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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.

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