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Major Glossectomy: End Results of 106 Cases

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Advanced cancers of the oral cavity continue to be a therapeutic challenge. Despite significant improvements in radiotherapeutic techniques and adjuvant chemotherapy, patients usually die after a short period. Recent progress in reconstructive techniques has made major glossectomy (subtotal, near total, total or extended total) a reasonable palliative and potentially curative approach. It is the purpose of this study to report a series of 106 patients treated from 1985 to 1994 regarding surgical complications and prognosis. All but 1 patient undergoing major glossectomy had squamous cell carcinoma. Primary tumour sites were oral tongue (50 cases), base of the tongue (18 cases), floor of the mouth (28 cases) and other parts of the mouth (10 cases). Tumour stages were: 25 T3, 57 T4, 24 Tx, 34 N0, 20 N1, 32 N2a–N3, 20 Nx. The types of glossectomy were as follows: 24 subtotal, 31 near total and 51 total. A total laryngectomy was performed in only 6 cases. A neck dissection was performed in all but 3 patients: 12 unilateral radical neck dissection (RND), 1 unilateral supra, omohyoid (SOH), 39 simultaneous bilateral RND, 8 simultaneous bilateral SOH, and 43 RND associated to contralateral SOH. A pectoralis major myocutaneous flap was used to repair the operative defect in 96 cases. Complications were seen in 52 cases (49%). The most common complications were wound infection (17 cases), flap necrosis (15 cases) and fistula (15 cases). Significant transient aspiration was seen in 8 patients. At the study closing date, 30 patients were alive without disease, 5 had recurrent disease, 47 died of cancer, 14 died of causes not related to cancer or treatment and 10 were lost to follow-up. The 5-year actuarial survival rates were, respectively, 45%, 18% and 18% for T3, T4 and Tx. Other significant variables were pN stage ($P = 0.0672$) and year of admission (0.0318). In conclusion a major glossectomy without laryngectomy whenever possible is a safe procedure for a selected group of patients with advanced tongue and floor of the mouth cancer. The actuarial survival rates presented suggests that, in a very select group of patients, major glossectomy is a surgical procedure to be considered. Copyright © 1996 Elsevier Science Ltd

Key words: oral cancer, surgery, glossectomy, survival analysis

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INTRODUCTION

The more advanced oral and oropharyngeal cancers are related to various major problems: severe pain, changes in swallowing, desnutrition and altered airway-protecting mechanisms. The role of multimodality approaches including surgery, radiotherapy and chemotherapy is particularly appealing in the treatment of such cases. In spite of the significant improvements in radiotherapy techniques and addition of adjuvant chemotherapy, loco-regional tumour control and ultimate survival after non-surgical treatments remain poor [1–3]. Furthermore, if conservative treatment fails, salvage is not usually possible [1].

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Only few years ago, major glossectomy was still taken as a heroic procedure of last resort. A small number of patients whose clinical status was not so debilitated, and recurrent primary tumours not so advanced, were candidates to this procedure. Surgical excision of advanced tongue and floor of the mouth cancer had been considered a formidable challenge because of associated early morbidity and mortality and delayed cosmetic and functional outcomes. The most recent skills and innovations with reconstructive techniques, i.e. myocutaneous and revascularised free flaps, made major glossectomy an acceptable mutilation [4–13]. Not only is it possible to obtain a reasonable palliative effect improving the quality of survival, but also long-term loco-regional control has been achieved in a significant number of cases [4–12]. Although comparisons of surgery and radiotherapy results are extremely difficult due to selection bias, the

reported survival rates after major glossectomy and postoperative radiotherapy are usually higher than those obtained by other single or multimodality treatments [1–14].

The present study was prompted by the need to evaluate complications and survival results in a series of 106 consecutive patients submitted to major glossectomy from 1985 to 1994.

PATIENTS AND METHODS

From 1985 to 1994, 106 consecutive patients with locally advanced carcinomas of the mouth and oropharynx underwent a major glossectomy at the Head and Neck Surgery Department at Hospital A.C. Camargo (São Paulo, Brazil). Major glossectomies were classified according to the structures resected in: (a) subtotal (entire oral tongue and part of genioglossus and geniohyoid muscles); (b) near total (resection of at least three-quarters of the entire tongue); (c) total (entire tongue). There were no significant modifications on management policy for all patients included in this series. Eligibility criteria included resectable lesions, good pulmonary function and a Karnofski's score of 60 or greater. Pretreatment staging evaluations included physical examination, mandible and chest X-rays, and haematological and biochemical laboratory tests. Regional computed tomographic (CT) scans and pulmonary tests were performed in selected cases. Definitive radiotherapy was the treatment for patients with unresectable tumours, those with a poor performance status and those who refused surgical treatment.

All diagnosis were confirmed histopathologically prior to surgery (104 squamous cell carcinomas; 2 minor salivary gland carcinomas). The patients' ages ranged from 24 to 76 years (median 55 years). There were 93 males (88%) and 13 females (12%). The primary tumour sites were as follows: oral tongue, 50; base of tongue, 18; floor of the mouth, 28; other parts of the mouth, 10. There was tumour extension to one adjacent site in 68 patients (64%), two sites in 31 (29%) and three sites in 3 (3%). 29 patients with recurrent tumours (2 surgical failures, 19 radiotherapy failures, and 8 failures after combined surgery and irradiation) were classified as TxNxM0. Patient charts were reviewed and previously untreated cases were restaged using the 1987 version of UICC–AJC classification on the basis of the initial clinical description: 24 T3, 53 T4, 28 N0, 18 N1, 31 N2a–N3.

The surgical procedures for primary tumour resection were 24 subtotal (23%), 31 near total (29%) and 51 total glossectomies (48%). The primary tumour resection was accompanied by a marginal mandibulectomy in 19 patients (18%) and by a hemimandibulectomy in 19 (18%). Total laryngectomy was performed in 5 cases (5%) with tumour extension posteriorly into the vallecula or supraglottic larynx. A Biller *et al.* [8] method of laryngoplasty to prevent aspiration was performed in 6 patients (6%) considered at high risk for aspiration. The larynx was used for floor of the mouth reconstruction in 1 patient. All but 3 patients were submitted to neck dissections (90 simultaneous bilateral dissections). The patients were distributed according to the surgical technique for cervical lymph node dissection as follows: 51 radical classical dissections (39 bilateral), nine supraomohyoid dissections (eight bilateral) and 43 simultaneous combinations of radical classical and supraomohyoid techniques. In all bilateral classical neck dissections, the internal jugular vein was preserved at the less involved side of the neck. The surgical defects were reconstructed by myocutaneous flaps in all but 2 cases (1 laryngeal transposition flap and 1 microvascular free rectus abdominis transfer). The pectoralis major myocutaneous flap was the most frequently employed (96 cases) followed by infrahyoid (4 cases), pectoralis minor (3 cases) and the association of a pectoralis minor and pectoralis major (1 case).

Postoperative radiotherapy was used as an adjuvant to surgery in 68 patients (64%): 4 (of 5) patients with involved surgical margins; 46 (of 67) with positive lymph nodes; 5 (of 7) with positive margins and metastatic lymph nodes. The reason for radiotherapy in 13 (of 27) cases with negative margins and pN0 neck stage was the subjective judgement of the surgeon that considered the operation not radical. The postoperative radiotherapy consisted of a wide field technique including both sides of the neck with a dose range of 20–70 Gy (median = 50 Gy).

Statistical analysis

Distribution of main complications and certain treatment variables were compared by means of the chi-square test. Product-limit estimates of survivorship function were used for the computation of the cumulative survival rates [15]. The overall survival time was defined as the interval between the date of surgery and date of last consultation for censored observations, and date of death for uncensored observations. Cox's regression model was used to estimate the hazard ratios of death due to the combined effect of two or more study factors [16]. A stepwise forward algorithm was used for variable selection and construction of models containing the most parsimonious subset of variables with independent predictive properties with respect to the risk of death. Inference was based on the partial likelihood ratio statistic between nested models (10% significance).

RESULTS

52 patients (49%) presented 79 postoperative complications. There were four postoperative deaths (4%). Local infection (23 cases), wound dehiscence and/or flap necrosis (15 cases), and fistula (15 cases) were the most frequent complications. Table 1 shows the distribution of the three most frequent complications according to selected therapeutic variables. There were no differences in the rates of wound infection and flap dehiscence/necrosis according to prior radiotherapy, type of glossectomy or neck dissection. On the other side, prior radiotherapy and type of glossectomy were significant factors related to the presence of orocutaneous fistula. 8 patients (8%) had significant persistent aspiration that delayed decanulation and removal of feeding tube (for more than 30 days), or caused respiratory infection. There was one death related to recurrent pneumonia and 1 patient had a severe and life-threatening lung abscess. A total laryngectomy due to persistent aspiration and recurrent respiratory infection was performed in 1 patient.

Surgical margins were involved in 12 cases (11%). The number of lymph nodes dissected and histologically examined from each case varied from two to 188 (median = 53). Among the 103 cases submitted to a neck dissection, histologically involved lymph nodes were found in 74 (42 unilat-

Table 1. Distribution of selected postoperative complications according to treatment variables

Variables	Categories	Infection No/yes*	P	Flap necrosis No/yes	P	Fistula No/yes	P
Pre-operative radiotherapy	No	63/16	0.5370	68/11	0.9087	75/4	<0.001
	Yes	20/7		23/4		16/11	
Type of glossectomy	Subtotal	19/5	0.9874	21/3	0.2644	22/2	0.0246
	Near total	24/7		24/7		30/1	
	Total	40/11		46/5		39/12	
Neck dissection	No	3/0	0.6504	3/0	0.7721	3/0	0.4974
	Unilateral	10/3		11/2		10/3	
	Bilateral	70/20		77/13		78/12	

*Number of cases.

eral, 4 contralateral and 28 bilateral). The number of positive ipsilateral nodes varied from one to nine and contralateral nodes from one to six. The distribution of involved ipsilateral lymph nodes were as follows: level 1 (2 cases), level 2 (14 cases), level 3 (14 cases), level 4 (4 cases) levels 1 and 2 (6 cases), levels 1 and 3 (4 cases), and other combinations in 22 cases (7 and 6 patients had, respectively, 3 and 4 levels involved). In 4 cases, the sites of positive nodes were not possible to determine retrospectively.

At the study's closing date, there had been 2176 patient-months of cumulative follow-up experience. The mean follow-up time was 20.5 months. Two- and 5-year rates for OS were 37 and 28%, respectively. 49 patients (46%) died because of cancer recurrence or treatment-related complications and 4 (4%) due to causes not related to cancer. The cause of death of 12 patients (11%) was not determined. At the study closing date, there were 30 patients (28%) alive with recent follow-up information (4 with tumour recurrence). An additional 11 patients (10%) were considered lost to follow-up, but contributed sufficient follow-up information to be included in survival analysis (2.9–56 months, mean 14.2 months). 49 patients presented 55 tumour recurrences or metastasis. They occurred at the primary site in 29 patients (9 oral cavity, 18 oropharynx, 2 larynx), the neck in 18 (14 ipsilateral, 4 contralateral), and at distant sites in 8 (5 lung, 2 bone, 1 liver).

Tables 2–4 show the exploratory univariate analysis of survival data for selected demographic, clinical, pathological and therapeutic characteristics. Although female patients

Table 2. Survival rates according to selected demographic and clinical characteristics

Variables	Categories (%)	2-year OS*	5-year OS	P
Sex	Male (88)	33	26	0.0878
	Female (12)	73	37	
Age	< 50 (34)	32	25	0.4434
	50–69 (59)	39	28	
	⩾ 70 (7)	36	36	
T stage	T3 (23)	57	49	0.0116
	T4 (50)	40	20	
	Tx (27)	29	23	
N stage	N0 (26)	41	41	0.2314
	N1 (17)	54	41	
	N2a–N3 (29)	31	0	
	Nx (27)	29	23	
Sites involved:				
Oral tongue	No (9)	33	33	0.3281
	Yes (91)	37	27	
Base of tongue	No (42)	39	34	0.2798
	Yes (58)	34	21	
Floor of mouth	No (43)	37	33	0.8342
	Yes (57)	36	25	
Inferior gingiva	No (87)	38	31	0.5746
	Yes (13)	29	0	
Retromolar	No (92)	36	27	0.6002
	Yes (8)	49	49	
Tonsil fossa	No (96)	37	27	0.7493
	Yes (4)	38	38	
Number of sites involved	1 (4)	25	25	0.3085
	2 (64)	39	37	
	3 (29)	34	0	
	4 (3)	0	0	

*Overall survival.

Table 3. Survival results according to pathological variables

Variables	Categories (%)	2-year OS*	5-year OS	*P*
Histology	Grade I SCC† (49)	36	23	0.3378
	Grade II–III SCC (49)	36	33	
	Other (2)	100	100	
Surgical margins	Uninvolved (89)	37	28	0.6836
	Involved (11)	37	37	
Sides of the neck with positive nodes	Negative nodes (27)	58	46	0.0951
	Only ipsilateral (40)	26	14	
	Only contralateral (4)	25	25	
	Bilateral (26)	28	28	
	No neck dissection (3)	50	50	
Number of positive nodes	Negative nodes (27)	58	46	0.0590
	1 (19)	37	30	
	2 (16)	3	16	
	3–15 (35)	18	18	
	No neck dissection (3)	50	50	
Number of ipsilateral positive nodes	Negative nodes (31)	54	43	0.1213
	1 (21)	35	28	
	2 (14)	31	0	
	3–9 (31)	19	19	
	No neck dissection (3)	50	50	
Number of contralateral positive nodes	Negative nodes (55)	39	30	0.8327
	1 (12)	37	37	
	2–6 (18)	20	20	
	No neck dissection (15)	45	0	
Number of levels with ipsilateral positive nodes	Negative nodes (31)	54	43	0.2325
	1 (32)	30	25	
	2 (18)	28	14	
	3–4 (12)	16	16	
	Ignored/no neck dissection (7)	31	31	

*Overall survival.
†Squamous cell carcinoma.

had higher 5-year OS than males, the difference failed to reach statistical significance in univariate analysis. Patients with T4 tumours, those with more than two metastatic lymph nodes, experienced significant decrease of OS (Tables 2 and 3). Except for postoperative irradiation, the other treatment-related variables lacked impact on prognosis (Table 4).

The multivariate predictive model built using Cox's regression technique identified the independent predictors of the risk of death. Of the several candidate prognostic factors shown in Tables 2–4, only T stage, number of metastatic lymph nodes and sex were selected independent prognostic predictors (Table 5). Patients with T4 tumours or radiation failures had a significant impairment on prognosis compared

Table 4. Survival rates according to treatment-related variables

Variables	Categories (%)	2-year OS*	2-year OS	*P*
Type of glossectomy	Subtotal (23)	43	27	0.7894
	Near total (29)	29	16	
	Total (48)	38	38	
Neck dissection	No (3)	50	50	0.9039
	Unilateral (12)	43	0	
	Bilateral (85)	35	29	
Type of neck dissection	No (3)	50	50	0.5892
	RND† (11)	37	0	
	SOH‡ (1)	100	0	
	Bilateral RND (37)	42	36	
	Bilateral SOH (8)	30	0	
	RND + SOH (41)	31	27	
Prior radiotherapy	No (75)	39	29	0.2847
	Yes (26)	30	24	
Postoperative radiotherapy	No (36)	26	22	0.0022
	Yes (64)	43	31	

*Overall survival.
†Radical neck dissection.
‡Supraomohyoid neck dissection.

Table 5. Cox regression model for the risk of death

Variables	Categories	HR*	95% CI†	*P*
T stage	T3	1.0	Ref.‡	0.0058
	T4	2.9	1.4–6.0	
	Tx	2.8	1.2–6.1	
Number of positive nodes	0	1.0	Ref.	0.0009
	1	3.1	1.4–6.8	
	2	3.5	1.5–8.2	
	3–15	4.2	2.0–8.7	
	No neck dissection	1.0	0.1–7.7	
Sex	Male	1.0	Ref.	0.0162
	Female	0.3	0.1–0.9	

*Hazard ratios.
†95% confidence interval.
‡Reference category.

with patients with T3 tumours. The analysis showed a significant and dose–response-like relation between the number of positive nodes and risk of death.

DISCUSSION

There is no general agreement in the literature on the proper treatment of oral cavity and oropharynx cancers. Radiotherapy or surgery appears equally adequate for stage I and some stage II cancers. Stage III and IV cancers involving the tongue are treated by radiotherapy, combined radiotherapy and chemotherapy or surgery (major glossectomy) [1, 4–14]. Given the functional and cosmetic results of radical surgery for patients, radiotherapy was used widely in the past in the hope of avoiding a mutilating operation, but in most cases there is a remnant tumour or recurrence after a short period [1–3]. The results of treatment did not improve significantly in spite of different combinations of treatment modalities [2, 3]. Furthermore, the problems in a salvage surgery cannot be overemphasised. The most important are the difficulty in evaluating the extent of resection due to fibrosis and the potential increase in the risk of postoperative complications. The main advantage of primary operation is that the surgical landmarks are not obscured by fibrous tissues and inflammation. A major glossectomy is a treatment alternative that probably should be considered earlier in the treatment rather than as a last resort [5, 6, 8, 13, 17, 18]. Considering the decision to resect a massive tongue carcinoma, according to Sessions *et al.* [6]: "it should be either based on the possibility of returning the patient to productive life or on the need for palliation of an intolerable clinical condition such as pain, hemorrhage, dyspnea, or disphagia".

The management policy and the surgical technique varied relatively little for all 106 patients studied. The pectoralis major myocutaneous flap is the method currently employed for the reconstruction of the oral and oropharyngeal extensive defects because of its versatility and reliability. It is not only a good source of skin for intraoral lining, but also provides a soft and well-irrigated muscle for coverage of the carotid artery. One additional advantage of this flap is the possibility of performing ablation of the tumour simultaneously with the preparation of the flap. The main disadvantage is that the intraoral hair growth that can be disturbing and may require removal at varying intervals. Although a larynx flap is a reliable option, the sacrifice of an intact organ can only be justified in the situation where a laryngectomy would be necessary for functional reasons.

There were four postoperative deaths in the 106 patients studied. The incidence of fatal and non-fatal complications in this study was similar to that reported in other series [5–13]. Our study showed evidence of statistical significance related to prior radiotherapy on the risk of orocutaneous fistula. Such differences can be imputed both to irradiation late effects and the need of larger resections associated with more complicated reconstruction.

Since total or near total loss of the tongue produces significant functional deficits, rehabilitation following a major glossectomy requires a motivated patient and the co-operation of the surgeon, prosthodontist and speech therapist. The patient must have an adequate pulmonary reserve to clear secretions. All patients require a tracheotomy, usually for several weeks after the operation, some patients have continued difficulty in swallowing and recurrent aspiration. Depending on the patient's ability to handle secretions, the tracheotomy is maintained for a variable period of time. The incidence of significant aspiration ranges from 10 to 37% [5, 12, 18]. The degree of aspiration is rarely significant to require total laryngectomy and usually declines with rehabilitation [5, 12, 13]. A total laryngectomy was necessary due to recurrent respiratory infection in only 1 patient of this series. Patients can no longer manage solids, but usually tolerate a soft or liquid diet. To improve the mechanism of swallowing after major glossectomies, several techniques have been described [8, 11–13]. Although speech initially can be extremely handicapped, most patients who have undergone a major glossectomy develop satisfactory speech [11, 13].

The frequency and distribution of lymph node metastases in this series were similar to those reported by others for advanced tongue cancer [5, 19]. Although the predominance of metastases were in levels 1 and 2, more than one-third of patients had three or more positive nodes. This emphasises the need for a comprehensive neck dissection in cases of clinically positive nodes. Elective neck dissection has now been used for more than four decades since treatment of occult metastasis is considered to be important to the management of oral cancers. Elective radical neck dissection (RND) used to be part of standard treatment of patients with advanced oral and oropharyngeal cancer. The main disadvantage of this procedure is that it can produce significant disability. For the last three decades, several reports support the concept that conservation of some structures, such as sternocleidomastoid muscle, internal jugular vein and/or accessory nerve, does not compromise survival. Supraomohyoid neck dissection became the standard elective procedure, since it is an anatomical and oncologically sound procedure based on the probability of metastasis [20].

Advanced squamous cell carcinoma of the tongue and floor of the mouth continues to be a problem of loco-regional control. 49 patients (46%) died because of cancer recurrence or treatment-related complications and 4 (4%) due to causes not related to cancer. At the study closing date, there were 30 patients (28%) alive with recent follow-up information (4 with tumour recurrence). An additional 11 patients were considered lost to follow-up, but contributed sufficient follow-up information to be included

in survival analysis. 45 patients presented 55 tumour recurrences or metastasis. They occurred in the primary site in 29 patients (18 in the oropharynx), the neck in 18 (14 ipsilateral) and distant sites in 8 patients. This is similar to the causes of death reported by Harrison [18] in 10 of 16 total glossectomy patients: residual disease at the lateral pharyngeal wall (3 patients), uncontrolled neck disease (2 patients), distant metastasis (3 patients) and cardiovascular accident (2 patients). Weber *et al.* [12] and Tiwari *et al.* [13] also reported that the most important cause of death was local and regional recurrences. These results emphasize the need to improve local and cervical control with first treatment. Probably the preservation of part of the base of the tongue (near total glossectomy) should not be recommended, and the tonsil fossa must be evaluated carefully by CT scan or MRI prior to the operation. Postoperative radiotherapy should be indicated as a routine for all patients undergoing major glossectomy, independent of margins or lymph node status, and should include the oropharynx in the portals.

In this series, the pathological description of surgical margin involvement did not contribute significantly in prediction of the overall survival results. Probably other factors, such as the inaccuracy in examining deep margins, and the presence of perineural invasion and/or vascular embolisation, can play a role. Unfortunately, their value could not be studied here because there was no information on most pathological reports.

The risk of death significantly varied as a function of T stage: the OS of recurrent tumours (Tx) and T4 tumours were lower than the observed in T3. In this series, clinical N stage was not a significant prognostic indicator, but the number of positive nodes diagnosed at pathological examination exerted a significant and dose–response-like effect on prognosis. The best prognosis identified for females can be attributed to the lower risk of death due to causes other than cancer.

A major glossectomy without laryngectomy whenever possible is a safe procedure for a selected group of patients with advanced tongue and floor of the mouth cancer. This study showed that major glossectomies can be carried out with acceptable morbidity and it is effective (28% 5-year overall survival). The high rate of local and regional recurrences suggests that a more extensive resection with appropriate reconstruction may be necessary in selected cases. Also, radiotherapy as an adjuvant modality should be indicated in all situations. The preliminary survival data presented suggest that, in a very selected group of patients, total glossectomy is the surgical procedure to be considered. The use of a myocutaneous flap associated with a team approach dramatically improves patient rehabilitation.

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