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Conservation laryngeal surgery for selected pyriform sinus cancer.

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Abstract *Aims*. This study reports the treatment of a cohort of patients with pyriform sinus squamous cell carcinoma, using conservative surgery and radiotherapy.

Methods. Thirty-four patients with pyriform sinus SCC were treated between 1986 and 2001, using partial laryngopharyngectomy with or without complementary radiotherapy. Seventy-six percent had stage III–IV lesions. Quality of life questionnaire and clinical examination were used for evaluation of laryngeal function.

Results. Conservation surgery was undertaken. All patients underwent neck dissection. Two thirds of the patients received post-operative radiotherapy. Reconstruction was achieved by local muscular flap in 13 cases, radial forearm free flap in 18 and pectoralis major flap in three. Five-year overall and disease-specific survival rates were 50 and 65%, respectively. Successful laryngeal function preservation with local control was achieved in 80% of the patients.

Conclusion. Partial laryngopharyngectomy is a suitable treatment for early and selected advanced stage pyriform sinus carcinoma with a good functional and oncologic outcome.

Introduction

Squamous cell carcinoma of the pyriform sinus has an unfavorable prognosis. Definitive radiation therapy is generally considered an effective therapeutic approach for T1 and selected T2 pyriform

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sinus carcinomas, whereas partial or total pharyngectomy and total laryngectomy with post-operative radiation therapy remains the most used conventional treatment for advanced, resectable stage III or IV tumours.[1-3] Despite this aggressive, highly morbid approach, the overall 5-year survival rate ranges from 25 to 40%.[4-7] Although not always agreed with some authors advocate nevertheless conservation surgery, and have reported favorable outcomes with partial laryngopharyngectomy.[8-10] The primary objective of the conservative approach is to lessen operative morbidity while increasing the chances for a better quality of life. It is our belief that partial laryngopharyngectomy, eventually combined with adjuvant radiation therapy, may meet these goals without worsening the survival rate.

The following report focuses on analysing the functional and oncologic results, as well as the global and specific survival rates, following voice-sparing partial supraglottic laryngopharyngectomy, in most of the cases followed by radiation therapy, in early and selected advanced cases of pyriform sinus cancer.

Patients and methods

Patients

From 1986 to 2001, 34 patients underwent formal or extended partial supraglottic laryngopharyngectomy for pyriform sinus squamous cell carcinoma. Criteria for patient selection for this type of surgery had included: (1) squamous cell carcinoma of the pyriform sinus, (2) absence of infiltration of the apex of the pyriform sinus or retro-cricoid and para-pharyngeal regions, (3) no extension to the thyroid cartilage. Patient charts were reviewed for: history of disease, clinical, radiological and pathologic characteristics of lesions, type of surgical reconstruction, radiation therapy modalities, delay for retrieval of tracheotomy and nasogastric feeding tube, complications and duration of local control. Three patients among the 34 initially included died within a few weeks following the operation and were, therefore, not taken into account for functional and loco-regional control assessment. All of the patients included in the present study were retrospectively staged by the TNM staging system as recommended by the 1997 American Joint Committee on Cancer on clinical staging.[11] Vocal cord mobility had been assessed by fiberoptic clinical examination. Pre-operative panendoscopies had been systematically undertaken to evaluate local extent of the tumour. In each case, pathologic examination revealed squamous cell carcinoma.

Surgical technique

The procedures were all performed by the same two attending head and neck surgeons and one plastic and reconstructive surgeon when reconstruction by a distant pedicled or free flap was needed. All patients were operated on according to either the technique described by Ogura[8] consisting of partial supraglottic laryngopharyngectomy, indicated for tumours limited to the medial wall of the pyriform sinus with possible extension to the aryepiglottic fold, or supraglottic laryngectomy associated with an extended partial pharyngectomy previously described,[12] indicated for tumours extending to the lateral wall of the pyriform sinus with possible extension to the posterior hypopharyngeal wall, equally preserving laryngeal function. In cases of hemilaryngeal fixation, a third technique was used as described by Urken[13] and consisting of partial laryngopharyngectomy, including the hemicricoid and hemithyroid cartilages and resection of the ipsilateral thyroid lobe. In this specific case, a free graft of costal cartilage was employed to restore laryngeal infrastructure in addition to the rest of the reconstruction. Neck dissection was bilateral in most cases. Primary closure was achieved with a local infrahyoid muscle flap in case of limited defect. In case of larger resection extending to the lateral wall of the pyriform sinus or to the posterior pharyngeal wall, or as salvage after previous radiotherapy, reconstruction was achieved with a radial forearm free flap, preferred for its greater versatility, or with a pectoralis major myofascial flap when no reliable vessels were available for microanastomoses.

Radiation therapy

Post-operative radiation therapy was delivered according to pN staging (positive lymph nodes, extracapsular spread) and prognostic factors such as borderline or positive margins, vascular and perineural involvement. Typically, patients were treated with parallel opposed lateral fields for the upper neck, including the primary site and an anterior field for the lower neck. Recently, a more conformal approach was used. Total dose administered ranged from 60 to 64 Gy at the ICRU reference point. Patients received daily 2 Gy fractions for 6–6.5 weeks.

Post-operative evaluation

At the end of the study, 20 living and traceable patients were contacted for functional evaluation. All received a quality of life questionnaire based on the EORTC QLQ-H&N 35 (quality of life questionnaire—head and neck 35 questions) model[14] with a special focus on vocal function, swallowing difficulties and social life. Five randomly chosen patients also returned to the outpatient clinic for specific vocal assessment with objective tests and independent observer ratings, and deglutition evaluation with barium X-rays.

Statistical methods

Patient survival curves were estimated using the Kaplan–Meier and product-limit methods.[15] Overall survival analysis was based on death from any cause. For the calculation of cause-specific survival, patients were censored if death was not directly related to the pyriform sinus cancer. Survival interval was measured from the date of surgery in the department to last consultation, phone inquiry or death. Comparisons between survival curves were made using the log-rank test with a significance level based on a *p*-value of less than 0.05.

Results

Patient population and treatment

Thirty-four patients with squamous cell carcinoma of the pyriform sinus were included in this study. Median age was 47.9 (range 40–69 years). There were 28 men and six women.

In most cases, disease was diagnosed at an advanced stage. Among the 34 patients, 26 presented with stage III or IV lesions. Six patients had primary lesions classified as T1, 25 as T2, 2 as T3 and 1 as T4. Nine patients had neck disease staged as N0, 8 as N1, 16 as N2 and 1 as N3 (Table 1). No patient had evidence of distant metastasis at time of initial diagnosis.

All patients were treated by partial laryngopharyngectomy: 13 according to the Ogura technique, 19 following the extended resection technique, and two using the Urken technique. Of these, 32 underwent bilateral neck dissection, when only two had unilateral neck dissection (ipsilateral to the primary lesion). Four patients had been referred for salvage treatment of recurrence after poor response to radiation therapy, and were considered suitable for conservation surgery. One other patient had received two cycles of a combination of carboplatin and fluorouracil as part of an oncological protocol of induction chemotherapy[16] and was operated on afterwards because no significant clinical response had been observed.

Reconstruction required in 13 cases a local infrahyoid muscle flap only (Ogura type resection), a radial free flap in 18 cases and a pectoralis major myofascial flap in three cases. Among the patients primarily operated, 66% (20/30) received post-operative definitive radiation therapy.

Pathologic examination of the resected tumour revealed disease free margins in 30 patients (86%), and microscopically positive or border-line in four cases on the initial resection margins. In these cases, margins were enlarged until histologically disease free on frozen section. Nodal metastases were histopathologically diagnosed in 26 patients (76%), among which two had bilateral involvement and nine were found to have extracapsular spread.

Complications

Three patients died in the immediate post-operative course; one patient died of massive pulmonary embolism, the second one died of acute asphyxia following accidental decannulation during an acute delirium tremens crisis and the third one died of sudden cardiopulmonary arrest. Because deaths were not related to the cancer itself, these patients

Table 1 Clinical T- and N-status (AJCC, 1997) at the time of diagnosis of 34 patients with piriform sinus squamous carcinoma

	T1	T2	T3	T4	Total
N0	1	7	1	-	9
N1	1	6	1	-	8
N2a	2	3	-	-	5
2b	1	6	-	1	8
2c	1	2	-	-	3
N3	-	1	-	-	1
Total	6	25	2	1	34

were hence excluded from the analysis of loco-regional recurrence and functional results.

Local complications occurred in nine out of 31 patients, mainly consisting in deep wound infection and fistulae. In seven cases, closure was obtained within 4 weeks with the use of pressure dressing. In two instances, surgical drainage was necessary. One patient developed free flap necrosis requiring a second procedure for reconstruction with a pectoralis major flap.

Functional results

Deglutition was assessed clinically and radiologically with modified barium swallow. Overall, in 50% of the patients, deglutition, with the ability to tolerate liquid and solid food was obtained and feeding tube removed by the 18th post-operative day. Thirty of the 31 patients achieved deglutition without aspiration by the end of the first post-operative month. One patient developed several episodes of pneumonia.

Tracheotomy tube was removed with a median delay of 2 weeks post-operatively (range: 8–73 days). Three patients required secondary micro-endoscopic CO_2 laser vaporization because of laryngeal oedema following radiation therapy. Tracheotomy was kept in one patient who rapidly developed pulmonary metastasis and was not functionally assessed. Overall, laryngeal function preservation (ability to speak, no tracheotomy and deglutition without symptomatic aspiration) was achieved in 27 of 30 functionally assessed cases (90%) at the end of the treatment.

Quality of life assessment

Of the 20 patients who received the EORTC QLQ H&N 35 questionnaire, 10 responded. All had been followed after the treatment for more than 24 months. Only one patient complained of occasional pain. Three patients reported having persistent moderate to severe swallowing difficulties with solid food, and two of these occasionally with liquids. Yet only one patient continued losing weight. Eight mentioned slight persistent xerostomia. Three patients reported moderate speech impairment (some difficulties in making themselves understood on the telephone). Only one patient admitted having a deteriorated social life.

Of the five patients seen for control evaluations in the outpatient clinic, none complained of swallowing difficulties. Although barium swallow demonstrated minimal aspiration in four, it was silent or completely cleared by the patients and none of them had a past of recurrent episodes of pneumonia. Equally, for these patients, no major vocal handicap was observed or reported. Maximum phonation time ranged between 10 and 21 s (reference range: 15–25 s). Vocal intensity, for all five, varied from a minimum of 67 dB to a maximum of 95 dB (reference range: 55–117 dB). Average frequency was 153 Hz. Vocal handicap index ranged between 16 and 25 out of 120 for four patients. One scored 61 but with excellent objective parameters.

Survival and loco-regional control

With a median follow-up of 45.2 months, the global overall actuarial survival rate was 62% at 3 years and 50% at 5 years and the cause specific actuarial survival rate was 80% at 3 years and 65% at 5 years (Fig. 1). The loco-regional control rate was 92% at 3 years and 86% at 5 years (Fig. 2). Survival and loco-regional control comparison in between stage groups, i.e. I+II and III+IV, showed a slight tendency to more favorable evolution in earlier stages, but it did not reach a statistically significant difference. Local recurrence occurred in three patients. Two of these patients also developed regional neck recurrence and were treated by palliative chemotherapy (combination of *cis*-platinum and fluorouracil). Distant metastases were found in four patients: one of them rapidly, 2 months after surgery while three other patients developed distant metastasis within one year after surgical treatment. Four patients developed a second primary during follow-up period. Overall, successful laryngeal function preservation with local control was achieved in 24 of the 30 assessed patients (80%).

Discussion

Pyriform sinus squamous cell carcinoma remains one of the most lethal cancers of the upper aero-digestive tract with consequently a low mean survival rate. Overall poor results obtained by current treatment regimens are related to an anatomic disposition predisposing to silent evolution and the rich lymphatic network draining the hypopharynx which increases the risk of cervical node metastasis.[17,18] Total laryngopharyngectomy with adjuvant radiation therapy remains the most widely used treatment in cases of high-staged disease.[17,19] However, the resulting permanent tracheostoma with the necessary loss of voice and the impaired deglutition account for significant post-operative morbidity. Moreover, whatever the

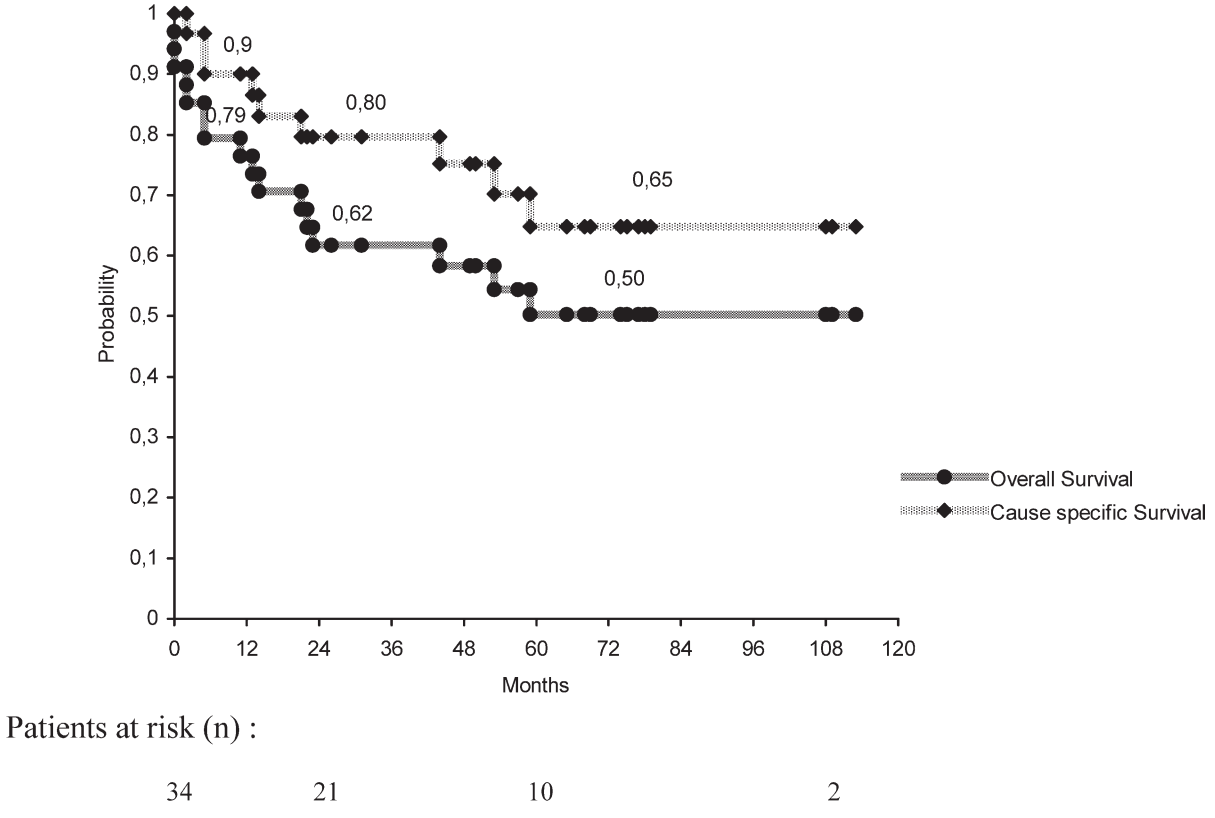

Figure 1 Overall and cause-specific survival.

therapeutic modality used, overall 5-year survival rates, as reported in the literature, do not exceed 50%.[17,20,21] These observations raise a major question: 'Can some of these patients be treated less aggressively by using laryngeal preservation approaches either surgically or non-surgically without compromising loco-regional control and survival?' Certain studies suggest that chemotherapy used as induction before radiotherapy or concomitant chemoradiation protocols are effective in advanced laryngeal and hypopharyngeal carcinoma while avoiding total laryngectomy in the majority of patients.[22-24] However, a recent large meta-analysis showed that there is a small significant survival benefit in favor of chemotherapy only when chemotherapy is given concomitantly to radiotherapy.[25] Besides, non-surgical larynx-preservation strategies are indicated for patients with operable tumours eligible for total laryngectomy or total pharyngolaryngectomy. Consequently, these treatment's protocols should clearly not challenge voice-sparing surgical procedures indicated for patients with locally less advanced tumours. Conservation surgery is unfrequently considered to be suitable in pyriform sinus carcinoma because of either oncologic reasons or patient factors such as inadequate pulmonary reserve and post-operative swallowing disorders.[1,26] Radiation therapy is generally considered adequate for early lesions of the hypopharynx.[1-3,27] However, the M.D. Anderson cancer center reported a rate of 41% of local or/and regional recurrence in a series of patients staged T2 treated by primary radiation therapy.[3] More recently, a Danish study reported disappointing results in a series of 101 patients with T1–T4 hypopharyngeal carcinoma primarily treated by

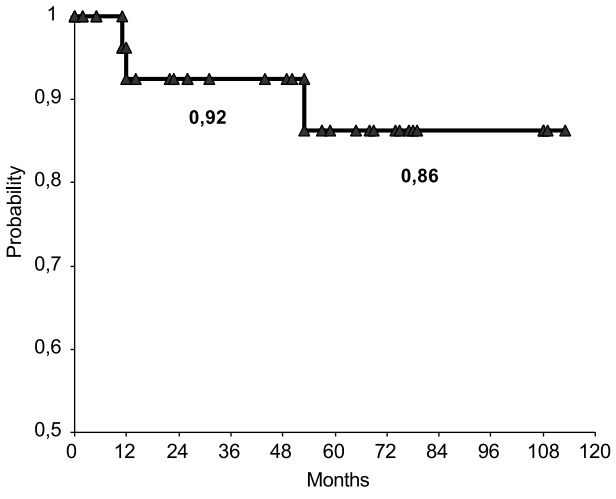

Figure 2 Loco-regional control.

radiation therapy. Sixty-one percent had local or/and regional recurrence and the 5-year overall and disease-specific survivals for T1–T2 patients reached only 17 and 32% respectively.[28]

A few decades back, partial laryngopharyngectomy had been proposed for early staged pyriform sinus carcinoma, with favorable oncologic results.[8,9,29,30] In our experience including a majority of stage III–IV lesions, 65% of the patients remained disease-free up to 5 years after treatment. Even though our study is based on a limited number of cases, this result is encouraging knowing the poor prognosis of such tumours and the high-staged diseases of our patients. Yet comparisons with other reported series in the literature must be cautious in that patient groups differ in disease advancement. Moreover, reports, as our present study, are most often based on retrospective analysis, and any statistically significant difference between treatment modalities needs to be interpreted prudently.

In particular, our series lacks a control group with exclusive radiation therapy or total laryngopharyngectomy. Until now, such a study has not been reported in the medical literature. However, in the absence of prospective randomization, patient groups would here again have been difficult to compare.

It may nonetheless be noted that the overall and disease-specific survival rates of our series of patients seems slightly better than that reported in previous studies, including generally less advanced tumours (Table 2).[10,21,29,31,34] Our surgical techniques may have been more aggressive, with wider, even though partial, laryngopharyngeal resection, knowing that large resection margins are necessary.

As most of the patients included in the study have been operated within the last 5 years, the survival curve cannot reasonably be interpreted on a long-term basis. However, none of the patients followed on the long-term developed any type of recurrence after the fifth post-operative year. The high 3–5-year survival rate does moreover confirm the possibility of good oncologic results even with conservation surgery.

The small number of patients limited subgroup analysis of this study. In particular, it does not seem reasonable to compare survival and functional results between patients having received post-operative radiation therapy (20 patients), those treated with exclusive surgery (10 patients) and those treated as salvage after radiation failure (four patients).

Functional results are generally satisfactory, comparing favorably with those previously reported,[32,33] although our patients' diseases were more advanced.

Conclusion

Pyriform sinus cancer, even early diagnosed, remains associated with a poor long-term overall survival. The patient outcome depends on loco-regional failure, the occurrence of second primary and distant metastases. Moreover, many of these patients have significant co-morbidity and are at

Table 2 Comparison of overall survival between previous reported series and the present series

Author	Stage	Protocol	Overall survival	
			%	Years
Ogura et al. (1980)[26]	T1-T2	Pre-op RT+CS ($n=85$)	59	3
Van den Brouck et al. (1987)[33]	T1 (+1 T2)	CS+RT ($n=18$)	67	3
			39	5
Baillet et al. (1996)[10]	T1-T2	CS+RT ($n=47$)	48	5
		RS+RT ($n=48$)	33.5	
		RT ($n=47$)	22	
Chevalier et al. (1997)[30]	T1-T2	CS+RT ($n=48$)	47	5
Kraus et al. (1997)	T1-T4	RS±RT ($n=88$)	54[a]	5
		CS±RT ($n=39$)		
Lecanu et al. (2000)[32]	T3-T4	CH+CS ($n=46$)	40	3
Eckel et al. (2001)[31]	T1-T2	CS±RT ($n=46$)	61.1	5
UCL-St Luc Study (2003)	T1-T4	CS±RT ($n=34$)	62	3
			52	5

CS, conservation surgery; RS, radical surgery; RT, radiotherapy; CH, chemotherapy.
[a] Disease-specific survival. Five year-overall survival of all patients was 30%.

risk of death from another disease than cancer. Therefore, we advocate that optimal loco-regional control with fairly good quality of life should be the primary goal. Compared with data from series using radiation therapy alone as primary treatment, conservative surgery alone or combined with post-operative radiotherapy appears to result in better loco-regional control, higher cause-specific and overall survivals, and yielding acceptable morbidity not only in early tumours but also in selected advanced carcinoma.

To our knowledge, there is currently no prospective study comparing the quality of life of the patients treated by conservation surgery and by non-surgical protocols. With similar outcomes in each group, quality of life assessments of the treated patients would be very informative to determine which therapeutic option is associated with the best functional outcome.

References

1. Mendenhall WM, Parsons JT, Cassisi NJ, Million RR. Squamous cell carcinoma of the pyriform sinus treated with radical radiation therapy. *Radiother Oncol* 1987;**9**:201–8.
2. Mendenhall WM, Parsons JT, Stringer SP, Cassisi NJ, Million RR. Radiation therapy alone or combined with neck dissection for T1–T2 carcinoma of the pyriform sinus: an alternative to conservation surgery. *Int J Radiat Oncol Biol Phys* 1993;**27**:1017–23.
3. Garden AS, Morrison WH, Clayman GL, Ang KK, Peters LJ. Early squamous cell carcinoma of the hypopharynx: outcomes of treatment with radiation alone to the primary disease. *Head Neck* 1996;**18**:317–22.
4. Brasnu D, Lacau-St-Guily J, Fabre A, Menard M, Bassot V, Laccourreye H. La survie dans les cancers du sinus piriforme après chimiothérapie d'induction. *Ann Oto Laryngol (Paris)* 1986;**103**:83–9.
5. Driscoll WG, Nagorsky MJ, Cantrell RW, Johns ME. Carcinoma of the pyriform sinus: analysis of 102 cases. *Laryngoscope* 1983;**93**:556–60.
6. Kajanti M, Mantyla M. Carcinoma of the hypopharynx: a retrospective analysis of the treatment results of a 25-year period. *Acta Oncol* 1990;**29**:903–7.
7. Kraus DH, Pfister DG, Harrison LB, et al. Larynx preservation with combined chemotherapy and radiation therapy in advanced hypopharynx cancer. *Otolaryngol Head Neck Surg* 1994;**114**:31–7.
8. Ogura JH, Jurema AA, Watson RK. Partial laryngopharyngectomy and neck dissection for pyriform sinus cancer. *Laryngoscope* 1960;**70**:1399–417.
9. Laccourreye H, Lacaux Saint guily J, Brasnu D, Fabre A, Menard M. Supracricoid hemilaryngopharyngectomy: analysis of 240 cases. *Ann Otol Rhinol Laryngol* 1987;**96**:217–21.
10. Baillet F, Simon JM, Rozec C, et al. Intérêt de l'association chirurgie paritelle- radiothérapie postopératoire pour le traitement des tumeurs de l'hypopharynx. Etude à propos de 142 T1–T2 traités par chirurgie partielle, chirurgie radicale ou radiothérapie exclusive. *Bull Cancer Radiother* 1996;**83**:65–9.
11. American Joint Committee on Cancer. *Cancer staging manual*. 5th ed. Philadelphia: Lippincott-Raven; 1998.
12. Hamoir M, Lengelé B, Rombaux P, Badr El-Din A, El Fouly P. Stretched radial forearm flap for reconstruction of the laryngopharynx: an alternative conservation procedure for radiation-failure carcinoma of the pyriform sinus. *Laryngoscope* 1999;**109**:1339–43.
13. Urken ML, Blackwell K, Biller HF. Reconstruction of the laryngopharynx after hemicricoid/hemithyroid cartilage resection. Preliminary functional results. *Arch Otolaryngol Head Neck Surg* 1997;**123**:1213–22.
14. Bjordal K, Ahlmer-Elmqvist M, Tollesson E, et al. Development of a European Organization for Research and Treatment of Cancer (EORTC) questionnaire module to be used in quality of life assessments in head and neck cancer patients 8 EORTC Quality of Life Study Group. *Acta Oncol* 1994;**33**:879–85.
15. Kaplan E, Meier P. Nonparametric estimation for incomplete observation. *J Am Stat Assoc* 1958;**53**:457–81.
16. Grégoire V, Beauduin M, Humblet Y, et al. A phase I–II trial of induction chemotherapy with carboplatin and fluorouracil in locally advanced head and neck squamous cell carcinomas: a report from the UCL-Oncology Group, Belgium. *J Clin Oncol* 1991;**9**:1385–92.
17. Shah JP, Shaha AR, Spiro RH, Strong EW. Carcinoma of the hypopharynx. *Am J Surg* 1976;**132**:195–9.
18. Rubin S. Pyriform sinus carcinoma. In: Silver CE, editor. *Laryngeal cancer*. New York: Thieme; 1991. p. 106–18.
19. Clayman GL, Weber RS, O'Mailley BB. Cancer of the hypopharynx and the cervical esophagus. In: Harrison LB, Sessions RB, Hong WK, editors. *Head and neck cancer: a multidisciplinary approach*. Philadelphia: Lippincott-Raven; 1999. p. 529–54.
20. Kramer S, Gelber RD, Snow JB, et al. Combined radiation therapy and surgery in the management of advanced head and neck cancer: final report of study 73-03 of the Radiation Therapy Oncology Group. *Head Neck Surg* 1987;**10**:19–30.
21. Kraus DH, Zelefsky MJ, Brock HA, Huo J, Harrison LB, Shah JP. Combined surgery and radiation therapy for squamous cell carcinoma of the hypopharynx. *Otolaryngol Head Neck Surg* 1997;**116**:637–41.
22. Lefebvre JL, Chevalier D, Luboinski B, Kirkpatrick A, Collette L, Sahmoud T. Larynx preservation in pyriform sinus cancer: preliminary results of European Organisation for Research and Treatment of Cancer phase III trial: EORTC Head and Neck Cancer Cooperative Group. *J Natl Cancer Inst* 1996;**88**:890–9.
23. Zelefsky MJ, Kraus DH, Pfister DG, et al. Combined chemotheray and radiotherapy versus surgery and post-operative radiotherapy for advanced hypopharyngeal cancer. *Head Neck* 1996;**18**:405–13.
24. The Department of Veterans Affairs Laryngeal Cancer Study Group. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. *N Engl J Med* 1991;**324**:1685–90.
25. Pignon JP, Bourhis J, Domenge C, Designe L. Chemotherapy added to locoregional treatment for head and neck squamous cell carcinoma: 3 meta-analyses of updated individual data. MACH-NC Collaborative Group. Meta-analysis of Chemotherapy on Head and Neck Cancer. *Lancet* 2000;**355**:949–55.
26. Ho CM, Ng WF, Lam KH, Wei WJ, Yuen AP. Submucosal tumor extension in hypopharyngeal cancer. *Arch Otolaryngol Head Neck Surg* 1997;**123**:959–65.
27. El Badawi SA, Goepfert H, Fletcher GH, Herson J, Oswald MJ. Squamous cell carcinoma of the pyriform sinus. *Laryngoscope* 1982;**92**:357–64.

28. Godballe C, Jorgensen K, Hansen O, Bastholt L. Hypopharyngeal cancer: results of treatment based on radiation therapy and salvage surgery. *Laryngoscope* 2002;**112**:834–8.
29. Ogura JH, Marks JE, Freeman RB. Results of conservation surgery for cancers of the supraglottis and pyriform sinus. *Laryngoscope* 1980;**90**:591–600.
30. André P, Pinel J, Laccourreye H. La chirurgie partielle verticale dans les cancers du sinus piriforme. *Ann Oto-Laryngol (Paris)* 1965;**82**:901–8.
31. Vandenbrouck C, Eschwege F, De La Rochefordière A, et al. Squamous cell carcinoma of the pyriform sinus: retrospective study of 351 cases treated at the Institut Gustave-Roussy. *Head Neck Surg* 1987;**10**:4–13.
32. Chevalier D, Watelet JB, Darras JA, Piquet JJ. Supraglottic hemilaryngopharyngectomy plus radiation for the treatment of early lateral margin and pyriform sinus carcinoma. *Head Neck* 1997;**19**:1–5.
33. Lecanu JB, Monceau G, Perie S, Angelard B, St Guily JL. Conservative surgery in T3–T4 pharyngolaryngeal carcinoma: an alternative to radiation therapy and to total laryngectomy for good responders to induction chemotherapy. *Laryngoscope* 2000;**110**:412–6.
34. Eckel HE, Staar S, Volling P, Sittel C, Damm M, Jungehuelsing M. Surgical treatment for hypopharynx carcinoma: feasibility, mortality and results. *Otolaryngol Head Neck Surg* 2001;**124**:561–9.