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Carcinoma of the Vocal Cord. Results after Subperichondral Cordectomy

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Abstract. *The clinical outcome of 110 patients operated upon by subperichondral cordectomy between 1982 and 1992 for T1s/T1a, NO, MO carcinomas of the vocal cord has been evaluated in this longitudinal epidemiological study. Patients have been followed up until the end of 1993 by examinations done once a month (first year), every three months (years 2 to 4), every six months (years 5 to 8), and then once a year. Life-tables have been computed according to Kaplan and Meier and raw survival has been 90.0%. Considering only the mortality due to any type of neoplastic disease, the survival reached 93.6%. Finally, considering only deaths due to recurrences or metastases of the primary tumor, the survival rate was 95.5%. Mortality after the first recurrence was 27.3%, after a second recurrence 50.0%. A correlation between number of cigarettes smoked and the risk of recurrence of the tumor could be observed ($p < 0.01$), while gross appearance and histologic grading of the vocal cord carcinoma proved to be uncorrelated with the risk of recurrences.*

Among the malignant neoplasms of the larynx the carcinoma confined to the vocal cord has a special position. Although in the vast majority of cases it is usually a histologically squamocellular carcinoma of high to poor differentiation, the scarce lymphatic drainage and the sanctuary-like location make it behave, at least for the first phases of its growth, like a local malignancy, closely resembling plant neoplasms (1,2,3,4,5,6,7,8,9,10,11,12,13). This justifies the therapeutic approach based on functional surgery, and makes it the laryngeal carcinoma with the best prognosis (14,15,16), both *quoad vitam* and *quoad validudinem*.

The mucosa of the vocal cord is exposed to carcinogenic stimuli such as cigarette smoke and alcohol as well as the oropharyngeal mucosa as a whole and together they ought to be considered as an oncologic functional unit. The surgical removal of the cord malignancy does not then modify the oncologic risk of the surrounding mucosa and this must be

kept in mind while considering the incidence of recurrences. Furthermore, the longer survival rates in these patients make the physician face a rising number of metachrone neoplasms arising independently from other mucosal sites of the upper and lower aerodigestive tracts. These neoplasms should not be interpreted as recurrences, but as true autonomous second tumours(17).

In this study we analysed the clinical records of T1a and T1s vocal cord squamocellular carcinomas treated by subperichondral cordectomy and followed up for at least one year from 1982 through 1993, in order to obtain data about survival rates, recurrences, node metastases, and metachrone neoplasms of the upper and lower aerodigestive tracts.

Materials and Methods

One hundred and ten patients were included in the study. All patients presented from January 1982 through December 1992 with T1a/T1s, NO, MO vocal cord squamous cell G1-G3 carcinoma (18) and were treated by subperichondral cordectomy (Table I). In four patients a temporary tracheotomy was performed as a part of the surgical approach. In each of these patients the tracheostomy was closed by the second postoperative day. No tracheotomy has been done since June 1984. To obtain a standardized group of subjects, all patients treated by surgical variants (*i.e.* enlarged cordectomy) were excluded from the study. No patient had any preoperative treatment, such as chemotherapy or radiotherapy. Twenty six patients (23.6%) with positive resection margins underwent postoperative radiotherapy (usually 65 G of TCT).

Patients were followed up until December 1993 by examinations done once a month (first year), every three months (years 2 to 4), every six months (years 5 to 8), and once a year after that. Only patients who submitted regularly to the follow up have been included in the study.

Survival rates were computed to 5 years according to Kaplan and Meier (19). Correlations between survival and specific risk factors such as number of cigarettes smoked, alcohol consumption, age, gross appearance and histologic grading of the primary vocal cord carcinoma were subjected to statistical analysis by the 2 test (20,21) and the use of the Yeats correction (22) when necessary.

Results

One hundred and six patients (96.4%) were males and 4 (3.6%) females. The mean age of the patients was 60.2 years, ranging between 41 and 82 years. The median age was 60.0 years. No side prevalence for the location of the primary vocal cord carcinoma could be seen: in 50.9% (56) of cases the left

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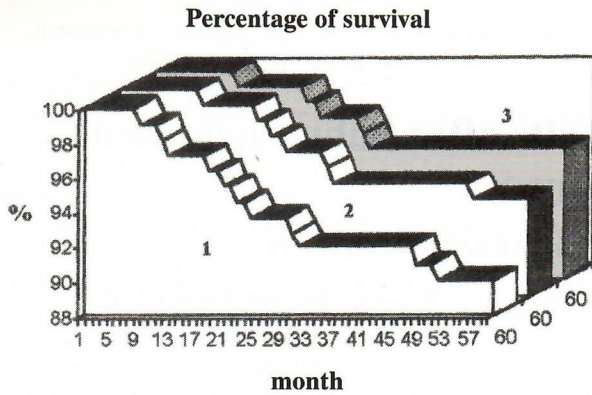


Figure 1. Percentage of survival.
 1-raw survival (all causes of death)
 2-death due to all types of neoplastic disease
 3-death due to primary tumour and its recurrences.

Table I. General data of examined population.

| | | | |
|--------------------------------------|---------|--------|------------|
| a. Number of cases | M | F | Tot |
| | 106 | 4 | 110 |
| | (96.4%) | (3.6%) | |
| b. Age | Min | Mean | Median Max |
| | 41 | 60.2 | 60.0 82 |
| | | | years |
| c. Number of cigarettes smoked daily | | | |
| | 0 | 17 | |
| | 1-10 | 13 | |
| | 11-20 | 47 | |
| | 21-30 | 16 | |
| | 31-40 | 10 | |
| | >40 | 7 | |

Table II. Morbid anatomy of the primary tumours.

| | | | |
|-------------------------|--------------------------------|----|---------|
| a. Gross morphology | Vegetating | 79 | (71.8%) |
| | Infiltrating | 15 | (13.6%) |
| | Ulcerated | 14 | (12.7%) |
| | Other | 2 | (1.9%) |
| b. Histological grading | | | |
| | G1 - well differentiated | 80 | (72.7%) |
| | G2 - moderately differentiated | 25 | (22.7%) |
| | G3 - poorly differentiated | 5 | (4.6%) |

vocal cord was involved, and in 49.1% (54) the right one. At gross examination the neoplasm appeared exophytic in 71.8% of the cases, in 13.6% it was infiltrating and in 12.7% it was ulcerated. Microscopic evaluation showed that all neoplasms were squamocellular carcinomas: 72.7% were well differentiated (G1), 22.7% moderately differentiated (G2) and 4.6% poorly differentiated (G3) (Table II).

After the subperichondral cordectomy complications could be seen in ten cases, with emphysema in six, subcutaneous oedema of the neck in two and wound infection in two patients.

Table III. Statistics and treatment of the first recurrence of tumour.

| | | | | |
|----------------------------------|------------|--|---------|-------------------|
| a. Total number of recurrences | M | F | Tot | % of Cordectomies |
| | 11 | 0 | 11 | 10.0% |
| b. Time from surgery (month) | Min | Med | Max | |
| | 5.7 | 18.7 | 46.4 | |
| | < 6 month | 1 | (9.1%) | |
| | 6-60 month | 10 | (90.9%) | |
| c. Site | | | | |
| | Laryngeal | 8 | (72.7%) | |
| | Neck | 1 | (9.1%) | |
| | Distance | 2 | (18.2%) | |
| d. Death due to first recurrence | | 3 | (27.3%) | |
| e. Treatment | | | | |
| Site of recurrence | N. | Treatment | | |
| Larynx | 8 | 1 Controlateral Chordectomy | | |
| | | 1 Glottectomy | | |
| | | 1 Frontolateral Laryngectomy | | |
| | | 3 Total Laryngectomy | | |
| | | 2 No further treatment | | |
| Larynx+neck | 1 | 1 Subtotal laryngec.(Piquet)+neck dissection | | |
| Lung metastasis | 1 | 1 Radiotherapy | | |
| Kidney+lung metastasis | 1 | 1 Chemotherapy+radiotherapy | | |

Table IV. Statistics and treatment of the second recurrence of tumour.

| | | |
|---|-----------------|--------------------------|
| a. Number of second recurrences | 4 | |
| b. Site | Laryngeal 1 | |
| | Neck 1 | |
| | Neck+distance 2 | |
| c. Death from second recurrence | 2 (50%) | |
| d. Treatment | | |
| Site of recurrence | N. | Treatment |
| Larynx | 1 | Total Laryngectomy |
| Neck + distance | 3 | 1 Radiotherapy |
| | | 1 Comb.Chemoradiotherapy |
| | | 1 no further treatment |
| e. Total death from recurrence (first + second) | 5(45.4%) | |

Table V. Second metachronous tumours.

| | | |
|------------------------|---|---|
| Gastrointestinal tract | 5 | (3 squamous cell and 2 adenocarcinomas) |
| Respiratory tract | 2 | (both adenocarcinomas) |

- Aspects of Cancer. (Goldfarb RH, ed). Kluwer Academic Publishers, 1989, pp. 33-34
- 6 Kaiser HE: The influence of the body structure on tumor development. *In: Kaiser HE (ed), Cancer Growth and Progression, Chapter 7, Vol. 1: Fundamental Aspects of Cancer.* (Goldfarb RH, ed), Kluwer Academic Publishers, 1989, pp.43-46.
 - 7 Kaiser HE: Comparative importance of the lymphatic system during neoplastic progression: lymphohematogenous spreading (with contribution of D. Berens von Rautenfeld and C. Hunneshage). *In: Kaiser HE (ed), Cancer Growth and Progression, Chapter 12, Vol. 1: Fundamental Aspects of Cancer* (Goldfarb RH, ed). Kluwer Academic Publishers, 1989, pp. 98-133.
 - 8 Kaiser HE: Neoplastic dissemination and spreading from the viewpoint of comparative pathology: Differences and similarities between animals and plants. *In: Kaiser HE (ed), Cancer Growth and Progression, Chapter 1, Vol. 5: Comparative Aspects of Tumor Development.* Kluwer Academic Publishers, 1989, pp.1-15.
 - 9 Kaiser HE: Characteristics and pattern of direct tumor spreading. *In: Kaiser HE (ed), Cancer Growth and Progression, Chapter 1, Vol. 7: Local invasion and spread of cancer* (Brunson KW ed) Kluwer Academic Publishers, 1989, pp. 1-16.
 - 10 Kaiser HE: Overview of metastatic spreading. *In: Kaiser HE (ed), Cancer Growth and Progression, Chapter 1, Vol. 8: Metastasis/Dissemination* (Gorelik E, ed). Kluwer Academic Publishers, 1989, pp. 1-20.
 - 11 Kaiser HE: Patterns of metastasis. *In: Kaiser HE (ed), Cancer Growth and Progression, Chapter 2, Vol. 8: Metastasis/Dissemination* (Gorelik E ed). Kluwer Academic Publishers, 1989, pp. 21-31.
 - 12 Bayer MH, Kaiser HE and Micozzi MS; Abnormal growth processes in plants and animals: A Comparison. *In Vivo* 8: 3-15, 1994.
 - 13 Kaiser HE: Comparison of direct spreading and local recurrence of neoplasm. *In Vivo* 8: 91-95, 1994.
 - 14 Ottaviani A, Ottaviani F and Broich G: Neoplastic secundarism after laryngeal surgery [Il secundarismo neoplastico dopo chirurgia laringea]. *In: Cortesina G (ed). International Workshop on Locoregional recurrences of tumours of the cervicofacial region.* University of Turin, 1992, pp. 299-310.
 - 15 De Campora E: Surgical treatment of laryngeal glottic cancer: Introduction to the surgery and indications for the surgery of the glottic cancer [Trattamento Chirurgico dei tumori glottici della laringe: Introduzione ed Indicazioni alla chirurgia del cancro glottico]. *Relazione Ufficiale LXXX Congresso SIO, Udine, 1993, pp. 347-356.*
 - 16 Ottaviani A and Sambataro G: Surgical treatment of laryngeal glottic cancer: The subperichondral cordectomy, vertical hemilaryngectomy, horizontal laryngectomy [Trattamento Chirurgico dei tumori glottici della laringe: La cordectomia sottopericondrale interna, l'emilaringectomia verticale, la glottidectomia orizzontale]. *Relazione ufficiale LXXX Congresso SIO, Udine, 1993, pp. 391-402.*
 - 17 Kaiser HE: Secondary primary cancers: An overview. *In: Kaiser HE (ed), Cancer Growth and Progression, Chapter 22, Vol. 6: Etiology of cancer in man* (Levine AS, ed), Kluwer Academic Publishers, 1989, pp. 200-213
 - 18 UICC: Hermanek P and Sobin LH (ed): TNM Classification of malignant tumours. IV ed. Springer, 1987.
 - 19 Kaplan EL and Meier P: Non parametric estimation from incomplete observations. *J Am Stat Ass* 53: 457-481, 1958.
 - 20 Barona R, Basterra J and Martorell A: Prognostic value of histopathologic parameters in epidermoid carcinoma of the vocal chords in T1 stage. *An Otorrinolaringol Ibero Am. 19: 467-474, 1992.*
 - 21 Eiband JD, Elias EG and Suter CM: Prognostic factors in squamous cell carcinoma of the larynx. *Am J Surg* 158: 314-317, 1989.
 - 22 Armitage P; *Statistical Methods in Medical Research*; New York, Wiley and Sons, 1971, pp. 124-125,
 - 23 Piquet JJ, Chevalier D: Subtotal laryngectomy with crico-hyoido-epigloto-pxy for the treatment of extended glottic carcinomas. *Am J Surg* 162: 357-361, 1991.
 - 24 Serafini I, Bernardi G and Ghirardo R: Results of the surgical treatment of glottic cancer. Our experience. [Risultati del trattamento chirurgico nei carcinomi glottici. Nostra esperienza]. *In: Serafini I (ed), Glottic and Subglottic carcinoma [Il carcinoma glottico e sottoglottico].* Piccin Padova, 1989, pp. 267-269.
 - 25 Antonelli AR, Bonetti B and Bovarini M: Comparison of the results of surgery and radiotherapy in T1 and T2 glottic cancer [T1 e T2 della glottide, confronto dei risultati di chirurgia e radioterapia]. *In: Serafini I (ed), Glottic and subglottic carcinoma [Il carcinoma glottico e sottoglottico].* Piccin Padova, 1989, pp. 271-279.
 - 26 Regina R, Cavalot A and Gedda F: Follow-up delle cordectomie. *Otorinolaringologia I: 80-83, 1988.*
 - 27 Olsen KD, Thomas JV, De Santo LW and Suman VJ: Indications and results of cordectomy for early glottic carcinoma. *Otolaryngol Head Neck Surg* 108: 277-282, 1993.
 - 28 Royal Society of Health: Smoking and health now. 90: 40-41, 1971.
 - 29 Rothman K and Keller A: The effect of joint exposure to alcohol and tobacco on risk of cancer of the mouth and oharynx. *J Chron Dis* 25: 711-716, 1972.
 - 30 Wynder EL: Environmental factors in cancer of the larynx. A second look. *Cancer* 38: 1591-1601, 1976.
 - 31 Barona R, Basterra J, Martorell MA, Garin L, Alvarez-Valdes R and Armengot M. Prognostic value of histopathological parameters in epidermoid carcinoma of the vocal cords in T-1 stage [Valor pronostico de los parametros histopatologicos en el carcinoma epidermoide de cuerda vocal en estadio T-1]. *An Otorrinolaringol Ibero Am 19: 467-474, 1992.*
 - 32 Pradier R, Gonzalez A, Matos E, Loria D, Adan R, Saco P and Califano L: Prognostic factors in laryngeal carcinoma. Experience in 296 male patients. *Cancer* 71: 2472-2476, 1993.
 - 33 Kaiser HE, Characteristics and pattern of direct tumor spreading. *In: Kaiser HE (ed), Cancer Growth and Progression, Chapter 1, Vol. 7: (ed Brunson KW) Local Invasion and Spread of Cancer.* Kluwer Academic Publ, 1989, pp. 1-12.
 - 34 Broich G; Comparison of the progression of selected, topographically particular, tumors in the head and neck region. *In: Kaiser HE (ed), Cancer Growth and Progression, Chapter 2, Vol. 7: (ed Brunson KW) Local Invasion and Spread of Cancer.* Kluwer Academic Publ, 1989, pp. 17-29.
 - 35 Mandravadi RVP, Haas RE, Liebner EJ, Skolnik EM and Aplebaum EL: Postoperative Radiotherapy for persistant tumor at the surgical margina in head and neck cancers. *Laryngoscope* 93: 1337-1340, 1983.
 - 36 Danidilidis J, Nikolau A and Symeonidi V: Our experience in the surgical treatment of T1 carcinoma of the vocal chord. *J Laryngol Otol* 104: 222-224, 1990.
 - 37 Kleinsasser O, Glanz H and Kimmech T: Endoscopic surgery in glottic carcinoma [Endoscopische Chirurgie bei Stimmlippenkarzinomen]. *HNO* 36: 412-416, 1988.
 - 38 Fein DA, Mendenhall WM, Parsons JT, Stringer SP, Cassini NJ and Million RR, Carcinoma *in situ* of the glottic larynx: the role of radiotherapy. *Int J Radiat Oncol Biol Phys* 27: 379-84, 1993.
 - 39 Small W Jr, Mittal BB, Brand WN, Shetty RM, Rademaker AW, Beck GG and Hoover SV: Role of radiation therapy in the management of carcinoma *in situ* of the larynx. *Laryngoscope* 103: 663-7, 1993.
 - 40 Kowalski LP, Batista MB, Santos CR, Scopel AA, Salvajoli JV, Novaes PE and Trippe N: Prognostic factors in glottic carcinoma clinical stage I and II treated by surgery or radiotherapy. *Am J Otolaryngol* 14: 122-7, 1993.
 - 41 Kaiser HE: Local recurrence. *In: Kaiser HE (ed), Cancer Growth and Progression, Chapter 7, Vol.7: (ed Brunson KW) Local Invasion and Spread of Cancer.* Kluwer Academic Publ., 1989, pp. 187-194
 - 42 Ott S, Klingholz F, Willich N and Kastenbauer E: Assessing the quality of the speaking voice after therapy of T1 and T2 vocal cord cancers [Die Bestimmung der Qualitat der Sprechstimme nach Therapie von T1- und T2-Stimmlippenkarzinomen]. *Laryngorhinootologie* 71: 236-41, 1992.
 - 43 McGuirt WF, Blalock D, Koufman JA and Feehs R\$: Voice analysis of patients with endoscopically treated early laryngeal carcinoma: *Ann Otol Rhinol Laryngol* 101: 142-146, 1992.

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