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Clinical outcome of early glottic carcinoma in Serbia

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ABSTRACT

Objective: Proposed methods for treating early glottic carcinoma are cordectomy through laryngofissure, laser cordectomy, and radiotherapy. The aim of the study was to conduct comprehensive study to evaluate oncological and functional results of different treatment modalities for Tis and T1 glottic carcinoma, identify prognostic factors for the outcome of treatment and decide where we stand in applying worldwide standards of early glottic carcinoma treatment.
Methods: Prospective study was conducted on 221 patients treated with Tis and T1 glottic carcinoma from 1998 to 2003 (72 patients were treated endoscopically with CO_2 laser, 75 patients with cordectomy through laryngofissure and 74 with radiotherapy), with follow-up period from 38 to 107 months. Important demographic and clinical variables were analyzed. Voice quality after the treatment was assessed using multidimensional voice analysis.
Results: Comparing oncological results of three modalities of treatment, there were no significant differences. Functional results of treatment were better after laser cordectomy and primary radiotherapy than following the open cordectomy. Five-year survival rate was almost identical in all three groups of patients, and important prognostic factors for survival were age and histological grade of the tumor.
Conclusion: Considering that the choice of treatment in our country is also greatly influenced by other paramedical factors, such as distance from treatment facility, reliability of follow-up, significant time delay of radiotherapy because of small number of radiology centers and strong patients' surgeon and treatment preference, we consider endoscopic laser surgery highly efficient and preferred choice of treatment for early glottic carcinoma.

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1. Introduction

Successful treatment of early glottic carcinoma demands radical tumor removal and preservation of laryngeal functions. There are still many questions about different possibilities of therapy and their true value. During the last century, radiotherapy and cordectomy through laryngofissure were preferred oncological approaches for these lesions in most European countries. In the last three decades, transoral laser microsurgery (TLM) emerged as a valuable alternative considering high cure rate, shorter hospitalization, lower morbidity, higher cost-effectiveness, and functional results [1]. Laser resection is used as standard treatment method of early glottic carcinoma at the Clinic for otorhinolaryngology and maxillofacial surgery in Belgrade since 1986.

Laryngeal carcinoma was the fifth most common malignancy in Serbia in 2009 [2]. Disinterest and very low health awareness in Serbian population in last two decades are causing the increase in number of patients treated from this disease. The treatment strategy for every patient treated for head and neck malignancy is decided on the Oncological board, depending on patient preference, comorbidity or anatomical limitation. Decision making of the Board was heavily influenced by other factors, such as availability and number of health centers which conduct radiotherapy and considerable waiting period for starting the therapy. Also, the number of patients who underwent classic surgery was noticeably

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high and influenced by a fact that there is small number of laryngeal surgeons trained for transoral microsurgery. Considering that two other methods of treatment-radiotherapy and transoral microsurgery are worldwide accepted, preferred and recommended, number of our patients treated with classic surgery is worrisome. Changing all these circumstances requires significant financial and human resources which are not available at this time. These facts forced us to conduct one comprehensive study to evaluate oncological and functional results of different available treatment modalities for Tis and T1 glottic carcinoma, identify prognostic factors for the outcome of treatment and decide where we stand in applying worldwide standards of early glottic carcinoma treatment.

2. Material and methods

Prospective study was conducted on 221 patients treated with Tis and T1a glottic carcinoma in 6-year period (January 1, 1998–December 31, 2003) in the Clinic for Otorhinolaryngology and Maxillofacial surgery of Clinical Centre of Serbia in Belgrade. This study was approved by the Institutional Ethical Committee, and all patients signed informed consent form prior to their inclusion in the study. Patients had no previous surgical or radiation treatment for cancer with curative intent.

Patients were staged using the TNM clinical classification of the International Union Against Cancer [3] as TisN0M0 and T1N0M0, based on clinical examination, laryngomicroscopy and histopathology. The modality of treatment for every patient was decided on the Oncological board (consisting of radiotherapist, head and neck surgeons, oncologist and histopathologist). Decision was made based on age and general state of the patient, their preference, and the macroscopic and histopathological characteristics of the tumor. Each patient was presented with treatment modalities, facts about their limitations, oncological and functional results, important for their decision making. Through laryngomicroscopy, extension, infiltration and size of the tumor were assessed, and histopathology result was confirmed. Group treated with transoral laser microsurgery involved patients with tumor localized on upper surface or free edge of one vocal fold with preserved mobility and tumor size up to 10 mm, without anterior commissure involvement. Patients with tumor localized on one vocal fold with preserved mobility, inadequate endoscopic tumor exposure, or tumor diameter greater than 10 mm with deeper infiltration were treated with surgical cordectomy. Surgery was strongly advised in treating tumors which were histological well and moderately differentiated. If any other diseases were present (pulmonary, cardiovascular, etc.) which carried high risk or contraindication for treatment in general endotracheal anesthesia, patients were treated with radiotherapy. Also some of the patients didn't want to undertake surgical treatment and decided on radiotherapy.

According to modality of treatment patients were divided in three groups. 72 patients (Transoral Laser Microsurgery – TLM group) were treated endoscopically with CO_2 laser (type I to IV, according to recommended ELS classification for endoscopic cordectomies) [4]. In 75 patients laryngofissure with cordectomy was conducted (Surgical Cordectomy – SC group). 74 patients underwent radiotherapy (Radiotherapy – RT group). Patients with surgical margins that were positive of malignancy received postoperative radiotherapy and were not included in this study.

Endoscopic cordectomies were conducted with Sharplan Lumenis 40C CO2 laser (Sharplan Lasers Inc., London, UK), with a Carl Zeiss Surgical OPMI Sensera optical microscope (Carl Zeiss Meditec Inc., Dublin, CA), in general endotracheal anesthesia. Open surgical approach involved laryngofissure with cordectomy in general endotracheal anesthesia. Radiotherapy was conducted in the Institute of Oncology and Radiology of Serbia and the patients primarily received doses from 60 to 64 Gy.

Duration of follow-up period was from 38 to 107 months. Patients were examined every month during first year, every three months during second and third year, every six months during fourth and fifth year, and every 12 months after fifth year of follow-up. Endovideostroboscopy was performed at each follow-up visit Storz Endovision Telecam DX 20 Pal i Storz Pulsar 20 (Karl Storz GmbH &Co., Tuttlingen, Germany). Repeated rigid laryngoscopy with biopsy in general anesthesia was performed in patients to confirm the existence of recurrent carcinoma.

Demographic variables like gender, age and smoking habits and clinical variables like T stage, histological differentiation grade for planocellular carcinoma (G1, G2, G3 and G4), existence of recurrent carcinoma, duration of hospitalization in days and complication of the treatment were followed. Local recurrence was defined as a carcinoma in situ or a carcinoma occurring after completion of primary treatment independent of the localization in any part of the glottis. Existence of postoperative complications was followed in all three groups of patients. For assessment of complications in RT group National Cancer Institute Common terminology criteria for adverse events was used [5]. Also, 5-year overall survival and disease-specific survival were calculated for all patients included in the study, and for every group of patients according to their modality of treatment.

Multidimensional voice analysis was done with Tiger DRS software (Tiger DRS, Inc., Seattle, WA), with every patient before treatment and 6 months after the treatment. Intensive voice therapy lasted two weeks, and was conducted with every patient, 5 to 8 weeks after the treatment. Acoustic parameters were determined by analyzing vocal results of patients pronouncing continuous vocal /a/ – fundamental frequency (F0, Hz), jitter, shimmer, Harmonic-to-noise ratio (HNR, dB) and maximum phonation time (s) with Vocal Assessment program.

Absolute and relative frequency distribution for every nominal variable was formed using cross tabulations. To evaluate and compare values between the groups Chi-squared test was used. Overall survival and disease-specific survival were calculated according to the Kaplan Meier method; the Log-rank test was used to compare survival parameters between the three patient groups. Univariate and multivariate analysis of survival time for different parameters were performed using Cox proportional hazards models with corresponding 95% confidence intervals. The parameters analyzed included age, gender, smoking habits, T category and histological grade of the tumor. Student's t test and Bonferroni multiple comparisons were used to compare values for acoustic and aerodynamic parameters among different groups of patients. P values less than 0.05 were considered significant and less than 0.01 highly significant. SPSS 11.5 program was used for statistical analysis (Statistical Package for Social Sciences, Chicago, Illinois).

3. Results

There were 72 patients treated with transoral laser microsurgery, 75 treated surgically with cordectomy through laryngofissure and 74 treated with radiotherapy. In patients treated with transoral laser microsurgery, type I cordectomy was done in 12 patients (16.7%) type II in 15 patients (20.8%), type III in 28 patients (38.9%) and type IV in 17 patients (23.6%) according to recommended ELS classification for endoscopic cordectomies.

Male patients dominated in all three groups (Table 1). Average age in TLM group was 59.5 years, in SC group 60.9 years and in RT group 62.9 years. The youngest patient was 31 years old treated endoscopically (TLM group) and the oldest 71 years old from the same group. There was a highly significant difference in age between groups ($F = 6.383$; $p < 0.01$). The differences between

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Table 1
Demographic and clinical variables in all three groups of patients.

Patient groups	Gender *n* (%)		T stage *n* (%)		Histological grade *n* (%)			Smoking *n* (%)		Existence of recurrent carcinoma *n* (%)		Total *N* (%)
	Male	Female	T0	T1a	G1	G2	G3	Yes	No	Yes	No	
TLM	65 (90.3)	7 (9.7)	28 (38.9)	44 (61.1)	64 (88.9)	5 (6.9)	3 (4.2)	69 (95.8)	3 (4.2)	3 (4.2)	69 (95.8)	72 (100.0)
SC	67 (89.3)	8 (10.7)	2 (2.7)	73 (97.3)	62 (82.7)	8 (10.7)	5 (6.7)	72 (96.0)	3 (4.0)	4 (5.3)	71 (94.7)	75 (100.0)
RT	67 (90.5)	7 (9.5)	0 (0)	74 (100)	66 (89.2)	5 (6.7)	3 (4)	72 (97.3)	2 (2.7)	5 (6.7)	69 (93.2)	74 (100.0)
Total *N* (%)	199 (90.0)	22 (10.0)	30 (13.6)	191 (86.4)	192 (86.9)	18 (8.1)	11 (4.9)	213 (96.4)	8 (3.6)	12 (5.4)	209 (94.5)	221 (100.0)

mean values of age among different groups were compared, using Fisher's Least Significant Difference test, and there was a significant difference in values between TLM and RT group ($p < 0.01$) and significant difference between SC and RT group ($p < 0.05$). The majority of the patients were smokers (94.4%).

There were no differences between groups comparing histological differentiation grade for planocellular carcinoma ($\chi^2 = 1.772$; $p > 0.05$). In all three groups dominant histological grade was G1 (88.9% in TLM group; 82.7% in SC group; 89.2% in RT group) (Table 1). Majority of the patients were classified as T1a stage accordingly to TNM classification (86.4%) ($\chi^2 = 58.557$; $p < 0.01$). Recurrence carcinoma rate for RT group was the highest (6.7%), and the lowest for TLM group (4.2%).

Average duration of hospitalization for TLM group was 3.7 days, for SC group 7.3 days and for RT group 32.1 days. Tracheotomy was done in one case, to a patient in RT group, because of the edema which occurred during the treatment (Table 2). In RT group 26 patients (35.1%) had grade I and II radiation mucositis and 21 (28.4%) had acute grade I of radiation dermatitis. Local infection was registered in 3 patients (4%) in SC group, and subcutaneous emphysema in 3 patients (4%) in SC group. There were no postoperative complications in TLM group.

3.1. Overall survival, disease-specific survival and prognostic factors for patients' survival

Overall survival and disease-specific survival were calculated according to Kaplan–Meier method (Table 3). Period of follow-up of patients was from 38 to 107 months. Five-year survival of patients was 96.8%, six-year survival 94.6% and eight-year survival 93.6%. The log rank test did not show significant difference between groups (Log rank = 0.07; $p > 0.05$). Over-all survival between in groups was similar. 15 patients died during the duration of the study, 8 from cardiovascular diseases, and 7 from malignancy. Five-year disease-specific survival was 99.1%, six-year survival 97.7% and eight-year survival 96.8%, again without significant differences between groups (Log rank = 0.08; $p > 0.05$).

Univariate analysis of parameters (gender, age, smoking habits, T stage and histological grade of the tumor) was done for all patients. Considering age parameter, patients were divided into two groups, patients younger than 60 years and patients of 60 and over years of age. Only statistically significant variable that influenced survival time in univariate analysis was histological grade (between G1 and G2 $\chi^2 = 12.30$, $p < 0.05$; and between G2 and G3 $\chi^2 = .050$, $p < 0.05$). Age and histological grade of the tumor significantly affected survival time according to multivariate analysis ($p < 0.05$) (Table 4).

Table 2
Postoperative complications for all groups of patients.

Patient groups	Local infection *N* (%)	Tracheotomy *N* (%)	Emphysema *N* (%)	Total *N* (%)
TLM	0/72 (0)	0/72 (0)	0/72 (0)	0/72 (0)
SC	3/75 (4)	0/75 (0)	3/75 (4)	6/75 (8)
RT	0/74 (0)	1/74 (1.3)	0/74 (0)	1/74 (1.3)
Total *N* (%)	3/221 (1.3)	1/221 (0.4)	3/221 (1.3)	7/221 (3.2)

3.2. Vocal analysis

Average values of acoustic parameters with standard deviation before the treatment and six months after the treatment are shown in Table 5. Student's test was used to compare the difference of average values for each parameter in all three groups. There was a highly significant change in values of F0, MPT, jitter and shimmer in all three groups of patients ($p < 0.01$). F0, jitter and shimmer increased significantly, and MPT decreased significantly for all three groups. HNR significantly increased for TLM and RT group, but no statistically significant changes were detected in SC group.

The differences between mean values of acoustic and aerodynamic parameters among different groups were compared, using Bonferroni multiple comparison, and shown in the Table 6. There is a highly significant difference in values of F0, shimmer and HNR between all groups ($p < 0.01$) before and six months after the treatment. There was little difference in mean values of MPT among TLM and RT group before had after the treatment, and in mean values of jitter between TLM and RT group six months after the treatment ($p > 0.05$).

4. Discussion

There were 90% male patients involved in the study, and only 10% female patients. Average age in TLM group was 59.5 years, in SC group 60.9 years and in RT group 62.9 years. According to the literature, laryngeal carcinoma is a "male disease", and it commonly involves males in fifth and sixth decade of life [6–11]. In the last few decades, there is a shift in male-female ratio, caused by increased consummation of cigarettes and alcohol in female population [12].

Considering histological differentiation grade for planocellular carcinoma most of the patients (87%) had tumors of histological grade G1 and were classified as T1a stage accordingly to TNM classification (86.4%). Some of the authors noticed that histological grade G1 was dominant in 70 to 90% in histological results [13], and others had percentage of well and moderate differentiated tumors under 30% [6].

Table 3
Overall survival and disease-specific survival rates for different groups of patients.

	TLM (%)	SC (%)	RT (%)	Total (%)
Overall survival rate				
5-year	97.2	97.3	95.9	96.8
6-year	94.4	96.0	93.2	94.6
8-year	91.7	96.0	91.9	93.2
Disease-specific survival rate				
5-year	98.6	98.7	100	99.5
6-year	97.2	97.3	98.6	98.6
8-year	95.8	97.3	97.3	97.7
$p > 0.05$				

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Table 4
Univariate and multivariate analysis of survival time for different prognostic factors.

Univariate analysis: survival time				Multivariate analysis of prognostic factors (Cox proportional hazards model)		
Factor	No. of patients (%)	Chi square	*p* value	Chi square	*p* value	HR (95.0% CI for HR)
Gender						
male	199 (90.0)	.024	.876	.409	.708	1.505 (.18–12.76)
female	22 (10.0)					
Age						
<60	78 (35.3)	2.235	.135	2.202	.048*	9.047 (1.02–80.38)
≥60	143 (64.7)					
Smoking habits						
yes	213 (96.4)	.427	.513	−12.689	.990	.000 (.000)
no	8 (3.6)					
T stage						
Tis	30 (13.6)	.509	.476	−.777	.349	.460 (.09–2.34)
T1a	191 (86.4)					
Histological grade						
G1	192 (86.9)	G1–G2 12.30	.000*	1.501	.000*	4.486 (2.06–9.77)
G2	18 (8.1)	G2–G3 .050	.004*			
G3	11 (5)	G1–G3 8.090	.823			

HR, hazard ratio; CI, confidence interval.
* $p < 0.05$.

Table 5
Acoustic parameters before the treatment and six months after the treatment for all groups of patients.

Group	TLM	SC	RT
F0 (Hz)			
before the treatment	131.4 ± 15.13	121.8 ± 13.17	127.2 ± 13.66
after the treatment	162.4 ± 14.68	151.2 ± 13.61	159.7 ± 14.15
Student's t test	29.3*	−34.9*	−37.2*
MPT (s)			
before the treatment	12.7 ± 2.05	11.6 ± 1.83	14.01 ± 1.71
after the treatment	15.3 ± 2.12	14.3 ± 1.82	17.6 ± 2.10
Student's t test	18.2*	36.2*	31.6*
Jitter (%)			
before the treatment	0.96 ± 0.09	0.78 ± 0.10	0.88 ± 0.13
after the treatment	1.08 ± 0.11	0.89 ± 0.11	0.91 ± 0.14
Student's t test	−26.6*	−31.2*	−5.9*
Shimmer (%)			
before the treatment	3.24 ± 0.31	2.12 ± 0.40	2.62 ± 0.59
after the treatment	3.75 ± 0.34	2.34 ± 0.39	2.76 ± 0.60
Student's t test	−22.4*	−32.1*	−66.3*
HNR (dB)			
before the treatment	13.7 ± 1.69	10.7 ± 1.21	12.9 ± 0.87
after the treatment	14.9 ± 1.87	12.8 ± 1.41	13.7 ± 0.88
Student's t test	−17.8*	−2.4	−38.5*

* $p < 0.01$.

In TLM group there was 4.2% of recurrent disease, in SC group 5.3% and in RT group 6.7%. In all patients with recurrent disease, total laryngectomy was done. No laryngeal preservation was done, mainly due to localization of the recurrent tumor. In 10 patients with recurrent disease, anterior commissure was involved and thyroid cartilage infiltrated according to control CT scans. Two patients had anterior commissure and subglottic extension, with enlarged pretracheal lymph nodes according to control CT scans. It is important to emphasize that initially, in cases of anterior commissure involvement, patients were not included in this study. Eckel had 11.2% local recurrence of carcinoma in his series of patients treated with transoral laser microsurgery [14]. Ansarin et al. had local recurrence in 6.7% of patients after transoral laser microsurgery with subsequent radicalization or radiotherapy as necessary [15].

Subcutaneous emphysema was detected in 4% of the patients in SC group. In this group there were 3 patients with mild local infection, successfully treated with antibiotics and local care of the wound. In post-treatment care, corticosteroids were administrated, and there were no cases of tracheotomy. Tracheotomy was done in one patient in RT group. In patients treated with transoral laser microsurgery there were no complications. Antibiotics and corticosteroid inhalations were administrated in postoperative course in all patients treated with transoral laser microsurgery and surgical cordectomy, which, in our opinion, was important for this result. De Diego et al. [6] in the series of 104 patients treated with cordectomy through laryngofissure had sero-hematoma in 26.9%, wound infection in 6.7%, postoperative bleeding in 5.8%, wound dehiscence in 3.8% and pharyngocutaneus fistula in 1% of the patients. Except acute grade I of radiation dermatitis in 21 (28.4%) patients and grade I and II radiation mucositis in 26 patients (35.1%), other complications in RT group were not noticed, according to CTCAE [5]. Gultekin et al., in series of 183 patients, had acute grade III skin complications (moist desquamation in 3% and acute grade III mucosal complications with diffuse coating and edema of the vocal cords in 7% of patients). They also noted that 9% of the patients required steroid administration for reversible

Table 6
Comparison of differences between mean values of acoustic parameters among different groups of patients.

		Bonferroni multiple comparison				
		F0 (Hz)	MPT (s)	Jitter (%)	Shimmer (%)	HNR (dB)
Before the treatment	TLM–SC	1.33**	9.23**	−0.19**	−1.12**	3.044**
	TLM–RT	−1.43**	3.84	−0.1**	−0.49**	0.824**
	SC–RT	−2.76**	−5.39*	0.09**	−0.62**	−2.219**
After the treatment	TLM–SC	1.29**	10.65**	−0.19**	−1.4**	2.241**
	TLM–RT	−2.19**	2.87	−0.03	−0.42**	1.434**
	SC–RT	−3.48**	−7.78**	0.16**	−0.98**	−0.807**

* $p < 0.05$.
** $p < 0.01$.

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laryngeal edema during RT [16]. Deglutition was preserved in all patients. Unilateral resection of ventricular folds which was done in some of the patients treated with type III and IV transoral laser microsurgery had no impact on the swallowing act.

Preoperative preparation was relatively short for patients in TLM and SC group, so patients in TLM group were hospitalized for average 3.7 days and in SC group for average of 7.3 days. For patients in RT group, average duration of hospitalization was 32.1 days. Patients in this group waited for 25 to 60 days to start the treatment, a significant period of time with great risk for tumor advancement. Some authors state that a percentage (32.6%) of patients with T1 glottic tumors who had undergone excision biopsies and were treated with radiotherapy were overtreated. Thus, before choosing radiotherapy, it would be advisable to perform an incision biopsy to obtain a diagnosis of carcinoma, conserving the maximum amount of healthy tissue and better voice quality after the treatment [17].

4.1. Overall survival, disease-specific survival and prognostic factors for patients' survival

In our study, there were no lethal outcomes in all three groups of patients, in first three years of follow-up. 5-year overall-survival rate was 96.8% and 8-year 93.2%. Five-year disease-specific survival was 99.5%, six-year survival 98.6% and eight-year survival 97.7%. Dinapoli et al. had 5-year disease-free survival for 97. 8% of T1a patients treated with radiotherapy and 86.5% of T1a patients treated with transoral laser microsurgery [18]. Stoeckli et al. had 2-year and 5-year overall survival of 96% and 85%, and disease-specific 2-year and 5-year survival was 96% and 96% for T1 tumors after transoral laser microsurgery. After radiotherapy 2-year and 5-year overall survival was 98% and 88% and disease-specific 2-year and 5-year survival was 98% and 93% for T1 tumors [7]. Over the years, different studies have similar 3-year survival rate in patients treated with transoral laser microsurgery, varying from 91.2% to 97.5% [10,19,20]. Comparing different surgical approaches, Karatzanis et al. had 5-year disease specific survival of 96.5% for T1a cases and no statistically significant differences noted between different types of procedures-cordectomy and transoral laser microsurgery [9].

Not many studies gave information of the impact of different factors on survival rate in patients with T1N0M0 glottic carcinoma. Jin et al. conducted a study on 238 T1N0M0 patients treated with radiotherapy alone, between 1958 and 1994, and 5- and 10-year overall-survival rates were 84.0% and 74.9%, respectively. Important prognostic factors for overall survival were age (for patients younger than 65 years – 87.9% and 66.6%, for patients of 65 years and older – 80% and 50.8%) and the existence of secondary primary tumor [21]. In a series of 432 T1aN0M0 patients treated with transoral laser microsurgery, Motta et al. published survival rate of 85% and adjusted survival rate of 97%. If the outcome was lethal, causes of death were other disease (9.2%), secondary tumor (7.4%), local recurrence (3.5%), nodal recurrence (0.5%) and distant metastasis (0.2%) [11]. According to our analysis, important prognostic factors were age and histological grade of the tumor ($p < 0.05$). In our patients, there was nine times greater risk for lethal outcome in patients older than 60 years of age, and 4.5 times greater risk if a tumor was histological less differentiated.

4.2. Vocal assessment

In both SC and TLM groups mean values of F0 were significantly higher comparing to those before the treatment. In patients followed by Honocodeevar–Boltezar and Zargi [22], a year after radiotherapy, average F0 values were 163.32 Hz, which is close to ours. Vilaseca et al. [23] had slightly higher values of F0 for type I–III transoral laser microsurgery in their follow-up period of 6–18 months; and also Haddad et al. [24], in patients treated with transoral laser microsurgery during a follow-up period between 3 and 36 months. Removing the vibrating tissue of the vocal cord in patients after classic cordectomy and transoral laser microsurgery leads to higher fundamental frequencies with lowering mass of the vocal fold [24]. Resected vocal cord tissue is replaced by scar tissue, which has lower mobility and elasticity, qualities essential for vibration. In RT group values of F0 were also higher after the treatment, probably as a result of the vocal fold fibrosis.

Values of jitter, shimmer and NHR were higher in all three groups 6 months after the treatment, probably as a result of irregular vibration pattern and patients' inability to compensate newly created insufficient glottis occlusion. Values of this parameters recorded in other studies differed from ours [22–24].

MPT was higher in all three groups after the treatment, without significant difference between TLM and RT group, but significantly better comparing to SC group. Early after the treatment, we can explain this with different degree of insufficient glottis occlusion and limited mobility of the remaining vocal fold part depending on the method of treatment. Motta et al. had similar values of MPT in their group of 51 patients treated with type III and IV cordectomy five months after the surgery [11]. Vilaseca et al. detected lower average values of MPT 6–18 months after transoral laser microsurgery in their patients [23]. Tamura et al. had very similar results of all voice parameters to ours, though on smaller groups, for transoral laser microsurgery on 22 and for radiotherapy on 8 patients, a year after the treatment [25]. According to our data, quality of voice was better in surgically treated patients six months after the treatment, comparing to the patients treated with radiotherapy. We can agree with other authors who also confirm postirradiational stiffness of the larynx, poor vibratory source and irregularities in vocal fold vibrations resulting in poor voice quality. These changes affect whole larynx, alter its biomechanical functions and are not limited only to the side of the tumor [26].

5. Conclusion

Comparing oncological results of three different modalities of treatment, there were no significant differences. Considering functional result, better voice quality was detected in patients treated surgically, six months after the treatment. Parameters in RT group were improving slowly in six months of follow-up, probably due to structural changes in the vocal fold tissue and inflammatory response to radiation in the beginning of the treatment. Five-year survival rate was almost identical in all three groups of patients, but there was slightly higher recurrence rate in patients treated with radiotherapy, compared to two other groups. Important prognostic factors for survival turned out to be age and histological grade of the tumor.

It is important that our first choice of therapy gives both good oncological results and high percentage of laryngeal preservation. Radiotherapy is considered the preferred treatment option in many countries, because of excellent voice quality and good locoregional control. From an oncological point of view, we have to keep in mind that recurrent disease after radiotherapy usually cannot be salvaged by conservative surgery. A total laryngectomy is frequently necessary in those cases, which we showed in our study. Barthel et al. stated that radiotherapy promotes laryngeal edema, which can make the detection of recurrences difficult, and lower the possibility of performing conservative surgery considerably [27]. Transoral laser microsurgery gives us possibility of larynx preservation with excision limited only to the tumor and excellent retreatment options after local recurrence. Classic surgery slowly falls behind other two treatment choices, with its probable postoperative complications, but still is a valuable

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option for patients not anatomically suitable for endoscopic surgery or for treatment of recurrent disease.

Having in mind facts and information for every modality of treatment, we must also consider deteriorating of health care in our country and lack of health awareness and responsibility in many of our patients. Our decision on the treatment is influenced by other factors, such as distance from treatment facility, reliability of follow-up, significant time delay of radiotherapy because of small number of radiology centers and strong patients' surgeon and treatment preference, very frequently based on scarce information of basic medical options and restrictions. Because of these facts, large numbers of patients are still treated with classic surgery, contradictory to better functional results and lower cost of other treatment options. Our main concern in the future is to promote endoscopic surgery and radiotherapy, along with educating not only the patients, but surgeons also, something that was done few decades ago in developed countries. Giving these circumstances, we consider transoral laser microsurgery highly efficient and preferred choice of treatment for early glottic carcinoma in our country.

Conflict of interest

None

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