

# Advanced laryngeal cancer with skin infiltration: Survival analysis

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## Objective

The objective of this study was to investigate T4 laryngeal cancer patients with skin infiltration regarding survival and different variables that may influence the survival.

## Study design

This was a retrospective analytic study.

## Materials and methods

This study included 14 patients suffering from laryngeal carcinoma, with tumor extending to involve the skin of the front of the neck. Total laryngectomy was performed for all patients together with excision of the overlying skin, and pectoralis major myocutaneous flap was used for reconstruction of the skin defect in all patients. Analysis of the preoperative, operative, postoperative, and follow-up patients' data was performed. The 1-, 2-, 3-, and 5-year survival rates were estimated.

## Results

The overall mean survival time for all patients was  $51.1 \pm 8.3$  months. The mean survival time for patients with recurrent disease was  $16.4 \pm 3.5$  months and for patients without recurrent disease was  $70.7 \pm 6$  months. The 1-, 2-, 3-, and 5-year survival rates were 92.9, 71.4, 64.3, and 50%, respectively. The univariate analysis revealed that previous treatment before definitive surgery was the only variable that had a statistical influence on the overall 5-year survival rate ( $P = 0.046$ ).

## Conclusion

Extended laryngectomy with skin removal offers reasonable 5-year survival rate for T4 laryngeal cancer patients with skin invasion, and reconstruction of the neck skin defect with a pectoralis major myocutaneous flap is a reliable method of repair.

## Keywords

Laryngeal cancer, skin infiltration, survival rate, pectoralis major myocutaneous flap

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## Introduction

Laryngeal cancer usually spreads along the mucosal surface or by submucosal infiltration. Fungation of laryngeal cancer through skin is a rare condition that requires extension of total laryngectomy to involve en-bloc resection of a wide area of skin of the front of the neck followed by reconstruction of the defect. The pectoralis major myocutaneous flap (PMMF) is considered to be the most suitable and reliable to close such a defect [1]. For early laryngeal cancer, the 5-year survival rate ranges between 53 and 84% with radiotherapy [2,3], whereas partial laryngectomy alone results in a 5-year survival rate of 86–100% [4]. However, in stage IV laryngeal cancer, the 5-year survival rate decreases to around 39% [5].

In this study, we decided to investigate T4 laryngeal cancer with skin infiltration in terms of survival and the different variables that may influence survival in such cases, namely previous therapy, preoperative tracheostomy, exact tumor location, and the nodal stage. The use of PMMF for reconstruction of the resultant skin defect was evaluated in terms of complications such as wound gap and pharyngocutaneous fistula.

## Materials and methods

This study included 14 patients suffering from laryngeal cancer, with tumor extending to involve the skin of the front of the neck. Diagnosis and treatment of the patients were carried out during the period from May 2006 to May 2008. We performed the surgeries in the Department of Otolaryngology — Head and Neck Surgery in Kasr El Aini University Hospital and new Kasr El Aini Teaching Hospital. This study was a retrospective analytic study including analysis of the preoperative, operative, postoperative, and follow-up patients' data. The preoperative patients' data included age, sex, primary tumor site, the clinical classification at presentation based on the TNM classification by the AJCC in 2007, direct extension to the skin whether fungating or nonfungating, preoperative radiotherapy, the presence of preoperative tracheostomy, and extension of the tumor to other extralaryngeal sites. Patients who underwent surgery were staged according to their clinical presentation at the time of surgery. The operative data were collected including the type of surgery performed for treatment of the primary tumor and the neck, method of reconstruction for

the neck skin defect, postoperative radiotherapy, and or radiochemotherapy. The data regarding the postoperative course included development of complications such as pharyngocutaneous fistula, delayed wound healing, and gap as well as the general postoperative complications.

### Follow-up

The minimum follow-up period was 5 years during which patients were evaluated for the occurrence of recurrent disease whether local, regional, or distant. The management of recurrent disease and its sequelae was included. The patients' survival in months was stated and the cause of death was documented.

### Statistical analysis

Descriptive and analytic statistics were carried out using the Statistical Package for the Social Sciences (SPSS IBM Corporation, Chicago, USA) program version 16 designed for Windows. The survival rates and the mean survival times were analyzed using the Kaplan–Meier method. The univariate analysis for the different variables namely previous treatment, preoperative tracheostomy, tumor site, and nodal stage was performed using the Cox regression model. Significance was set at a *P* value of 0.05.

## Results

### Preoperative details

The 14 patients in this study were all men and their ages ranged from 48 to 70 years, with a mean of 57 years. In the classification according to the primary tumor site, five (35.7%) patients were glottic, two (14.3%) were supraglottic, and seven (50%) were transglottic. All patients were in the T4 stage owing to extralaryngeal spread with infiltration of skin of the front of the neck. The skin infiltration was either with a clinically evident fungating mass ( $n = 3$ ; 21.4%) or with skin fixation to the underlying neck mass ( $n = 11$ ; 78.6%). The preoperative computed tomography findings revealed infiltration of the strap muscles in all patients, infiltration of the thyroid gland in four (28.6%) patients, and extension to the cervical trachea in two (14.3%) patients; however, there was no infiltration of other extralaryngeal sites. According to the nodal stage, eight (57.1%) patients were classified as N0, two (14.3%) patients as N1, one (7.1%) patient as N2a, two (14.3%) patients as N2b, and one (7.1%) patient as N3. Nine (64.3%) patients underwent preoperative tracheostomy for relief of airway obstruction, with a duration ranging from 7 to 180 days before surgery and a mean of 52 days. Four (28.6%) patients received prior treatment elsewhere in the form of radiotherapy ( $n = 1$ ; 7.1%), radiochemotherapy ( $n = 2$ ; 14.3%), or surgery

in the form of supraglottic laryngectomy ( $n = 1$ ; 7.1%). The duration between the previous treatment and the development of recurrence that necessitated surgery ranged from 6 to 11 months, with a mean of 8 months. Ten (71.4%) patients did not receive any type of treatment previously. Table 1 shows the preoperative details.

### Treatment details

Total laryngectomy was performed for all patients for treatment of the primary tumor together with excision of a variable area of the overlying skin for excision of the whole tumor. Pedicled PMMF was used for reconstruction of the resultant skin defect in the front of the neck in all patients. Nine (64.3%) patients underwent hemithyroidectomy, whereas five (35.7%) patients underwent total thyroidectomy for adequate surgical control of the primary tumor. According to the site of the primary tumor and the nodal stage, all patients underwent bilateral neck dissection corresponding to 28 neck dissections; these were in the form of three radical neck dissections, five modified radical neck dissections, and 20 selective neck dissections. All surgical resection margins were free of tumor tissue in the 14 patients. Eleven patients received postoperative radiotherapy. Six (42.9%)

**Table 1 Preoperative details**

	<i>N</i> (%)
Tumor site	
Glottic	5 (35.7)
Supraglottic	2 (14.3)
Transglottic	7 (50)
Skin infiltration	
Fungating	3 (21.4)
Nonfungating	11 (78.6)
Thyroid gland invasion	
Yes	4 (28.6)
No	10 (71.4)
Extension to trachea	
Yes	2 (14.3)
No	12 (85.7)
Nodal stage	
N0	8 (57.1)
N1	2 (14.3)
N2a	1 (7.1)
N2b	2 (14.3)
N3	1 (7.1)
Preoperative tracheostomy	
Yes	9 (64.3)
No	5 (35.7)
Previous treatment	
Yes	4 (28.6)
Radiotherapy	1 (7.1)
Radiochemotherapy	2 (14.3)
Supraglottic laryngectomy	1 (7.1)
No	10 (71.4)

patients developed postoperative complications. Pharyngocutaneous fistula occurred in four (28.6%) patients and all of them were managed conservatively, where the fistula healed between 2 and 5 weeks; of the patients with pharyngocutaneous fistula, one received prior radiotherapy and one received radiochemotherapy. Wound failure occurred in two patients, where one of them received prior radiotherapy; of these two patients, one required freshening of the skin edges with resuturing and the other healed with repeated dressings. Postoperative hematoma occurred in one patient, where it required reopening of the wound with evacuation of the hematoma and control of the bleeding source that was from the inferior thyroid artery.

#### Follow-up details and survival analysis

In the analysis of recurrence during the course of the follow-up, five (35.7%) patients developed recurrent disease. Of those patients, two had local recurrence after 8 and 13 months from definitive surgery, one had regional recurrence 12 months after surgery, one had locoregional recurrence 5 months after surgery, and one developed metastatic recurrence 25 months after surgery. The time for recurrent disease ranged from 5 to 25 months, with a mean of 12.6 months. Of those five patients, only one underwent surgery for resection of the recurrent disease but 7 months later he developed extensive neck recurrence and died from carotid blow out, and the other four patients were managed by chemotherapy or palliative treatment as the extent of the recurrent disease was not suitable for surgery and died from the recurrent disease.

The overall mean survival time for all patients was  $51.1 \pm 8.3$  months. The mean survival time for patients with recurrent disease was  $16.4 \pm 3.5$  months and for patients without recurrent disease was  $70.7 \pm 6$  months. The 1-, 2-, 3-, and 5-year survival rates were 92.9, 71.4, 64.3, and 50%, respectively. The univariate analysis of different variables using the Cox regression model revealed that previous treatment before definitive surgery had a statistical influence on the overall 5-year survival rate; however, preoperative tracheostomy, tumor site, and nodal stage did not have a statistical impact on the 5-year survival rate as shown in Table 2. On studying the influence of the nodal stage on survival and upon grouping N+ patients together, it was found that of the eight N0 patients five were alive and three were dead after 5 years, and of the six N+ patients two were alive and four were dead after 5 years; however, the better survival outcome of the N0 patients did not reach a statistical significance as shown in Table 2.

**Table 2 Comparative univariate analysis of the 5-year survival using Cox regression model**

Variables	5-year survival		P value
	Alive	Dead	
Age (mean)	57.8	57.4	0.52 (NS)
Previous treatment			
Yes	1	3	0.046 (S)
No	6	4	
Preoperative tracheostomy			
Yes	5	4	0.61 (NS)
No	2	3	
Tumor site			
Glottic	4	1	0.091 (NS)
Supraglottic	1	1	
Transglottic	2	5	
Nodal stage			
N0	5	3	0.89 (NS)
N1	1	1	
N2a	1	0	
N2b	0	2	
N3	0	1	
N4	0	0	
Nodal stage			
N0	5	3	0.59 (NS)
N+	2	4	

Nodal stage, upon grouping of the N+ cases together; NS, not significant; S, significant.

#### Discussion

T4 laryngeal cancer with anterior extension to involve the skin of the anterior of the neck is a rare situation but yet a surgical challenge since invasion of the soft prelaryngeal tissues; the thyroid gland as well as the skin of the neck can no longer be controlled by the routinely performed organ surgery. A widened forward surgery consisting of total laryngectomy together with removal of the prelaryngeal muscles, fascia, and a more or less large area of the anterior cervical skin is needed [6]. In this study, we reviewed 14 laryngeal cancer patients with neck skin invasion, who were managed surgically. The overall 5-year survival rate of 50% is comparable with the 5-year survival rates for advanced laryngeal cancer, which was 51% in an observational cross-sectional study reported by Chen *et al.* [7]. In addition, this is not far less than the overall 5-year survival rate for laryngeal cancer patients with different stages and treatment modalities, which was 64.2% in another survival meta-analysis study [8]. Treatment of such patients with extended laryngectomy surgery is considered to be worthy owing to the acceptable survival rate. Supporting this observation, the 1-, 2-, and 3-year survival rates in our study were 92.9, 71.4, and 64.3%, respectively, which are considered acceptably good survival rates. In this study, the univariate analysis revealed that the only factor that had a negative impact on the survival rate was previous failed treatment for the laryngeal cancer; of our four patients who received prior treatment and

later developed recurrence with skin invasion, three died because of the recurrent disease and this was found to be statistically significant ( $P = 0.046$ ). Other variables such as age, prior tracheostomy, tumor site, and nodal stage did not have a significant impact on the survival rate.

The thickness of the PMMF in addition to its constant blood supply makes it a suitable and reliable flap for reconstruction of wide-neck resections [9,10]. In a study conducted by Patel and Keni [11], they reported that the use of PMMF in salvage laryngectomy following radiotherapy significantly reduced the incidence of pharyngocutaneous fistula from 50 to 0%. In this study, the resultant skin defect in the front of the neck following laryngectomy with skin resection was reconstructed using a PMMF. Pharyngocutaneous fistula in our study occurred in four patients representing an incidence of 28.6%, and it is worth mentioning that two of these patients received prior radiotherapy. The reported incidence of pharyngocutaneous fistula following total laryngectomy ranges from 3 to 65% [12,13]. Mclean *et al.* [14] in a recent study reported a comparable pharyngocutaneous fistula rate of 26.5% in their group of patients. Other complications namely wound infection and dehiscence occurred in two patients representing an incidence of 14.3%, which is still comparable with the 23% overall incidence of postoperative wound infection and dehiscence after major head and neck surgery [15]. This supports the better choice of using PMMF for reconstruction of the skin defect in our study and in other similar studies [1,6].

## Conclusion

Although T4 laryngeal cancer with skin invasion is rare, it carries a reasonable 5-year survival rate. Extended laryngectomy with skin removal offers adequate cure rates. Recurrent laryngeal cancer with skin invasion carries a lower survival than de-novo patients. Reconstruction of the neck skin defect with PMMF is a reliable method of repair with a low complication rate.

## Acknowledgements

### Conflicts of interest

None declared.

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