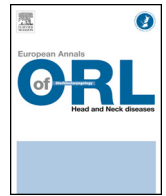




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Original article

# Primary total laryngectomy and pharyngolaryngectomy in T4 pharyngolaryngeal cancers: Oncologic and functional results and prognostic factors

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## ARTICLE INFO

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## ABSTRACT

**Objectives:** The aims of this study were to assess oncologic and functional outcome in primary total laryngectomy or pharyngolaryngectomy (TL/TL/TPL) for laryngeal or hypopharyngeal cancer with extra-laryngeal extension (T4) and to determine the predictive factors of these results.

**Material and methods:** A retrospective analysis was performed on the computerized medical records of all patients undergoing primary TL/TPL for T4 larynx or hypopharynx squamous cell carcinoma between 2000 and 2014 at our institution. Predictive factors of oncologic and functional outcome were investigated on univariate and multivariate analysis.

**Results:** Sixty-three patients (58 men, 5 women; mean age,  $68.8 \pm 9.7$  years) were included. Overall and disease-specific survivals were 69% and 80% at 3 years, and 56% and 69% at 5 years, respectively. On multivariate analysis, gender (female,  $P < 0.001$ ), ASA score ( $ASA \geq 3$ ;  $P = 0.006$ ) and vascular embolism ( $P = 0.006$ ) had significant pejorative impact on overall survival. Six months after end of treatment, 90% of patients had recovered independent oral feeding and 83% of those with tracheoesophageal voice prostheses had recovered an intelligible voice.

**Conclusion:** Primary TL/TPL remains the gold standard treatment for T4 larynx or hypopharynx cancer. It provides satisfactory oncologic and functional outcomes.

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## 1. Introduction

Indications for total laryngectomy or pharyngolaryngectomy (TL/TPL) are tending to give way to laryngeal preservation protocols or are increasingly reserved to oncologic salvage situations of tumor recurrence in previous radiation therapy sites [1,2]. Primary TL/TPL however, remains indicated in case of transcartilage extension (T4), massive subglottal extension or contraindications for neoadjuvant chemotherapy, and second-line TL/TPL may be indicated in case of previous cervical radiation therapy. In practice, transcartilage extra-laryngeal extension is the main indication for first-line radical surgery [3–5], where laryngeal preservation protocols have been shown to offer poorer survival [3,6]. To allow reliable comparison, however, it seems important to reassess oncologic and functional results for TL/TPL in the light of present-day reconstruction options (free flap in circumferential TL/TPL)

and progress in postoperative treatment (concomitant radio-chemotherapy).

The present study therefore assessed oncologic and functional results of primary TL/TPL for larynx or hypopharynx cancer with extra-laryngeal extension (T4), and sought to determine predictive factors.

## 2. Material and methods

A retrospective study included all patients undergoing primary TL/TPL for squamous cell carcinoma of the larynx or hypopharynx staged T4 (extra-laryngeal transcartilage extension) in our institution between 2000 and 2014. Computerized medical files provided the following clinical and histologic data: age, gender, comorbidities, tumor site and stage, postoperative treatment, pathologic specimen analysis, tumor recurrence, death and cause of death, and feeding and phonation quality.

Comorbidity was assessed on the American Society of Anesthesiologists (ASA) score. Tumor stage was determined on the 2009 American Joint Committee on Cancer (AJCC) TNM classification.

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Overall, disease-specific and recurrence-free survivals were assessed following Kaplan-Meier.

Functional results were assessed at 6 months posttreatment (TL/TPL and any postoperative treatment) in surviving patients and checked oncologically on the department's standardized assessment form, with a score from 0 to 2 for quality of feeding and of the tracheoesophageal prosthetic voice; this assessment is used systematically in our department for laryngectomy follow-up.

Feeding quality was assessed as follows:

- 2: normal or slightly impaired swallowing; slight difficulty with certain solid foods;
- 1: moderately impaired swallowing; feeding limited to soft or semi-liquid foods;
- 0: swallowing severely impaired or impossible; enteral feeding (nasogastric tube or gastrostomy) alone or supplementing oral feeding.

Prosthetic voice quality was assessed as follows:

- 2: easy phonation with good intelligibility;
- 1: difficult phonation, requiring repetition but intelligible;
- 0: no or generally unintelligible vocal production.

The impact of the following factors on oncologic and functional results was assessed: gender, age (>/<70 years), comorbidity (ASA score </≥3), tumor site (larynx/hypopharynx), circumferential TL/TPL, clinical N stage (</≥1), histologic N stage (</≥1), vascular embolism, perineural spread, capsule rupture, and postoperative radiation or radio-chemotherapy. Oncologic results underwent univariate analysis on log-rank test and multivariate analysis on Cox models. Functional results underwent univariate analysis on Chi<sup>2</sup> test confirmed by Fisher exact test and multivariate analysis on logistic regression. Variables with  $P \leq 0.05$  on univariate analysis were carried over to multivariate analysis. Analyses used R.2.10.1 software for Windows, with the significance threshold set at 5% for 2-tailed tests.

### 3. Results

#### 3.1. Patient characteristics

Sixty-three patients were included: 58 male, 5 female; mean age,  $68.8 \pm 9.7$  years. All had squamous cell carcinoma of the larynx ( $n=46$ ) or hypopharynx ( $n=17$ ). TL/TPL was circumferential in 7 cases. There were no patients with history of head and neck radiation therapy. Fourteen patients did not receive postoperative radiation therapy, for the following reasons: death ( $n=2$ ); age >80 years with no lymph node invasion ( $n=6$ ); or safe resection margins, with no lymph node invasion or other negative pathology criteria except stage T4 ( $n=6$ ). Clinical and histologic data are shown in Table 1.

#### 3.2. Oncologic results

Median follow-up was 43.9 months (95% CI [confidence interval], 29.1–75.9 months). Table 2 shows 2-, 3- and 5-year overall, disease-specific and recurrence-free survivals; Fig. 1 shows overall and disease-specific survival curves. Table 2 shows predictive factors for oncologic results. On multivariate analysis, female gender ( $P < 0.001$ ; OR [odds ratio], 15.2; 95% CI, 3.1–74.7), ASA score  $\geq 3$  ( $P = 0.006$ ; OR, 4.5; 95% CI, 1.5–13.5) and vascular embolism ( $P = 0.006$ ; OR, 4.6; 95% CI, 1.5–13.8) showed significant negative impact on overall survival; female gender ( $P = 0.04$ ; OR, 7.6; 95% CI, 1.1–56.9), hypopharyngeal location ( $P = 0.005$ ; OR, 10.8;

**Table 1**

Clinical and histologic characteristics of the 63 included patients.

Characteristics	Number of cases (n=63)	Percentage
Gender: male/female	58/5	92/8
Age: </>70 years	38/25	60/40
ASA score: </≥3	30/33	48/52
Tumor location: larynx/hypopharynx	46/17	73/27
N stage: N0/N1/N2a-c/N3	39/7/17/0	62/11/27/0
pN stage: N0/N1/N2a-c/N3	36/10/17/0	57/16/27/0
Positive margins	0	0
Perineural spread	18	29
Vascular embolism	16	25
Capsule rupture	18	29
Exclusive postoperative RT	35	56
Postoperative RTCT	14	22

pN stage: histologic N stage; RT: radiation therapy; RTCT: concomitant radiation and chemotherapy

**Table 2**

Oncologic results and predictive factors.

Results	Overall S.	Disease-specific S.	Recurrence-free S.
<i>Survival (%)</i>			
2 years	82	92	63
3 years	69	80	55
5 years	56	69	50
<i>Predictive factors</i>			
Gender: male/female	p (UV)/(MV) 0.002/<0.001	p (UV)/(MV) <0.001/0.04	p (UV)/(MV) 0.008/0.006
Age: </>70 years	0.80/-	0.24/-	0.89/-
ASA score: </≥3	0.001/0.006	0.03/0.57	0.009/0.11
Tumor location: larynx/hypopharynx	0.002/0.94	<0.001/0.005	<0.001/0.71
History of tracheotomy	0.58/-	0.36/-	0.96/-
N stage: N0/N ≥ 1	0.003/-	0.001/-	<0.001/-
pN stage: N0/N ≥ 1	0.003/0.70	<0.001/0.81	0.003/0.51
Perineural spread	0.17/-	0.04/0.26	0.14/-
Vascular embolism	0.001/0.006	<0.001/0.03	<0.001/<0.001
Capsule rupture	0.02/0.32	<0.001/0.16	0.01/0.04
Postoperative RT or RTCT	0.59/-	0.28/-	0.78/-

S.: survival; p (UV)/(MV):  $P$ -value on univariate (log-rank) and multivariate (Cox model) analysis. When N and pN (histologic N) stages were both significant on univariate analysis, only pN stage was carried forward in multivariate analysis (intercorrelated variables); RT: radiation therapy; RTCT: concomitant radiation and chemotherapy.

95% CI, 1.9–58.6) and vascular embolism ( $P = 0.03$ ; OR, 5.9; 95% CI, 1.1–30.1) showed significant negative impact on disease-specific survival; and female gender ( $P = 0.006$ ; OR, 5.6; 95% CI, 1.7–18.2), vascular embolism ( $P < 0.001$ ; OR, 5.1; 95% CI, 2.1–12.4) and capsule rupture ( $P = 0.04$ ; OR, 2.4; 95% CI, 1.1–5.4) showed significant negative impact on recurrence-free survival.

#### 3.3. Functional results

Table 3 shows functional results at 6 months posttreatment. Two patients died in the postoperative period (1 myocardial infarction, 1 infectious pneumopathy) and 1 patient showing early tumor progression could not be assessed for feeding at 6 months. Forty-nine patients out of the 60 assessed (82%) had feeding score = 2 (normal or slightly impaired): 10 (out of 15: 67%) with hypopharyngeal tumor and 39 (out of 45: 87%) with laryngeal tumor. Vocal results are presented for the 51 patients receiving a tracheoesophageal voice prosthesis (42 primary and 9 secondary) earlier than 4 months posttreatment (i.e., for >6 months for primary fitting and  $\geq 2$  months for secondary fitting). Four of the seven patients with circumferential TL/TPL received a voice prosthesis (1 primary, 3 secondary).

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