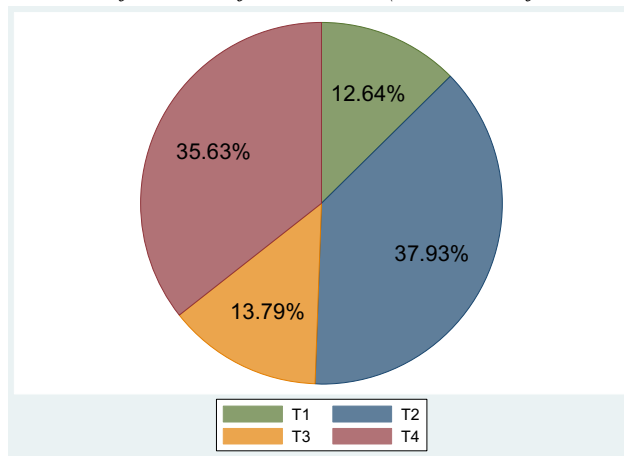
3.1 Description of the population

Our population is composed of 87 patients among whom 51 (59%) are men. Mean age of the population is 65.8 years (standard deviation 9.6 years).

Most of patients (52/87, i.e. 60%) present a tumor of the oropharynx and 40% present a tumor in the oral cavity.

According to the TNM classification, 11 patients present a T1 tumor, in other words a small one (smaller than or equal to 2 cm in its largest dimension). The group of patients with a T2 tumor (size from 2 through 4 cm) is the largest, with 33 subjects. Twelve patients are classified T3 (tumor larger than 4 cm) and 31 present a tumor invading surrounding structures (T4) (Figure 1).

Figure 1: Distribution of patients as a function of tumor size (TNM classification: criterion T)



Several data are missing from TNM classification category N. Even so, 22 subjects do not present involvement of regional lymph nodes.

About the different treatments, most of patients have undergone tumor surgery (84%), lymph node surgery (87%), radiotherapy treatment (94%) and/or chemotherapy (55%). These treatments may have been proposed alone or in various combinations: 5 surgery alone (tumor and nodes), 14 (Chemo)radiotherapy alone (5 radiotherapy alone including nodes surgery before or after in 4 cases, and 9 chemoradiotherapy including node surgery before or after in 2 cases), and 68 surgery associated with (chemo)radiotherapy (including 38 chemoradiotherapy). In this last group only 3 patients don't have a node surgery.

Also, 58 patients are surgically reconstructed while 27 don't get any reconstruction (2 missing data). No analysis is made about the type of reconstruction, because of many missing data in that field (38) and 15 different types of them with few subjects in each one.

In order to define the chronic nature of the speech disorder, treatment must have over at least six months before evaluation, with an extreme value of 239 months for one patient, i.e. almost 20 years post-treatment. The median value is 39 months (3 years 3 months).

The characteristics of our population is given in table 1.

Table 1: Characteristics of the 87 patients included in this study

| | | |
|--|--|---------------|
| Age (years) | | |
| Extreme values | | 36-87 |
| Shapiro-Wilk test: P | | 0.63 |
| Mean (standard deviation) | | 65.8 (9.6) |
| Time since the end of treatment | | |
| Extreme values | | 6-239 |
| Shapiro-Wilk test: P | | < 0.001 |
| Median [interquartile ranges] | | 39 [21,91] |
| Intelligibility of speech disorder | | |
| Extreme values | | 1.2-10 |
| Shapiro-Wilk test: P | | < 0.001 |
| Median [interquartile ranges] | | 7.6 [6.8,9.5] |
| Severity of speech disorder | | |
| Extreme values | | 0.6-9.7 |
| Shapiro-Wilk test: P | | 0.005 |
| Median [interquartile ranges] | | 6.3 [4.2,8] |
| Sex: n (%) | | |
| Men | | 51 (59) |
| Women | | 36 (41) |
| Anatomical region involved: n (%) | | |
| Oral cavity | | 35 (40) |
| Oropharynx | | 52 (60) |
| TNM classification: T (tumor size): n (%) | | |
| T1 | | 11 (13) |
| T2 | | 33 (38) |
| T3 | | 12 (14) |
| T4 | | 31 (35) |
| TNM classification: N (presence of regional lymph nodes): n (%) | | |
| Missing data | | 17 |
| 0 | | 22 (32) |
| 1 | | 17 (24) |
| 2 | | 3 (4) |
| 2a | | 5 (7) |
| 2b | | 13 (19) |
| 2c | | 5 (7) |
| 3 | | 5 (7) |
| Surgery on the tumor: n (%) | | |
| Yes | | 73 (84) |
| No | | 14 (16) |
| Lymph node surgery: n (%) | | |
| Yes | | 76 (87) |
| No | | 11 (13) |
| Radiotherapy: n (%) | | |
| Yes | | 82 (94) |
| No | | 5 (6) |
| Chemotherapy: n (%) | | |
| Yes | | 48 (55) |
| No | | 39 (45) |

3.2 Univariate analysis: experts' results

The results of expert scores are listed in table 2.

Table 2: Means of experts' scores, from 0 (most deteriorated speech) to 10 (most preserved speech)

| | Mean | Median | Min. | Max. | Interquartile range |
|-----------------|------|--------|------|------|---------------------|
| Severity | 6.06 | 6.33 | 0.58 | 9.67 | 4.2-8 |
| Intelligibility | 7.61 | 8.67 | 1.2 | 10 | 6.83-9.5 |

The standard deviation is not shown because no distribution followed a normal distribution ($p < 0.01$, Shapiro-Wilk test).

The mean severity score is lower than the intelligibility one. Moreover, interquartile ranges show the existence of a ceiling effect towards extreme high values that is greater for the evaluation of intelligibility than in the

case of severity.

Finally, inter-expert reliability, measured with the inter-class correlation coefficient, is good, with a coefficient of 0.77 (95% confidence interval: 0.70-0.83) for intelligibility, and 0.69 (95% confidence interval: 0.62-0.77) for severity.

Table 3 lists the means of each scoring according to the tumor size and the anatomical region involved.

Table 3: Mean scores of scorings by experts according to the tumor size and the anatomical region involved, standard deviations in brackets (Tx: criterion T, tumor size according to TNM classification; OC = oral cavity; OP = oropharynx)

| | Criterion T (TNM classification) | | | | Anatomical region involved | |
|-----------------|----------------------------------|-------------|-------------|-------------|----------------------------|-------------|
| | T1 | T2 | T3 | T4 | OC | OP |
| Severity | 6.77 (1.71) | 6.95 (2.01) | 5.62 (2.83) | 5.02 (2.39) | 5.44 (2.47) | 6.46 (2.24) |
| Intelligibility | 8.71 (1.03) | 8.55 (1.85) | 6.95 (3.14) | 6.47 (2.71) | 6.83 (2.70) | 8.12 (2.23) |

The mean score of severity is always lower than the intelligibility one. A tumor size effect exists, with lower scores for more advanced stage tumors, regardless of the test (advanced tumors are T3 and T4, while T1 or T2 correspond to earlier stages). Finally, higher scores are obtained when the oropharynx is involved (thus better performance), compared to oral cavity involvement.

3.3 Modelling intelligibility

Following the bivariate analysis of each variable with mean scores of intelligibility, we conducted a robust analysis of covariance (because of the residual heteroscedasticity of the restricted model) including significant variables at the threshold of $p=0.20$ in bivariate, as well as variables for which literature indicates they may have an influence on speech disorders.

All results are listed in table 4.

Table 4: Modeling intelligibility of the speech disorder

| Intelligibility | Bivariate analysis | | Multivariate analysis | | |
|---|--------------------|------------|-----------------------|---------------|--------------------|
| | Coeff. | P | Coeff. | 95% CI | P |
| Constant | | | 8.72 | 6.35 ; 11.1 | <0.001 |
| Female (ref.: H) | | 0.28 (1) | | | |
| Age (ref.: first quartile) | | 0.56 (2) | | | |
| 2 nd quartile | | | -0.28 | -1.62 ; 1.07 | 0.68 |
| 3 rd quartile | | | -0.43 | -1.93 ; 1.08 | 0.58 |
| 4 th quartile | | | -0.73 | -2.14 ; 0.67 | 0.30 |
| Region: involvement of the oropharynx (ref.: oral cavity) | | 0.01 (1) | 0.89 | -0.24 ; 2.02 | 0.12 |
| Tumor surgery (ref.: no) | | <0.001 (1) | -1.43 | -2.21 ; -0.65 | <0.001 * |
| Lymph node surgery (ref.: no) | | 0.06 (1) | | | |
| Radiotherapy (ref.: no) | | 0.49 (1) | | | |
| Chemotherapy (ref.: no) | | 0.51 (1) | | | |
| Tumor size: TNM T (ref.: T1) | | 0.006 (2) | | | |
| T2 | | | -0.17 | -1.03 ; 0.68 | 0.69 |
| T3 | | | -1.86 | -3.89 ; 0.17 | 0.07 |
| T4 | | | -1.93 | -3.16 ; -0.70 | 0.003 * |
| Invasion of lymph nodes TNM N | | 0.37 (2) | | | |
| Time since the end of treatment (months) | 0.13 | 0.25 (3) | | | |

Brackets in the first column: reference categories used to calculate coefficients.

Bivariate analysis, P value from the following tests: 1 = Mann-Whitney U test; 2 = Kruskal-Wallis test; 3 = Spearman correlation coefficient

Significant P values (5%) are in boldface and indicated by *

Several variables significantly associated with intelligibility in bivariate analysis disappear in the multivariate analysis because of collinearity phenomena with other more significant variables. After adjustment for age

class and anatomical region of the tumor, surgery on the tumor significantly degrades intelligibility of speech ($p < 0.001$). On average, surgery reduces the intelligibility score by 1.43 point. Tumor volume also affects intelligibility performance ($p = 0.003$). The largest tumors (T4) reduce the intelligibility score by an average of 1.93 point. Even if p values of other tumor sizes are not significant, the larger the tumor, the more decreased the mean intelligibility score is.

3.4 Modelling severity of the disorder

The same robust multivariate analysis of the mean severity score was also done. All results are listed in table 5.

Table 5: Modelling severity of the speech disorder

| Severity | Bivariate analysis | | Multivariate analysis | | |
|---|--------------------|-----------|-----------------------|---------------|----------------|
| | Coeff. | P | Coeff. | 95% CI | P |
| Constant | | | 7.45 | 5.06 ; 9.84 | < 0.001 |
| Female (ref.: H) | | 0.30 (1) | | | |
| Age (ref.: first quartile) | | 0.63 (2) | | | |
| 2 nd quartile | | | -0.78 | -2.12 ; 0.57 | 0.26 |
| 3 rd quartile | | | -0.61 | -1.98 ; 0.75 | 0.37 |
| 4 th quartile | | | -0.72 | -2.08 ; 0.65 | 0.30 |
| Region: involvement of the oropharynx (ref.: oral cavity) | | 0.07 (1) | 0.61 | -0.51 ; 1.74 | 0.28 |
| Tumor surgery (ref.: no) | | 0.001 (1) | -1.60 | -2.59 ; -0.61 | 0.002 * |
| Lymph node surgery (ref.: no) | | 0.08 (1) | | | |
| Radiotherapy (ref.: no) | | 0.48 (1) | | | |
| Chemotherapy (ref.: no) | | 0.80 (1) | | | |
| Tumor size: TNM T (ref.: T1) | | 0.01 (2) | | | |
| T2 | | | 0.16 | -1.03 ; 1.35 | 0.79 |
| T3 | | | -1.11 | -3.16 ; 0.95 | 0.28 |
| T4 | | | -1.36 | -2.73 ; 0.005 | 0.05 |
| Invasion of lymph nodes TNM N | | 0.40 (2) | | | |
| Time since the end of treatment (months) | 0.11 | 0.31 (3) | | | |

Brackets in the first column: reference categories used to calculate coefficients.

Bivariate analysis, P value from the following tests: 1 = Mann-Whitney U test; 2 = Kruskal-Wallis test; 3 = Spearman correlation coefficient

Significant P values (5%) are in boldface and indicated by *

After adjustment for published variables associated with speech disorders (age, anatomical region, tumor size), only surgery has a significant impact on severity of the speech disorder ($p = 0.002$): the score decreases on average by 1.60 point after surgery. The size of the tumor is unrelated to the perceptive score of severity of the disorder at the threshold of 5%, even if the p value of the largest T4 tumors is only slightly higher than this threshold.

3.5 Intelligibility and severity according to reconstruction

For patients treated by a tumor surgery, a complementary analysis was performed to assess the impact of a reconstruction procedure. Results are shown in table 6.

Table 6: Intelligibility and severity results according to reconstruction for patients with a tumor surgery

| | With reconstruction (n = 55) | Without reconstruction (n = 12) | Test |
|------------------------|---------------------------------|------------------------------------|----------------------------------|
| Intelligibility (mean) | 6.91 | 8.57 | Mann-Whitney: $p = 0.037$ |
| Severity (mean) | 5.33 | 7.06 | t-test (Student): $p = 0.022$ |

Speech performances are lower for patients surgically reconstructed, for both intelligibility and severity.

4. DISCUSSION

The results of our study show that surgery has an impact on chronic speech disorders, whether in terms of severity of the disorder, or degradation of intelligibility.

Although surgery is the only significant factor increasing the speech severity, in terms of intelligibility tumor size also plays a negative role (the larger the tumor, the lower intelligibility score). These conclusions are consistent with the definitions of severity of the disorder and intelligibility.

Tumor mass affects primarily intelligibility capacities because of the direct effect on the restriction of the mobility of the structures affected. Specific phonetic productions to a phoneme or phonetic sequences are deteriorated and so oral production is altered preferentially.

Surgery has often a major effect on the morphological modification of oral cavity or oropharyngeal structures. It is often accompanied by surgical reconstructions, for example with flaps or plates, to compensate the defect due to the mass removal. Thus, these anatomical changes modify the dynamic of oropharyngeal segments involved in articulating speech (explaining its relationship with intelligibility) but also the volume of resonance cavities. Then, in addition to phonetic deterioration, modifications of vocal timber and/or resonance can change the acoustic vocal signal and increase the speech disorders severity.

Among patients who have undergone tumor surgery, the functional impact on speech is more important in reconstructed patients (both on intelligibility and severity scores). Complementary bivariate analyzes were conducted, between reconstruction on the tumor site and the other variables of interest. The proportion of reconstructed patients is significantly different depending on the size of the tumor ($p = 0.001$, Fischer test). In fact, patients with larger tumors (T3 and T4) are more reconstructed than patients with smaller ones (Table 7).

Table 7: patients surgically reconstructed according to tumor size

| Tumor size | Reconstruction | |
|------------|----------------|-----|
| | No | Yes |
| T1 | 5 | 6 |
| T2 | 17 | 15 |
| T3 | 2 | 9 |
| T4 | 3 | 28 |
| | 27 | 58 |

However, the previous results of this study highlight the impact of tumor size on patient performance. It is then highly probable that reconstructed patients have worse results in speech because they initially have tumors of bigger volume. In addition, the reconstruction does not compensate for the loss of volume of surgically removed structures. Thus, comparisons of speech performance between patients probably make sense only at equivalent resection volume.

In contrast to studies mentioned by Dwivedi et al. [3], we did not find in our population any statistically significant association between severity of the disorder or speech intelligibility, and age or anatomical region involved.

The results of Borggreven et al. [2] showed a significant relationship between anatomical area and speech disorder. Their work involved 80 subjects having a higher percentage with tumors of the oral cavity (48%) compared to ours (40%). Furthermore, our study included all tumor sizes, whereas these authors included only tumors whose TNM classification was higher than or equal to T2. Moreover, the high proportion of T4 in our study (35 %) increases the proportion of tumor involving several anatomical areas and can be an explanation to the lack of significance of main areas (oropharynx and oral cavity in our study), which could be different with more particular data about the specific location of the tumor.

The lack of significance of the age factor in our study may be explained by the fact that the mean age of our population was 65.8 years, higher than in Matsui et al. [6] which was 59.1 years. With increasing age, subjects are more likely to be affected by other phenomena that could affect their speech (auditory loss, aging of muscles involved in articulation, etc.), and oncology treatment may become only one factor among others involved in chronic speech disorders, and therefore reduce or eliminate their significance.

Finally, published data remain very sparse regarding the impact of the extension of the tumor process and of particularly sensitive anatomical regions.

5. CONCLUSION

Among the factors that influence intelligibility and severity of chronic speech disorders of patients treated for an oral or oropharyngeal cancer, our study has shown the prominent impact of surgery and also the specific role of tumor size on speech intelligibility deterioration. However, the influence of tumor location, as gathered in our study, does not provide information on how different treatments affect speech production. Further studies that include more precise data on the extension of tumors and on surgical resection are required.

Author Version

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