

Options for salvage after failed initial treatment of anterior vocal commissure squamous carcinoma

Patrick J. Bradley · Alfio Ferlito · Carlos Suárez ·
Jochen A. Werner · Eric M. Genden ·
Ashok R. Shaha · C. René Leemans ·
Johannes A. Langendijk · Alessandra Rinaldo

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Abstract Persistence or recurrent cancer in the anterior commissure (AC) after primary radiotherapy may remain localized to its pretreatment anatomical site. If so, endoscopic CO₂ laser excision, in experienced hands, may achieve complete tumor excision and result in cure for many patients. Occasionally, second and third recurrences may be similarly salvaged by further endoscopic surgery. The use of the vertical hemilaryngectomy is an alternative treatment for similar localized lesions, with a higher first time surgical tumor eradication rate, but with a more protracted hospitalization and a less satisfactory voice and swallowing outcome. In both types of such surgical salvage, CT scanning must demonstrate no evidence of cartilage invasion or destruction. When there is evidence of minimal thyroid cartilage invasion,

then the supracricoid partial laryngectomy is an alternative conservation option, and is likely to result in a cure, with the retention of a voicing larynx without a stoma. When the tumor has increased in size from the original pretreatment dimension and/or site, then imaging must be used to identify possible cartilage invasion, in which case the likelihood of tumor eradication by endoscopic or external vertical partial laryngectomy is highly unlikely. The indications for the routine use of total laryngectomy for the treatment of recurrent or persistent cancer involving the AC must be reviewed; there is current evidence that cure can be achieved by a less radical procedure. However, total laryngectomy may remain the only treatment option for advanced or aggressive first time recurrence, or in patients who develop

P. J. Bradley
Department of Otorhinolaryngology-Head and Neck
Surgery, Queens Medical Centre, Nottingham, UK

A. Ferlito (✉) · A. Rinaldo
Department of Surgical Sciences, ENT Clinic,
University of Udine, Policlinico Universitario,
Piazzale S. Maria della Misericordia, 33100 Udine, Italy
e-mail: a.ferlito@uniud.it

C. Suárez
Department of Otolaryngology,
Hospital Universitario Central de Asturias,
Oviedo, Spain

C. Suárez
Instituto Universitario de Oncología del Principado de
Asturias, Oviedo, Spain

J. A. Werner
Department of Otorhinolaryngology-Head and Neck
Surgery, Philipp-University Marburg, Marburg, Germany

E. M. Genden
Department of Otolaryngology-Head and Neck Surgery,
The Mount Sinai Medical Center,
New York, NY, USA

A. R. Shaha
Head and Neck Service,
Memorial Sloan-Kettering Cancer Center,
New York, NY, USA

C. R. Leemans
Department of Otolaryngology-Head and Neck Surgery,
VU University Medical Center,
Amsterdam, The Netherlands

J. A. Langendijk
Department of Radiation Oncology,
University Medical Center Groningen,
University of Groningen, Groningen, The Netherlands

subsequent recurrence following previous less aggressive surgery (endoscopic or external).

Keywords Anterior vocal commissure squamous carcinoma · Laser surgery · Partial laryngeal surgery · Supracricoid laryngectomy · Total laryngectomy · Radiotherapy

Introduction

Treatment for early stage glottic squamous carcinoma continues to be controversial, with some clinicians advocating surgery and others radiotherapy [1, 2]. It is reported that treatment can be equally effective with either partial laryngectomy (transoral endoscopic or open surgical resection) or external beam radiotherapy [3]. Failure rates with primary radiotherapy are reported to be 5–10% for T1 and 20–40% for T2 glottic cancers [4]. Tumors involving the anterior vocal commissure (AVC) are associated with a higher local persistence and recurrence rate than those without AVC involvement treated by radiotherapy [5]. A prospective clinical study [6] demonstrated that the results of 5 years survival in patients with cancers of the AVC treated by primary surgery were significantly better compared with results obtained by radiotherapy.

Kirchner and Carter [7] and Kirchner [8] found that T1a and T1b carcinomas rarely penetrated the anterior commissure (AC) tendon to invade the thyroid cartilage. AVC tumors that demonstrate cartilage invasion typically display surface invasion of the infrapetiolar region or extension to the subglottis (T2 by surface stage). Sessions et al. [9] recognized that the cartilage invasion associated with surface spread above and below the insertion of the vocal cords was a reflection of greater tumor volume rather than a predisposition of soft tissue disease at the AVC to invade cartilage. It has been stated that tumors of the AVC with supraglottic and/or subglottic extension also present a discrete propensity for extralaryngeal spread through the thyrohyoid membrane superiorly and the cricothyroid space inferiorly [10].

Treatment options for recurrent squamous carcinoma involving the AVC include conservation surgery options, principally endolaryngeal CO₂ laser surgery or vertical partial laryngectomy, supracricoid laryngectomy or radical surgery in the form of total laryngectomy [11].

Treatment options after failed primary radiotherapy

Transoral laser surgery

de Gier et al. [12] reported on a group of 17 patients with glottic cancer previously treated by radiotherapy

all extending into the AVC and all first recurrences treated by laser surgery. Twelve patients (71%) developed a second recurrence. Two of them had another laser procedure and were cured; the other ten patients required a total laryngectomy. Two of these developed a recurrence after total laryngectomy and died of their disease. Casiano et al. [13] reviewed the role of conservation surgery for radiation recurrent laryngeal carcinoma and reported an overall 5 years cure rate of 51% in previously irradiated patients vs. 62% in the nonirradiated group. However, if the AVC was involved, the probability of successful salvage laser surgery was significantly reduced, 45% vs. 65%, also agreed with Sewnaik et al. [14], 42% vs. 67%. A number of authors [15], including Casiano et al. [13] concluded that in case of tumor extension into the AVC, excision of the adjacent thyroid cartilage was indicated, and thus was considered to be a contraindication to laser surgery. de Gier et al. [12] also found that there was a higher recurrence rate after irradiation when the AVC was involved (71% vs. 46%). In this series, 40 patients who recurred after radiotherapy were treated by laser surgery. In 23 patients the recurrence did not extend into the AC and in 57% of this group a total laryngectomy could be avoided. At variance, only in 41% of 17 patients at whom the recurrence did extend into the AC a total laryngectomy was avoided. Based on these findings, they concluded that a total laryngectomy or partial laryngectomy through an external approach would have been preferable. In addition, they advocated that in case of tumor extension into the AVC laser surgery was a contraindication. This corresponds directly to the results described by Eckel [16] who was able to identify the AC as being the location with most local recurrences after initial laser microsurgery.

Steiner et al. [17] reported on their experience with CO₂ laser surgery in 34 patients with local recurrent squamous cell carcinoma of the glottis after full-course radiotherapy, including 21 patients (62%) with involvement of the AVC. Restaging was performed with preoperative magnifying laryngoscopy and CT scan, and none of the patients had thyroid or cricoid cartilage involvement. The authors experienced increased difficulty with identifying tumor in irradiated tissues and that the use of frozen section should be employed routinely. Moreover, all margins must be confirmed by permanent section in the post-operative period. Twelve out of the 21 patients (57%) with recurrent tumor after radiotherapy extending into the AC developed a second recurrence. Six patients underwent a total laryngectomy as salvage in this group of patients. The authors observed little difference in the number of subsequent recurrences between patients with and

without AVC involvement (57% vs. 54%); however, there was a difference between the two groups with respect to salvage laryngectomy in patients with commissural tumors (29% vs. 8%). Steiner et al. [17] stated that larger margins were necessary in resecting these tumors. In their series, in case of any evidence of tumor infiltration during laser surgery, a part of the thyroid cartilage was removed using the laser. In addition, the authors stated that only surgeons with great expertise should perform laser resections for recurrent carcinomas. An experienced surgeon and technical innovations for adequate exposure will contribute to success, so that AC involvement should not be considered an absolute contraindication to laser treatment. They recommend that contraindications for the use of CO₂ laser include: (1) fixation of both vocal cords or arytenoid cartilages, (2) gross infiltration of thyroid or cricoid cartilage detected by CT or MRI, and (3) extensive infiltration of the soft tissue of the neck.

The use of radiologic imaging is emphasized when the lesions involve the AC, and probably should be performed before starting any treatment of tumors involving the AVC [18]. The question arises on which modality of current imaging is better, CT or MRI? It has been reported [19] that either modality can detect extensive tumor infiltration passing completely through cartilage. In the non-irradiated patient evaluation of cartilage invasion has shown that MRI is more sensitive but less specific than CT (MRI tends to overestimate neoplastic cartilage invasion) [20, 21]. However, neither imaging modality could effectively define tumor involvement of the inner perichondrium. The problem remains how to identify tumor within the cartilage itself. However, there seems to be no work performed on the assessment in the irradiated cartilage, especially the AC. A novel method is warranted to overcome these difficulties and to identify suitable patients before embarking on certain laryngeal preserving operations. Barbosa et al. [22] set out to compare laryngoscopy and helicoidal axial CT scan for staging tumors involving the AC in a non-treated group of patients. They found that endoscopic evaluation understaged tumors, whereas helicoidal axial CT scan reformatted to 1.0 mm thick represented a highly effective approach to identifying invasion of the AC.

Many clinicians do not undertake routine imaging for T1 and early T2 glottic cancer. However, it has to be emphasized that before undertaking any form of salvage procedures it is extremely important to avoid an underestimation of the involvement of the visceral spaces and cartilaginous framework [23, 24]. If there is evidence of supraglottic or subglottic extension of

tumor located at the AVC, there is a great propensity for extralaryngeal spread and this should be suspected at the time of rigid endoscopy or when undertaking imaging. If doubt remains, an infrapetiolar exploration must be undertaken to exclude the presence of laryngeal framework involvement [24, 25]. If one or more of these diagnostic findings suggests cartilaginous infiltration, an endoscopic approach has a high risk of failure and exposes the patient to the persistence of disease.

In addition to cartilage infiltration, inferior extension has been cited as a potential pitfall to staging and treatment planning [26]. This may be difficult to assess using conventional imaging and is often not identified until the time of surgery. Intraoperative frozen section analysis is essential to provide assurance that the tumor has not been understaged. Other methods for identifying inferior extension include the use of rigid 30°, 45° and 90° endoscopes during the time of preoperative endoscopy. The rigid endoscope provides high magnification and excellent view of the infraglottic and subglottic regions.

Vertical partial surgery

In the 1950s the use of vertical partial laryngectomy had been generally recommended as an option for the treatment of early glottic cancer failure following curative doses of radiotherapy [27]. In the 1990s, a number of authors reported on larger series of patients treated with vertical partial surgery for recurrent tumor with AVC involvement. Kooper et al. [28] treated 61 patients and achieved local control in 85% of the cases. DelGaudio et al. [29] treated 22 patients with a control rate of 82%, Lavey et al. [30] treated 25 patients with a 96% control rate. Although the local control rates achieved with hemilaryngectomy were higher compared with those achieved with endoscopic procedures, hemilaryngectomy produces a longer hospitalization and a greater risk of complications, including soft tissue wound infection, chondritis, persistent laryngeal edema, and a higher rate of thoracic infections when compared with endoscopic approaches. Postoperative complications were reported to occur in up to 20% of cases [28]. All patients required a temporary tracheostomy—which was permanent in some cases.

Furthermore, Sewnaik et al. [14] compared the results of two types of partial laryngectomies in patients with radiation failures: group I received endoscopic laser surgery ($n = 42$), and group II frontolateral partial laryngectomy ($n = 21$). With CO₂ laser treatment, 14 of 24 patients (58.3%) with no involvement of

the AC and 8 of 18 patients (44.4%) with involvement of the AC were cured. With the frontolateral partial laryngectomy, they achieved local control in 15 of 21 patients (71.4%).

In a series reported by Ganly et al. [3], 23 out of 43 patients (54%) who underwent salvage surgery following primary radiotherapy for T1–T2 glottic tumors, between 1984 and 1998 at the Memorial Sloan–Kettering Cancer Center, New York, had involvement of the AC. Most of these patients (77%) underwent total laryngectomy. The 5 years overall survival was 68% for the entire group and 89% among those that underwent partial laryngectomy. One out of 21 patients (5%), that underwent partial laryngectomy salvage procedures developed a local recurrence and was ultimately treated by total laryngectomy. Based on these findings, the authors concluded that careful selection of patients with early stage tumors that recur or progress after radiation allows for successful treatment by partial laryngectomy with excellent survival outcome. In that series, patients requiring a total laryngectomy experienced poorer survival outcome, which was mainly due to the adverse prognostic factors, including AVC involvement and subglottic involvement at presentation.

The main question is which patients are candidates for partial laryngectomy for local recurrence following radiotherapy. A number of authors stated that recurrent and/or persistent disease should not extend beyond its original limits [31–33]. The same authors emphasized the need to achieve surgical excision margins greater than 1 mm, thus recommending the use of intraoperative frozen section. However, based on the findings of their own series, Lydiatt et al. [34] questioned reliability of the marginal status of the resection specimen when performing salvage partial laryngeal surgery following radiotherapy. They found that the margins were always relatively close in conservation laryngeal surgery and that the pathological report frequently was not consistent with the intraoperative findings of the surgeon. This requires the surgeon to make an intraoperative judgment call regarding the adequacy of the resection margins. A surgeon dissatisfied with the completeness of the resection is an indication for further treatment, i.e., additional surgery almost always in the form of total laryngectomy. However, it would seem logical that surgical attempts must be made to excise all tumors by whatever methods of surgery employed [35]. It is mandatory that all such patients treated by vertical hemilaryngectomy should be followed up closely using symptom documentation especially pain, endoscopy, imaging and biopsy if necessary to ensure that their treatment is successful and

that further tumor growth is not developing in the laryngeal remnant [36].

Supracricoid laryngectomy

Laccourreye et al. [37] described their experience with the use of the supracricoid partial laryngectomy for primary recurrence after radiotherapy not amenable to vertical or horizontal partial laryngectomy. Seven out of their 9 patients had glottic cancer with AVC involvement and the majority of these patients had tumor that exceeded the original limits. In their series, there were two local failures reported but relevant details of these two patients were not described. However, it was found that the duration of the tracheostomy was twice as long (15 days on average) in the non-irradiated patients previously treated by supracricoid partial laryngectomy versus the post-irradiated patients. They concluded that, though retrospective, their results were encouraging.

In another series, Spriano et al. [38] reviewed 15 patients who underwent supracricoid partial laryngectomy. In two patients the pathology of the thyroid cartilage specimens showed infiltration by tumor (pT4), although the CT scan performed before surgery was negative. Both patients were still alive at follow-up 39 and 98 months, respectively. The authors stated that their indications and contraindications for performing supracricoid partial laryngectomy after failure of radiotherapy were similar to those specified for patients with previously untreated laryngeal tumors. The only exception was selected T4 lesions demonstrating infiltration of the thyroid cartilage, in which they do not perform supracricoid laryngectomy.

Another series [39] reported on 23 patients, in which supracricoid partial laryngectomy was performed for salvage after failure of radiation therapy in patients with T1–T2 glottic cancer. Sixteen of these cases had extension of tumor to involve the AVC. No patient had subglottic extension of more than 5 mm or an extension to the cartilage on the CT scan. Four of the patients who had AVC invasion recurred within 24 months and were controlled by total laryngectomy. Of interest was that no recurrences were recorded for the two patients staged T1b who had histological extension to the anterior part of the thyroid cartilage (pT4).

Finally, Rifai et al. [40] performed a supracricoid laryngectomy in 45 cases of recurrent AC carcinoma with a rate of control of local spread at 2 years of 95.4%. These results indicate that supracricoid laryngectomy is a suitable alternative to total laryngectomy under oncologic and functional points of view in most of the cases of AC involvement.

Treatment options after failed conservation primary surgery

Transoral laser surgery

The use of the CO₂ laser does not preclude its further use for persistent or multiple recurrent disease [12, 17]. However, recurrences in patients treated by external surgical methods require a total laryngectomy.

Total laryngectomy

Performing a total laryngectomy for persistence or recurrent treated AC carcinoma is certainly the most likely method of eradicating tumor and preserving life in the majority of patients who have failed previous conservation treatments. Some surgeons considered salvage laryngectomy as the safest choice in patients with recurrence in the AC [17]. Experienced clinicians consider that surgical salvage is often performed by total laryngectomy because of lack of experience in the technique of conservation surgery of the larynx, as well as some believe that partial laryngectomy of irradiated cartilage is associated with an increased risk on complications and that negative tumor margins are difficult to achieve in a fibrotic edematous larynx [3].

The use of imaging has also been emphasized as part of the selection of patients for partial or total laryngectomy [34, 36] and it is recommended that a total laryngectomy be performed if there is gross cartilage invasion, vocal cord fixation, extensive subglottic disease, or recurrence beyond the original limits seen on the CT scan or MRI.

Performing a total laryngectomy may be the treatment of choice for all patients who develop recurrences after primary radiotherapy [41], and usually reflects the local surgical expertise or nursing support. Total laryngectomy may be indicated when other conservation attempts have failed, such as endoscopic CO₂ laser surgery [12, 14, 17], vertical partial laryngectomy (any type) [3, 11, 14, 28, 29, 35], or even partial supracricoid laryngectomy [14, 37, 39], without compromising ultimate local control in the majority of patients. Peristomal recurrence has been seldom reported [29].

It would appear that performing supracricoid partial laryngectomy has extended the surgical aggressiveness to achieve cancer eradication in selected cases, including some selected patients who have minimal thyroid cartilage invasion. Complete excision of the tumor should be the goal, whereas the voice and swallow quality may not be as good as that achieved by endoscopic laser surgery, and also a lesser quality of function is noted than following vertical partial surgery.

Radiotherapy

The use of radiotherapy after transoral laser surgery, vertical partial laryngectomy or supracricoid laryngectomy is a treatment option, which has not been reported in the series reviewed. A single case of local recurrence after supracricoid laryngectomy cured by radiotherapy, has been reported by Laccourreye et al. [42]. It is very likely that other cases have been treated in the past with salvage radiotherapy, but specifically may not have been cancers involving the AC. Patients previously treated surgically who recur locally are likely to have tumors that are very large, with soft tissue involvement and thus unlikely to be suitable for treatment with curative intent using radiotherapy. However, in selected patients or in patients who are unwilling to consider losing their larynx, then the use of modern radiotherapy methods, such as IMRT or the addition of chemotherapy, may indeed achieve organ preservation and control of the cancer. Such patients need to be identified and reported to support salvage radiotherapy after failed primary partial laryngeal surgery for cancers involving the AC.

Evaluation and management of the neck

In patients who present after failed primary treatment, it must remain the goal of the treating clinician to evaluate the patient totally and commence with the re-staging of the disease. This not only includes the primary site, but the other likely mucosal bearing areas, as well as the possibility of neck node metastases. It is well recognized that early tumors that persist, or if there are close tumor margins, then the possibility of nodal metastases is increased. Therefore, as part of the evaluation of such patients, imaging of the primary tumor, the neck, as well as the chest must be performed and appropriate management offered depending on the findings.

In conclusion, in selected cases, different salvage partial laryngectomy procedures are available for early glottic cancer that invades the AVC, and thus allowing for more patients to avoid total laryngectomy.

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