



Working together
www.rcis.ro

Revista de Cercetare și Interventie Sociala

ISSN: 1583-3410 (print), ISSN: 1584-5397 (electronic)

QUALITY OF LIFE AND SOCIAL IMPACT IN PATIENS WITH LARYNGEAL TUMORS AFTER RADIOTHERAPY

*Adriana NEAGOS, Cristian OLTEANU, Daniela MANUC, Oana Roxana BITERE,
Mihail Dan COBZEANU, Marius Valeriu HINGANU, Romica Sebastian COZMA*

Revista de cercetare și intervenție socială, 2020, vol. 71, pp. 149-161

<https://doi.org/10.33788/rcis.71.10>

Published by:
Expert Projects Publishing House



On behalf of:
„Alexandru Ioan Cuza” University,
Department of Sociology and Social Work
and
HoltIS Association

REVISTA DE CERCETARE SI INTERVENTIE SOCIALA
is indexed by Clarivate Analytics (Social Sciences Citation Index),
SCOPUS and CROSSREF

Quality of Life and Social Impact in Patients with Laryngeal Tumors after Radiotherapy

Adriana NEAGOS¹, Cristian OLTEANU², Daniela MANUC³,
Oana Roxana BITERE⁴, Mihail Dan COBZEANU⁵,
Marius Valeriu HINGANU⁶, Romica Sebastian COZMA⁷

Abstract

Malignant laryngeal tumor occupies an important place among ENT malignancies, representing 26% of head and neck cancers. The control of the disease and especially the quality of life are parameters often overlooked. The term “quality of life”, has social impact too. The aim of this retrospective, observational study, is to evaluate the quality of life of patients with laryngeal tumors and the social impact in patients after the radiotherapy or radiochemotherapy. The group of study included 52 patients, diagnosed with histopathologically confirmed laryngeal

- ¹ Department of Otorhinolaryngology, “George Emil Palade” University of Medicine, Pharmacy, Science and Technology, Tirgu Mures, ROMANIA. E-mail: neagos.adriana@gmail.com
- ² Orthodontic Department, Faculty of Dentistry, “Iuliu Hatieganu” University of Medicine and Pharmacy, Cluj-Napoca, ROMANIA. E-mail: cristidolteanu@yahoo.com
- ³ Public Health, Faculty of Dentistry, “Carol Davila” University of Medicine and Pharmacy, Bucharest, ROMANIA. E-mail: d_manuc@yahoo.com
- ⁴ Department of Otorhinolaryngology, Faculty of Medicine, “Grigore T. Popa” University of Medicine and Pharmacy, Iasi, ROMANIA. E-mail: oana.bitere@gmail.com
- ⁵ Department of Otorhinolaryngology, Faculty of Medicine, “Grigore T. Popa” University of Medicine and Pharmacy, Iasi, ROMANIA. E-mail: cobzeanu_dan@yahoo.com (*Corresponding author*)
- ⁶ Department of MorphoFunctional Sciences I, Faculty of Medicine, “Grigore T. Popa” University of Medicine and Pharmacy, Iasi, ROMANIA. E-mail: hanganu.marius@yahoo.com
- ⁷ Department of Otorhinolaryngology, Faculty of Medicine, “Grigore T. Popa” University of Medicine and Pharmacy, Iasi, ROMANIA. E-mail: scozma2005@yahoo.com (*Corresponding author*)

tumors. The evaluation of the quality of life was done before and after surgery and during the radiotherapy and chemotherapy, weekly, for 8 weeks. The tools used to assess the quality of life, were the questionnaires EORTC QLQ-30 version 3.0, and EORTC QLQ 35. EORTC QLQ-30 version 3.0 showed a low score on scales such as fatigue, pain and sleep problems, from the beginning of therapy. The symptoms that appeared during the treatment, with statistical significance were: fatigue, nausea / vomiting, pain and appetite problems. EORTC QLQ-35 signals from the beginning of therapy problems with the senses, voice, social life, cough, which increase in severity as the radiation dose increases. At the end of treatment, pain scales, senses, social life and dry mouth were affected. In conclusion, the patients with laryngeal tumors present an important degradation of the quality of life and social integration after the treatment and radiotherapy or chemoradiotherapy, situation that we must take into account in the therapeutic plan.

Keywords: laryngeal tumor, cancer, survival, quality of life, radiotherapy, laryngectomy, social life, social impact.

Introduction

Malignant laryngeal pathology occupies an important place among otorhinolaryngological oncology, representing 26% of head and neck cancers (Unguras & Stamate, 2013). The treatment has evolved a lot, helping to preserve the function of phonation, respiration, offering therapeutic strategies such as surgery, radiotherapy and chemotherapy, used in various combinations (Unguras & Stamate, 2013; Teodorescu, 2019; Gillison *et al.*, 2014; Wiegand, 2016). However, side effects remain a major problem, as they have a negative impact on the quality of life. The oral cavity is the most frequently involved. It is estimated that every year 30% - 35% of patients receiving chemotherapy develop local complications such as: mucositis, stomatitis, candidiasis, which eventually lead to taste disorders (Shuman *et al.*, 2017; Ponticelli *et al.*, 2017) and, in the case of radiotherapy, the changes occur in 85%-95% of patients. These are considered to be the most serious and unpleasant side effects, often underestimated, and can lead to a number of complications that will affect the quality of life (Ponticelli *et al.*, 2017; Solyom, Csiszer, & Neagos, 2014). In many cases the patients with laryngeal tumors present apnea symptoms during the sleep, due to the tumor development or to the association with other pathological conditions such as: tonsils hypertrophy, different types of allergy or obesity (Solyom, Csiszer, & Neagos, 2014).

The control of the disease, toxicity and survival are the traditional key points of each study in cancer patients and quality of life is a parameter often overlooked. Cella *et al.* (2007) defined the quality of life as the assessment, made by a patient, and satisfaction with the current level of functioning compared to what was expected to be possible or ideal. Patients with laryngeal cancer have problems

with swallowing, voice quality, smell, taste and hearing after radiotherapy, so these elements are very important for them to be evaluated (Hovan *et al.*, 2010; Kannan *et al.* 2016). The side effects after surgical and oncological treatment, changing nutritional status, tissue regeneration, energy levels, social relationships and daily habits, affect the quality of life (Solyom, Csiszer, & Neagos, 2014; Kannan *et al.*, 2016; Latifi *et al.*, 2012; Lansaat *et al.*, 2017). Current guidelines point to problems related to quality of life in laryngeal cancer, which are important because: first of all, the tumor affects the basic physiological functions such as chewing, breathing, swallowing; secondly, alters the senses: hearing, smell, taste; in the third line, affects human characteristics like voice and appearance (Salturk *et al.*, 2016). The “quality of life” is a relatively new topic in the medical field, very little studied, but whose change has an impressive social impact. Some studies have begun to focus on this aspect, leading to highlighting of some results that have the role of sensitizing the medical staff to certain aspects that disturb the oncological patient and to the adoption of new therapeutic approaches (Solyom, Csiszer, & Neagos, 2014; Kannan *et al.*, 2016).

EORTC (*The European Organization for Research and Treatment of Cancer Quality of Life Study Group*) developed and standardized validated questionnaires, based on studies that have the role of helping the clinician to evaluate the parameters related to quality of life (Aaronson *et al.*, 1993). In this context, by using the existing questionnaires, the research of the quality of life is facilitated, benefiting from the direct appreciation of the patient taking into account the medical stages he went through and the subjective satisfaction regarding the results of the therapeutic strategies he benefited from. The aim of this paper is to evaluate the social impact and quality of life of patients with laryngeal tumors who needed surgery and radio and chemotherapy.

Methodology

A retrospective, observational study was performed. It included a group of 52 patients, hospitalized and treated between 2016-2017 at Otorhinolaryngology Clinic of Tirgu Mures, who were diagnosed with histopathologically confirmed laryngeal tumors, as squamous laryngeal carcinoma. All regulations related to data confidentiality were implemented, the study receiving the approval of the Ethics Commission.

The patients included in the study have met the following criteria: to be diagnosed histopathologically with squamous cell laryngeal carcinoma, for which different types of surgery were performed and to follow oncological treatment - radiotherapy (RT) or radiotherapy-chemotherapy (RTCT). The exclusion criteria were: the existence of associated neurological diseases, severely affected functional status, inability to understand the language of questionnaires.

The evaluation of the quality of life took place weekly, for each patient, for 8 weeks, starting with the week 0 (W0 - before the surgery) and continuing after the intervention, during the radiotherapy and chemotherapy sessions until the 7th week (W7). The radiotherapy program followed by patients was an external one - IMRT (*Intensity Modulated Radiotherapy*).

The tools used to assess the quality of life consisted of two questionnaires, bearing the EORTC mark: EORTC QLQ-30 version 3.0, respectively EORTC QLQ-35. The time required to answer these questionnaires was approximately 8 minutes. The evaluator assisted in completing them if a certain aspect was not understood by the patient. Both questionnaires are multimodal, standardized and validated (Fayers *et al.*, 2001; Aaronson *et al.*, 1993; Karlsson *et al.*, 2016; Karlsen *et al.*, 2017; Dinescu *et al.*, 2016). The Romanian version was obtained from the center in Brussels, Belgium (Quality of Life Unit of EORTC) being accompanied by a user manual.

EORTC QLQ-30 version 3.0 is a cancer-specific questionnaire. It contains 30 questions that can be assessed on a Likert scale by each participant. There are four answer options, numbered from 1 to 4: not at all, a little, quite a lot, a lot. The questions are grouped into functional scales and symptoms, including: 5 functional scales such as: physical, emotional, cognitive and role; 9 symptoms: fatigue, nausea/vomiting, pain, dyspnea, insomnia, loss of appetite, constipation, diarrhea, financial difficulties and Global Health Status that assesses the patient's satisfaction and appreciation of the new way of life and functioning. The scale was rated between 1 (very poor) and 7 (excellent). It is recommended to use abbreviated terms for easier handling of the data provided (Fang *et al.*, 2004; Hamilton *et al.*, 2016; Tribius *et al.*, 2015; Braam *et al.*, 2007). Abbreviations as well as the structure of the scales and included symptoms are presented in the *Table 1*.

Table 1. Abbreviations and number of questions for functional scales and symptoms included in the EORTC QLQ-30 (version 3.0)

	Scale	Number of questions
Global health status	QL	2
<i>Functional scales</i>		
Physical functioning role	PF	5
Role functioning	RF	2
Emotional functioning	EF	4
Cognitive functioning	CF	2
Social functioning	SF	2

<i>Symptoms/items</i>		
Fatigue	FA	3
Nausea and Vomiting	NV	2
Pain	PA	2
Dyspnoea	DY	1
Insomnia	SL	1
Appetite loss	AP	1
Constipation	CO	1
Diarrhoea	DI	1
Financial Difficulties	FI	1

EORTC QLQ 35, a specific questionnaire for head and neck malignancy; includes 35 questions that assess the symptoms and side effects of the treatment: social life, body image, sexuality. The first 30 questions have answers similar to the first questionnaire, and the last five have answers with two options: 1 - “no” and 2 - “yes”. They investigate some general aspects such as: the use of anti-inflammatory drugs, nutritional supplements, the presence of the gastric tube, body weight variations. Likewise, the first 30 questions are grouped into functional scales and symptoms. Functional scales represented by: pain, swallowing, senses (smell and taste), voice problems, social life and sexuality and the included symptoms (problems with the teeth, opening of the mouth, dry mouth, sticky saliva, cough, altered general condition etc.) are shown in *Table 2*.

Table 2. Abbreviations and number of questions for functional scales and symptoms included in the EORTC QLQ-35

	Scale	Number of questions
<i>Functional scales</i>		
Pain	HNPA	4
Swallowing	HNSW	4
Senses problems	HNSE	2
Speech problems	HNSP	3
Trouble with social eating	HNSO	4
Trouble with social contact	HNSC	5
Less sexuality	HNSX	2

<i>Symptoms/items</i>		
Teeth	HNTE	1
Opening mouth	HNOM	1
Dry mouth	HNDR	1
Sticky saliva	HNSS	1
Coughing	HNCO	1
Felt ill	HNFI	1
Pain killers	HNPk	1
Nutritional supplements	HNNU	1
Feeding tube	HNFE	1
Weight loss	HNWL	1
Weight gain	HNWG	1

All these aspects were evaluated starting from the week before the surgery and seven weeks afterwards, in order to evaluate the improvements or the deteriorations of the quality of life of the patient. These two questionnaires were designed by specialists who recommend to be used together for a better assessment.

The instruction manual received from the center contains information on how to interpret the data. Thus, the answers given by patients were linearly transformed into scales ranging from 0 to 100, which was done using specific formulas, calculated in the statistical program SPSS version 24. The results obtained after the calculation represent scores that can be interpreted. Therefore, the scores obtained for both the functional and symptoms scales are between 0 and 100. For their interpretation, the following rule are applied to the EORTC QLQ 30 questionnaire: a high score for a functional scale represents a good/healthy level of functioning; a high score for overall health status is a good quality of life; a high score for a symptom means a high level of symptomatology/problem. In the case of EORTC QLQ 35, for all scales and symptoms, a high score means problems and a low score means good functioning (Fang *et al.*, 2004; Hamilton *et al.*, 2016).

Because the assessment was done weekly, the visual scale can also be used to interpret the data in progress based on the scores variations (decreases or increases), which means: less than 10 points - small effect; between 10 and 20 points - moderate effect; over 20 points - high effect.

Statistical analysis of the data was performed with the SPSS software (version 24), for the description of qualitative data using percentages and for the quantitative ones using averages and standard deviations (SD). The normality tests applied were Shapiro-Wilk tests and Kolmogorov-Smirnov. Data with Gaussian distribution (normal) were evaluated with the Mean-test and those with non-

Gaussian distribution (abnormal) by nonparametric tests: Wilcoxon signed rank test- $p < 0.05$ and $CI > 95\%$ were used as significant statistical values.

Results

The group of study included 52 patients with the following demographic distribution: 51 males and 1 female, aged between 44 and 82 years (mean value of 63.13 ± 7.21).

EORTC QLQ-30 version 3.0 showed a low score on scales such as emotional (EF), role (RF) and symptoms: fatigue (AF), pain (PA) and sleep problems (SL) even from the first evaluation at the beginning of the therapy. During the seven weeks of radiotherapy, we found a decrease in scores on most scales, and an increase in symptoms. Thus, at the end of the therapeutic protocol, making a comparison of the means using the Mean t-test for data with Gaussian distribution, between W0 and W7, we found as statistically significant affected the following scales: functional role (RF), emotional (EF), cognitive (CF) and social (SF). The symptoms that occurred during the treatment with statistical significance are: fatigue (AF), nausea/vomiting (NV), pain (PA) and appetite problems (AP). The differences between the scores, more specifically, between the first evaluation and the last one, in order to better evaluate the amplitude of the effect, are highlighted in *Table 3*, as well as the p value, the statistical significance sustaining the clinical observations. By statistical evaluation of clinical and symptomatic data, we observed that the scales start from a high score and end up decreasing towards the end, denoting an affected quality of life and the symptoms starting from a low score are increasing to the end, signaling the deepening of the symptomatology.

Table 3. Functional scales and symptoms from W0 to W7: differences and statistical significance (p value) for the EORTC QLQ-30 questionnaire

	W0	W7	Δ W0-W7	p Value
PF	62.82	61.79	1.03	$p = 0.811$
RF	49.35	31.08	18.27	$p = 0.0012$
EF	56.89	44.39	12.5	$p = 0.0091$
CF	80.12	71.15	8.97	$p = 0.0138$
SF	76.28	46.47	29.81	$p < 0.0001$
FA	38.46	52.13	-13.67	$p = 0.0008$
NV	9.61	22.75	-13.14	$p = 0.0035$
PA	42.94	66.02	-23.08	$p < 0.0001$
DY	40.38	31.41	8.97	$p = 0.167$

SL	55.76	49.35	6.41	p = 0.289
AP	22.43	48.07	-25.64	p = 0.0002
CO	23.07	0	23.07	/
DI	0.64	0	0.64	/
FI	14.74	19.23	-4.49	p = 0.370

The Global Health Status scores, calculated after its evaluation by each patient, are relatively constant during the eight weeks of observation. The scores are at the middle level, neither too high nor too low. A slight decrease can be observed along the weeks 3 and 4, with a return towards the end of therapy to the initial value (*Figure 1*).

EORTC QLQ-35, which was created specifically for laryngeal malignancy, signalized problems with the senses (HNSE), voice (HNSP), social life (HNSO, HNCS), cough (HNCO) and sticky saliva (HNSS) starting from the beginning of therapy and increasing in severity as the radiation dose increases.

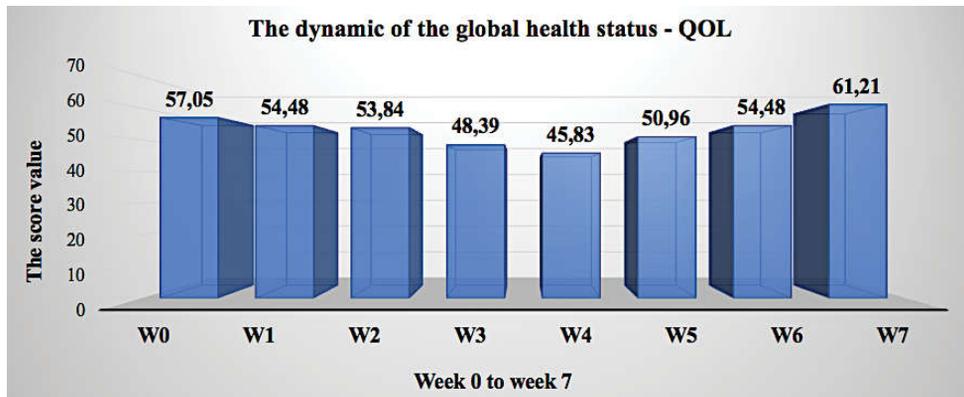


Figure 1. The evolution of the global health status – QOL from the W0 to the W7

At the end of the treatment, we found affected, both clinically and statistically, the scales for pain (HNPA), senses (HNSE), social life (eating in public, physical contact - HNSO, HNCS) and symptoms such as dry mouth (HNDR), cough (HNCO) and altered general condition (HNFI), as it is shown in the *Table 4*.

Table 4. Functional scales and symptoms from W0 to W7: differences and statistical significance (p value) for the EORTC QLQ-35 questionnaire

	W0	W7	Δ W0-W7	p Value
HNSA	65.86	46.31	19.55	p = 0.0001
HNSW	59.29	31.08	-1.12	p = 0.825
HNSE	56.89	44.39	41.67	p < 0.0001
HNSP	80.12	71.15	1.28	p = 0.725
HNSO	76.28	46.47	20.19	p < 0.0001
HNSC	38.46	52.13	19.62	p < 0.0001
HNSX	9.61	22.75	7.37	p = 0.119
HNTE	42.94	66.02	0	p = 1.000
HNOM	40.38	31.41	0	p = 1.000
HNDR	55.76	49.35	-14.11	p = 0.0476
HNSS	22.43	48.07	4.49	p = 0.602
HNCO	23.07	0	21.79	p = 0.0018
HNFI	0.64	0	-15.39	p = 0.0221

Discussion

Using EORTC QLQ 30 version 3.0, the study found a low score on scales such as role and emotional and a high one for symptoms such as fatigue, pain, insomnia right from the beginning of the evaluation in the first week. One possible explanation would be the impact of finding out the diagnosis and the traumatic period that patients went through: surgery, respectively accepting that they can no longer use their voice at the level before the surgery and will be dependent on the tracheostomy and/or phonatory prosthesis. During radiotherapy sessions, which are the second traumatic factor, these scores decreased or increased. At the end of the treatment, we found that the following scales were affected: role, emotional, cognitive, social as well as the following symptoms: fatigue, nausea/vomiting, pain and loss of appetite. The symptoms indicate the existence of some problems that will influence the nutritional status: loss of appetite, caused by loss of taste, lack of pleasure to enjoy meals, or the side effect of radiation therapy, nausea and vomiting, and bad emotional status. All this leads to depression and anxiety, often highlighted in the literature.

Some studies have found all scales and symptoms to be problematic, with the exception of nausea and vomiting at the end of treatment (Kannan *et al.* 2016). Patients assessed their health as well as the quality of new functioning, with degrees between 4 and 5, leading to relatively constant scores, without a statistical

significance between W0 and W7. A slight increase in the grading was observed in the last weeks of the RT, (W6 and W7), the explanation given by them being a simple one: their discharge from the hospital and their reintegration into the family environment made them increase their own assessment. With the help of EORTC QLQ 35, specific to laryngeal malignant pathology, a better highlighting of treatment-related problems was achieved. As in the previous questionnaire, the most affected scales by cancer therapy from the beginning were: pain, swallowing, senses, speech and social life.

The pain scale is affected from the beginning, a fact supported by the first questionnaire, due to the presence of the tracheostomy tube and the short period elapsed after surgery (approximately 1 month). The problem of voice loss is obvious after total laryngectomy, which leads to problems with social life, the patient no longer enjoys going out in public. Comparing the problems from the first week with the last one, statistically significant scales variations were detected for pain, senses, social life and also for symptoms such as dry mouth, cough and affected general condition. Other studies have shown similar data with this paper. What needs to be pointed out, however, is the magnitude of the problems, especially for the senses. Some authors have conducted long-term studies which evaluated, using EORTC QLQ 35, the quality of life, wanting to capture the persistence or regression of certain symptoms. The senses have great chances to return to normal, but only in one year after the end of the radiotherapy (Tribius *et al.*, 2015), as well as symptoms such as dry mouth and sticky saliva, but not earlier than 5 years or 10 years (Braam *et al.*, 2007; Nordgren *et al.*, 2008; Fischer *et al.*, 2006), denoting that these senses, in some cases, return to the starting line (Tribius *et al.*, 2015; Braam *et al.*, 2007). No statistically significant difference was demonstrated for the speech scale, because the voice is affected immediately after the surgery and the patient has to use the esophageal voice to communicate, so the scores on this scale are constant, remaining at a low value. Quality of life is influenced in patients with total laryngectomy, as well as in patients with sleep disorders associated with laryngeal tumors and laryngeal malformations, as it is demonstrated in many studies (Nordgren *et al.*, 2008; Riechelmann *et al.*, 2006).

Social life is affected due to physical appearance, in some cases, or due to communication problems in other, as shown also by previous studies (Dinescu *et al.*, 2016; Tribius *et al.*, 2015; Nordgren *et al.*, 2008; Riechelmann *et al.*, 2006; Fischer, Neagos, & Pirsig, 2005).

Conclusion

There are few studies focusing on the evaluation of the quality of life in patients with operated laryngeal tumors and radiochemotherapy. Therefore, this assessment is a topical one, studying the quality of life with standardized international tools.

It has been shown that the patient with laryngeal tumor, who has been laryngectomized and who underwent radiochemotherapy has a severely impaired quality of life. Survivors of this disease may have many problems with the senses, voice, swallowing and respiratory symptoms, alteration of general status, social life deterioration, symptoms that could increase in severity along the postoperative treatment.

The improvement of the quality of life in patients with operated and irradiated laryngeal tumors represents a great challenge and depends on the development of new strategies of therapeutical approach which have to reduce in the end the socio-economic impact of this pathology.

Recommendations

Monitoring the quality of life of patients with treated laryngeal tumors should be a concern in all clinics where laryngectomy is performed and in all oncology services. The specific questionnaires can support the decisions for an adapted assistance to each case.

The results of recent studies on this topic support the necessity to train specialists in order to provide for patients with operated and treated by radiochemotherapy laryngeal tumors special programs dedicated to the rehabilitation of breathing, swallowing and speech.

Acknowledgments

All authors have equally contribution as the first author to this study.

References

- Aaronson, N.K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N.J., Filiberti, A., Flechtner, H., Fleishman, S.B., de Haes, J.C.J.M., Kaasa, S., Klee, M.C., Osoba, D., Razavi, D., Rofe, P.B., Schraub, S., Sneeuw, K.C.A., Sullivan, M., & Takeda, F. (1993). The European Organisation for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute*, 85, 365-376, DOI: 10.1093/jnci/85.5.365.
- Braam P.M., Roesink J.M., Raaijmakers P.J., Busschers W.B., Terhaard C.H.J. (2007). Quality of life and salivary output in patients with head-and-neck cancer five years after radiotherapy. *Radiation Oncology*, 2, 3, DOI: 10.1186/1748-717X-2-3.
- Cella, D., Yount, S., Rothrock, N., Gershon, R., Cook, K., Reeve, B., Ader, D., Fries, J.F., Bruce, B., & Rose M. (2007). The Patient-Reported Outcomes Measurement Information System (PROMIS) Progress of an NIH Roadmap Cooperative Group During its First Two Years. *Medical Care*, 45(5 Suppl 1), S3-S11, DOI: 10.1097/01.mlr.0000258615.42478.55.

- Dinescu, F.V., Tiple, C., Chirila, M., Muresan, R., Drugan, T., & Cosgarea, M. (2016). Evaluation of health-related quality of life with EORTC QLQ 30 and QLQ-H&N35 in Romanian laryngeal cancer patients. *European archives of oto-rhino-laryngology*, 273, 2735-2740, DOI: 10.1007/s00405-015-3809-0.
- Fang, F.M., Liu, Y.T., Tang, Y., Wang, C.J., & Ko, S.F. (2004). Quality of life as a survival predictor for patients with advanced head and neck carcinoma treated with radiotherapy. *Cancer*, 100, 425-432, DOI: 10.1002/cncr.20010.
- Fayers, P.M., Aaronson, N.K., Bjordal, K., Groenvold, M., Curran, D., Bottomley, A., on behalf of the EORTC Quality of Life Group. (2001). *The EORTC QLQ-C30 Scoring Manual* (3rd Edition). Brussels: European Organisation for Research and Treatment of Cancer.
- Fischer, Y., Neagos, A., & Pirsig W., (2005). Sleep-related breathing disorders. Sleep anamnesis questionnaire and determination of clinical results within the framework of staged diagnostics. *HNO*, 53(11), 995-1008, DOI: 10.1007/s00106-005-1314-2.
- Fischer, Y., Neagos, A., Gronau, S., & Rettinger, G. (2006), Examiner variability of clinical findings in Patients with Sleep Related Breathing Disorders. *Laryngorhinootologie*, 85(5), 338-343, DOI: 10.1055/s-2005-870571.
- Gillison, M.L., Castellsague, X., Chaturvedi, A., Goodman M.T., Snijders, P., Tommasino, M., Arbyn, M., & Franceschi, S. (2014). Eurogin Roadmap: comparative epidemiology of HPV infection and associated cancers of the head and neck and cervix. *International journal of cancer*, 134, 497-507, DOI: 10.1002/ijc.28201.
- Hamilton, D.W., Bins, J.E., McMeekin, P., Pedersen, A., Steen, N., De Soyza, A., Thomson, R., Paleri, V., & Wilson, J. A. (2016). Quality compared to quantity of life in laryngeal cancer. *Head & Neck*, 38, 631-637, DOI: 10.1002/hed.24061.
- Hovan, A.J., Williams, P.M., Stevenson-Moore, P., Wahlin, Y.B., Ohrm, K., Elting, L.S., Spijkervet, F., & Brennan, M.T. (2010). A systematic review of dysgeusia induced by cancer therapies. *Supportive care in cancer*, 18, 1081-1087, DOI: 10.1007/s00520-010-0902-1.
- Kannan, P., Mukherji, A., Saravanan, K., Reddy, K.S., Vivekanandam, S., Shamsudheen, C., & Santhosh, V. (2016). Change in the quality of life in oropharyngeal, laryngeal and hypopharyngeal cancer patients treated with volumetric modulated arc-based concomitant boost radiotherapy. *The Gulf Journal of Oncology*, 1, 36-45.
- Karlsen, T., Sandvik, L., Heimdal, J.H., Hjermland, M.J., Aarstad, A.K., & Aarstad, H. J. (2017). Health-related QOL as studied by EORTC QOL and voice handicap index among various patients with laryngeal disease. *Journal of Voice*, 31(2), 251.e17-251.e26, DOI: 10.1016/j.jvoice.2016.07.009.
- Karlsson, T., Bergstrom, L., Ward, E., & Finizia, C. (2016). A prospective longitudinal study of voice characteristics and health-related quality of life outcomes following laryngeal cancer treatment with radiotherapy. *Acta Oncologica*, 55, 693-699, DOI: 10.3109/0284186X.2016.1150604.
- Lansaat, L., Kleijin, B.J., Hilgers, F.J.M., Van der Laan, B.F.A.M., & Van den Brekel, M.W.M. (2017). A prospective multicenter clinical feasibility study of a new automatic speaking valve for postlaryngectomy voice rehabilitation. *European archives of oto-rhino-laryngology*, 274, 1005-1013, DOI: 10.1007/s00405-016-4304-y.

- Latifi, H., Mikaili, P., Latifi, K., & Torbati, H. (2012). Squamous cell carcinoma of larynx in northwestern Iran. *European Journal of Experimental Biology*, 2, 242-246.
- Nordgren, M., Hammerlid, E., Bjordal, K., Ahlner-Elmqvist, M., Boysen, M., & Jannert, M (2008). Quality of life in oral carcinoma: a 5-year prospective study. *Head & Neck*, 30, 461-470, DOI: 10.1002/hed.20735.
- Ponticelli E., Clari M., Frigerio S., De Clemente A., Bergese I., Scavino E., Bernardini A., & Sacerdote C. (2017). Dysgeusia and health-related quality of life of cancer patients receiving chemotherapy: A cross-sectional study, *European journal of cancer care (Engl.)*, 26, 1-7, DOI: 10.1111/ecc.12633.
- Riechelmann, H., Neagos, A., Netzer, U., Yilmaz, U., Gronau, S., Scheithauer, M., & Rockemann, M.G. (2006). The ASA Score as a comorbidity index in patients with Cancer of the Oral Cavity and Oropharynx. *Laryngorhinootologie*, 85(2), 99-104, DOI: 10.1055/s-2005-870291.
- Salturk, Z., Arslanoglu, A., Ozdemir, E., Yildirim, G., Aydogdu, I., Kumral, T.L., Berkiten, G., Atar, Y., & Uyar Y. (2016). How do voice restoration methods affect the psychological status of patients after total laryngectomy? *HNO*, 64, 163-168, DOI: 10.1007/s00106-016-0134-x.
- Shuman A., Larkin K., Thomas D., Palmer F.L., Fins J., Baxi S., Lee N., Shah J., Fagerlin A., & Patel S.H. (2017). Patient reflections on decision making for laryngeal cancer treatment, *Otolaryngology--head and neck surgery*, 156, 299-304, DOI: 10.1177/0194599816683377.
- Solyom, R., Csiszer, I., & Neagos, A. (2014). Tonsillar hypertrophy implications in sleep disorders in children and adults. *Romanian journal of morphology and embryology*, 55(2Suppl), 603-606.
- Teodorescu, D. (2019), *Psihologie sociala*, Editura Polirom, Iasi.
- Tribius, S., Raguse, M., Voigt, C., Munscher, A., Grobe, A., Petersen, C., Krull, A., Bergelt, C., & Singer S. (2015). Residual deficits in quality of life one year after intensity-modulated radiotherapy for patients with locally advanced head and neck cancer. *Strahlentherapie und Onkologie*. 191, 501-510, DOI: 10.1007/s00066-015-0824-4.
- Unguras, C., & Stamate, M. (2013). Studiu statistic privind cancerul laringian în clinica O.R.L. Coltea. *Acta Medica Transilvanica*, II (4), 52-53.
- Wiegand, S. (2016). Evidence and evidence gaps of laryngeal cancer surgery. *GMS current topics in otorhinolaryngology, head and neck surgery*, 15, Doc03, DOI: 10.3205/cto000130.