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Original article

Salvage surgery for recurrence of laryngeal and hypopharyngeal squamous cell carcinoma: A retrospective study from 2005 to 2013

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ABSTRACT

Objectives: Salvage surgery is the gold-standard treatment for locoregional recurrence of laryngeal and hypopharyngeal cancer following radiation therapy. Imperfect oncologic and functional results, however, require patient selection. The main objective of the present study was to determine preoperative factors for survival. Secondary objectives were to study 5-year overall and disease-free survival, general and locoregional complications, and functional results in terms of feeding and tracheotomy closure.
Patients and method: A retrospective multicenter study included 52 patients treated by salvage surgery for recurrence of laryngeal or hypopharyngeal squamous cell carcinoma after radiation therapy between 2005 and 2013.
Results: Factors associated with improved 3-year overall survival on univariate analysis comprised laryngeal primary ($P = 0.001$), laryngeal recurrence ($P = 0.026$), rT1, rT2 or rT3 rather than rT4 tumor ($P = 0.007$), previous chemotherapy ($P = 0.036$), and neck dissection during salvage surgery ($P = 0.005$), the last of these being confirmed on multivariate analysis. Five-year overall survival was 36.0% (range, 27.6–44.4%), for a median 23.04 months (95% CI, 19.44–26.64). Five-year disease-free survival was 23.5% (range, 16.0–31.0%), for a median 8.04 months (95% CI, 2.04–14.04).
Conclusion: Salvage surgery for laryngeal or hypopharyngeal cancer is difficult, and survival is not good. Laryngeal primary and recurrence location, moderate tumor volume and extension (<T4), prior chemotherapy and neck dissection during salvage surgery were associated with better overall and disease-free survival, which should enable better patient selection.

1. Introduction

With increasing use of concomitant radiation-chemotherapy in locally advanced cancer [1] and organ-preservation protocols [2], so-called "salvage" surgery in irradiated tissue is increasingly performed.

Surgery remains the gold-standard curative treatment in locoregional recurrence in these patients, for whom repeat radiation therapy is often precluded. However, it incurs complications rates often exceeding 60%, taking all complications together [3,4], with non-negligible perioperative mortality and sometimes long hospital stay, while survival can be poor: some teams reported 19% 2-year overall survival, with a median 19.4 months [4,5]. Palliative chemotherapy offers an alternative to salvage surgery, maintaining quality of life, which is a primordial concern for these patients. Impairment of quality of life following heavy surgery should be as short as possible and can only be justified by improved survival.

It would be useful to be able to select patients liable to find real benefit from salvage surgery, by identifying preoperative prognostic factors. Some studies have already sought to achieve this, proposing the following criteria: stage [4,6,7], patient age [6], local or regional relapse [4], primary location [8,9], and interval since primary therapy [7]. Samples, however, have either been homogeneous for tumor location but small [3], or larger but heterogeneous for location [4,8].

The main objective of the present study was to assess preoperative prognostic factors for overall and disease-free survival after salvage surgery for laryngeal or hypopharyngeal squamous cell carcinoma. Secondary objectives comprised assessment of functional results and local and general complications rates.

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2. Patients and method

Patients operated on for laryngeal or hypopharyngeal squamous cell carcinoma between January 1, 2005 and December 31, 2013, with history of locoregional radiation therapy for previous upper airway tumor were included. All medical data-files concerning total laryngectomy and total pharyngolaryngectomy performed in 2 university hospital centers in Lyon (France) between January 1, 2005 and December 31, 2013 were examined. History of radiation therapy was screened for to constitute the study sample. Fifty-two patients met the inclusion criteria.

Overall and disease-free survival were analyzed. Overall survival was defined as the interval between salvage surgery and death from all causes; surviving patients were censured at the date of last follow-up. Disease-free survival was defined as the interval between salvage surgery and onset of local, regional or remote recurrence; disease-free patients were censured at the date of last follow-up. Last follow-up was defined as the last follow-up appointment at time of study data harvesting.

Resection margins were classified on pathology as R0 (> 5 mm from resection edge), R borderline (< 5 mm from resection edge), R1 (in contact with resection edge), or R2 (macroscopically invaded margin).

Functional assessment concerned respiration and swallowing. Feeding was classified as normal, mixed (soft plus liquids) or enteral by nasogastric tube or gastrostomy. Fistula was screened for systematically at postoperative day 10 by a radionuclide esophageal transit.

Prognostic factors were defined in the light of the literature; age > 60 years, performance status (PS), tumor and lymph-node stage, primary radiation dose ≥ 60 Gy, history of chemotherapy, neck dissection during salvage surgery, local relapse, second location or progression, and ≥ 12 months' interval after end of radiation therapy.

Overall and disease-free survival were calculated following Kaplan-Meier. Associations between clinical parameters and overall and disease-free survival were tested on univariate and multivariate Cox models. All statistical analyses were performed on SPSS Statistics® software (version 23.0; SPSS Inc., Chicago, IL).

3. Results

3.1. Population characteristics

Fifty-two patients were included: 4 female, 48 male; mean age, 62.9 years. There were 17 hypopharyngeal (32.7%) and 35 laryngeal locations (67.3%). One patient with laryngeal recurrence had a single pulmonary metastasis accessible to laryngeal and bronchial curative surgery. Table 1 shows patient characteristics. Table 2 shows oncologic progression (tumor progression, local recurrence or second location) according to primary stage.

Table 1
Population data.

Characteristics	Patients (n = 52)	Percentage
Gender		
Male	48	92.3
Female	4	7.7
Age		
< 60 years	23	44.2
> 60 years	29	55.8
Mean	62.90	
Initial T stage		
T1	13	25
T2	20	38.5
T3	15	28.8
T4	4	7.7
Initial N stage		
N0	41	78.8
N1	4	7.7
N2a	0	0
N2b	3	5.8
N2c	2	3.8
N3	2	3.8
Initial M stage		
M0	51	88.1
M1	1	1.9
rT stage		
rT1	0	0
rT2	16	30.8
rT3	23	44.2
rT4	13	25
rN stage		
rN0	46	88.5
rN1	3	5.8
rN2a	2	3.8
rN2b	1	1.9
rN2c	0	0
rN3	0	0
rM stage		
rM0	51	88.1
rM1	1	1.9
Performance status (PS)		
PS0	0	0
PS1	49	94.3
PS2	2	3.8
PS3	1	1.9
PS4	0	0
Recurrence location		
Hypopharynx	17	32.7
Larynx	35	67.3
Primary location		
Oral cavity	2	3.8
Oropharynx	9	17.3
Hypopharynx	8	15.4
Larynx	33	63.5
Time to recurrence		
Progression (< 6 months)	12	23.1
Local recurrence (> 6 months)	22	42.3
Second location	18	34.6
Primary treatment		
Radiation therapy only	15	28.8
Surgery + radiation therapy	24	46.2
Induction chemotherapy + radiation therapy	14	26.9
Radio-chemotherapy	15	28.8
Type of primary radiation therapy		
Internal radiation therapy	2	3.8
T	15	28.8
N	1	1.9
T + N	35	67.3
Mean primary dose (Gray)		
T	67	
N	52	

3.2. Salvage surgery

Forty-eight procedures sacrificing the larynx (92%) and 4 sparing the larynx (8%) were performed. Larynx-sacrificing procedures comprised: 36 total laryngectomies (69%), 1 total laryngectomy with tongue-base extension (2%), 1 total laryngectomy with voice prosthesis in the same step (2%) and 12 total pharyngolaryngectomies (23%). Larynx-sparing procedures comprised: 2 supracricoid hemipharyngolaryngectomies (4%), 1 supraglottic laryngectomy with tonsillectomy (2%), and 1 tracheal resection and anastomosis (2%).

One patient (2%) received preoperative induction chemotherapy, with 2 courses of docetaxel and 5-fluorouracil, without cisplatin due to kidney failure, with partial response estimated at 50%; subsequently, tracheal resection and anastomosis and repeat radiation therapy were performed.

Fig. 1 shows the distribution of neck dissection performed during salvage surgery. Thirty-three patients (63.5%) had neck

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