Impact of preoperatative tracheostomy on tracheostome recurrence and overall survival in patients undergoing laryngectomy

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Background
The development of tracheostomerecurrence after total laryngectomy is a complication with a dismal prognosis .The average survival rate of tracheostome recurrence (TR) is 7.5%, ranging from 1.7% to 40%The TR consists of diffuse infiltration of tumor into the soft tissues of the neck and mediastinum; hence the control of this disease is difficult.

Objective
To analyze the impact of preoperative tracheostomy ontracheostome recurrence (TR), regional recurrence (RR), and overall survival (OS) in patients undergoing primary laryngectomy.

Material and methods
Thirty three consecutive patients, who underwent primary total laryngectomy for locally advancedlaryngeal squamous cell carcinoma, were enrolled in this study. Patients whounderwent primary chemo-radiotherapy, partial laryngectomyor those treated palliatively wereexcluded from the study.Patient factors analyzed included age,gender, primarytumor site, TNM classification, type of procedure, thyroid gland management, extent of neck dissection and preoperative tracheostomy (POT). The timeinterval between tracheostomy and definitive surgery was calculated.

Results
A total of 33 patients underwent total laryngectomy(TL) for squamous cell carcinoma of the larynx.Thirty patients (90.9%) were males, while 3 (9.1%) patients were females. Their mean age was 57.7 (±11.6) years, 26 (78.8%) of them were smokers, their follow up mean time was 23 (±6.6) months. Tracheostomy recurrence occurred in 3 (9.1%) patients and regional recurrence in another 3(9.1%) patients. The 2 years survivalfor the whole patients was 84.8% and overall survival was 81.1%. Nineteen patients had POTbetween 10 to 21days (median 15)prior to TL surgery. Fourteen patients had their tracheostomy at the time of surgery .There was no statistical significant difference between both groups as regard overall survival, stomal recurrence and regional recurrence.

Conclusion
Our results are in keeping with more recent studies, which suggest that POT is notnecessarily related to stomal recurrence or poor oncological outcome.

Keywords:
regional recurrence, squamous cell carcinoma, total laryngectomy, tracheostome recurrence

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Introduction

Tracheostome recurrence (TR) following primary total laryngectomy (TL) for squamous cell carcinoma (SCC) occurs in 2–15% [1,2] and has been defined as 'a diffuse infiltration of neoplastic tissue at the junction of the trachea and skin' [1]. It is associated with very poor prognosis despite aggressive surgery or radiotherapy. Factors that are thought to predispose patients to TR include advanced T stage and N stage, subglottic involvement, and preoperative tracheostomy [3]. Other predisposing factors include insufficient tracheal resection margins and thyroid gland invasion [4].

Most cases are diagnosed within the first year following TL, but some cases present as late as 3.5 years after surgery [4]. It is associated with 90% mortality, with more than 80% of the patients dying within the first 24 months [5].

Preoperative tracheostomy (POT) is one of several factors associated with an increased risk for TR. Several articles have reported a poor outcome with POT [6–8], whereas others could not find a significant relation [9,10]. It seems plausible that POT might disrupt the primary tumor or seed the tracheal tract and lead to reduced local control.

The different treatment modalities for these recurrences include surgery, radiotherapy, and radiochemotherapy. All these modalities have not been satisfactory in controlling the recurrence and therefore, special attention should be given to the prevention of such pathologies [2,11,12].

Many methods have been proposed to prevent recurrence in the tracheostomy area, such as a broader surgical margin by resecting the trachea at a lower level, excision of lymph-nodes located in the paratracheal area, emergency laryngectomies rather than preoperative tracheostomy if the patients present with significant airway obstruction, and postoperative radiotherapy including the tracheostomy and the upper mediastinum [1,6,13,14]. Theoretically, any delay between the POT and the definitive TL would allow the seeded tumor cells to more effectively establish themselves in the fresh tracheostomy.

In this study, we present our experience with a series of laryngectomy patients, with the aim of analyzing the impact of POT on TR, regional recurrence, and overall survival (OS) in patients undergoing primary laryngectomy.

Patients and methods

This study was conducted after approval by the Institutional Review Board of Ain Shams University Hospitals and obtaining informed consent from all participants.

This is a prospective study, carried out between January 2011 and October 2013. Thirty-three consecutive patients who underwent primary TL for locally advanced laryngeal SCC were enrolled in this study. Patients who underwent primary chemoradiotherapy or partial laryngectomy, and those treated palliatively were excluded from the study.

Patient factors analyzed included age, sex, primary tumor site, tumor, node, metastasis classification, type of procedure, thyroid gland management, extent of neck dissection, and POT.

The time interval between tracheostomy and definitive surgery was calculated. All patients who had undergone POT had the tracheal window excised and sent for histological analysis. All patients underwent primary TL, with or without unilateral or bilateral neck dissection. Histological features, such as the degree of differentiation, and the adequacy of the pathological margin of excision were documented. The decision to administer postoperative radiotherapy or radiochemotherapy to the patients was recorded.

Statistical analysis was carried out on a personal computer using MedCalc© version 11.4 (MedCalc© Software, Mariakerke, Belgium).

The Kolmogorov–Smirnov goodness-of-fit test was used to test the normality of numerical data distribution. Normally distributed numerical data are presented as mean and SD, and differences between the two groups were compared using the unpaired Student *t*-test. Skewed numerical data are presented as median and interquartile range, and the Mann–Whitney *U*-test was used to compare intergroup differences. Categorical data are presented as number and percentage, and differences between the two groups were compared using the Pearson χ^2-test and the χ^2-test for trends for nominal and ordinal data, respectively. Fisher's exact test was used in place of the χ^2-test if greater than 20% of cells in any contingency table had an expected count of less than 5.

The Kaplan–Meier method was used to create curves for survival and for the time to stomal or regional recurrence in the two groups. The Kaplan–Meier curves of both groups were compared using the log-rank test. All *P*-values are two-sided. *P* less than 0.05 is considered statistically significant.

Results

A total of 33 patients underwent TL for SCC of the larynx. Thirty patients (90.9%) were male, whereas three (9.1%) patients were female. Their mean age was 57.7 (±11.6) years; 26 (78.8%) of them were smokers; their mean follow-up period was 23 (±6.6) months. TR occurred in three (9.1%) patients, two of them were Sisson's stage II and one was Sisson's stage IV, and regional recurrence occurred in another three (9.1%) patients. The 2-year survival for the entire patient group was 84.8%, and the OS was 81.1%.

Nineteen patients had undergone POT between 10 and 21 days (median 15) before TL surgery. Fourteen patients underwent tracheostomy at the time of surgery [intraoperative tracheostomy (IOT)]; demographic data are shown in Table 1.

In the POT group, 18 (94.73%) patient were male and one (5.27%) was female; their mean age was 58 years (±14.3 years); 16 (84.2%) of them were smokers. Their median follow-up period was 26 months (21–28 months). Of the 19 POT patients,

Table 1 Demographic data of the study groups

Variable	Intraoperative tracheostomy (*n* = 14)	Preoperative tracheostomy (*n* = 19)	*P*-value
Gender, M/F	12/2	18/1	0.561
Age (yr)	57.2 (6.9)	58 (14.3)	0.836
Smokers [*n* (%)]	10 (71.4)	16 (84.2)	0.422
Tracheostomy-to-laryngectomy time (days)	–	15 (10–21)	n/a

nine (47.4%) had transglottic, six (31.6%) had supraglottic, two (10.5%) had glottic, and two (10.5%) had subglottic carcinomas. There were 14 patients (73.7%) with T3 tumors and the rest had T4 tumors. Four patients (21.1%) had no neck nodes; 15 patients (78.9%) presented with N+ cervical lymphadenopathy. Unilateral neck dissection was performed in 13 of these patients (68.4%), whereas bilateral neck dissection was performed in four patients (21.1%). Total thyroidectomy was carried out in 12 patients (63.2%), whereas hemithyroidectomy was performed in six patients (31.6%). On histopathological examination, 12 patients (63.2%) showed moderately differentiated carcinomas and seven (36.8%) showed poorly differentiated carcinomas. Seven (36.8%) patients underwent postoperative radiotherapy, whereas eight (42.1%) underwent postoperative chemoradiotherapy (Table 2). One (5.3%) patient developed stomal recurrence, which was diagnosed 21 months after surgery, and one patient (5.3%) had regional recurrence. The 2-year survival was 84.02%.

In the IOT group, 12 (85.71%) patients were male, whereas two (14.29%) were female; their mean age was 57.2 years (±6.9%); 10 (71.4%) of them were smokers. Their median follow-up period was 26.5 months (19–28 months). Of the 14 POT patients, 11 (78.6%) had transglottic, two (14.3%) had supraglottic, and one (7.1%) had glottic carcinomas. There were 10 patients (71.4%) with T3 tumors and the rest had T4 tumors. Nine patients (64.3%) had no neck nodes and five (35.7%) presented with N+ cervical lymphadenopathy. Unilateral neck dissection was performed in eight (57.1%) of these patients, whereas bilateral neck dissection was performed in two patients (14.3%). Total thyroidectomy was carried out in five patients (35.7%), whereas hemithyroidectomy was performed in five patients (35.7%). On histopathologic examination, five patients (35.7%) showed well-differentiated, five (35.7%) showed moderately differentiated, and four (28.6%) showed poorly differentiated carcinomas. Five (35.7%) patients underwent postoperative chemoradiotherapy (Table 2). Two (14.3%) patients developed stomal recurrence, which was diagnosed 26 months after surgery; in addition, two patients (14.3%) had regional recurrence (Table 3). The 2-year survival was 85.7% (Table 4).

There were no statistically significant differences between the two groups in age, sex, smoking habits, T and M stage, tumor differentiation, or tumor site. Significant differences were observed in the tumor stage, with the POT group having a higher clinical stage and cervical nodal metastases (Table 2).

Further subgroup analysis was carried out using the T-classification. Again POT was not predictive of

Table 2 Surgical and pathological data of both groups

Variable	Intraoperative tracheostomy (*n* = 14) %	Preoperative tracheostomy (*n* = 19) %	*P*-value
T stage			
T3	10 (71.4)	14 (73.7)	1.000
T4	4 (28.6)	5 (26.3)	
N stage			
N0	9 (64.3)	4 (21.1)	0.042
N+	5 (35.7)	15 (78.9)	
M stage			
M0	14 (100.0)	19 (100.0)	–
Clinical stage			
Stage III	9 (64.3)	4 (21.1)	0.012
Stage IV	5 (35.7)	15 (78.9)	
Differentiation			
Well differentiated	5 (35.7)	0 (0.0)	0.067
Moderately differentiated	5 (35.7)	12 (63.2)	
Poorly differentiated	4 (28.6)	7 (36.8)	
Tumor site			
Glottic	1 (7.1)	2 (10.5)	0.379
Transglottic	11 (78.6)	9 (47.4)	
Supraglottic	2 (14.3)	6 (31.6)	
Subglottic	0 (0.0)	2 (10.5)	
Neck dissection			
No neck dissection	4 (28.6)	2 (10.5)	0.588
Unilateral neck dissection	8 (57.1)	13 (68.4)	
Bilateral neck dissection	2 (14.3)	4 (21.1)	
Thyroidectomy			
No thyroidectomy	4 (28.6)	1 (5.3)	0.155
Hemithyroidectomy	5 (35.7)	6 (31.6)	
Total thyroidectomy	5 (35.7)	12 (63.2)	
Auxiliary treatment after surgery			
Nil	9 (64.3)	4 (21.1)	0.009
Radiotherapy	0 (0.0)	7 (36.8)	
Radiotherapy plus chemotherapy	5 (35.7)	8 (42.1)	

Data are presented as number (%).

Table 3 Follow-up and outcome

Variable	Intraoperative tracheostomy (*n* = 14)	Preoperative tracheostomy (*n* = 19)	*P*-value
Follow-up time (months)	26.5 (19–28)	26 (21–28)	0.679
Stomal recurrence *n* (%)	2 (14.3%)	1 (5.3%)	0.561
Regional recurrence *n* (%)	2 (14.3%)	1 (5.3%)	0.561
Mortality *n* (%)	3 (21.4%)	3 (15.8%)	1.0

Data are presented as median (interquartile range) or number (%).

Table 4 Two-year survival and overall survival in patients subjected to intraoperative or preoperative tracheostomy

Variables	Intraoperative tracheostomy (*n* = 14) [*n* (%)]	Preoperative tracheostomy (*n* = 19) [*n* (%)]	*P*-value
Two-year survival	12 (85.7)	16 (84.2)	1.0
Overall survival	11 (78.6)	16 (84.2)	1.0

outcome in either subgroup when analyzed separately. POT remained a nonsignificant prognostic factor in the outcome analysis of the T-classification subgroups that is, T3 POT versus T3 IOT and T4 POT versus T4 IOT.

On the basis of Kaplan–Meier survival curves for the IOT and POT groups, there was no statistically significant difference between both groups with regard to OS [hazard ratio = 0.717, 95% confidence interval (CI) = 0.142 to 3.631, $P = 0.680$; Figure 1 and Table 4]. In other words, POT was not statistically significantly associated with poorer outcome in terms of OS.

Kaplan–Meier survival curves for stomal recurrence and regional recurrence in the IOT and POT groups showed that there was no statistically significant difference between the two groups (hazard ratio = 0.342, 95% CI = 0.034–3.422, P=0.357 and hazard ratio = 0.373, 95% CI = 0.038–3.672, P = 0.401) (Figs. 2 and 3) and (Table 3). This result indicates that there was no statistically significant association between POT and regional or stomal recurrence.

Discussion

Development of TR after TL is a complication with a dismal prognosis [14]. The average survival rate of TR is 7.5%, ranging from 1.7 to 40% [15].

TR includes diffuse infiltration of tumors into the soft tissues of the neck and the mediastinum; hence, control of this disease is difficult [15]. Stomal recurrence prevention is therefore of paramount importance and seems to be the only means of reducing incidence [15,16]. It has been categorized by Sisson, and this classification is known to be correlated with the selection of appropriate management and outcome [16].

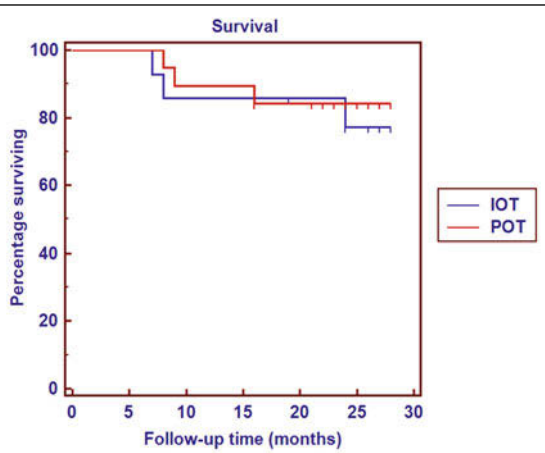
The study by Keim *et al.* [1] reported a 14% incidence of stomal recurrence if laryngectomy was performed at the time of emergency tracheostomy, compared with a 41% incidence if laryngectomy was performed more than 2 days after tracheostomy. Other studies stated that there is no relation between the two [9,10].

The main aim of this study was to evaluate patients who had undergone TL and study the impact of POT on stomal recurrence, regional recurrence, and OS.

Thirty-three consecutive patients who had undergone TL for SCC of the larynx at our unit were studied. Thirty patients (90.9%) were male, whereas three (9.1%) were female; this indicates the male predominance of the disease, which is in agreement with the findings from other studies [17]. The mean age of the patients was 57.7 (±11.6) years; 26 (78.8%) of them were smokers; and their mean follow-up period was 23 (±6.6) months. Stomal recurrence occurred in three (9.1%) patients; this is in agreement with a study conducted by Breneman *et al.* [18], in which only two (11%) stomal recurrences occurred among 18 laryngectomy patients with POT. In addition, Yotakis *et al.* [13] in their review of 352 patients reported only 21 (6%) to have developed a stomal recurrence.

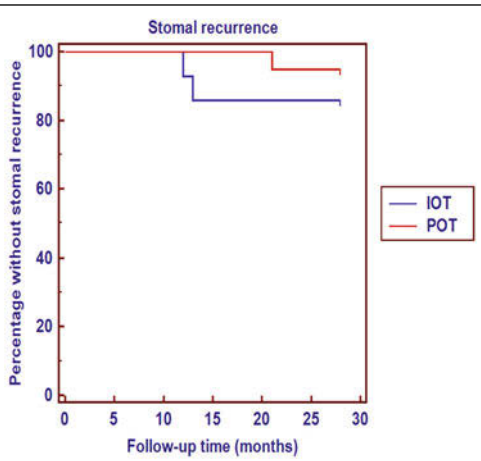
This study showed that there was no significant difference in the development of stomal recurrence between the group that underwent POT and the group that underwent intraoperative tracheostomy during TL. This is in agreement with the findings of Pezier

Figure 1



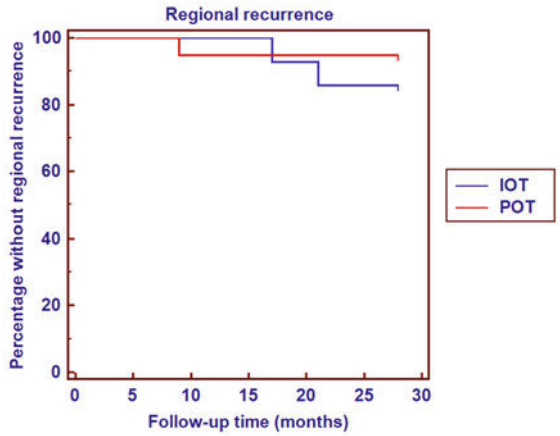
Kaplan–Meier survival curves for the IOT and POT groups; there was no statistically significant difference between both groups with regard to overall survival (P = 0.680). IOT, intraoperative tracheostomy; POT, preoperative tracheostomy.

Figure 2



Kaplan–Meier survival curves for stomal recurrence in the IOT and POT groups showing that there is no statistically significant difference between the two groups (P = 0.357). IOT, intraoperative tracheostomy; POT, preoperative tracheostomy.

Figure 3



Kaplan–Meier survival curves for the IOT and POT groups showing that there is no statistically significant difference between the two groups with regard to regional recurrence (P = 0.401). IOT, intraoperative tracheostomy; POT, preoperative tracheostomy.

et al. [19], who concluded that there is no statistically significant difference in OS, disease-specific survival, and local recurrence-free survival between patients undergoing POT and those undergoing intraoperative tracheostomy during TL. In addition, Yotakis *et al.* [13] reported that there was no significant difference in the rate of stomal recurrence between those undergoing emergency tracheostomy (23.3%) and those undergoing intraoperative tracheostomy (18.2%).

In contrast, Halfpenny and McGurk [20] found in their study that three (1%) of 265 patients developed a stomal recurrence. All recurrences occurred in the group in which tracheostomy had been performed before laryngectomy; all these three patients had N+ disease. They concluded that the timing of tracheostomy placement is important in reducing the risk for stomal recurrence.

Kaplan–Meier survival curves for the IOT and POT groups show that there is no statistically significant difference between both groups with regard to overall survival, stomal recurrence, and regional recurrence (P = 0.680, 0.357, and 0.401, respectively; Figs. 1–3). POT was therefore not statistically associated with a poorer outcome in terms of OS, regional recurrence, and stomal recurrence.

This article targets an important issue in the management of laryngeal cancer, namely the impact of POT on survival. We need larger series and multicenter studies with longer periods of follow-up for these patients to support the evidence that POT is not a risk factor for poor outcome.

Conclusion

Management of the compromised airway in advanced laryngeal carcinoma remains a challenge; our results are in keeping with more recent studies, which suggest that POT is not necessarily related to higher stomal recurrence or poor oncological outcome.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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