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Original scientific paper

Influential Factors, Complications and Survival Rate of Primary and Salvage Total Laryngectomy for Advanced Laryngeal Cancer

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A B S T R A C T

This is a retrospective review of patients with advanced malignant neoplasms of the larynx treated with total laryngectomy. 387 total laryngectomies for advanced squamous cell carcinoma of larynx performed in the period between 1995 and 2007 were analyzed. Primary total laryngectomy (PRT) was performed in 316 patients, while initial radiotherapy radiotherapy (60–70 Gy) and concomitant chemotherapy (cisplatin-5 fluorouracil) with radiotherapy were applied in totally 71 patients who later received salvage total laryngectomy (STL). All the laryngectomies were performed by four surgeons, using the same routine surgical technique. Postoperative clinical examination was made every three months during five years. We documented the occurrence of: local and general complications, survival rate, residual and recurrent disease, lymph node metastasis, and other changes. Salvage total laryngectomy after previous radiotherapy (STL-pRT) and after chemoradiotherapy (STL-pCTRT) caused more frequent local complications than primary total laryngectomy (PTL). TNM stage and localization of primary laryngeal tumor had significant influence on five year survival rate. It amounted: 61.4% for PTL, 52.6% for STL-pCTRT, and 48.5% for STL-pRT. Incomplete response to initial treatment produced low survival rate. Salvage total laryngectomy caused more frequent local complications, especially after chemoradiotherapy whan compared to primary laryngectomy. Survival rate was increased when chemotherapy is added to radiotherapy. Five year survival rate depended on TNM stage and localization of primary tumor.

Key words: *larynx, squamous cell carcinoma, total laryngectomy, five year survival, complications*

Introduction

Recent advances in surgical techniques and multidisciplinary treatment procedures have improved the management of malignant neoplasms of upper aerodigestive tract. However, these malignancies have high recurrence rates, low survival, and significant alterations in speech and swallowing function. Thus, carefully consideration of morbidity and outcome within the context of the patient's medical condition is needed[1,2]. Larynx preservation approach using chemoradiotherapy for potential preservation of voice and swallowing and with similar survival rate to primary laryngectomy was proposed. Salvage laryngectomy is used for failure of treatment, when persistent disease or when biopsy proven recurrent tumor are present. However, salvage surgery is accompanied with significantly more frequent complications[1,3]. Complications after total laryngectomy can be local (fistula, infection, chyle leak, carotid rupture, and flap necrosis), and general (pulmonary, myocardial infarction, metabolic, urinary infection), as well as airway and swallowing difficulties. They significantly affect morbidity, hospitalization and costs of the treatment[4–6]. Randomized comparison of primary and salvage laryngectomy is very rare in medical references. Adequate conclusions are difficult because of different surgical techniques, insufficient number of cases, and many variables that are influential[4,7,8].

A retrospective review of the patients with malignant neoplasms of larynx treated with primary and salvage to-

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tal laryngectomy is reported to compare the results, complications and factors of outcome of the treatment. This study was conducted on a large number of patients in a single institution and uniform treatment protocol.

Patients and Methods

In the period between 1996 and 2007 we performed 387 total laryngectomies for advanced squamous cell carcinoma of larynx. Primary total laryngectomy (PRT) was applied in 316 patients, while in 38 patients initial radiotherapy (60–70Gy), and in 33 patients chemotherapy (cisplatin-5 fluorouracil) with radiotherapy were introduced becauce of refusal of primary surgery, and they later received salvage total laryngectomy (STL).

ENT examination, CT of the neck, panendoscopy with biopsy, as well as laboratory, cardiologic and pulmonary examination were performed preoperatively. Staging was made with the help of computed tomography (extent of disease at the primary site, status of lymph nodes in the neck, and evaluation for metastatic disease). Age, sex, medical comorbidity, smoking and drinking habit were also documented.

TABLE 1
LARYNGEAL CARCINOMA PARAMETERS, STATUS, SURGERY, AND COMPLICATIONS (NS=NON SIGNIFICANT)

PARAMETER	PTL		STL-pRT		STL-pCTRT		TOTAL		P
	No	%	No	%	No	%	No	%	
Site									
supraglottic	96	30.4	20	52.6	15	45.4	131	33.9	
glottic	170	53.3	10	26.3	10	30.3	190	49.1	NS
transglottic	50	15.3	8	21.14	8	24.3	66	17.0	
cT stage									
T1	0	0	0	0	0	0	0	0	
T2	0	0	5	13.2	0	0	5	1.3	NS
T3	184	58.2	15	390.5	22	66.7	221	57.1	
T4	132	41.8	18	47.3	11	33.3	161	41.6	
cN stage									
N0	23	7.3	3	7.9	0	0	26	6.7	
N1	81	25.6	4	10.5	1	3.0	86	22.2	NS
N2	127	40.2	20	52.6	22	66.7	169	43.7	
N3	85	26.9	11	28.8	10	30.3	106	27.4	
cTNM									
stage I	0	0	0	0	0	0	0	0	
stage II	0	0	3	7.9	0	0	3	0.8	P<0.05
stage III	81	25.6	4	10.5	2	6.1	87	22.5	
stage IV	235	74.4	51	88.6	31	93.9	297	76.7	
Comorbidity									
Yes	16	5.1	21	28.9	3	8.3	30	7.8	P<0.01
No	300	94.9	27	71.1	30	91.7	357	92.2	
Reconstruction									
No	316	100	36	94.7	29	87.9	381	98.5	NS
Yes	0	0	2	5.3	4	12.1	6	1.5	
Dissection									
RND	95	30.0	12	31.6	22	65.7	129	33.3	
SND	162	51.3	22	57.9	11	33.3	195	50.4	NS
No	59	18.8	4	10.5	0	0	63	16.3	
Infection									
No	277	87.6	30	78.8	20	60.6	327	84.5	P<0.01
Yes	39	12.3	8	21.1	13	39.4	60	15.5	
Fistula									
No	279	88.3	30	78.9	23	69.7	332	85.8	P<0.01
Yes	37	11.7	8	21.1	10	30.3	55	14.2	
Swallow dif.									
No	298	94.3	26	68.4	24	72.7	348	89.9	P<0.01
Yes	18	5.7	12	31.6	9	27.3	39	10.1	

All the laryngectomies were performed by four surgeons, using the same routine surgical technique. Briefly, pharynx was closed linearly or in T shape, with 3-0 Vicryl single stitches, muscular reinforcement was made using the same material, and nasogastric tube was used for 7 days.

Postoperative clinical examination was performed every three months during five years. Local and general complications, survival rate, residual and recurrent disease, lymph node metastasis, and other changes were noted. Suspected residual or recurrent disease was confirmed by endoscopy and biopsy.

χ^2-test was used to find out the differences between the groups of the patients (p value less than 0.05 confirmed the presence of a statistically significant difference).

Results

Age of the patients was under 50 years in 54.7%, while the rest were older than 50 years. Male patients were present in 84.2%. Smoking habit was reported in 91.5%, and drinking habit in 88.6%. There was no statistically significant difference between the groups of treatment.

The most frequent tumor site was glottic with 49.1%, followed by supraglottic in 33.9%, and subglottic or transglottic localization in 17.0%. T3 stage (57.1%) was more frequent than T4 stage of the disease. N2 stage predominated with 43.7%, while N3 and N1 were less frequent. Only 6.7% of patients presented without affected neck nodes. Thus, 76.7% of the patients were in the stage IV, and only 22.5% in the stage III. No significant differences for all these parameters between PTL, STL-pCT, and STL-pCTRT groups were found (Table 1).

Medical comorbidity was verified in 7.8% of patients with laryngeal cancer, and it was statistically more frequent in the group of the patients that were treated by primary radiotherapy.

The interval between the initial treatment and salvage laryngectomy ranged from two to 43 months (median 5.1 months). Surgical complications for PTL and STL were absent. The mean length of hospitalization after primary total laryngectomy was 12.4 days, compared to 18.5 days after salvage surgery. Nasogastric tube was in place for average 16.5 days after STL.

Selective neck dissection was the most frequent type of dissection performed (50.4%), without significant difference between the groups. The biggest number of radical neck dissections was performed in STL-pCTRT group. Neck dissection specimens after radiotherapy were positive for metastatic cancer in 57,7%, while after chemoradiotherapy in 73,5%, which correlated to the N stage.

Pectoral myocuteneous flap was mainly used for reconstruction in STL-pCTRT group, and less frequent in the STL-pRT group, while no reconstruction was needed after primary laryngectomy.

Wound infection was confirmed in 19.4%, and pharyngocutaneous fistula in 16.3%. Statistically significant increase of local complications in salvage laryngectomy group was found. Patients with laryngeal cancer receiving chemoradiotherapy developed postlaryngectomy fistula twice more frequently than for primary laryngectomy. The mean time for spontaneous closure of fistulas was 25±3 days. Totally 88.4% of fistulas closed spontaneously, with local care and specific antibiotic treatment. Spontaneous closure of fistulas after radiotherapy was verified in 81.2%, while after previous chemoradiotherapy it was only in 67.7%. The persistent fistulas were closed after one month by local flap, or rarely using pectoral myocutaneous flap. Swallowing problems were significantly more frequent in STL groups. Carotid artery rupture was very rare in laryngeal cancers (0.5%). Immediate surgical ligation and musculocutenous flaps for covering of exposed vessels were performed in such cases. Airway and systemic complications were not significantly different between the groups.

Five year follow-up of the patients was complete in 90.1% of the patients with advanced laryngeal cancer. The overall survival rate after total laryngectomy was 59.5%. TNM stage of the disease was very significant factor for the survival, so for T4 it was 55.0% (Figure 1).

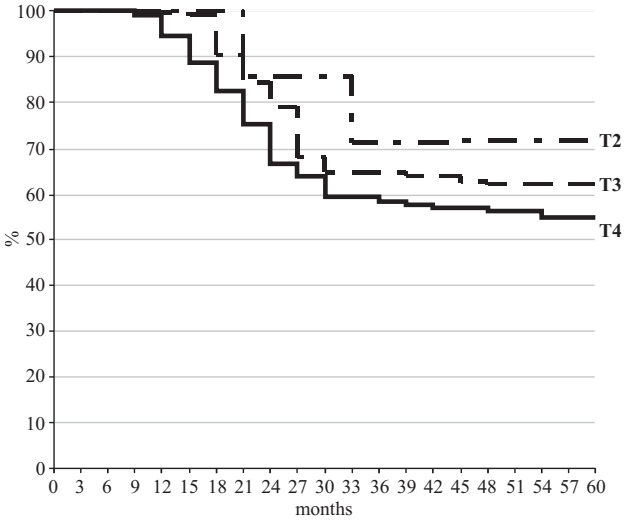

Fig. 1. Five year survival rate for laryngeal carcinoma after total laryngectomy depending on the t stage (Kaplan Meier).

Similar results were present when N stage was analyzed (Figure 2). Stage IV of the disease gave five years survival in 56.0% (Figure 3). The worst survival rate was verified for transglottic and subglottic cancer (Figure 4). The survival rate of primary was significantly better amounting: 61.4% for PTL, 52.6% for STL-pCTRT, and 48.5% for STL-pRT (Figure 5). Five years survival rate for patients who responded completely to initial treatment was favourable. After STL-pCTRT it was 68.4%, and after STL-pRT 63.2%. Incomplete response to initial treatment had five year survival rate totally in about only one third of the patients (Figure 6).

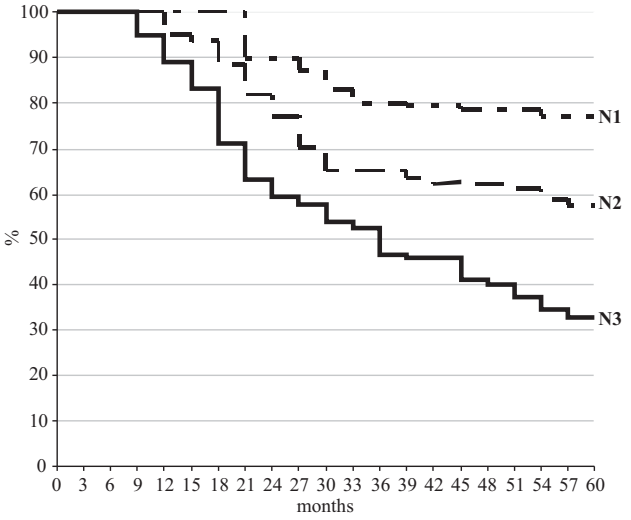

Fig. 2. Five year survival rate for laryngeal carcinoma after total laryngectomy depending on the N stage (Kaplan Meier).

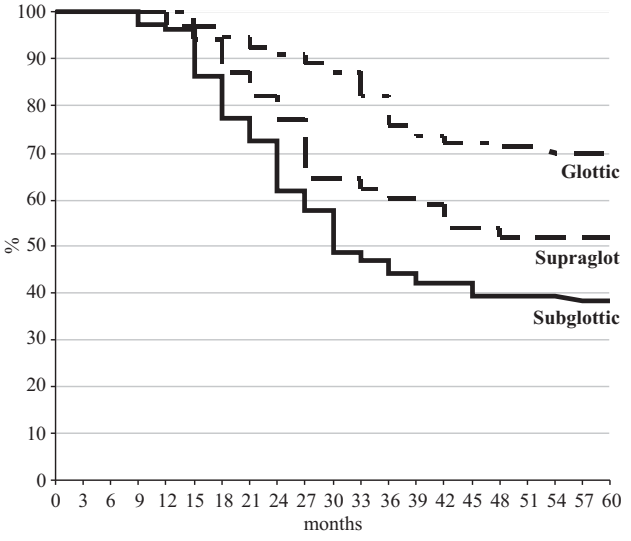

Fig. 3. Five year survival rate for laryngeal carcinoma after total laryngectomy depending on the stage of the disease (Kaplan Meier).

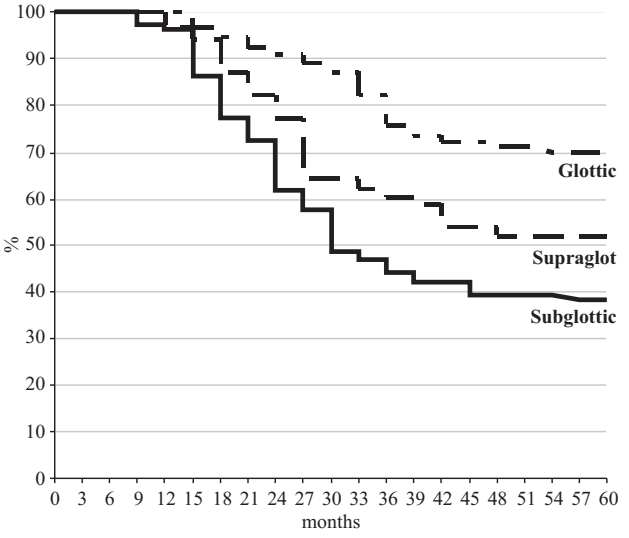

Fig. 4. Five year survival rate for laryngeal carcinoma after total laryngectomy depending on the localization of primary tumor (Kaplan Meier).

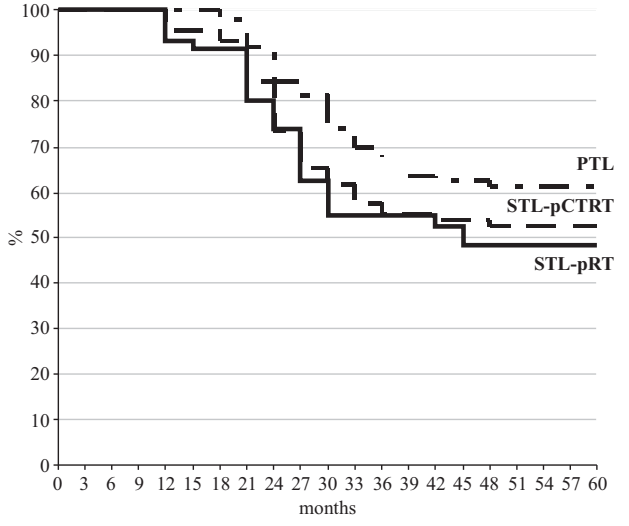

Fig. 5. Five year survival rate for laryngeal carcinoma after total laryngectomy depending on the previous treatment (PTL=primary total laryngectomy, STL-pRT=salvage total laryngectomy after radiotherapy, STL-pCTRT=salvage total laryngectomy after chemo-radiotherapy) (Kaplan Meier).

Discussion

Laryngeal preservation means larynx in place, no residual tumor, no tracheotomy and no feeding tube. Also, preservation of function is more important to the patients than just anatomic integrity of the larynx[8,9]. Multi-institutional studies in the United States support organ preservation for management of the primary site in head and neck squamous cell carcinoma. However, large study of treatment of laryngeal cancer in the US confirmed higher survival when patients had primary laryngectomy[10]. Also, none of the nonsurgical approaches to treatment of laryngopharyngeal cancer gave a better survival than initial radical surgery[11,12]. There are insufficient data on salvage laryngeal surgery after initial radiochemotherapy. Proper detection of tumor, determination of surgical margins, adequate resection, and complication rate, are difficulties associated with salvage total laryngectomy[8,13]. Postlaryngectomy pharyngocuteneous fistula is found in the range from 3% to 65%. Metacentric study on postlaryngectomy fistula denoted the significance of: preoperative hemoglobin, prior tracheotomy, previous radiotherapy and neck dissection. There are insufficient data to confirm the importance of suture material, antibiotics, positive surgical margins, pharyngeal myotomy, blood transfusion and type of radiotherapy[14–16]. Some au-

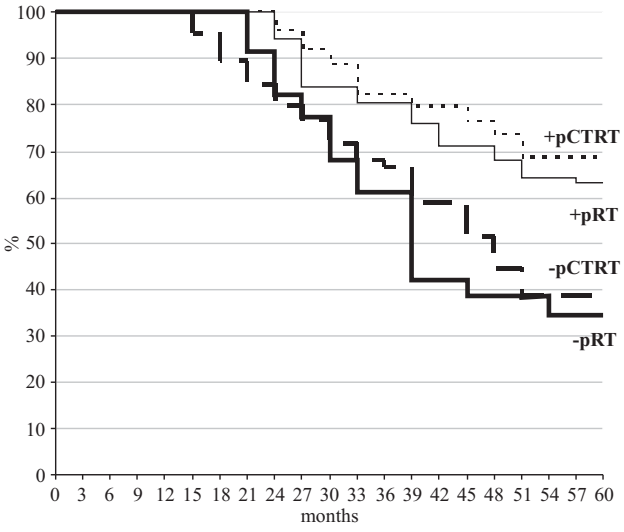

Fig. 6. Five year survival rate for laryngeal carcinoma after total laryngectomy depending on the response to initial therapy (+pRT= complete reaction after radiotherapy, -pRT=incomplete reaction after radiotherapy, +pCTRT= complete response after chemoradiotherapy, -pCTRT= incomplete response after chemoradiotherapy) (Kaplan Meier).

thors do not place nasogastric tubes, and start oral feeding after three days from the surgery[17,18]. More frequent fistulas after radiotherapy, especially when bigger fields and doses were used were found. Nowadays, the reported rate is slightly less, probably because of advances in radiotherapy and surgery, as well[3,13,19]. Chemotherapy was important factor that increased wound complications in treated patients, and the rate is even bigger when radiotherapy is added[20]. Independent risk factors for survival in this study were: advanced clinical stage of the disease, tumor localization, incomplete response to initial therapy and previous therapy. Stage IV caused low survival of the patients. Transglottic and subglottic localization were particularly associated with low survival that was caused by local propagation and advanced neck stage. Salvage total laryngectomy produced worse results than for primary surgery. The addition of chemotherapy to radiotherapy significantly improved the outcome. Since the differences in the stage of the disease between the groups were not significant, these results imply the advantage of primary surgery. CT, MRI and ultrasound have limitations in detecting recurrent carcinoma, especially after salvage surgery. The reduction of the interval from initial therapy to salvage surgery could improve the survival rate[20–23].

Conclusion

Primary total laryngectomy (PTL) for laryngeal carcinoma was associated with pharyngocutenoues fistula in 11.7%, while salvage total laryngectomy after previous radiotherapy (STL-pRT) had fistula in 21.1%, and after chemoradiotherapy (STL-pCTRT) in 30.3%. Salvage total laryngectomy was also accompanied by increase of wound infection and swallowing problems. Five year survival rate was significantly influenced by TNM stage and localization of primary laryngeal tumor, amounting: 61.4% for PTL, 52.6% for STL-pCTRT, and 48.5% for STL-pRT. Incomplete response to initial treatment caused survival rate only 37.5% after chemoradiotherapy and 34.2% after radiotherapy.

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DOPRINOSEĆI FAKTORI, KOMPLIKACIJE I STUPANJ PREŽIVLJAVANJA PRIMARNE I SEKUNDARNE TOTALNE LARINGEKTOMIJE KOD UZNAPREDOVALOG KARCINOMA LARINKSA

S A Ž E T A K

Provedena je r*etrospektivna analiza pacijenata sa uznapredovalim malignim tumorom grkljana tretiranih totalnom laringektomijom. Ukupno 387 totalih laringektomija kod uznapredovalih carcinoma grkljana načinjeno je u periodu od 1995 do 2007. godine. Primarna totalna laringektomija (PTL) obavljena je u 316 pacijentas, dok je inicijalna radioterapija (60–70 Gy) i konkomitantna kemoterapija (cisplatin-5 fluorouracil) sa radioterapijom primenjena u 71 pacijenta, a koji su kasnije tretirani sekundarnom totalnom laringektomijom (STL). Sve laringektomije obavila su četiri kirurga primenom klasične kirurške tehnike. Postoperativni klinički pregled vršen je svaka tri mjeseca tokom pet godina. Dekumentirano je prisustvo: lokalnih i općih komplikacija, stupanj preživljavanja, rezidualna i rekurentna bolest, limfogene metastaze i druge promjene. Sekundarna totalna laringektomija poslije radioterapije (STL-pRT) i kemoterapije (STL-pCTRT) uvjetovala je češće lokalne komplikacije nego primarna totalna laringektomija (PTL). TNM stadij i lokalizacija primarnog tumora grkljana imali su značajan udio na petogodišnje preživljavanje. Ono je iznosilo: 61.4% za PTL, 52.6% za STL-pCTRT, kao i 48.5% za STL-pRT. Nekompletan odgovor na početni tretman dao je nizak stupanj preživljavanja. Sekundarna totalna laringektomija uvjetuje više lokalnih komplikacija, posebno poslije kemoterapije, a u uporedbi sa primarnom totalnom laringektomijom. Stupanj preživljavanja se povećava primjenom kemoterapije uz radioterapiju. Petogodišnje preživljavanje zavisi od TNM stadijuma i lokalizacije primarnog tumora.*