

Laser Surgery versus Radiotherapy for T1–T2N0 Glottic Cancer: A Meta-Analysis

Yan Feng Binquan Wang Shuxin Wen

Otorhinolaryngology Head and Neck Surgery, The First Affiliated Hospital of Shanxi Medical University, Taiyuan, China

Key Words

Early glottic cancer · Radiotherapy · Laser surgery · Meta-analysis

Abstract

Background: Laser surgery and radiotherapy are commonly used to treat glottic cancer. **Objective of Review:** To compare outcomes and cost of laser surgery versus radiotherapy for T1–T2N0 glottic cancer. **Type of Review:** Meta-analysis. **Search Strategy:** The Cochrane Central Register of Controlled Trials, Ovid MEDLINE® In-Process & Other Non-Indexed Citations, Embase, Web of Science (1990–2010) were searched electronically. Three Chinese journals in otolaryngology were searched manually. **Evaluation Method:** Retrieved studies were analyzed with Review Manager 5.0 software. Methodological and outcome heterogeneity was analyzed using the χ^2 test and the I^2 test. Homogeneous and heterogeneous data were analyzed using a fixed random effect model. **Results:** Eleven studies involving 1,135 patients were included in the analysis. The cure rate did not differ between patients receiving laser surgery versus radiotherapy. Results on voice preservation were inconclusive. The overall cost for laser surgery was lower. **Conclusions:** The quality of the reported clinical studies is limited.

No level I data are available. Nonetheless, our analysis suggests that laser surgery and radiotherapy produce comparable outcomes.

Copyright © 2011 S. Karger AG, Basel

Laryngeal carcinoma is one of the most common head and neck cancers. According to the most recent estimate, 151,000 new cases (approximately 2.0 men and 0.3 women in every 100,000 population) of laryngeal carcinoma were diagnosed worldwide in 2008 [1]. In recent years, however, the incidence rate of laryngeal carcinoma has been increasing in China, apparently due to cigarette smoking, alcohol consumption and industrial pollution [2].

Laryngeal carcinoma may occur in the glottis, supraglottis or subglottis. The prevalence of larynx cancer in the glottis and supraglottis varies with geographic locations; the vast majority of laryngeal carcinoma in China and the United States are glottic cancers. Supraglottic laryngeal carcinoma is relatively rare, and occurs most commonly in Europe and other parts of the world [3]. Glottic cancer is often at its early stage (Tis or T1–T2N0M0, based on the TNM staging system) upon diagnosis for the following reasons: (1) lesions in the true vo-

cal cords produce readily noticeable voice changes [3]; (2) the true vocal cords in the glottis region of the larynx are devoid of lymphatic drainage [4].

Early glottic cancer has a relatively good prognosis [5, 6]. The most common treatment options are endoscopic laser surgery and radiotherapy. The goal of the treatment for T1–T2N0M0 glottic cancer is to cure the disease while preserving the vocal cords. Both laser surgery and radiotherapy could achieve high cure rates, but which treatment is superior in voice preservation remains controversial [7–10]. Superior voice quality has been reported after radiotherapy in several studies [9–11] whereas one study reported superior voice quality after laser treatment [7].

There are a few reviews on the use of endoscopic laser surgery and radiotherapy in the treatment of early glottic cancer [11, 12], and none of these reviews comprehensively assessed cure rates, voice function-preserving capacity and treatment costs. The present meta-analysis is based on reports published in the past two decades. Specifically, carbon dioxide endoscopic laser surgery was compared to radiotherapy in patients with T1–T2N0M0 glottic cancer. Parameters included overall survival, voice preservation and cost.

Methods

Search Strategy

The search was limited to reports published in the English and Chinese languages. Databases were searched using a combination of free text and MESH terms. For the English literature, the following databases were electronically searched: the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 2, 2009), Ovid MEDLINE, Ovid MEDLINE® In-Process & Other Non-Indexed Citations, Embase and Web of Science. The reference lists of identified articles/reviews were manually searched for additional trials. For the Chinese literature, the *Journal of Clinical Otorhinolaryngology Head and Neck Surgery*, the *Chinese Archives of Otolaryngology-Head and Neck Surgery* and the *Chinese Journal of Otorhinolaryngology Head and Neck Surgery* were manually searched. The time period of the search was from January 1990 to December 2010. The bibliographies listed in the selected articles were cross-examined to identify additional literature. The authors of the original articles were contacted in case of ambiguity with regard to the design and data.

Inclusion Criteria

All reports included in this review met the following criteria: (1) patients with previously untreated early-stage glottic cancer (i.e. T1–T2N0M0, based on the TNM system); (2) the intervention was carbon dioxide endoscopic laser surgery versus radiotherapy (without salvage procedure). The primary outcome measure was local control rate. The secondary outcome measures included voice handicap index (VHI), quality of life and treatment cost.

Quality Assessment of Included Studies

Retrieved articles were assessed by two independent researchers. The methodological quality of the articles was evaluated by using the ABC rating scale as previously described [13]: level A, high-quality randomized controlled trials; level B, well-designed, nonrandomized clinical trials, and level C, consensus or expert opinions.

Data Collection and Analysis

For each study, the following data were collected: first author, publication year, study design, number of patients, tumor stage, patient sex, treatment and outcome. The data were analyzed using Review Manager 5.0 software (Nordic Cochrane Centre, Copenhagen, Denmark). We statistically synthesized dates of eligible studies if appropriate. For dichotomous outcomes, relative risk (RR) and 95% confidence intervals (CIs) were utilized to compare the event rate. For continuous outcomes, data were summarized using weighted mean difference.

Clinical and methodological heterogeneity was assessed using the χ^2 test and I^2 test. Meta-analyses were performed whenever appropriate. When there was no significant heterogeneity, a fixed-effect model was employed; otherwise, a random-effect model was adopted and the results from each study were individually described without pooling of the data.

Results

Eligible Studies

Of the 25 potentially eligible trials, 14 were excluded [10, 14–26]. The reasons for exclusion are shown in table 1. Eleven studies [27–37] met all inclusion criteria and were included in the final analysis. None of the 11 studies was completely randomized in design; 1 was prospective [35] and all others were retrospective. A total of 1,135 participants were included: 539 were treated with laser surgery and 596 with radiotherapy. Detailed information is presented in table 2.

Local Control Rate

Local control rate was reported in 5 studies [31, 32, 34, 35, 37]. Two studies evaluated the 2-year local control rate [31, 32], 2 evaluated the 3-year local control [34, 35], and 3 evaluated the 5-year local control [32, 34, 37]. A meta-analysis of the 5 studies failed to show a significant difference in local control rate at any time (2-year: RR = 0.55, 95% CI: 0.28–1.09; 3-year: RR = 0.84, 95% CI: 0.48–1.47; 5-year: RR = 0.90, 95% CI: 0.59–1.39; fig. 1).

Voice Handicap Index

The VHI was reported in 6 trials [27–31, 36]. Significant heterogeneity prevented a meta-analysis. No significant difference in total VHI score was found in 3 studies [28, 29, 31]. Two studies reported significantly lower VHI

Table 1. Characteristics of excluded studies

Study ID	Reasons for exclusion recorded
Phillips et al. [14]	Early glottic cancer study with Tis, T1, T2. Data on T1–T2N0M0 glottic cancer patients could not be separated
Mlynarek et al. [15]	Patients in surgery group did not undergo carbon dioxide endoscopic laser surgery. They underwent endoscopic microsurgical resection using a cold-knife technique
Loughran et al. [16]	Early glottic cancer study with Tis, T1, and T2. Data on T1–T2N0M0 glottic cancer patients could not be separated
Krengli et al. [17]	No outcome of interest reported
Jones et al. [18]	Early laryngeal cancer study with supraglottic, glottic, subglottic. Data on T1–T2N0M0 glottic cancer patients could not be separated
Tamura et al. [19]	No outcome of interest reported
Wedman et al. [20]	No outcome of interest reported
Spector et al. [21]	Not all participants in surgery group received carbon dioxide endoscopic laser surgery
Grégoire et al. [22]	For laser surgery, cost included postoperative radiotherapy applied in 30% of patients
Rosier et al. [10]	This study includes 11 cases who had a previous history of malignant disease
Foote et al. [23]	Early glottic cancer study with Tis, T1 and T2. Data on T1–T2N0M0 glottic cancer patients could not be separated
Rydell et al. [24]	No outcome of interest reported
McGuirt et al. [25]	No outcome of interest reported
Chen et al. [26]	Open surgery was included

scores ($p < 0.05$) in patients receiving radiotherapy [27, 30]. The remaining study claimed significantly higher VHI scores ($p < 0.05$) in patients receiving radiotherapy [36]. Data with regard to emotional and functional changes were also conflicting. Better emotional scores were achieved by patients receiving laser surgery by Goor et al. [31] whereas Nunez Batalla et al. [30] and Dinapoli et al. [27] reported better emotional scores in patients receiving radiotherapy. Sjögren et al. [29] reported no difference. Better functional scores were reported by Nunez Batalla et al. [30] in patients receiving radiotherapy while Dinapoli et al. [27], Sjögren et al. [29] and Goor et al. [31] found no difference between the two groups.

Quality of Life

The quality of life was assessed in 2 studies [28, 31]. Goor et al. [31] used the COOP/Wonca chart and found no significant difference between patients receiving laser surgery versus radiotherapy. Patients receiving radiotherapy seemed to do be better in physical fitness and

social activities but poorer in mental well-being and daily activities. The differences, however, were not statistically significant. Oridate et al. [28] used Voice-Related Quality of Life and also failed to find significant difference between the two treatment modalities.

Treatment Cost

Two studies [31, 33] described the costs. Both revealed significantly lower total cost for laser surgery. None of the 2 studies assessed loss of income during treatment. In this respect, laser surgery is probably more economical as the treatment typically requires <2 days hospital stay whereas radiotherapy typically takes 5 or 6 weeks.

Discussion

Strong and Jako [38] began to use carbon dioxide laser to treat malignant lesions of the larynx in 1972. In the following decades, minimal tissue resection has been in-

Table 2. Characteristics of the studies included in the meta-analysis

Study ID	Design	Groups	Sample size	Stage included	Mean or median age, years	Radiation dose/ number of fractions	Length of follow-up, months	Outcomes
Dinapoli et al. [27]	R	LS RT	33 49	T1a, T1b	63 64.5	70 Gy/35; 70.2 Gy/39; 69.6 Gy/58	less than 180 less than 96	VHI
Mahler et al. [35]	P	LS RT	188 163	T1a	67 66	66–70 Gy/30–35	29 (minimum)	LC
Oridate et al. [28]	R	LS RT	10 43	T1a, T1b	79 71	65 Gy	24 (median) 6 (median)	VHI; QOL
Schrijvers et al. [37]	R	LS RT	49 51	T1a	64 67	60–70 Gy/33	60 (minimum)	LC
Sjögren et al. [29]	R	LS RT	18 16	T1a	67 69	NR	45 (mean) 60 (mean)	VHI
Nunez Batalla et al. [30]	R	LS RT	19 18	T1a T1a, T1b	64 67	6,525 cGy/29	30 (mean) 43 (mean)	VHI
Goor et al. [31]	R	LS RT	54 31	T1a T1a	64.7 63.8	60 Gy/24	22.5 (mean) 23 (mean)	LC; VHI; QOL; Cost
Peeters et al. [36]	R	LS RT	56 46	T1a T1a	66 64	50–70 Gy/20–35	24 (minimum)	VHI
Stoekli et al. [32]	R	LS RT	65 75	T1, T2	63	70.2 Gy/39; 68 Gy/34	60 (mean) 70 (mean)	LC
Brandenburg [33]	R	LS RT	30 44	T1a, T1b	64.5 63.2	65–70 Gy	64.5 (median)	Cost
Epstein et al. [34]	R	LS RT	17 60	T1a T1a, T1b	62 63	66 Gy/33; 64–70 Gy/35–36; 68 Gy/34; 66–70 Gy/35–37	31 (median) 59 (median)	LC

P = Prospective; R = retrospective; LS = laser surgery; RT = radiation therapy; LC = local control; VHI = voice handicap index; QOL = quality of life; NR = not reported.

creasingly accepted in clinical practice [39, 40]. Such a change of attitude led to an increase in the popularity of laser surgery as the primary management for early glottic cancer [41].

The most commonly used types of treatment for early glottic cancer are radiotherapy and CO₂ laser surgery [42]. The choice seems to vary significantly across countries. Radiotherapy is preferred in northern Europe whereas patients are more likely to be treated with surgery in the United States and southern Europe [18]. A number of original studies comparing the oncologic and functional outcomes, quality of life and costs of laser surgery and/or radiotherapy in the treatment of early-stage carcinoma were excluded from our meta-analysis because they did not meet the inclusion criteria. Our analy-

sis demonstrated a similar cure rate for radiotherapy [7, 10, 33, 43] and laser surgery [7, 10, 33, 44–46], at 66–95% and 76–96%, respectively. The results with regard to voice preservation are inconclusive. Five studies [10, 20, 25, 47, 48] reported no significant difference between the two treatments. Four studies reported [24, 34, 49] better voice quality after radiotherapy. Very few studies concluded that voice quality was better after laser surgery. The costs for T1a glottic cancer are substantially greater in patients treated with radiotherapy than in patients treated with laser surgery [7, 33, 41, 50]. In all, both treatments achieve high and comparable cure rates. However, there remains controversy over voice quality, quality of life, risk of complications and cost.

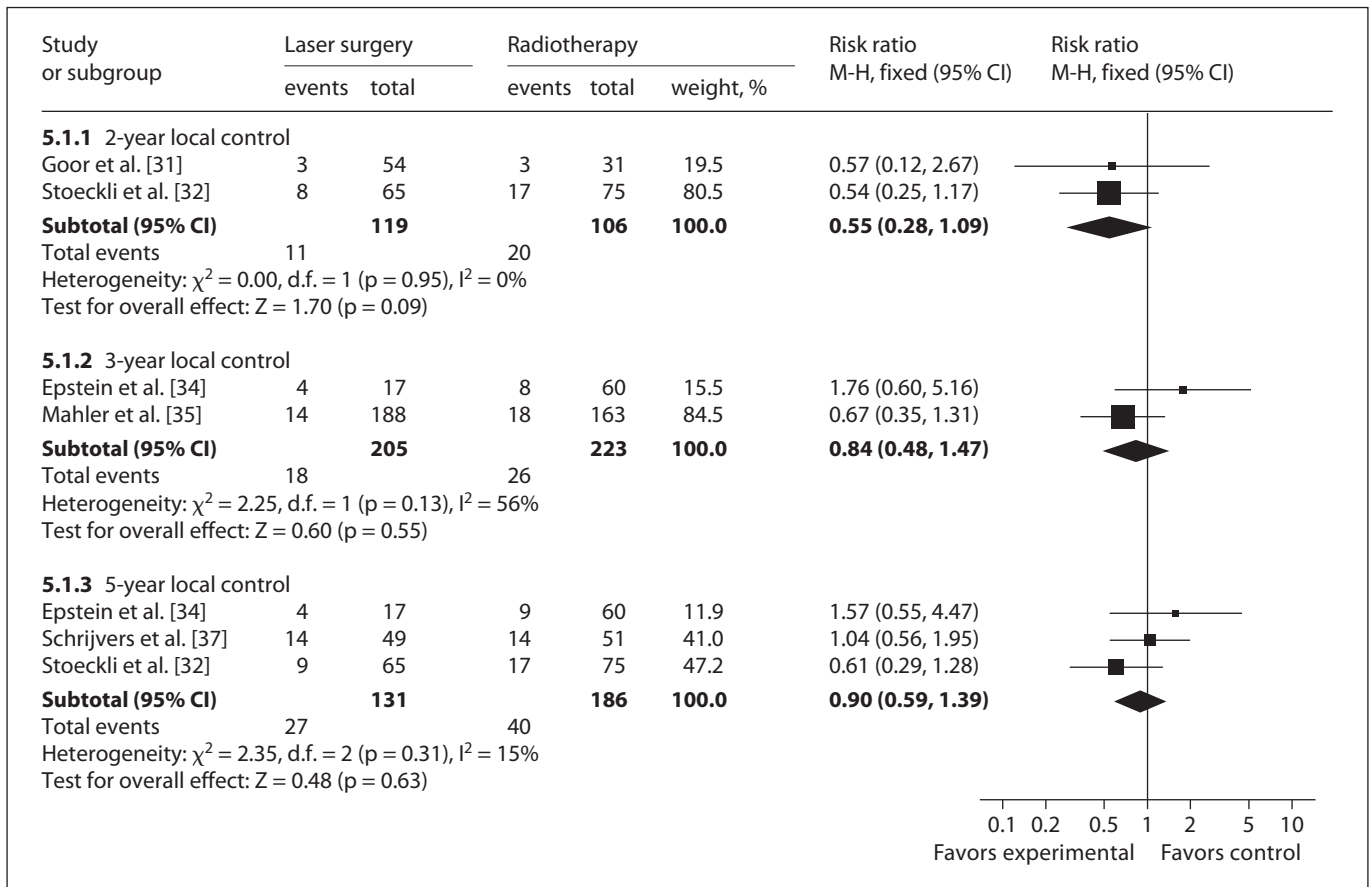


Fig. 1. Comparison of local control rate of laser surgery versus radiotherapy for early glottic cancer.

Our meta-analysis failed to show a significant difference between CO₂ laser surgery and radiotherapy in the rate of local control at 2, 3 and 5 years (fig. 1). However, there was significant heterogeneity in patient selection (T1a vs. T1-T2, T1 vs. T1a, T1 vs. T1a vs. T1-2). Also, there is no significant difference between CO₂ laser surgery and radiotherapy in quality of life. Total cost of radiotherapy is significantly higher than that of CO₂ laser surgery.

The current study has several limitations. None of the included studies were randomized controlled clinical trials. Only one study was prospective in design; the remaining studies were retrospective and had a relatively small sample size. Moreover, there was significant heterogeneity in tumor stage, dosing and schedule of radiotherapy, duration prior to voice assessment and the follow-up. Expanding the search to languages beyond English and Chinese might have identified more good-quality studies.

Conclusion

Our analysis reveals a lack of well-designed prospective studies. Our analysis of the limited evidence failed to identify any difference in local control in patients with early glottic cancer receiving laser surgery versus radiotherapy. The effects on voice preservation require further study. Treatment cost is lower with laser surgery. Based on these findings, we believe that laser surgery is a more attractive option for patients with early glottic cancer based on economic considerations.

Disclosure Statement

We do not have any potential financial conflicts of interest or otherwise.

References

- 1 Ferlay J, Shin H, Bray F, Forman D, Mathers C, Parkin D: Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010;127:2893–2917.
- 2 Wight R, Paleri V, Arullendran P: Current theories for the development of nonsmoking and nondrinking laryngeal carcinoma. *Curr Opin Otolaryngol Head Neck Surg* 2003;11:73–77.
- 3 Hoffman HT, Porter K, Karnell LH, Cooper JS, Weber RS, Langer CJ, Ang KK, Gay G, Stewart A, Robinson RA: Laryngeal cancer in the United States: changes in demographics, patterns of care, and survival. *Laryngoscope* 2006;116:1–13.
- 4 Woodhouse RJ, Quivey JM, Fu KK, Sien PS, Dedo HH, Phillips TL: Treatment of carcinoma of the vocal cord. A review of 20 years' experience. *Laryngoscope* 1981;91:1155–1162.
- 5 Ton-Van J, Lefebvre JL, Stern JC, Buisset E, Coche-Dequeant B, Vankemmel B: Comparison of surgery and radiotherapy in T1 and T2 glottic carcinomas. *Am J Surg* 1991;162:337–340.
- 6 Mittal BRD, Marks JE, Perez CA: Role of radiation in the management of early vocal cord carcinoma. *Int J Radiat Oncol Biol Phys* 1983;9:997–1002.
- 7 Cragle SP, Brandenburg JH: Laser cordectomy or radiotherapy: cure rates, communication, and cost. *Otolaryngol Head Neck Surg* 1993;108:648–654.
- 8 Davis RK, Kelly SM, Parkin JL, Stevens MH, Johnson LP: Selective management of early glottic cancer. *Laryngoscope* 1990;100:1306–1309.
- 9 Pellitteri PK, Kennedy TL, Vrabec DP, Beiler D, Hellstrom M: Radiotherapy. The mainstay in the treatment of early glottic carcinoma. *Arch Otolaryngol Head Neck Surg* 1991;117:297–301.
- 10 Rosier JF, Grégoire V, Counoy H, Octave-Prignot M, Rombaut P, Scalliet P, Vanderlinden F, Hamoir M: Comparison of external radiotherapy, laser microsurgery and partial laryngectomy for the treatment of T1N0M0 glottic carcinomas: a retrospective evaluation. *Radiother Oncol* 1998;48:175–183.
- 11 Radiotherapy versus open surgery versus endolaryngeal surgery (with or without laser) for early laryngeal squamous cell cancer. *Cochrane Database Syst Rev* 2002:CD002027.
- 12 Higgins KM, Shah MD, Ogaick MJ, Enepekides D: Treatment of early-stage glottic cancer: meta-analysis comparison of laser excision versus radiotherapy. *J Otolaryngol Head Neck Surg* 2009;38:603–612.
- 13 Siwek J, Gourlay ML, Slawson DC, Shaughnessy AF: How to write an evidence-based clinical review article. *Am Fam Physician* 2002;65:251–258.
- 14 Phillips TJ, Sader C, Brown T, Bullock M, Wilke D, Trites JR, Hart R, Murphy M, Taylor SM: Transoral laser microsurgery versus radiation therapy for early glottic cancer in Canada: cost analysis. *J Otolaryngol Head Neck Surg* 2009;38:619–623.
- 15 Mlynarek A, Kost K, Gesser R: Radiotherapy versus surgery for early T1–T2 glottic carcinoma. *J Otolaryngol* 2006;35:413–419.
- 16 Loughran S, Calder N, MacGregor FB, Carding P, MacKenzie K: Quality of life and voice following endoscopic resection or radiotherapy for early glottic cancer. *Clin Otolaryngol* 2005;30:42–47.
- 17 Krengli M, Policarpo M, Manfreda I, Aluffi P, Gambaro G, Panella M, Pia F: Voice quality after treatment for T1a glottic carcinoma – radiotherapy versus laser cordectomy. *Acta Oncol* 2004;43:284–289.
- 18 Jones AS, Fish B, Fenton JE, Husband DJ: The treatment of early laryngeal cancers (T1–T2 N0): Surgery or irradiation? *Head Neck* 2004;26:127–135.
- 19 Tamura E, Kitahara S, Ogura M, Kohno N: Voice quality after laser surgery or radiotherapy for T1a glottic carcinoma. *Laryngoscope* 2003;113:910–914.
- 20 Wedman J, Heimdal JH, Elstad I, Olofsson J: Voice results in patients with T1a glottic cancer treated by radiotherapy or endoscopic measures. *Eur Arch Otorhinolaryngol* 2002;259:547–550.
- 21 Spector JG, Sessions DG, Chao KS, Haughey BH, Hanson JM, Simpson JR, Perez CA: Stage I (T1 N0 M0) squamous cell carcinoma of the laryngeal glottis: therapeutic results and voice preservation. *Head Neck* 1999;21:707–717.
- 22 Grégoire V, Hamoir M, Rosier JF, Counoy H, Eeckhoudt L, Neymark N, Scalliet P: Cost-minimization analysis of treatment options for T1N0 glottic squamous cell carcinoma: comparison between external radiotherapy, laser microsurgery and partial laryngectomy. *Radiother Oncol* 1999;53:1–13.
- 23 Foote RL, Buskirk SJ, Grado GL, Bonner JA: Has radiotherapy become too expensive to be considered a treatment option for early glottic cancer? *Head Neck* 1997;19:692–700.
- 24 Rydell R, Schalen L, Fex S, Elnor A: Voice evaluation before and after laser excision vs radiotherapy of T1a glottic carcinoma. *Acta Otolaryngol* 1995;115:560–565.
- 25 McGuiert WF, Blalock D, Koufman JA, Feehs RS, Hilliard AJ, Greven K, Randall M: Comparative voice results after laser resection or irradiation of T1 vocal cord carcinoma. *Arch Otolaryngol Head Neck Surg* 1994;120:951–955.
- 26 Chen WC, Chen LH, Leung WM, Tang SG, Tsai MH, Liao CT, See LC: Comparison of radiotherapy and surgical results of early stage glottic cancer: a retrospective analysis. *J Formos Med Assoc* 1993;92:1076–1083.
- 27 Dinapoli N, Parrilla C, Galli J, Autorino R, Micciche F, Bussu F, Balducci M, D'Alatri L, Marchese R, Rigante M, Di Lella G, Liberati L, Almadori G, Paludetti G, Valentini V: Multidisciplinary approach in the treatment of T1 glottic cancer. The role of patient preference in a homogenous patient population. *Strahlenther Onkol* 2010;186:607–613.
- 28 Oridate N, Homma A, Suzuki S, Nakamaru Y, Suzuki F, Hatakeyama H, Taki S, Sakashita T, Nishizawa N, Furuta Y, Fukuda S: Voice-related quality of life after treatment of laryngeal cancer. *Arch Otolaryngol Head Neck Surg* 2009;135:363–368.
- 29 Sjögren EV, van Rossum MA, Langeveld TP, Voerman MS, van de Kamp VA, Friebel MO, Wolterbeek R, Baatenburg de Jong RJ: Voice outcome in T1a midcord glottic carcinoma: laser surgery vs. radiotherapy. *Arch Otolaryngol Head Neck Surg* 2008;134:965–972.
- 30 Nunez Batalla F, Caminero Cueva MJ, Senaris Gonzalez B, Llorente Pendas JL, Gorris Gil C, Lopez Llamas A, Alonso Pantiga R, Suarez Nieto C: Voice quality after endoscopic laser surgery and radiotherapy for early glottic cancer: OBJECTIVE measurements emphasizing the voice handicap index. *Eur Arch Otorhinolaryngol* 2008;265:543–548.
- 31 Goor KM, Peeters AJ, Mahieu HF, Langendijk JA, Leemans CR, Verdonck-de Leeuw IM, van Agthoven M: Cordectomy by CO₂ laser or radiotherapy for small T1a glottic carcinomas: costs, local control, survival, quality of life, and voice quality. *Head Neck* 2007;29:128–136.
- 32 Stoeckli SJ, Schnieper I, Huguenin P, Schmid S: Early glottic carcinoma: treatment according patient's preference? *Head Neck* 2003;25:1051–1056.
- 33 Brandenburg JH: Laser cordotomy versus radiotherapy: an objective cost analysis. *Ann Otol Rhinol Laryngol* 2001;110:312–318.
- 34 Epstein BE, Lee DJ, Kashima H, Johns ME: Stage T1 glottic carcinoma: results of radiation therapy or laser excision. *Radiology* 1990;175:567–570.
- 35 Mahler V, Boysen M, Brondbo K: Radiotherapy or CO₂ laser surgery as treatment of T1a glottic carcinoma? *Eur Arch Otorhinolaryngol* 2010;267:743–750.
- 36 Peeters AJ, van Gogh CD, Goor KM, Verdonck-de Leeuw IM, Langendijk JA, Mahieu HF: Health status and voice outcome after treatment for T1a glottic carcinoma. *Eur Arch Otorhinolaryngol* 2004;261:534–540.
- 37 Schrijvers ML, van Riel EL, Langendijk JA, Dikkers FG, Schuurin E, van der Wal JE, van der Laan BF: Higher laryngeal preservation rate after CO₂ laser surgery compared with radiotherapy in T1a glottic laryngeal carcinoma. *Head Neck* 2009;31:759–764.

- 38 Strong MS, Jako GJ: Laser surgery in the larynx. Early clinical experience with continuous CO₂ laser. *Ann Otol Rhinol Laryngol* 1972;81:791-798.
- 39 Steiner W: Results of curative laser microsurgery of laryngeal carcinomas. *Am J Otolaryngol* 1993;14:116-121.
- 40 Pearson BW, Salassa JR: Transoral laser microresection for cancer of the larynx involving the anterior commissure. *Laryngoscope* 2003;113:1104-1112.
- 41 Shah JP, Karnell LH, Hoffman HT, Ariyan S, Brown GS, Fee WE, Glass AG, Goepfert H, Ossoff RH, Fremgen A: Patterns of care for cancer of the larynx in the United States. *Arch Otolaryngol Head Neck Surg* 1997;123:475-483.
- 42 Mendenhall WM, Werning JW, Hinerman RW, Amdur RJ, Villaret DB: Management of T1-T2 glottic carcinomas. *Cancer* 2004;100:1786-1792.
- 43 Kaiser TN, Sessions DG, Harvey JE: Natural history of treated T1N0 squamous carcinoma of the glottis. *Ann Otol Rhinol Laryngol* 1989;98:217-219.
- 44 Thomas JV, Olsen KD, Neel HB 3rd, DeSanto LW, Suman VJ: Recurrences after endoscopic management of early (T1) glottic carcinoma. *Laryngoscope* 1994;104:1099-1104.
- 45 Myers EN, Wagner RL, Johnson JT: Micro-laryngoscopic surgery for T1 glottic lesions: a cost-effective option. *Ann Otol Rhinol Laryngol* 1994;103:28-30.
- 46 Koufman JA: The endoscopic management of early squamous carcinoma of the vocal cord with the carbon dioxide surgical laser: clinical experience and a proposed subclassification. *Otolaryngol Head Neck Surg* 1986;95:531-537.
- 47 Hirano M, Hirade Y, Kawasaki H: Vocal function following carbon dioxide laser surgery for glottic carcinoma. *Ann Otol Rhinol Laryngol* 1985;94:232-235.
- 48 Delsupehe KG, Zink I, Lejaegere M, Bastian RW: Voice quality after narrow-margin laser cordectomy compared with laryngeal irradiation. *Otolaryngol Head Neck Surg* 1999;121:528-533.
- 49 Elnor A, Fex S: Carbon dioxide laser as primary treatment of glottic T1s and T1a tumours. *Acta Otolaryngol Suppl* 1988;449:135-139.
- 50 Smith JC, Johnson JT, Cognetti DM, Landsittel DP, Gooding WE, Cano ER, Myers EN: Quality of life, functional outcome, and costs of early glottic cancer. *Laryngoscope* 2003;113:68-76.