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 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 ± 8.3 months. The mean survival time for patients with recurrent disease was 16.4 ± 3.5 months and for patients without recurrent disease was 70.7 ± 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

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.
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.

| Table 1 Preoperative details | N (%) |
|------------------------------|-------|
| 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 ± 8.3 months. The mean survival time for patients with recurrent disease was 16.4 ± 3.5 months and for patients without recurrent disease was 70.7 ± 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 of the N+ cases 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                  | Alive | Dead | P value |
|----------------------------|-------|------|---------|
| 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    |         |
| Nodal stage, upon grouping of the N+ cases together | 2  | 4 | 0.59 (NS) |

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.

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**Conflicts of interest**

None declared.

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**References**

1. Rifai M, Mebed H, Bassiouni M. Direct extension of laryngeal carcinoma to the skin of the neck. J Laryngol Otol 1990; 104:824–826.
2. Jin J, Liao Z, Gao L, Huang X, Xu G. Analysis of prognostic factors for T1N0M0 glottic cancer treated with definitive radiotherapy alone: experience of the cancer hospital of Peking Union Medical College and the Chinese Academy of Medical Sciences. Int J Radiat Oncol Biol Phys 2002; 54:471–478.
3. Haugen H, Johansson K-A, Mercke C. Hyperfractionated-accelerated or conventionally fractionated radiotherapy for early glottic cancer. Int J Radiat Oncol Biol Phys 2002; 52:109–119.
4. Back G, Sood S. The management of early laryngeal cancer: options for patients and therapists. Curr Opin Otolaryngol Head Neck Surg 2005; 13:85–91.
5. Spector GJ, Sessions DG, Lenox J, Newland D, Simpson J, Haughey BH. Management of stage IV glottic carcinoma: therapeutic outcomes. Laryngoscope 2004; 114:1438–1446.
6. Croce A, Moretti A, Bianchetti M, Neri G, Falcone G. Widened forwarding total laryngectomy (‘squared laryngectomy’). Hints of surgical techniques and personal experience. Acta Otorhinolaryngol Ital 1995; 15:355–360.
7. Chen AY, Fedewa S, Zhu J. Temporal trends in the treatment of early-and advanced-stage laryngeal cancer in the United States, 1985–2007. Arch Otolaryngol Head Neck Surg 2011; 137:1017–1024.
8. Rudolph E, Dyckhoff G, Becker H, Dietz A, Ramroth H. Effects of tumour stage, comorbidity and therapy on survival of laryngeal cancer patients: a systematic review and a meta-analysis. Eur Arch Otorhinolaryngol 2011; 268:165–179.
9. Ariyan S, Cuono CB. Use of the pectoralis major myocutaneous flap for reconstruction of large cervical, facial or cranial defects. Am J Surg 1980; 140:503–506.
10. Leemans CR, Balm AJM, Gregor RT, Hilgers FJM. Management of carotid artery exposure with pectoralis major myofascial flap transfer and split-thickness skin coverage. J Laryngol Otol 1995; 109:1176–1180.
11. Patel UA, Keni SP. Pectoralis myofascial flap during salvage laryngectomy prevents pharyngocutaneous fistula. Otolaryngol Head Neck Surg 2009; 141:190–195.
12. Bresson K, Rasmussen H, Attrup Rasmussen P. Pharyngo-cutaneous fistulae in totally laryngectomized patients. J Laryngol Otol 1974; 88:835–842.
13. Thawley SE. Complications of combined radiation therapy and surgery for carcinoma of the larynx and inferior hypopharynx. Laryngoscope 1981; 91:677–700.
14. Mclean JN, Nicholas C, Duggal P, Chen A, Grist WG, Losken A, Carlson GW. Surgical management of pharyngocutaneous fistula after total laryngectomy. Ann Plast Surg 2012; 68:442–445.
15. Grau C, Johansen LV, Hansen HS, Andersen E, Godballe C, Andersen LJ, et al. Salvage laryngectomy and pharyngocutaneous fistulae after primary radiotherapy for head and neck cancer: a national survey from Dahanca. Head Neck 2003; 25:711–716.