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ORIGINAL ARTICLE

Prognostic value of the status of resection margins after endoscopic laser cordectomy for T1a glottic carcinoma

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KEYWORDS
Head and neck cancer;
Larynx;
Laser cordectomy;
Recurrence

Summary
Objectives: The small size of endoscopic laser cordectomy (ELC) specimens frequently leads the histopathologist to assess excision margins as pathologic. The present study sought to assess the prognostic value of margin status in terms of overall and of recurrence-free survival in a population of T1a glottic carcinoma operated on by ELC.
Material and methods: Sixty-four records of T1a squamous-cell carcinoma treated between 1996 and 2006 were retrospectively analyzed. Overall and recurrence-free survival for the group with negative margins (group 1) and with positive margins (group 2) were analyzed following Kaplan-Meier. The influence of resection margin histologic status was assessed on Log Rank test.
Results: Six female and 58 male patients were included. Forty (62.5%) had negative margins (group 1) and 24 (37.5%) positive margins (group 2). Overall five-year survival was 97% (95% in group 1 and 100% in group 2). Five-year recurrence-free survival was 94% (91.7% in group 1 and 95% in group 2). There was no significant difference in overall or recurrence-free survival according to resection margin histologic status.
Conclusions: The present results show that margins considered positive after laser resection do not significantly impact carcinologic course, while still requiring close surveillance. The most generally recommended attitude is control endoscopy with biopsy at 10 weeks.

Introduction

Endoscopic laser surgery has developed since the mid-1980s [1]. It is based on the same principle of *en bloc* resection as partial laryngectomy, but the endoscopic approach shortens hospital stay and simplifies postoperative course, notably avoiding tracheotomy [2,3]. Alongside radiation therapy, it

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is now one of the reference attitudes in incipient T1 and T2 glottic cancer [4—6]. No complementary treatment such as radiation therapy is usually indicated when resection margins are negative [6]; but these margins are often narrow (1—2 mm) because of the need to spare as much tissue as possible for functional reasons, making them hard to analyze [2,7,8]. Several authors recommended extemporaneous biopsy, but this runs up against practical problems of availability in certain centers and technical difficulties related to the unreliability of extemporaneous small fragment analysis [6]: it is not unusual for final histological analysis to be less favorable than the extemporaneous analysis, discovering non-negative margins. The problem for the clinician is then to decide between surveillance, surgical revision and radiation therapy.

Resection margin analysis following endoscopic surgery in incipient glottic cancer is problematic: the large number of margins judged positive seems not to be reflected clinically in a corresponding number of recurrences or treatment failures. The issue is very present in the literature [1,8—10]. The present study assessed the carcinological evolution of patients managed by endoscopic laser cordectomy (ELC) in our center whose resection margins were judged positive on definitive anatomopathological examination.

Material and method

A retrospective study was carried out on all patients managed by ELC for T1a glottic cancer in our center between 1996 and 2006. All had well to moderately differentiated invasive squamous-cell carcinoma on initial biopsy; in situ carcinoma was excluded.

ELC was indicated by perfect exposure of the anterior commissure, which never showed invasion in the present series. The absence of invasion of this region and of the fundus of the ventricle was checked during endoscopy using 0° and 70° scopes and by palpation under the operative microscope. ELC consisted in radical resection of a specimen including the tumor itself and a margin of about 1—2 mm of macroscopically healthy tissue. No extemporaneous biopsies were performed. The procedure was determined according to the European Laryngological Society Working Committee system [11,12]. All ELCs were performed by the same surgeon, experienced in laryngeal surgery, using a CO^2 laser (Lumenis 40-C; Sharplan, Tel Aviv, Israel), coupled to an operative microscope (Zeiss, Oberkochen, Germany), at 7—12 W in pulsed or superpulsed mode or, as of 2004, with the Lumenis AcuBlade system. The type of cordectomy performed was independent of the equipment (with or without AcuBlade).

Histological resection margin analysis was performed by the same team in all cases, with the same technique and criteria. Surgical specimens were fixed in 4% formaldehyde for 72 h, inked on their superficial (mucosal) and deep sides with two different colored inks before inclusion in their entirety and then sliced axially (parallel to the vocal folds) with 3—4 mm thickness. Positive margins were defined by in situ or invasive carcinoma in contact with the margin. All the study specimens were reassessed by an anatomopathologist.

A database was created on FileMaker Pro® (version 5) software. Statistical analysis of overall and recurrence-free survival used the Kaplan-Meier method. Prognostic factors were explored for by Log Rank test. All analyses used SPSS® software.

Results

Sixty-four patients were included: 9.9% of all glottic cancers managed over the study period ($n = 645$). There were 58 males (90.6%) and six females (9.4%); mean age at diagnosis, 61 years (range, 39—88 yrs). Twenty-six type-III (transmuscular) and 38 type-IV (complete) ELCs were performed.

Mean follow-up was 40 months (range, 6—149 mo), and comprised clinical examination by epipharyngoscope and/or flexible laryngoscope every 3 months for 2 years, then every 6 months. When recurrence was suspected clinically, cervicothoracic CT was performed, followed by endoscopy with biopsy under general anesthesia. There was no resort to postoperative radiation therapy.

Overall five-year survival in the series as a whole was 97%, and recurrence-free survival 94%.

In 40 patients (62.5%), margins were judged negative (group 1) and in 24 (37.5%) positive (group 2).

In group 1, two patients (5%) showed local recurrence, leading in one case to successful repeat ELC and in the other to total laryngectomy. Two patients (5%) died: one from recurrence (pulmonary and adrenal metastases) and one from a metachronic lung cancer. Mean interval to recurrence was 25.5 months. In group 1, overall 5-year survival was thus 95% and recurrence-free survival 91.7%.

In group 2, four cases of local recurrence (16.6%) were all successfully managed by ELC. One patient died of hepatocarcinoma 7 years after ELC. Mean interval to recurrence was 18.5 months (range, 6—31 mo). Overall five-year survival was 100% and recurrence-free survival 95%.

No significant difference between the two groups emerged for overall or recurrence-free survival according to margin status ($P = 0.524$ and $P = 0.55$, respectively; Figs. 1 and 2).

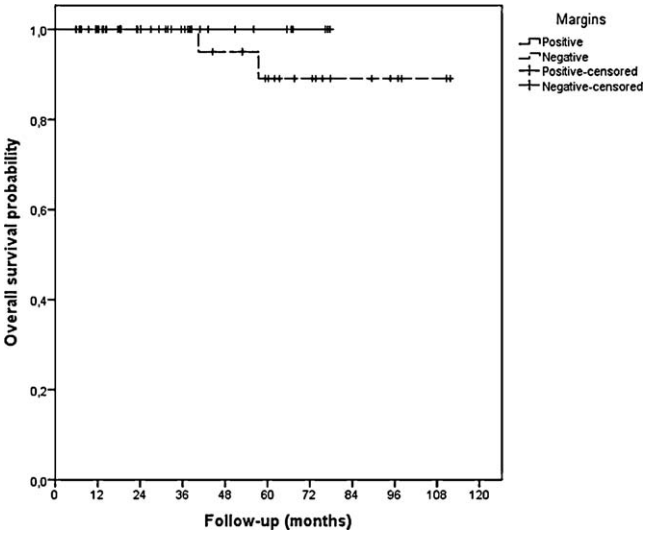

Figure 1 Overall survival in T1a glottic carcinoma according to margin status (Kaplan-Meier method).

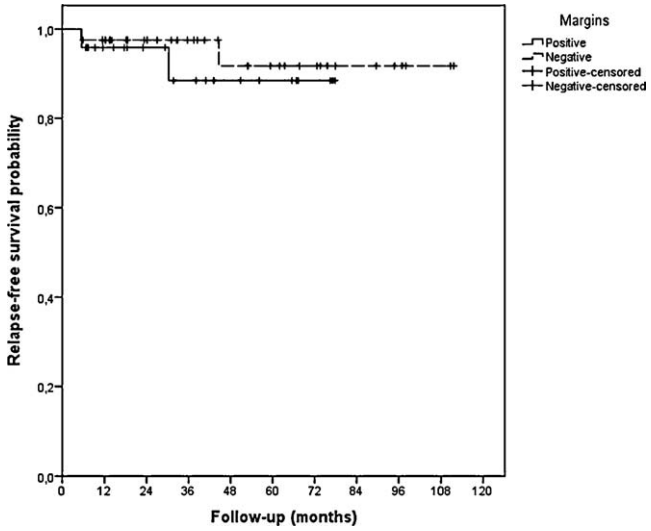

Figure 2 Recurrence-free survival in T1a glottic carcinoma according to margin status (Kaplan-Meier method).

Ten of the 24 group-2 patients underwent endoscopy under general anesthesia with biopsy targeting the pathologic resection region, 2—3 months after initial ELC: all proved negative, except one who was managed by repeat ELC; the others were followed up clinically, and by three monthly flexible laryngoscope surveillance over the first 2 years.

Five-year laryngeal conservation in the series as a whole was 98.4%.

Discussion

The objective of the present study was to analyze the prognostic value of resection margin status after ELC in T1a glottic carcinoma. In this series, margin status did not significantly influence overall or recurrence-free survival.

These survival results are in agreement with the literature. In 2004, Mendenhall et al. reported 80—90% local control after endoscopic laser surgery in T1 tumor [8]. Mortuaire et al., in 2006, reported 75% five-year recurrence-free survival, with recurrence correlating with pTNM status (22% in T1a) [13]. In 2007, Bronbo et al., reported 9.9% overall recurrence in 171 T1a glottic tumors after laser cordectomy [3]. Recurrence rates following ELC in glottic cancer ranged from 6 to 22% according to the series [13—17].

In 2000, Peretti et al. demonstrated that positive margins did not affect local control [18]; this was confirmed elsewhere [1,13]. In the present series, there was no significant difference in five-year overall or recurrence-free survival according to margin status. The present findings for both negative and positive margins agree with the literature.

In case of positive margins, most authors recommend control endoscopy with targeted biopsy [7]. In 2007, Jackël et al. reported that only 70 out of 382 patients (18%) undergoing systematic revision for positive margins showed neoplastic cells in the revision specimens [19]. The present study confirmed the absence of impact of negative or positive resection margins on overall survival or local recurrence. These findings, however, are to be interpreted with caution, as presence of cancerous cells cannot be considered a negligible fact. However, the large number of negative biopsy results a few weeks after resection margins had been assessed as positive testifies to the unreliability of a diagnosis of positive margin, probably due to small specimen size, thermal effects induced by the laser and/or tissue retraction. Biopsy of the tissue remaining after resection has been recommended, but is equally difficult to interpret, since there may be neoplastic cells in between the biopsy sites, making this safeguard illusory. According to Jackël et al., it is neoplastic cells in the revision specimen that counts as a prognostic factor for poor local control, rather than a positive margin in the initial specimen [19]. Peretti et al., in a study of 595 patients, reported that deep positive margins after laser revision had a negative impact on local control and laryngeal conservation without, however, affecting specific survival [20]; they recommended complementary treatment in case of laser revision of positive margins, stressing that such cases are rare and can be avoided by rigorous preoperative assessment [19,20].

There is no consensus as to the role of extemporaneous examinations in ELC. Our own team do not conduct them systematically. A recent study by Remacle et al., however, found they had a negative predictive value of 95% [9], enabling cordectomy to be extended in 10% of cases.

There is consensus on the non-indication of adjuvant treatment in case of initial positive margins [7,20]. The most frequent attitude in case of macroscopically negative but microscopically positive margins is endoscopy under general anesthesia some 10 weeks after ELC, with biopsies targeting the regions interpreted as being positive [7,19,20]; the interval allows the larynx to heal and provides histologically reliable results. Our own multidisciplinary meeting has recommended this attitude since 2006, before which, with no literature recommendations, the strategy was not applied — and thus not applied in the present study. The attitude in case of tumoral cells in targeted biopsy samples is currently discussed on a case-by-case basis in the multidisciplinary meeting.

Conclusion

The present study found that margins interpreted as being positive on anatomopathology after careful resection in macroscopically healthy tissue (i.e., ''satisfactory'' according to the surgeon) are not a pejorative factor for overall or recurrence-free survival in T1a patients operated on endoscopically. Adjuvant treatment such as radiation therapy or systematic surgical revision therefore does not seem indicated. The most frequently recommended attitude is control endoscopy with biopsy at 10 weeks.

Disclosure of interest

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

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