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*For further information about this article or if you need reprints, please contact:*

Payam Eghtesadi-Araghi  
Apartment No. 5, 37th (Eastern),  
First Golzar St.,  
Ashrafi Esfahani Bulv.,  
Ponak Sq., Tehran 1476783476,  
Iran

Tel/Fax: ++98 21 44454814

## Assessment of the Recurrence Rate of Laryngeal Cancer in Tracheostoma in Patient Undergoing Laryngectomy

<sup>1</sup>Mohammad Sadeghi Hassanabadi, <sup>1</sup>Shabnam Shadabi,  
<sup>1</sup>Seyed Mousa Sadr-Hosseini, <sup>1</sup>Masoud Motesadi Zarandi and  
<sup>2</sup>Payam Eghtesadi-Araghi

The purpose of this study is to evaluate the recurrence rate of laryngeal cancer in tracheostoma and its influential factors in patient undergoing laryngectomy. The data of 112 patients undergoing laryngectomy in Imam-Khomeini and Amir-Alam Hospitals from 2002 to 2004 were evaluated in a cohort study. The data of the age, gender, subglottic invasion, pre-operative radiation, thyroid condition during operation, staging of the tumor, pre-operative tracheostomy and primary site of the tumor of the patients were recorded. The patients were examined for stomal recurrence at 3, 6 and 12 months after operation. Suspected cases underwent more advanced diagnostic methods such as CT-scan, MRI, bronchoscopy, esophagoscopy and finally biopsy to verify presence or absence of stomal recurrence. The data of 83 patients were finally analyzed. There were 9 cases (10.84%) of recurrence in patients with tracheostoma. The number of pre-operative tracheostomy, prevalence of higher stages (T4) of cancer, thyroid resection, subglottic invasion and pre-operative radiation, were significantly higher in patients with recurrence of tracheostoma. The primary site of the tumor and the mean age of the patients did not affect the rate of recurrence. The death rate was also significantly higher in these groups. Pre-operative tracheostomy and radiation, higher stages of cancer (T4), subglottic invasion and thyroid resection as a sign of spread of tumor, are assumed as risk factors for osteomal recurrence while the primary site of the tumor was not influential.

**Key words:** Tracheostoma, risk factor, recurrence, laryngectomy

**INTRODUCTION**

Laryngeal carcinoma has good prognosis in cases of prompt diagnosis and proper treatment. One of the most common complications in patients with advanced laryngeal carcinoma is stomal recurrence (Onakoya *et al.*, 2004). Stomal recurrence is a common controversial issue on head and neck oncology (Ferlito *et al.*, 2002). Stomal recurrence is a dramatic, late complication with poor prognosis. Despite the remarkable advances in laryngeal surgery and introduction of modern plastic techniques, stomal recurrence is still accounted as an important cause of death in patients with laryngeal cancer (Martin Villares *et al.*, 2000). The common sites of recurrence include tracheostoma region, neopharynx, neck and distant metastases (Ferlito *et al.*, 2002). Identification and follow-up of risk factors in high-risk groups and detection of stomal recurrence at early stages plays the main role in the treatment (Imauchi *et al.*, 2002). Regarding this issue, there have been numerous studies in different countries like Spain (Esteban *et al.*, 1993; Leon *et al.*, 1996; Martin Villares *et al.*, 2000), Japan (Imauchi *et al.*, 2002), Hong Kong (Yuen *et al.*, 1996). To our knowledge, there have not been any studies in this field in Iranian patient, so we decided to evaluate the patients undergoing surgery in Imam Khomeini and Amir-Alam Hospitals for stomal recurrence and its risk factors at specific times. The purpose of this study was to assess the rate of tracheostoma recurrence in patients who had undergone laryngectomy in addition to its risk factors in a specific population. Identification of these risk factors and prompt diagnosis and follow-up of stomal recurrences at early stages (Type I, II) facilitates application of more conservative surgical methods with/without chemoradiotherapy.

**MATERIALS AND METHODS**

After approval of research deputy and ethics committee of Tehran University of Medical Sciences, the patients undergoing laryngectomy in Imam Khomeini and Amir-alam Hospitals from 2002 to 2004 were enrolled in a cohort study. The data of the age, gender, subglottic invasion, pre-operative radiation, thyroid condition during operation, staging of the tumor, pre-operative tracheostomy and primary site of the tumor of the patients were recorded. The patients were examined for stomal recurrence at 3, 6 and 12 months after operation. Suspected cases underwent more advanced diagnostic methods such as CT-scan, MRI, bronchoscopy,

esophagoscopy and finally biopsy to verify presence or absence of stomal recurrence.

Analysis of quantitative data was done applying independent t-test and qualitative data were analyzed utilizing chi-square and exact Fischer test in SPSS ver. 12.0. p-value below 0.05 was assumed significant.

**RESULTS AND DISCUSSION**

The data of 112 patients were recorded, but due to different reasons including change of address or phone number, etc., we could follow only 83 patients and the results of these 83 patients were analyzed. The mean of follow-up period was 15.6±4.8 months (min = 6 and max = 24). The mean age of the patients was 62.54±9.8 years (min = 42 and max = 84). All patients were male. Other demographic variables and the characteristics of the tumor and recurrence are summarized in Table 1 and 2.

There were 9 cases (10.84%) of tracheostomal recurrence. There was no significant difference in mean age of the patients with and without tracheostoma recurrence. The prevalence of pre-operative tracheostomy, higher stages of cancer (T4), thyroid resection, subglottic invasion and pre-operative radiation was significantly higher in patients with tracheostoma recurrence. The primary site of the tumor did not affect the rate of recurrence. Finally, 17 patients (20.48%) died, while the mortality rate was significantly higher in patients with tracheostoma recurrence (Table 3).

Table 1: The absolute and relative frequencies of the patients based on the characteristics of the patients, tumor and recurrence

| Variable name              | Absolute frequency | Relative frequency (%) |
|----------------------------|--------------------|------------------------|
| Male gender                | 83                 | 100.00                 |
| Subglottic invasion        | 12                 | 14.46                  |
| Pre-operative radiation    | 5                  | 6.02                   |
| Thyroid lobectomy          | 39                 | 46.99                  |
| Pre-operative tracheostomy | 11                 | 13.25                  |
| Stomal recurrence          | 9                  | 10.84                  |
| Mortality                  | 17                 | 20.48                  |

Table 2: The absolute and relative frequencies of the patients based on the characteristics of the tumor

| Variable name             | Absolute frequency | Relative frequency (%) |
|---------------------------|--------------------|------------------------|
| Tumor staging             |                    |                        |
| T1                        | 0                  | 0.00                   |
| T2                        | 0                  | 0.00                   |
| T3                        | 73                 | 87.95                  |
| T4                        | 10                 | 12.05                  |
| Primary site of the tumor |                    |                        |
| Glottic                   | 50                 | 60.24                  |
| Supraglottic              | 18                 | 21.69                  |
| Subglottic                | 0                  | 0.00                   |
| Undetermined              | 15                 | 18.07                  |

**Table 3: The comparison of absolute and relative frequencies of the risk factors of tracheostoma recurrence after laryngectomy**

| Variable name           | Without stomal recurrence | With stomal recurrence | Odds ratio   | 95% confidence interval |
|-------------------------|---------------------------|------------------------|--------------|-------------------------|
| Age                     | 62.70±10.01               | 61.33±8.70             |              |                         |
| Subglottic invasion     | 3(4.05%)                  | 8(88.89%)              | 190          | 18-2042                 |
| T4 tumors               | 4(5.41%)                  | 6(66.67%)              | 35           | 6-194                   |
| Primary                 | 46(62.16%)                | 4(44.44%)              |              |                         |
| Glottic tumor           |                           |                        |              |                         |
| Thyroid lobectomy       | 30(40.54%)                | 9(100.0%)              | Incalculable |                         |
| Subglottic invasion     | 3(4.05%)                  | 9(100.0%)              | Incalculable |                         |
| Pre-operative radiation | 3(4.05%)                  | 3(33.33%)              | 12           | 2-72                    |
| Mortality               | 10(13.51%)                | 7(77.78%)              | 22           | 4-123                   |

**DISCUSSION**

There have been a variety of reports of stomal recurrence after laryngectomy. Ferlito *et al.* (2002) evaluated the stomal recurrence after laryngectomy in a review article of the articles published up to 2002 and reported its prevalence to be from 1.7 to 25%, 94% of which was in the first 2 years and 80% of which occurred between 6 and 12 months after operation. Resendiz-Colosia *et al.* (2003) mentioned the stomal recurrence between 1.7 and 40% with the mean of 7.5% in different studies.

Although our search found most of the results after these studies in the same range, there were also some studies reporting higher rates. Onakoya *et al.* (2004) stated that stomal recurrence rate to be 38.9%. Our results showed a recurrence rate of 10.84% (9 in 83 patients).

We evaluated 8 risk factors that might be influential in stomal recurrence. All patients in our study were male, thus, we could not assess the effect of gender in stomal recurrence. We also found no significant difference in the mean age of the patients with and without tracheostoma recurrence.

Other studies have accounted pre-operative tracheostomy as a common risk factor of parastomal recurrence; however, there is still controversy over this. (Ferlito *et al.*, 2002) Some studies have showed that parastomal recurrence is significantly higher in patients who had undergone tracheostomy (emergency or elective) prior to surgery (Zbaren *et al.*, 1996). Sato *et al.* (1989) showed the same relationship for emergency tracheostomy and Brenman *et al.* (1988) verified that. Yuen *et al.* (1996) indicated that airway obstruction and emergency tracheostomy have significant relationship with stomal recurrence. Santoro *et al.* (2003) reported the same results. Our study revealed that prevalence of pre-operative tracheostomy was significantly higher in patients with stomal recurrence (88.89 vs. 4.05% with odds ratio = 189 and 95% confidence interval of 18 to 2042). However, Reddy *et al.* (2001) showed that emergency tracheostomy does not affect stomal recurrence in T1 glottic cancer. Yotakis *et al.* (1996) indicated that there was no significant relationship

between pre-operative or intra-operative tracheostomy and stomal recurrence. Mantravadi *et al.* (1981) verified these results. The main reason of this controversy seems to be the effects of the site of the emergency tracheostomy. Imauchi *et al.* (2002) indicated that the primary site of pre-operative tracheostomy can be a risk factor for stomal recurrence.

Based on these studies, application of laryngectomy in prevention of stomal recurrence in patients undergoing tracheostomy is controversial (Ferlito *et al.*, 2002). Some researchers have mentioned pre-operative tracheostomy as an indication for emergency laryngectomy in order to prevent stomal recurrence (Griebie *et al.*, 1987; Keim *et al.*, 1965; McCombe *et al.*, 1991) while Rockley *et al.* (1991) found no clues showing a decrease in stomal recurrence by emergency laryngectomy.

The patients with higher stages of cancer experience higher rates of stomal recurrence. Our results revealed that the prevalence of higher stages of cancer (T4) was significantly higher in patients with stomal recurrence (66.67 vs. 5.41% with odds ratio = 35 and 95% confidence interval of 6 to 194) which was verified by Yotakis *et al.* (1996) and Zbaren *et al.* (1996). Screening of patients with higher stages of cancer may decline the stomal recurrence rate.

Another important factor is the size of the primary involvement and the amount of involved tissue resection. Regardless of the cause of stomal recurrence, wide infiltration of the tumor into soft tissue of the neck and mediastinum affects this issue and makes the control of the tumor very difficult (Resendiz-Colosia *et al.*, 2003). We used 2 variables to assess the size of involvement: thyroid invasion and paratracheal lymph node involvement. Thyroid invasion can be an important influential factor in parastomal recurrence (Ferlito *et al.*, 2002). Residual cancer in thyroid can absolutely be an important factor affecting the stomal recurrence. We found out that thyroid resection was significantly higher in patients with stomal recurrence (100 vs. 40.54% with incalculable odds ratio). This implies that stomal recurrence can be due to high stage of the disease and its wide distribution in these patients.

Paralaryngeal, paratracheal and pre-tracheal lymph node involvement is also an influential factor in stomal recurrence in laryngeal carcinomas that are biologically invasive (Ferlito *et al.*, 2002). Paratracheal lymph node involvement is especially effective in stomal recurrence (Mantravadi *et al.*, 1981). Imauchi *et al.* (2002) showed that paratracheal lymph node involvement is significantly higher in patients with stomal recurrence. Resendiz-Colosia *et al.*, (2003) Liu *et al.* (2002 and 2001) and Petrovic *et al.* (2004) found the same results. In spite of the importance of this variable, it was not possible to be reported because of the shortages in reporting system and the pathology reports of the hospitals of our study.

Furthermore, we did not found a significant difference in stomal recurrence in patients with primary glottic or subglottic involvement. We did not have any cases with subglottic invasion. The primary subglottic cancers, originating in subglottic area, are rare and are associated with a long asymptomatic period. More commonly the subglottic area is invaded by the tumors originating from glottic or supraglottic and spread by paraglottic space invasion. Subglottic invasion of this type is associated with high rate of stomal recurrence due to paratracheal lymph node involvement (Chiesa *et al.*, 2001).

Subglottic involvement or remaining non-resected malignant tissues in cancers of the glottic area are statistically the most important risk factor of stomal recurrence (Mantravadi *et al.*, 1981). Reddy *et al.* (2001) indicated that subglottic invasion of the primary glottic tumor is associated with a remarkable increase in stomal recurrence. They showed that all patients with subglottic invasion experienced stomal recurrence, while stomal recurrence happened in only 6% of patients without subglottic invasion. Our study revealed the same results (100% vs. 4.05% with incalculable odds ratio). Many other studies showed the same relationship (Barr *et al.*, 1990; Leon *et al.*, 1996; Liu *et al.*, 2002, 2001; Resendiz-Colosia *et al.*, 2003; Rubin *et al.*, 1990; Yotakis *et al.*, 1996; Yuen *et al.*, 1996; Zbaren *et al.*, 1996).

Pre-operative radiation has also been accounted as a risk factor of stomal recurrence. There have been studies revealing that the rate of stomal recurrence was higher in patients undergoing high-dose radiation and then laryngectomy. Our study verified this relationship (33.33 vs. 4.05% with odds ratio = 11.83 and 95% confidence interval of 2 to 72). This can be due to the facts that: 1) pre-operative radiation is performed in patients not willing to undergo surgery at early stages and after progression of the cancer, they had to undergo surgery and 2) low-dose pre-operative radiation may stop the patient from undergoing proper dose of radiation after the operation (Breneman *et al.*, 1988).

Our study showed a significantly higher mortality rate in patients with recurrence of tracheostoma (77.78 vs. 13.51% with odds ratio = 22.4 and 95% confidence interval of 4.1 to 123). This is verified by the results of Onakoya *et al.* (2004) who reported a mortality rate of 70% in patients with stomal recurrence versus 30% in others. Stomal recurrence following laryngectomy is assumed incurable (Petrovic and Djordjevic, 2004) and the survival is very low despite the development of surgery, chemotherapy and radiation for treatment of this disease. The treatment choices are very limited and confined to radical surgery (Ferlito *et al.*, 2002).

Finally, as laryngectomy is a frequent operation in ENT wards, identification of the risk factors of stomal recurrence and close monitoring of these patients can yield a more promising outcome.

Based on our results, pre-operative tracheostomy, higher stages of cancer (T4), thyroid resection as a sign of spread of cancer, subglottic invasion and pre-operative radiation were risk factors of stomal recurrence, while the primary site of the tumor did not have a significant relationship with it. The mortality rate was significantly higher in patients with stomal recurrence which can be an emphasis on closer follow-up of these patients. It is recommended to evaluate paratracheal lymph node involvement, post-cricoid invasion and evolution of a second cancer in addition to other variables and also the alterations of the rate of stomal recurrence and the mortality and survival rates of patients with laryngeal cancer over the time.

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