

Current treatment of T1N0 squamous cell carcinoma of the glottic larynx

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The optimal treatment of patients with T1N0 squamous cell carcinoma (SCC) of the glottic larynx remains controversial [1–3].

T1 glottic SCC as defined by the AJCC/UICC system [4] is “Tumor limited to the vocal cords (which may involve the anterior or posterior commissure) with normal mobility”. This disease stage is further subdivided into T1a: tumor limited to one vocal cord, and T1b: tumor involving both vocal cords. Accurate assessment of the true T stage of glottic SCC (disease invasion of contiguous tissues) requires careful clinical, endoscopic and

stroboscopic examination. Radiological imaging methods to determine the extent of disease is usually not needed in T1 glottic SCC except for tumors at the anterior commissure [5]. The use of functional assessment of voice, both pre-treatment and again at an agreed upon post-treatment time (12 months) may be very useful in evaluating vocal function. However, no standard test of voice quality has been universally accepted although standardized protocols for functional assessment have been suggested [6].

Treatment options for T1 glottic SCC include radiotherapy (RT), transoral laser resection (TLR), and open partial laryngectomy [7–10]. Voice quality after open partial laryngectomy is significantly worse compared to RT and TLR so that this alternative is rarely employed. The

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role of chemotherapy alone in early stage laryngeal cancer (including glottis) remains investigational [11, 12].

The decision whether to select RT or TLR for the treatment of T1 glottic SCC depends on a number of factors, including the location and extent of the tumor, the medical condition of the patient, the likelihood of tumor control after treatment, anticipated functional outcome (voice quality), the expertise of the attending physicians and logistical considerations. In this complex decision-making process, we should also include patient preference, after an informed discussion of the pros and cons of each treatment modality.

Controversies regarding the best option for treatment exist because of the lack of high-quality prospective randomized trials comparing these modalities of treatment [3, 13]. Both treatment options are characterized differently. TLR can be done as a single procedure on an outpatient basis, whereas RT is delivered once daily on weekdays over 5–7 weeks. The likelihood of local control after RT or TLR is equivalent and is approximately 85–95 % [1–3]. However, in the reporting of local control after TLR, there is a difference between local control after the first procedure and “ultimate” local control after a subsequent TLR. In interpreting these data, one needs to understand that selection bias may exist in choosing the treatment employed. An advantage of RT is that it is applicable to all patients with T1N0 SCCs. TLR is usually applied in less-advanced tumors as most physicians keep in mind the fact that the more of the glottis that is involved with SCC, requiring a wider resection, the poorer the voice quality after resection [8, 14]. Thus it is likely that the more favorable cases are included in the reports on outcomes from TLR.

In some patients with very limited midcord lesions, the biopsy taken for diagnostic purposes may in fact have completely removed the small and superficial tumor; a fact demonstrated if followed by TLR but remaining in question if followed by radiotherapy. However, the absence of tumor in the re-excision specimen implies that it has either been completely removed by the biopsy or is not found (missed) by the pathologist. The only way to know whether a diagnostic biopsy has completely removed the tumor is to serially section the biopsy specimen for margins and administer no additional treatment, either TLR or RT.

Voice quality is reported to be comparable for both treatment modalities but again a selection bias may have been introduced in retrospective analyses [5, 8, 15], and although both TLR and radiotherapy have been found to offer similar objective measurement results, it seems that, from the patient’s perception, there is a reduced impact on voice quality after RT [16, 17]. Another advantage of TLR is that it can be repeated several times in contrast to RT. The ability to repeat TLR may contribute to the fact that

the likelihood of laryngeal preservation may be higher when TLR can be offered as initial treatment [3, 5]. Many patients with recurrences after RT will undergo total laryngectomy. However, laryngeal preservation may be feasible with salvage open partial laryngectomy or TLR in selected patients after radiation failure [18–20]. About one-third of such recurrent cancers are suitable for conservation surgery [21]. Patients with anterior commissure involvement will provide technical challenges and, even in experienced hands, may have local control rates that are somewhat lower compared with T1 SCCs without anterior commissure invasion [5, 22]. Efficacy of RT is not affected by involvement of the anterior commissure. However, voice quality is likely to be worse after TLR in these cases. Patients with significant medical co-morbidities who are poor candidates for anesthesia may be better treated with RT. On the other hand, some frail elderly patients may prefer the short procedure of a TLR over a full course of radiotherapy. Another important point to be taken into consideration is that in several studies TLR appeared to be the most cost-effective treatment of early glottic SCC, radiation therapy being two- to fourfold more expensive [15, 23]. The presence and extent of a cost differential will vary with the medical system.

The selection of patients for either treatment modality depends on all of the above-mentioned factors and this may also explain the lack of prospective randomized trials comparing both modalities. To randomize patients with T1 glottic SCC between RT and TLR without consideration of the above-mentioned factors such as, e.g. extent and depth of invasion of the tumor (rather than T classification as such), occupation and social context of the patient, patient preferences, comorbidity, etc., may be considered unethical and will make the design of a prospective study very difficult. Attempts at conducting such a trial have met with significant difficulties in accrual, and it has been deemed to be nearly impossible to conduct such a trial [13].

The only prospective comparison of RT and TLR for T1aN0 glottic SCC reported so far included only 56 patients over a 10-year period [24]. At 24 months post-therapy, a more breathy voice and wider glottis gap were found after TLR. Also, irradiated patients reported less hoarseness-related inconvenience in daily living, although overall voice quality and local control were similar between the two groups. Small patient numbers not allowing identification of eventual further differences between the treatments, short follow-up and absence of information on important voice quality modifying parameters (e.g. smoking habits, also having an adverse effect during RT) preclude firm conclusions. It seems, however, that RT may be preferred treatment option for patients with more demanding requirements for voice quality.

In case RT is the selected treatment modality, a successful fractionation schedule for T1 glottic cancer is 63 Gy in 28 once-daily fractions [25, 26]. Despite the very low probability of a significant complication after this treatment, many radiation oncologists prefer a more protracted schedule [25]. The reimbursement schedule in some countries, including the United States, increases with the number of fractions (treatments) thus creating a potential conflict of interest. For whatever reason, many radiation oncologists (in North America and elsewhere) select a commonly employed fractionation schedule that consists of 66 Gy in 33 fractions, which produces a significantly inferior result [25, 26]. Recently, the American College of Radiology (ACR) Expert Panel on Radiation Oncology—Head and Neck Cancer developed consensus recommendations for treatment of T1 glottic SCC. They concluded that “Treatment planning is complex and decisions nuanced”. And “Best treatment for a particular cancer cannot be defined without consideration of the lesion’s location, extent, depth of invasion, and quality of surgical exposure during direct laryngoscopy” [26]. But regardless of the modality chosen, physicians should track their own patient’s functional and disease-free survival data rather than rely on the best reported (published) results from the most experienced institutions. Analysis of outcomes should include tumor control, survival, functional outcomes (quality of voice) and larynx preservation rates.

In conclusion, the choice between treatment modalities for early stage glottic SCC should be based on careful considerations of all the factors discussed above, and made by the clinician and the patient. For optimal decision-making, the anticipated oncological and functional outcome from each treatment strategy should be considered. It is important to bear in mind that any physician or a specialist treatment center for early glottic SCC, is aware of their own outcome results.

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