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PRIMARY RADIOTHERAPY FOR GLOTTIC LARYNGEAL CARCINOMA STAGE I AND II

A retrospective study with special regard to failure patterns

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Abstract

A retrospective study has been made of 302 patients with vocal cord carcinoma stage I and II treated between 1963 and 1983, emphasizing treatment failure patterns. The primary treatment modalities were radiotherapy for 266 patients and surgery for 36 patients. The minimum follow-up was 4 years. After primary radiotherapy there were 63 local recurrences and 7 neck lymph node recurrences, all appearing outside the target volume. The actuarial loco-regional recurrence-free rates at 5 years were 78% for T1, 76% for T2a (normal cord mobility) and 60% for T2b (imparied cord mobility) tumors. The actuarial regional lymph node recurrence-free rates at 5 years were 99, 100 and 93% for T1, T2a and T2b tumors respectively. The actuarial corrected survivals at 5 years were 95, 96 and 79% for T1, T2a and T2b tumors with primary radiotherapy and salvage surgery for recurrence. Salvage surgery was less successful in T2b compared to T1 and T2a tumors. In conclusion, after primary radiotherapy with salvage surgery the loco-regional control rate was high and very similar for glottic cancer T1 and T2a but less satisfactory for T2b tumors. Regional lymph node metastases were not a large problem in any of the subgroups. More effective radiotherapy with higher dose levels or an altered fractionation might increase the local control rate for T2 tumors with impaired cord mobility.

Key words: Radiotherapy, glottic carcinoma.

Early glottic cancer limited to the vocal cord stages as T1 is generally considered to be radiocurable and in most treatment centres radiotherapy alone is the treatment of choice. Very high cure rates have been reported and in about 90% of the patients the larynx can be preserved (1–4). Failures after radiation treatment can usually be rescued by laryngectomy or sometimes by more conservative surgical procedures. For T2 tumors as well, radiotherapy alone has given excellent local control rates with surgical rescue (4–6). For larger lesions, however, where fixation of the vocal cord is seen, considerable controversy exists concerning a similar therapeutic approach. It has been suspected that radiotherapy alone for such tumors gives so much lower local control rates that despite successful rescue surgery, the survival of patients could be jeopardized (4, 7–9). In the UICC classification glottic cancers are staged as T2 because of either mucosal supra- or subglottic extention or limited cord mobility. For the latter subgroup a worse prognosis has also been reported by some authors (4, 6, 10, 11). One suggested reason for this is an earlier regional spread. Carcinomas limited to the true vocal cords practically never give lymph node metastases, while such metastases not infrequently occur in cancers extending beyond the true cords. This difference is probably due to differences in the capillary network between the vocal cords and the surrounding tissues. Therefore, different treatment policies exist regarding definition of the target volume for radiotherapy based on different views on the risk of spread to regional lymph nodes.

In the series now reported, in which mainly radiotherapy was the primary treatment for T1 and T2 glottic cancers with surgery reserved for failures, the regional lymph nodes were not included in the target voume. The impact of such a policy on local control, regional spread and survival will be discussed on the basis of a retrospective analysis.

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Material and Methods

Totally 302 patients with primary carcinoma of the vocal cords stage I and II (UICC 1978 (12)) were referred to the Sahlgrenska Hospital between 1963 and 1983 and all had histologically confirmed squamous cell carcinoma. All patients were seen and discussed by both head and neck surgeons and radiation oncologists concerning treatment modality. The primary treatment modality was curative radiotherapy for 266 patients and surgery for 36 patients. Since 1978, all patients with glottic cancer T1 N0 M0 and T2 N0 M0 have received radiotherapy as the primary treatment. In retrospect, from the medical records, it was not possible to find any clear reasons why in some patients primary surgery was used instead of radiotherapy.

The ages of the patients in the radiotherapy group ranged from 34 to 92 years (mean 64 ± 11 SD years). The treatment failure analysis was done separately for T1a N0 M0, T2a N0 M0 (normal cord mobility) and T2b N0 M0 (impaired cord mobility). The subdivision of T2 tumors has been suggested by serveral authors on a prognostic basis (4, 6, 10, 11). The number of patients in each subgroup is presented in Table 1.

Primary radiotherapy. All tumors were irradiated with ^{60}C-γ-beams or 5 MV photon beams in most of the patients with 2 oblique wedge filter beams (Fig. 1). The field size ranged between 4 cm × 4 cm and 7 cm × 7 cm, on average slightly larger for T2 than for T1 tumors. Some patients were irradiated with two lateral opposed fields and larger field size. Histograms over the used field size are presented in Fig. 2.

During the 20-year period the total dose as well as the fractionation schedules were made to vary. The total dose

Table 1

Primary treatment, glottic cancer stage I and II, 1963–1983

Stage	Radiotherapy n	Surgery n
T1	134	3
T2a	79	19
T2b	53	14

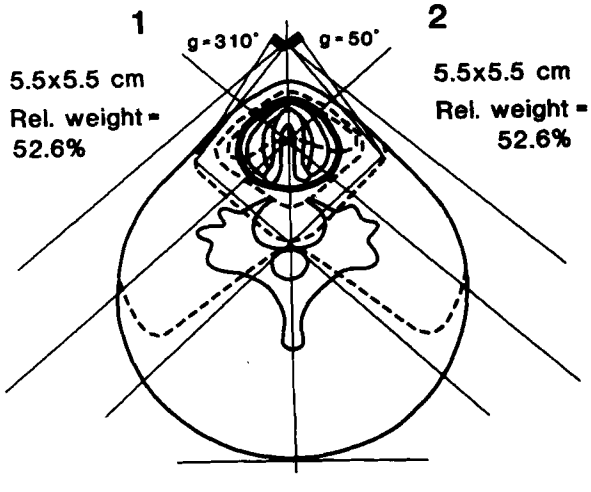

Fig. 1. Dose distribution for treatment of glottic T1, T2a and T2b tumors. Solid line: tumor area. Dashed line: isodoses of 100% (inside the tumor area), 95% (surrounds the tumor area) and the dose gradient represented by the 50% and 20% isodoses.

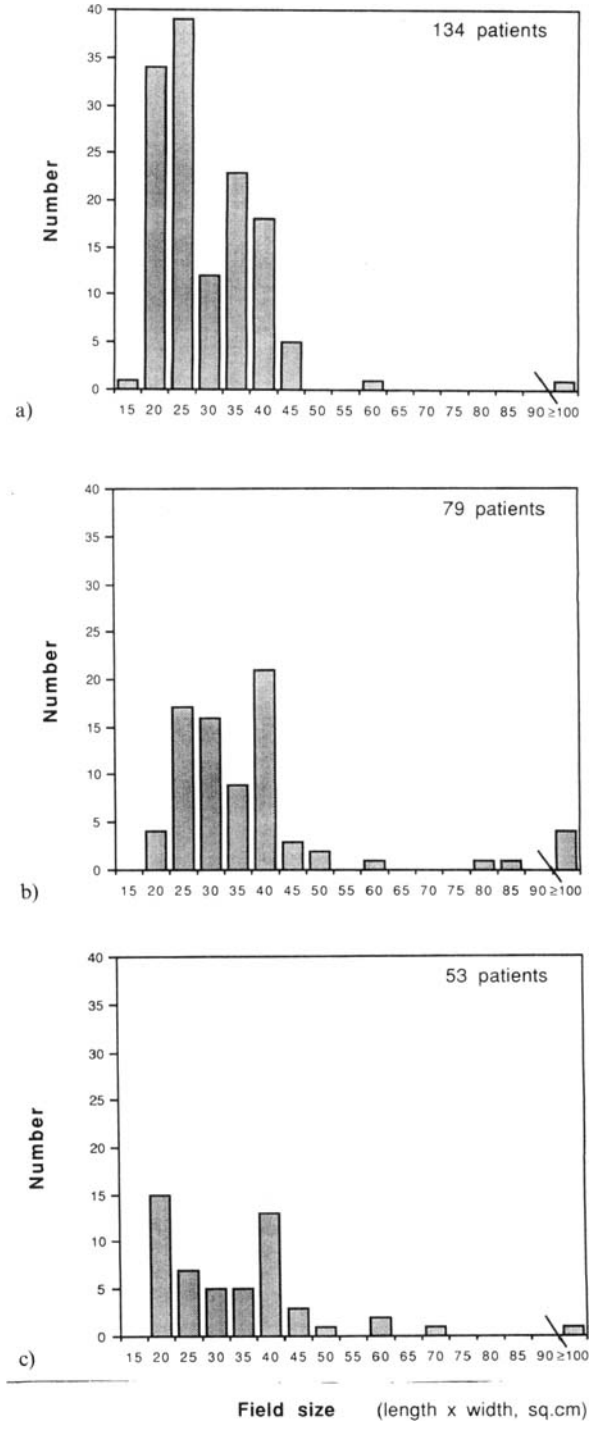

Fig. 2. Filed size distribution for radiotherapy of glottic tumors. a) T1; b) T2a; c) T2b tumors.

varied between 46.2 and 83.8 Gy. Four to 5 fractions/week and also 2 fractions/day were used. The fraction size varied between 1.4 and 3.9 Gy and the overall treatment time between 16 and 159 days. Split course radiotherapy was fairly common. On average T2 tumors received slightly higher total doses than T1 tumors. Otherwise, there were no systematic differences in fractionation between the 3 subgroups. A separate fractionation and dose-response analysis will be presented in a later paper.

Primary surgery. Three patients with T1 were operated by partial laryngectomy. Of the 19 patients with T2a tumors, 11 had laryngectomy plus neck dissection; 7 patients in each group had preoperative radiotherapy. One patient had partial laryngectomy only. Of the 14 patients with T2b tumors, 7 had laryngectomy and 7 laryngectomy plus neck dissection; 5 patients in each group had preoperative radiotherapy. The preoperative radiotherapy was usually given with laterally opposed fields including the anterior neck lymph node chain.

Treatment failure analysis. The local and regional recurrence-free rates and corrected survival were calculated by the life-table method (13). Results were calculated from the first day of treatment. Patients who died from intercurrent disease without known recurrence were censored from the calculations of recurrence-free rate and survival rate on the day of their death. All patients were followed up regularly 6 times the first year and then 3 to 4 times a year for 5 years followed by 1 to 2 times a year up to 10 years. Thereafter the patients' health was checked by questionnaire once a year. The minimum follow-up of this patient group was 4 years. All histologically verified malignancies after treatment elsewhere in the larynx or in a neck lymph node were registered as recurrence.

Results

Recurrence rates after primary radiotherapy

Figs 3–5 present the actuarial recurrence-free rates after primary radiotherapy for stages T1, T2a and T2b versus follow-up and the absolute number of recurrences for the following 4 categories: 1) local recurrence only, 2) regional recurrence only, 3) local plus regional recurrences, and 4) local and/or regional recurrences, which means categories 1–3 altogether.

Local recurrence. For T1, T2a and T2b tumors the numbers with local recurrence were 27, 18 and 15 out of 134, 79 and 53 treated patients respectively, and the local recurrence-free rates were 79, 77 and 70% at 5 years and 79, 72 and 65% at 10 years (Figs 3–5).

Regional lymph node recurrence. For T1, T2a and T2b tumors the number of regional node recurrence were 1, 0 and 3 respectively and the regional node recurrence-free rates were 99, 100 and 93% at 5 and 10 years (Figs 3–5).

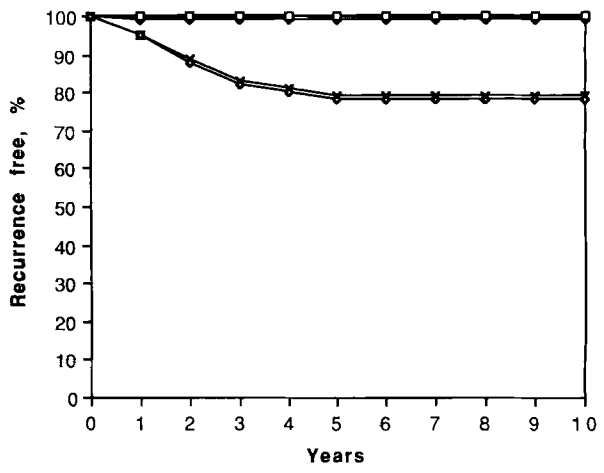

Fig. 3. Actuarial recurrence-free rates during 10 years follow-up of 134 patients with glottic T1 tumors. —×— local recurrence only (n = 27); —◆— regional node recurrence only (n = 1); —⊟— both local and regional recurrence (n = 0); —◇— all locoregional recurrences (n = 28).

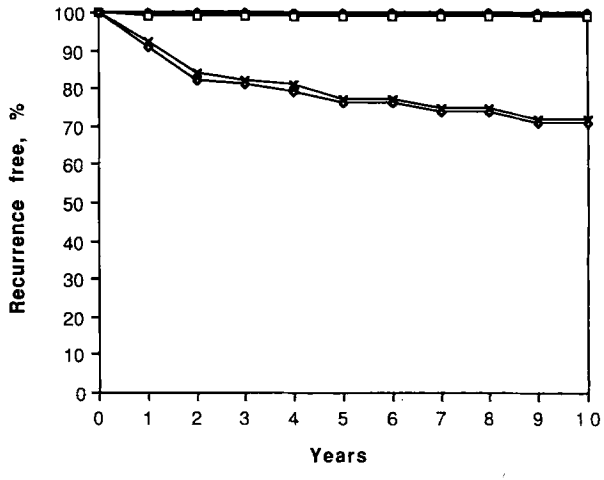

Fig. 4. Actuarial recurrence-free rates during 10 years follow-up of 79 patients with glottic T2a tumors. —×— local recurrence only (n = 18); —◆— regional node recurrence only (n = 0); —⊟— both local and regional reccurrence (n = 1); —◇— all locoregional recurrences (n = 19).

Local plus regional lymph node recurrences. For T1, T2a and T2b the numbers with both local and regional node recurrences were 0, 1 and 2 respectively and the recurrence-free rates were 100, 99 and 95% at 5 and 10 years (Figs 3–5).

Local and/or regional recurrences. For T1, T2a and T2b the total numbers of loco-regional recurrences were 28, 19 and 20 respectively and the recurrence-free rates were 78, 76 and 60% at 5 years and 78, 71 and 55% at 10 years (Figs 3–5).

Irrespective of stage, the rates of regional lymph node metastases are very low compared to the rates of recurrence of the primary tumor of the vocal cords; there were

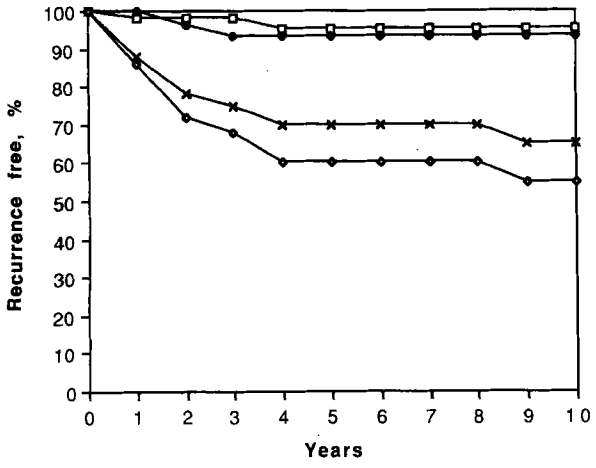

Fig. 5. Actuarial recurrence-free rates during 10 years follow-up of 53 patients with glottic T2b tumors. —×— local recurrence only (n = 15); —◆— regional node recurrence only (n = 3); —⊟— both local and regional recurrence (n = 2); —◇— all locoregional recurrences (n = 20).

totally 7 node recurrences versus 63 local recurrences in this patient group. All neck node recurrences appeared outside the treated volume.

Influence of field size. The field size, s, was divided into three subgroups: $s \leqslant 30\,cm^2$, $30 < s \leqslant 40\,cm^2$, and $s > 40\,cm^2$. The 5-year local control rates were 81, 77 and 68% for T1, 69, 83 and 77% for T2a and 73, 61 and 51% for T2b.

Recurrence rates after primary surgery

Table 2 presents the rate of regional neck lymph node metastases for T1, T2a and T2b among the patients who had primary surgery. There were only 2 patients with node metastases, both in the T2a (stage IIa) group. The node recurrence in the preoperative group appeared within the treated volume given 20 Gy. The node recurrence in the operated group appeared in one of the patients treated with primary laryngectomy only. There was no stomal recurrence after primary surgery but 2 local recurrences after partial laryngectomy (one in the T1 group and one in the T2a group).

Table 2

Glottic cancer (n = 36). Primary laryngectomy, 1963–1983

	Stage		
	I	IIa	IIb
Preop. radiotherapy	0/0	1/14 (7)	0/10 (5)
No preop. radiotherapy	0/3	1/5 (0)	0/4 (2)

Figures in parentheses = also primary neck dissection

Cumulative recurrence rate, salvage surgery and survival after primary radiotherapy

After primary radiotherapy the cumulative loco-regional recurrence rates were 31, 64, 79, 88 and 94% at 1, 2, 3, 4 and 5 years. There were no differences in this pattern between T1, T2a and T2b tumors. The remaining recurrences appeared at 83, 98, 104 and 193 months. All these engaged the vocal cords and 3 of them appeared at the primary site.

Table 3 presents the number of patients salvaged by surgery out of the radiotherapy failures. Totally 47 patients out of 60 (78%) with local recurrence were salvaged by surgery. Considering T1, T2a and T2b separately the percentages salvaged by surgery were 81, 83 and 67% respectively. Two patients out of 4 with nodal recurrence were cured by neck dissection. None of the 3 patients with both local and regional recurrence were rescued by surgery.

After primary radiotherapy and surgery of failures the corrected survival rates at 5 and 10 years were 95 and 94% for the T1 groups, 96 and 92% for the T2a group, and 79 and 79% for the T2b group. The difference between stages T2a and T2b reflects the less successful surgery of local recurrences in T2b tumors. After primary surgery 1/3 in the T1 group, 1/19 in the T2a group and 0/14 in the T2b group died from their glottic cancer.

Discussion

Data in the present report confirm that most stage T1 and T2 glottic tumors can be loco-regionally controlled with primary irradiation, thereby preserving the patients' voices. This is evidenced by an actuarial loco-regional recurrence-free rate at 5 years of about 80% for T1 tumors, 75% for T2 tumors with freely mobile vocal cords

Table 3

Salvage surgery of radiotherapy failures

	Stage		
	I	IIa	IIb
Local recurrence	22/27	15/18	10/15
Regional recurrence	1/1	0/0	2/3
Local-regional recurrence	0/0	0/1	0/2
Total	22/28 (79%)	15/19 (79%)	12/20 (60%)

(T2a) and about 60% for T2 tumors where cord mobility is impaired (T2b). It is quite evident from this analysis that regional failure in the neck is not the main problem in radiotherapy of T1 and T2 glottic cancers. With the present definition of target volume, where nodes in the neck were not irradiated only one out of 134 T1 patients primarily failed in this region. No patient out of 79 with T2a tumors and only 3 out of 53 patients with T2b tumors showed regional failure. In the T2a and T2b groups there were an additional 1 and 2 failures respectively for which the regional failure could not be separated in time from the local failure. This very low regional recurrence rate should be compared to the much higher rate of local recurrences in the larynx itself, which occurred in 63 out of 266 patients.

Concerning the treatment volume Olszewski et al. (14) concluded from an analysis of 137 patients with glottic T1 tumors that fields sized 30 cm^2 were associated with higher local recurrence rate than fields sized $>30\ cm^2$. In the present study this could not be confirmed for T1, nor for T2a or T2b tumors.

Improved radiotherapy of T1 and T2 glottic cancers should therefore aim at a better sterilization of tumor cells in the larynx. Elective irradiation of the neck nodes increases treatment morbidity, especially if glands along the mandible, the submandibular, subdigrastric or upper jugular or the paratracheal glands are included in the target volume. Too heavy acute mucosal reactions often make a rest period of 2–3 weeks during treatment necessary for these reactions to subside. Data are now piling up, showing that a long treatment time is negatively correlated to local control (15–17). There are also non-randomized studies showing better local control with accelerated fractionation schedules, when more than 10 Gy per week were given to patients allocated for a full-dose radiotherapy regimen (18, 19). Therefore we cannot rule out the possibility of elective irradiation of regional nodes in the neck precluding the sterilization of the primary tumor. In a transverse section just below the mandible, the regional upper jugular nodes are situated just behind the anterior part of the spinal cord, and so any irradiation technique intended to cover all potential regional spread in the neck will lead to a more heterogenous dose distribution in the treatment volume. We therefore use two lateral opposed photon fields which are reduced posteriorly after spinal cord tolerance has been reached, and treatment to the posterior target volume is then complemented with electrons until an absorbed dose of 50 Gy is obtained in the nodes. In the junction area of photon and electron beams, often located in the lateral pharyngeal walls, significant areas receive 110% during this course of treatment.

If higher dose levels or accelerated treatment regimens are planned to improve local control in the larynx, i.e. for T2 tumors, acute morbidity may be substantial and the overall treatment time prolonged.

In the present series 93% of the patients with normal cord mobility and 79% with impaired cord mobility achieved a 10-year loco-regional control after radiotherapy and surgery used for salvage. The salvage rate by the surgical procedure was high and only 7% of the patients died from uncontrolled cancer. The radiotherapy could possibly be made more effective by increasing the doses for slowly regressing tumors or tumors with impaired cord mobility or by altered radiation fractionation schedules.

Concerning the T2b group, Van den Bogaert et al. (9) analysed the prognostic significance of the extension to the supra- or subglottic region combined with (20 patients) or not combined with (8 patients) impaired mobility of the vocal cord. They concluded that impaired mobility by itself is a bad prognostic factor only when it is combined with tumor extension. However, this conclusion could not be verified in the present analysis. Eleven out of the 53 patients with T2b tumors had impaired mobility without extension. The loco-regional recurrence-free rates at 5 years were 61% without extension and 60% with extension combined with impaired mobility. The disparity between the results of these two studies can of course be related to the smallness of the patient groups.

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