Partial laryngectomy as salvage surgery after radiotherapy: Oncological and functional outcomes and impact on quality of life. A retrospective study of 20 cases

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Summary The gold standard for the management of laryngeal squamous cell carcinoma in a previously irradiated patient is "salvage" total laryngectomy, but surgical management by partial laryngectomy can sometimes be proposed in selected patients.

Objectives: This study was designed to review the functional and oncological outcomes of patients treated by open partial laryngectomy for recurrent squamous cell carcinoma after failure of radiotherapy or involving previously irradiated tissues and to define prognostic criteria for the selection of patients eligible for this treatment strategy.

Materials and methods: In this retrospective study, 20 patients underwent partial laryngectomy between 2000 and 2011 for recurrence or second primary stage I or II laryngeal squamous cell carcinoma in an irradiated territory (11 vertical partial laryngectomies; 9 horizontal partial laryngectomies).

Results: The 3-year overall survival rate in patients with negative resection margins was 66%, with higher survival rates for tumours confined to the glottis, and the 2-year local control rate was 67%. Positive resection margins requiring total laryngectomy were observed in 20% of cases. The 3-year overall survival rate was 56% in these patients. Exclusive oral feeding was restored in 75% of patients after an average of 32 days. The tracheotomy tube was removed after an average of 18 days in 90% of patients. The disease-free functional larynx preservation rate was 45%.

Conclusions: Salvage partial laryngectomy in irradiated tissues is an alternative treatment option to total laryngectomy in selected patients.

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Introduction

Laryngeal cancer is the fifth most common cancer in men. France has one of the highest laryngeal cancer incidence and mortality rates in Europe [1].

Various treatment modalities are available for early stages: radiotherapy either alone or in combination with chemotherapy, endoscopic and open partial laryngectomies. Each treatment option presents specific advantages for each stage and provides comparable cancer control results [2], but the functional results, particularly in terms of voice preservation, are often considered to be better with radiotherapy [3,4].

Failure rates reported for exclusive radiotherapy range from 2 to 18% for stage T1 glottic tumours and up to 31% for stage T2 glottic tumours, with higher failure rates for supraglottic tumours (up to 25% and 35% for stage T1 and T2, respectively [5,6]). In parallel, the recurrence or second primary tumour rate after a first stage T1 or T2 laryngeal tumour is 20%, and 91% of these recurrences or second tumours occur at the site of the primary tumour [4]. Progressive disease or recurrence are treated surgically depending on the extent of the tumour: this post-irradiation surgery is called salvage surgery.

The primary objective of partial laryngectomy is preservation of upper aerodigestive tract function. Historically, partial laryngectomy is not indicated in previously irradiated tissues due to the risks of poor wound healing and poor recovery of speech, swallowing and respiratory functions. Endoscopic resection of resectable tumours gives good functional and oncological results [7]. Salvage total laryngectomy for stage T1 and T2 squamous cell carcinoma of the larynx ensures cancer control in 75% of patients [8].

This retrospective study, based on a series of patients undergoing open partial laryngectomy for squamous cell carcinoma confined to the larynx arising in irradiated tissues, was designed to evaluate the oncological and functional outcome of post-irradiation salvage partial laryngectomy.

Material and methods

Study population

This study retrospectively reviewed 20 patients treated by open partial laryngectomy in irradiated tissues at Nantes university hospital between September 2000 and May 2011. These patients presented squamous cell carcinoma not controlled by radiotherapy (recurrence or progressive disease) or a secondary primary squamous cell carcinoma in previously irradiated mucosa. Tumours were classified according to the 2002 TNM classification.

This population had a mean age of 64 years (range: 48 to 84 years) with a sex ratio of 9 (18 men for 2 women). Mean postoperative follow-up was 2.5 years (± 1.9 years).

Treatment of the primary tumour consisted of exclusive radiotherapy at a mean dose of 67.5 Gy (range: 60 to 72 Gy). Primary tumour sites were essentially glottic (60%) and oropharyngeal (30%); only one tumour arose in the laryngeal vestibule and another arose in the oral cavity. All primary tumours were limited stage T1 (n = 12) or T2 (n = 8) tumours.

Patients were managed surgically after a mean interval of 5 years and 2 months (± 5.3 years) following completion of radiotherapy. Most patients presented a recurrence or a second primary (n = 17), while three patients presented progressive disease.

All 20 patients were managed surgically after endoscopic and radiological assessment (contrast-enhanced CT examination of the neck and chest). Operative indications were discussed in multidisciplinary consultation meetings. None of the patients presented a contraindication to partial laryngectomy. No lymph node dissection was performed concomitantly with the laryngeal procedure (all patients were NO).

Statistical analysis

Data were collected retrospectively using Microsoft® Excel 2010 software to calculate the mean, standard deviation and correlation coefficients. Overall survival and disease-free survival rates were estimated by the Kaplan-Meier method using IBM® SPSS Statistics 19 software. Functional prognostic factors were identified by calculating Pearson’s correlation coefficient. The results were considered to be statistically significant for P < 0.05.

Results

Oncological outcome

Fifteen (75%) of the 20 partial laryngectomies were considered to present negative resection margins (not requiring any adjuvant therapy). Four of the five cases with positive resection margins required total laryngectomy after a mean interval of 5.5 months (± 6); two of these four patients initially refused this complementary surgery and one of them was re-irradiated. The mean 2-year overall survival rate for these five patients was 45% with a primary site disease-free survival rate of 60%. Positive resection margins for these five partial laryngectomy specimens were mainly inferior for vertical partial laryngectomies (2/2), and anterosuperior for horizontal partial laryngectomies (2/3). The 3-year overall survival rate for this series of 20 patients was 56% (Fig. 1).

Fifteen patients therefore underwent partial laryngectomy with negative resection margins (8 vertical partial laryngectomies with epiglottic reconstruction [VPLER], 5 horizontal supraglottic partial laryngectomies [SPL], 1 horizontal supracricoid partial laryngectomy [SCPL], and 1 supraglottic hemiaryngolaryngectomy). Histological examination of these 15 operative specimens revealed 1 pT3 tumour, 7 pT2 tumours and 7 pT1 tumours. The mean 3-year overall survival rate was 66% (Fig. 1) and the mean 3-year disease-free survival rate was 52% for these 15 patients.

The local recurrence rate for these 15 patients was 20% (n = 3) with a mean recurrence-free survival of one year (range: 5 to 16 months). The 2-year local control rate was 67% and the main causes of local failure were recurrence or second primary (oropharyngeal tumour for 2 patients). Only one patient presented postoperative lymph node recurrence concomitant with local tumour recurrence. No cases of metastatic disease were observed.
The 3-year overall survival in the group of patients under the age of 65 years \( (n = 11) \) was 52% versus 65% for patients over the age of 65 years \( (n = 9) \). No correlation was observed between age at diagnosis and overall survival \( (r = 0.15) \).

Survival analysis according to tumour size showed better overall survival for limited tumours: the 3-year overall survival was 64% for stage T1 tumours versus 53% for T2 tumours \( \text{(Fig. 2)} \). The mean survival difference between these two groups was not significant \( (P = 0.07) \).

Survival analysis according to tumour site showed better 3-year overall survival for glottic tumours (66%) compared to supraglottic tumours (47%) \( \text{(Fig. 3)} \). The mean overall survival of patients with a glottic tumour was significantly better than that of patients with a supraglottic tumour \( (P = 0.04) \).

**Surgical and functional results**

No early postoperative deaths were observed. Several postoperative complications were observed: three patients (15%) developed documented aspiration pneumonia between D5 and D12, and another patient experienced upper gastrointestinal bleeding from an oesophageal ulcer on D3.

Oral feeding was restored for 15 of the 20 patients. The mean time to resumption of oral feeding was 32 days \( \pm 13 \). All patients received postoperative swallowing and speech therapy. Six patients in whom spontaneous feeding was difficult to restore attended a specialized swallowing consultation with video swallow study.

The tracheostomy tube was permanently removed in 18 (90%) of the 20 patients, after an overall mean interval of 18 days \( \pm 17 \) (13 days for VPLER, 16 days for SPL, 60 days for the SCPL with cricothyroidopexy, 5 days for SCPL with cricothyroidoepliglottopexy, 55 days for hemipharyngolaryngectomy). Two patients were treated by endoscopic laser disobstruction after VPLER for laryngeal oedema, allowing rapid removal of the tracheostomy tube without recannulation.

The disease-free functional larynx preservation rate was 45% \( (n = 9) \) in this series of 20 patients. Two patients subsequently underwent total laryngectomy for functional reasons, as decannulation was not possible, requiring frequent suction for severe aspiration and bronchopulmonary congestion. Video swallow studies confirmed these persistent episodes of severe aspiration, justifying the indication for total laryngectomy. No episode of aspiration pneumonia
was observed for the 45% of patients in local remission after partial laryngectomy.

No correlation was observed between age at diagnosis and duration of enteral feeding ($r = 0.38$) or duration of tracheostomy ($r = 0.28$) and no correlation was observed between the time to resumption of oral feeding and duration of tracheostomy ($r = 0.18$).

**Discussion**

Partial laryngectomy is an attractive solution for surgeons, as it allows preservation of laryngeal function: speech, breathing without tracheostomy, exclusively oral feeding. However, in order to be applied in the post-radiotherapy setting, this surgery must provide equivalent oncological results and better functional results than those of radical surgery.

The first-line treatment in our institution for patients with tumours amenable to partial laryngectomy is surgery: neoadjuvant radiotherapy is rarely proposed for T2 tumours amenable to partial laryngectomy. However, some authors have reported equivalent oncological results for partial laryngectomy and exclusive radiotherapy for stage T2 glottic tumours, but with better functional results [9], while other studies have shown that partial laryngectomy ensures better local control than radiotherapy [10, 11]. The attitude based on first-line surgery is designed to preserve the possibilities of irradiation in the case of a second primary tumour. The possibility of salvage partial laryngectomy is therefore considerably reduced in some centres in which the reference treatment is external radiotherapy for stage T2 tumours.

This retrospective study therefore shows:

- a local control rate of 65% for selected patients with negative resection margins;
- a 3-year overall survival of 66% for these selected patients with significantly longer survival for patients with a tumour confined to the glottis;
- a 3-year overall survival of 56% for all operated patients.

In the literature, total laryngectomy salvage surgery, all stages combined, classically ensures 5-year overall survival rates of 43 to 55%. Total laryngectomy is part of the management of patients with positive resection margins and the detailed treatment plan must be explained to the patient prior to partial laryngectomy in irradiated tissues. Partial laryngectomy in non-irradiated tissues ensures a local control rate of 90% with a 5-year overall survival rate of 80% (46 to 100%), while the local control rate of partial laryngectomy in irradiated tissues is only 61% (61 to 96%) with a 3-year overall survival of 66 to 85% [9, 12–14].

However, it is difficult to compare the results of these various series, as the populations differ from one series to another, with different tumour stages and different sites. Marked differences in overall survival and local control rates are observed for glottic and supraglottic tumours following failure of radiotherapy: supraglottic tumours have a poorer prognosis with a 3-year overall survival rate of 66% versus 80 to 88% for glottic tumours [15–18].

As reported in the literature [15], the lymph node recurrence rate was very low in the present series, validating our attitude in relation to lymph nodes. In view of the high morbidity associated with post-radiotherapy prophylactic bilateral lymph node dissection, simple lymph node surveillance appears to be legitimate in N0 patients. The main cause of failure of local control in this series was the appearance of a second primary. As part of the long-term follow-up of these patients, the surgeon must stress the importance of permanent avoidance of exposure to risk factors (essentially smoking).

However, survival is not directly related to successful surgery, as it is also influenced by the patient’s general state of health. The general eligibility criteria for partial laryngectomy have not been clearly defined, as some authors systematically perform pulmonary function tests, while others do not. The patient’s general health (cardiorespiratory) should be assessed, together with age, swallowing function and the patient’s preoperative motivation, as all of these factors determine the postoperative outcome, the quality of rehabilitation and survival.

The morbidity of partial laryngectomy is controversial: postoperative complication rates vary considerably from one study to another (10 to 70% [16]): aspiration pneumonia, chondronecrosis, perichondritis and postoperative fistulas are the complications most commonly reported. The early postoperative complication rate is probably decreased by systematic prescription of prolonged prophylactic antibiotics in the post-radiotherapy setting, despite the absence of guidelines and formal proof of the benefit of this treatment.

The tracheostomy decannulation and functional total laryngectomy rates in this series were similar to those reported in the literature [11] for partial laryngectomy in patients not previously treated by radiotherapy. However, it is difficult to compare the tracheostomy weaning or enteral nutrition times, as they are dependent on each team’s standard practices. The rates observed in this study reflect good preservation of laryngeal function despite the previous radiotherapy.

The results of this study and those of the literature therefore suggest that partial laryngectomy in irradiated tissues is a valid treatment option in selected patients that provides satisfactory cancer control.

**Conclusion**

This study shows that post-radiotherapy partial laryngectomy is a valid treatment option. Oncological selection criteria as well as the patient’s general state must be thoroughly evaluated before considering this type of resection. The postoperative course in selected patients is favourable. Various studies [19, 20] have demonstrated the functional and oncological benefits of transoral endoscopic resection in irradiated tissues. These robot-assisted techniques will probably result in new indications, allowing equivalent cancer control with a simpler postoperative course.

**Disclosure of interest**

The authors declare that they have no conflicts of interest concerning this article.
References


