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Squamous-cell carcinoma of the lower lip: A retrospective study of 58 patients

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The charts of 58 patients with squamous-cell carcinomas of the lower lip, treated at the General Hospital of the University of São Paulo Medical School from January 1980 to December 1989, were retrospectively analyzed. In addition to regular demographic data, all available information was collected regarding: smoking and drinking habits; sun exposure; clinical stage; macroscopic features of the primary lesions; type of treatment; and follow-up. A meticulous pathological analysis, comprising the histologic differentiation grade, maximal tumor thickness, sun elastosis, perineural spread, vascular and muscular invasion, surgical margins, peritumoral inflammatory infiltrate, and positive lymph nodes, with or without extracapsular spread, was undertaken as well. The evaluation of the overall 5-year survival showed significant statistical differences, with prognostic implications, for the following variables: maximal tumor thickness, T-stage and positive nodes.

UNITERMS: Lip cancer. Lip neoplasm. Squamous-cell carcinoma, prognostic factors. Head and neck cancer.

INTRODUCTION

Among the diseases treated by the head and neck surgeon, cancer is by far the most important, not only due to the frequency of its occurrence in this region of the human body, but also because of its prognostic implications. Of all malignant tumors in this area, lip cancer is the second most frequent, preceded only by skin cancer,¹⁰ and is also the most frequent among oral

cavity tumors.^{2, 20} Owing to the location and greater exposure to sunlight, the lower lip is affected in nearly 90 percent of all cases.^{17, 63} Among histologic types observed, squamous-cell carcinoma is identified in 95 percent of all cases, whereas basal-cell carcinoma, more common on the upper lip, and adenocarcinomas arising in minor salivary glands, constitute the rarest types.⁶⁴ Most authors agree that the evolution, at times favorable, of such tumors may be complicated by local recurrence, or lymphatic dissemination, whether local-regional or distant, which may lead to the patient's demise.^{9, 31}

Thus, the present study was undertaken to assess the tumoral and individual factors which may influence and determine the main prognostic aspects in regard to the recurrence and risk of death caused by the lower lip squamous-cell carcinoma.

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PATIENTS AND METHODS

Our study is based on the retrospective analysis of the charts of 58 patients with lower lip squamous-cell carcinoma treated at the Central Institute of the General Hospital of the University of São Paulo Medical School from January 1980 to December 1989.

Patients included in the study were those who:

- a. had a histologically-confirmed diagnosis of lower lip squamous-cell carcinoma;
- b. had not been previously treated;
- c. had been submitted to surgery, as a first treatment, with curative intent;
- d. Had records containing all clinical and anatomopathological data regarding the tumor; hence, incomplete records were excluded;
- e. had demographic data which was as complete as possible.

Thus, among the 141 patients listed on the computer of the General Registry at General Hospital with lip cancer treated during the period mentioned, we were able to select 58 cases. The main causes of record exclusion were:

- a. not in dead files
- b. imprecise tumor data
- c. the impossibility of reviewing the anatomopathological data.

We must stress that as this facility is a general hospital, the cases of the present study were treated in three departments, as follows: Dermatology, 27 patients

(46.5 percent); Otorhinolaryngology, 9 (15.5 percent); and Head and Neck Surgery, which was responsible for 22 patients (38.0 percent), 4 of whom (6.9 percent) had been referred by the Dermatology Department, where they had been submitted to the first resection (Fig. 1).

The protocol of each case included:

1. Patient's full name and hospital registration number.
2. Sex.
3. Age, in years.
4. Race: White/other races.
5. Place of origin: urban/rural area.
6. Occupation: outdoor/indoor activities.
7. Duration of complaint, in months.
8. Habits: smoker/non-smoker; consumed alcohol/ consumed no alcohol.
9. Local physical examination; this contained accurate data about the tumor lesion, as well as lesion type, size in centimeters (T), and site.
10. Treatment received: the data of the first surgery was the basis for estimating each patient's actuarial survival, in months. The type of hospital treatment received by patients enabled us to organize 4 groups, as follows:

Group I - Patients submitted to tumor resection (R) with primary closure (PC) of the surgical defect (R + PC);

Group II - Patients submitted to tumor resection with surgical defect reconstruction (REC) by means of some kind of flap (R + REC);

Group III - Patients submitted to tumor resection combined with any type of neck dissection (ND), without adjuvant radiotherapy (R + ND);

Group IV - Patients submitted to tumor resection and adjuvant radiotherapy (RDT), with or without neck dissection (SUR + RDT).

Our intent, when organizing the four groups, was to correlate treatment intensity with patient survival. Fifteen patients (25.9 percent) were classified into Group I; 21 (36.2 percent) into Group II; 7 (12.2 percent) into Group III; and the remaining 15 cases (25.9 percent) into Group IV. Eleven patients (19.0 percent) underwent neck dissection, and 4 (6.9 percent) with cervical metastasis were given radiotherapy (Fig. 1).

11. Follow-up: this involved observations on the development of recurrences, regional metastases, other malignant tumors, or evolution with no evidence of disease.

12. Anatomopathological study: biopsies and surgical specimens of the patients included in our study, whether of the primary tumor

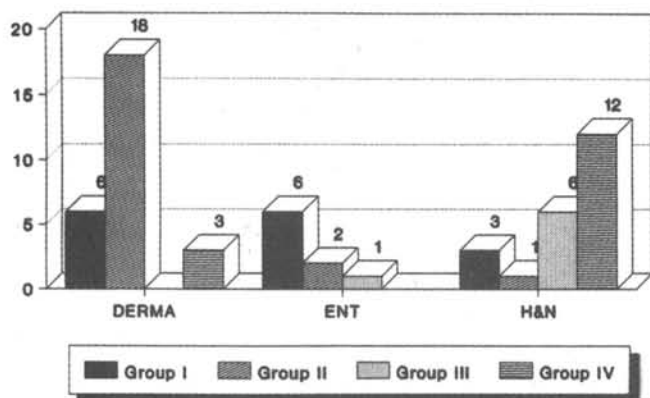


Figure 1 - Case distribution at the General Hospital. Number of patients treated by Dermatology (DERMA), Otorhinolaryngology (ENT) and Head and Neck Surgery (H&N).

or recurrences, as well as the products of neck dissection, were reviewed by two experienced pathologists at the General Hospital. Thus, we were able to analyze in detail:

12.1. Histologic grade: according to the classification proposed by BRODERS⁷ in 1926, by which these neoplasms are divided into four grades, mainly considering the cellular differentiation percentage in the squamous-cell carcinoma.

12.2. Maximal tumor thickness: utilizing a 0.1 mm accuracy optical micrometer, the maximal thickness of each tumor was measured vertically, with the exclusion of keratin, from the surface layers of viable cells, down to the deep region of the neoplasm which borders on the corium.

12.3. Solar elastosis: the alteration of the elastic fiber layer provoked by ultraviolet radiation, causing solar or senile elastosis was analyzed as present or absent.

12.4. Perineural invasion: this was defined as the visualization of a well-defined infiltration of the perineural space. The compression of nervous fillets by the neoplasm was not considered to be an invasion.

12.5. Muscular invasion: the neoplastic infiltration of the lip muscles was also analyzed as present or absent.

12.6. Vascular invasion: the presence of the tumor infiltrating the vascular wall was analyzed.

12.7. Surgical margins: the tumor resection margins on the lip after the cancer excision procedures had been completed.

12.8. Inflammatory response: the degree of inflammatory response on the tumor periphery was assessed through the discreet, moderate or intense presence of global reactional cellular infiltrate.

12.9. Analysis of cervical lymph nodes: in order to record data relative to the presence or absence of neoplastic involvement, rupture and extracapsular tumoral spread, cervical lymph nodes were divided, in the conventional fashion, into levels I to V, on both sides.⁶⁰

For the analysis of the different variables examined in the patients, a microcomputer (Microtec XT-1002) and specific statistical analysis programs were utilized. All data contained in the protocols were analyzed in regard to information coherence, with attempts to select variables which might best contribute to the discrimination of prognosis-determining factors. Cumulative survival rates and curves were generated by the Kaplan & Meier method. Comparisons among survival distributions for categories of the same variable were made using the Mantel-Cox test. The KMSURV microcomputer program¹² was utilized for all actuarial analyses relative to overall survival.

RESULTS

The collection and tabulation of the demographic data concerning the patient group analyzed showed that 50 (86.2 percent) were men and 18 (13.8 percent) were women, and both sexes were predominantly white (55 or 94.8 percent). A larger number of patients came from urban zones (33 or 56.9 percent) rather than rural areas (25 or 43.1 percent). Outdoor jobs, and consequently, more prolonged exposure to the sun, were reported by 30 (51.7 percent) of the patients, whereas the remaining 28 (48.3 percent) conducted activities indoors, thus affording greater protection. The actuarial or overall survival regarding these four variables did not reveal statistically significant differences among the categories.

Ages ranged from 18 to 84 and case distribution was as follows: 10 patients (17.2 percent) were under the age of 40; 21 patients (36.2 percent) were aged 41-60, and 27 (46.6 percent) were over the age of 61. The overall 5-year survival for these three categories did not reveal a statistical difference.

The duration of complaint varied from 2 to 36 months. This was shorter than 1 year in 25 cases (43.1 percent), and 1 or more years in 33 cases (56.9 percent). Survival at 5 years was not statistically different between these two categories.

A smoking habit was reported by 42 patients (72.4 percent). Normal cigarettes were mentioned by 32 (55.2 percent), handrolled cigarettes by 8 (13.8 percent), and pipes only by 2 of these patients (3.4 percent). There were no references to smoking in 12 cases (20.7 percent), and 4 patients (6.9 percent) stated they were non-smokers.

Moderate drinking was reported by 25 of these patients (43.1 percent), whereas 19 (32.8 percent) did not drink at all, and in 12 cases (20.7 percent) such information was lacking. Two cases (3.4 percent) of alcohol abuse were recorded.

In regard to tumor size, 20 patients (34.5 percent) exhibited T1 lesions; 32 cases (55.2 percent) showed T2; in 5 cases the tumor was recorded as T3; and only 1 patient (1.7 percent) had a T4 tumor. For patients with T1 tumors, the overall 5-year survival was 68.3 percent, with a standard error of 10.8. For T2 cases, such survival was 75.1 percent (SE: 8.3) for T3 + T4, it was zero, showing a statistically significant difference ($p=0.00001$).

The lesion exhibited by 45 patients (77.6 percent) was described as ulceroinfiltrative, whereas verrucose or vegetating lesions were seen in the remaining 13 (22.4 percent) patients. The lesion was noted on the left side in

24 of these cases (41.4 percent); on the mid-portion of the lip in 16 (27.6 percent); and on the right side in an equal number of cases.¹⁶ It was described as reaching the left commissure in 1 case (1.7 percent), and to have been inaccurately recorded in only 1 case (1.7 percent). Survival values for the type of lesion did not show statistically significant differences.

The situation of cervical lymph nodes was carefully examined and no suspicious cervical lymph nodes were encountered in 44 patients (75.9 percent), who were labeled as N0. Six patients (10.3 percent) were classified as N1; 2 (3.4 percent) as N2a; 4 (6.9 percent) as N2b; and 2 (3.4 percent) as N2c. For the survival analysis, the variable was divided into two categories: N0 and N+. Thus, the overall 5-year survival for patients with N0 classifications was 70.4 percent (SE: 7.2) and was 47.6 percent (SE: 14.0) for the 14 patients (24.1 percent) with palpable lymph nodes (N+), showing a statistically significant difference ($p=0.00929$).

As none of the patients presented evidence of distant metastasis, they were all considered M0. Our staging by TNM classification had been completed. Thus, there were 16 Stage I patients (27.6 percent); 22 Stage II (37.9 percent); 11 Stage III (19.0 percent); and 9 Stage IV (15.5 percent) at initial treatment.

These patients were submitted to six different forms of treatment, as follows:

- tumor resection with primary closure of defect in 15 cases (25.9 percent);
- resection and closure of defect using a regional flap in 21 cases (36.2 percent);
- tumor resection combined with unilateral neck dissection in 4 cases (6.9 percent);
- tumor resection associated with bilateral neck dissection in 3 cases (5.2 percent);
- tumor resection with neck dissection combined with postoperative radiotherapy in 11 patients (19.0 percent);
- primary tumor resection and neck radiotherapy in 4 cases (6.9 percent).

Considering the distribution by treatment groups, the overall 5-year survival for the 15 Group I patients (25.9 percent) was 67.7 percent (SE: 13.3); for the 21 Group II cases (36.2 percent), survival was 90.2 percent (SE: 6.6); for the 7 Group III cases (12.2 percent), it was zero; and for the 15 Group IV patients (25.9 percent), survival was 36.0 (SE: 13.2). A highly significant difference was evident among the categories ($p = 0.00009$).

During our data collection, we found that 33 patients (56.9 percent) were still alive, whereas 25 had died; 12

(20.7 percent) had died because of the lip tumor and 13 patients (22.4 percent) due to other causes.

Survival varied from 1 to 129 months; mean survival time was 54 months. There were 44 (75.9 percent) disease-free patients, including those who had died, and neoplastic recurrence in 14 patients (24.1 percent) was distributed as follows:

- 7 cases (12.0 percent) with neck recurrence;
- 6 cases (10.3 percent) with local and neck recurrences;
- 1 case (1.7 percent) with local, cervical recurrences, and distant metastasis.

Recurrence time was from 3 to 30 months and was detected within the first postoperative year in 8 patients (13.8 percent); between the first and second year in 5 cases (8.6 percent); and after two years in only 1 patient (1.7 percent).

The development of a second tumor was documented in 7 patients (12.0 percent). It was located on the skin in 5 cases (8.6 percent), in the oral cavity of 1 patient (1.7 percent), and elsewhere in the remaining case (1.7 percent). Other clinical ailments were recorded during the follow-up of 14 patients (24.1 percent). There was 1 patient (1.7 percent) with AIDS.

The accurate histologic analysis of the specimens on file at the General Hospital Department of Pathology revealed interesting and quite important data for this study. Thirty patients (51.7 percent) had Grade 1 tumors in regard to cellular differentiation; 22 (37.9 percent) had Grade 2; and 6 (10.3 percent), Grade 3. Survival at 5 years showed no statistically significant differences among these three categories.

Tumor thickness ranged from 0.6mm to 61.8mm, with median thickness approaching 4mm and was distributed among the patients as follows (Fig. 2):

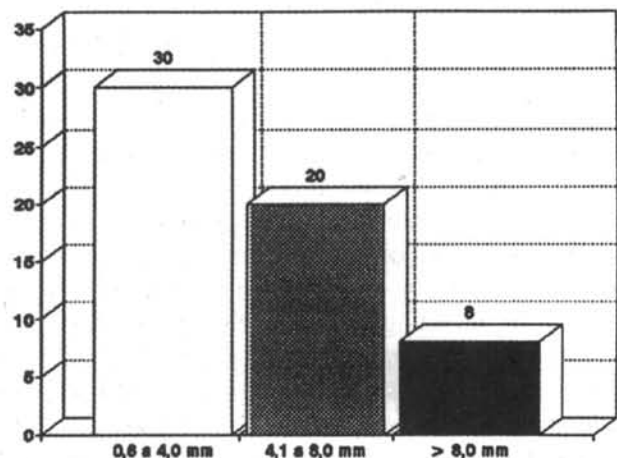


Figure 2 - Case distribution according to tumor thickness.

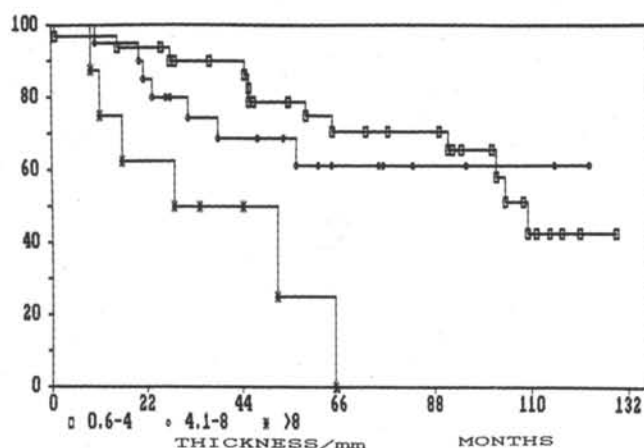


Figure 3 - Curves of cumulative survival and tumor thickness.

- 0.6-4 mm in 30 cases (51.7 percent);
- 4.1-8 mm in 20 cases (34.4 percent);
- > 8 mm in 8 cases (13.9 percent).

The overall 5-year survival for this variable was significantly different:

- 74.5 percent (SE: 8.4) for patients with tumors of 0.6-4mm;
- 60.9 percent (SE: 11.9) for those with tumors of 4.1-8.0mm;
- 25.0 percent (SE: 19.8), with $p=0.00467$ (Fig. 3) for those with tumors > 8 mm.

Solar elastosis was present in 44 cases (75.9 percent). Perineural tumor invasion was seen in 21 cases (36.2 percent). Muscular invasion was present in 39 cases (67.2 percent). No vascular invasion was detected in 52 cases (89.7 percent). The overall 5-year survival for the three invasion variables showed no statistical differences.

The peritumoral inflammatory cellular infiltrate was intensely evident in 33 cases (56.9 percent), moderately evident in 22 (37.9 percent), and discreet in only 3 (5.2 percent). It should be noted that lymphocytes and plasmocytes were detected in all cases, while no histiocytes, neutrophils or eosinophils were present in 8 cases (13.8 percent), 37 (63.8 percent), and 25 cases (43.1 percent), respectively. The analysis of the overall 5-year survival relative to inflammatory infiltrate forms revealed:

- a 60.9 percent (SE: 10.0) moderate and discreet infiltrates;
- a 67.1 percent (SE: 8.0) intense infiltrate ($p=0.8021$).

Eighteen (31.0 percent) of the patients treated underwent some form of neck dissection, as already detailed.

The analysis of lymph node involvement by cancer among the different levels of cervical distributions showed, as expected, a greater implication of levels I, II and III in 15 (25.9 percent), 10 (17.2 percent), and 10 (17.2 percent) patients, respectively. Among the patients submitted to neck dissection, there was no lymph node involvement in 6 (10.3 percent), whereas invasion of 1 to 4 lymph nodes was detected in 7 patients (12.1 percent), and 5 to 55 lymph nodes positive for carcinoma were noted in the remaining 5 cases (8.6 percent). No neck dissection (ND) was performed in 40 patients (69.0 percent) (Fig. 4). The overall 5-year survival for patients submitted to neck dissection and with histologically negative lymph nodes was 66.7 percent (SE: 19.2); 34.3 percent (SE: 19.5); for those with involvement of 1 to 4 lymph nodes for those with involvement of 5 to 55 lymph nodes, such survival was 40.0 percent (SE: 21.9) and, for those not submitted to neck dissection, the rate was 92.5 percent (SE: 4.2). Such differences were statistically significant ($p=0.00041$) (Fig. 5).

Lymph node capsule rupture and extracapsular neoplastic spread were identified in 8 (13.8 percent) of the 18 patients (31.0 percent) with neck dissection. For this variable, the overall 5-year survival also showed statistically significant results ($p=0.00111$) among the three categories represented:

- patients with no capsular rupture in involved lymph nodes had an overall survival of 58.3 percent (SE: 6.1);
- patients presenting lymph node capsule rupture had an overall survival of 33.3 percent (SE: 18.0);

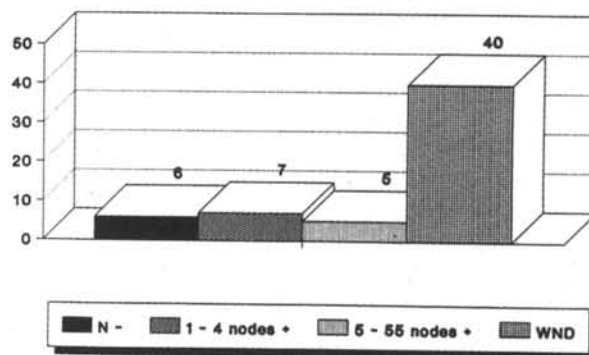


Figure 4 - Case distribution according to the number of histologically-positive lymph nodes.

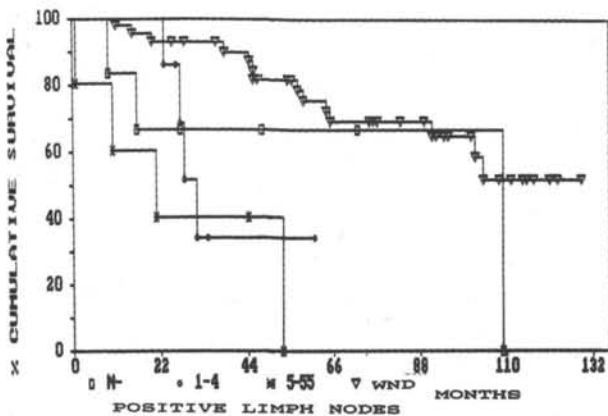


Figure 5 - Curves of cumulative survival and the number of histologically-positive lymph nodes.

- patients not submitted to neck dissection had an overall 5-year survival of 92.5 percent (SE: 4.2).

DISCUSSION

The literature shows quite different findings when analyzing lip cancer incidence worldwide. In Australia, this incidence represents 17 percent of all malignant tumors of the head and neck, 3.2 percent of all tumors, and 62.1 percent of mouth cancers.⁶² In Italy, lip cancer corresponds to 25 percent of mouth cancers,⁵⁶ in Canada, to three percent all tumors,⁵⁹ and in the United States this incidence varies from 0.6 percent²⁸ to 2.2 percent⁴² of cases treated as cancer in general. In Brazil, particularly in São Paulo, the annual incidence rate for 1978 was 3.8 cases per 100,000 population for males, and 1.0 case per 100,000 for females.⁴⁴ Cancer mortality in São Paulo was 0.18 per 100,000 population⁴³ in 1978.

In regard to demographic data, the literature has been quite unanimous in showing a far greater proportion of cases among men than women. In the large number of cases detailed, the number of male patients with cancer in the lower lip varied from 77.7 percent (24) to 100 percent.⁴ In our cases, comprised of 50 male patients (86.2 percent), such marked male predominance was also found.

The unanimity found in the literature is repeated when the patients' ethnic group is analyzed. All studies consulted report a higher incidence of lip cancer among

white patients. BERNIER & CLARK,⁵ among 835 cases collected, reported only 4 (0.47 percent) black patients. MORA & PERNICIARO⁴⁶ published a study with the largest number of black patients found in the literature reviewed: 36, treated between 1948 and 1979. Nevertheless, no race comparison is made in their study. SCOPP's hypothesis⁵⁴ seems plausible, as it states the melanin pigment, more abundant in blacks, affords greater protection from the sun. Our percentage of white patients (94.8 percent) agrees with the literature.

For the age group of greater lip cancer incidence, data were also somewhat uniform, with the age bracket between the 60's and the 80's being referred to by most authors.^{2,3,8,15,22-24,27,32,34,38,46,49,50,62} BERNIER & CLARK⁵ described the lowest mean age found in the literature consulted - 37 years - based on the sample of patients from the army included in their cases. Patients with lip cancer aged 18 and 19 years are described. The oldest patient, aged 97, is described in BRODERS' series.⁸ The age bracket in our series relates with the literature described; 46.6 percent of the patients are over the age of 61.

The place of origin of patients is associated with the importance attached by the authors to a more prolonged sun exposure as a relevant etiologic factor in lower lip cancer.^{8,17,29,34,57} Areas with predominantly sunny climates, as well as daily activities characterized by sun exposure, whether at work or leisure, seem to play a role in the development of lower lip cancer. In the present series, 56.9 percent of the patients came from urban areas. In a country with a predominantly tropical climate like Brazil, sun exposure, even in urban areas, may be more prolonged when activities are conducted outdoors (51.7 percent of our patients). Thus, the case distribution in our study relates with the literature. None of the variables mentioned above, when studied in our series, proved to be statistically important for patient prognosis.

The easy examination of the lip, as pointed out by ELFENBAUM,¹⁹ whether by the individual himself or by dentists or physicians, makes it possible to obtain diagnostic and therapeutic resources at quite an early stage. Thus, the duration of complaint is not long. BRODERS⁸ had mentioned a mean duration of 2.5 years, whereas for BERNIER,⁴ it was less than 1 year. The longest time of tumoral complaint in our series was 36 months.

Among habits considered to be harmful to one's health, smoking is quite constantly mentioned by

authors^{8,17,21,34} as an important etiologic factor in the development of lip cancer. The large number of pipe smokers found by BRODERS⁸ has not been confirmed by other authors.^{29, 59} Alcohol abuse did not prove to be an etiologically important factor in lip cancer.²¹ Our study has not added anything to these data, which are devoid of prognostic value.

Few series include advanced tumors.⁵⁸ In virtually all publications dealing with treatment, T1 and T2 tumors represent the majority of cases. For PETROVICH et al.,⁴⁹ 93 percent of a total of 250 patients were T1 and T2; MEHREGAN & ROENIGK⁴¹ reported 100 percent of T1 and T2 in 44 lesions; ZURRIDA et al.⁶⁵ detected 100 percent of T1 and T2 in their group of 131 patients; GROVER et al.²⁴ found 98.8 percent of T1 and T2 among their 180 cases; and BAKER & KRAUSE² reported 81.7 percent among 317 carcinomas. Such predominance of quite early clinical stages is invariably accompanied by high overall survival rates at 5 years, regardless of the therapeutic mode. Thus, following surgical treatment, survival was >90 percent for BAKER & KRAUSE;² 94.2 percent for MOHS & SNOW;⁴⁵ and 85 percent for ZURRIDA et al.⁶⁵ TAN⁶² reported 87.1 percent of overall 5-year survival for patients treated with radiotherapy. For larger lesions (T3 and T4), there was an impairment in the 5-year survival; 71.4 percent for T3, and 50 percent for T4.² In our series, only the patients with T1 and T2 tumors survived 5 years (68.3 percent SE: 10.8, and 75.1 percent SE: 8.3, respectively). All patients with T3 and T4 tumors died before the 5-year period. The literature seems to indicate that advanced or recurrent tumors and/or positive cervical lymph nodes can be more effectively managed by surgical treatment. Advantages, such as better assessment of the primary tumor, better and faster healing, and absence of local radiotherapeutic complications, are cited by BAILEY.¹ The author advocates radiotherapy only for elderly patients with small, localized lesions.

The ulcerous tumor lesion was the most frequently described.^{13,33,35} The same occurred in our series, with no statistical significance as to survival rate variation.

According to the literature, the lymph node involvement at initial consultation was quite infrequent.^{25,49} In our series, this was 34.1 percent, with statistical tests showing significant difference of survival rates of N0 and N+ categories.

The presence or absence of cervical metastases at initial consultation is a relevant factor for the choice of therapeutic mode. On the basis of his 2,696 cases, MAHONEY³⁷ noted an important decline in overall survival at 5 years when comparing patients without

metastasis with patients with positive neck metastasis (from 97.8 percent to 37.4 percent, respectively). HELLER & SHAH²⁶ detected primary metastases in 10 percent of their cases, which led them not to indicate the prophylactic neck dissection. However, with an overall 5-year survival of 70 percent, the authors recommended the therapeutic radical neck dissection, following a suprahyoid dissection which had detected the presence of metastasis. The same recommendation was made by others.^{1,39,64} It must be stressed that PETROVICH et al.⁴⁸ found lymph node metastases in only 5 percent of patients with T1 and T2 lesions, whereas 67 percent of T3 and T4 cases had metastasized. EGGERT et al.¹⁸ also reported a 5-year survival of 64.7 percent among patients treated with elective neck dissection,⁴⁰ as opposed to only 10 percent for patients submitted to therapeutic neck dissection.

The significant difference in the survival of the four treatment groups in our series should not be overestimated, as the present study was not designed to analyze therapeutic forms. Nevertheless, such difference does help to reinforce the likelihood of a fatal evolution of advanced lip cancer.⁵¹

Local or cervical recurrence is undoubtedly a factor of poorer prognosis. DARGENT et al.¹⁶ reported a 5-year survival of 60 percent for patients treated for the first time, and 32 percent for those treated for recurrence. In our series, neoplastic recurrence was detected in 24.1 percent (14 patients), with neck recurrence in 7 cases (12.0 percent). The mortality rate of recurring patients was 85.7 percent (12 patients), and the 5-year survival rate was 15.3 percent (2 patients).

The purpose of the present study was the analysis of the factors related to the tumors in 58 patients. Although BRODERS⁷ and FRIERSON & COOPER²² have encountered significant differences in the prognosis of patients with Grade 3 and 4 tumors, such differences were not found in our study. The vascular invasion cited by LUND et al.,³⁶ the nerve invasion described by BYERS et al.,¹¹ in addition to others,^{42,53} all with marked influences on patients' evolution, showed no statistical difference in our series, either.

The peritumoral lymphoplasmocytic cellular response, stressed by LUND et al.⁵⁶ through their tumoral scores, and by SYRJANEN et al.,⁶¹ who reported that such scores correlated directly with the survival rates and inversely with the frequency of metastases, was investigated in our histologic analysis. Our results confirmed the constant presence of lymphocytes and plasmocytes (100 percent of cases); however, this was not statistically significant.

Muscular invasion is described as quite frequent, owing to the superficiality of the orbicular muscle. Invasion was reported as present in 84 percent of the lesions operated on by MEHREGAN & ROENIGK⁴¹. Despite being present in 67.2 percent of the cases in our series, muscular invasion had no prognostic significance.

The maximal tumor thickness analyzed by FRIERSON & COOPER²² and by MEHREGAN & ROENIGK⁴¹ was even more prominent in our study. The former described the minimal thickness of 6 mm to be statistically significant in terms of prognosis, whereas the latter described the variation interval of 0.33 mm to 2.44 mm encountered in operated patients, without relating thickness to prognosis. After tabulating our data, we obtained the value of 8 mm, above which survival is less likely (Fig. 3).

The lymph node involvement by the neoplasm was included as a prognosis-predicting factor by NOONE et al.⁴⁷ In the present series, overall survival curves for lymph node involvement showed significant values, even when the group of patients not submitted to neck dissection was included (Fig. 5). The overall 5-year survival for patients with positive lymph nodes was 34.3 percent (SE: 19.5) for 1 to 4 lymph nodes, and 40.0 percent (SE: 21.9) for 5 to 55 lymph nodes, as opposed to 66.7 percent (SE: 19.2) for those with no involved lymph nodes. The lymph node chains more frequently involved were those of levels I, II and III on the tumor side. Dissemination to other levels is far less common, as demonstrated by SHAH et al.⁵⁵ in 1990.

NOONE et al.⁴⁷ also described the presence of extracapsular spread as an important factor of poorer prognosis. SACK & FORD⁵² reported a 3-year survival rate as low as 18 percent among patients with extracapsular invasion. Our case analysis showed the occurrence of capsular rupture in 13.8 percent of cases (8 patients), with

a 5-year survival similar to that found in patients with no capsular rupture.

Thus, the factors with an actual prognostic value encountered in the present study were: tumor size, maximal tumor thickness, and histologically-proven lymph node involvement. Factors such as N, of the TNM clinical stage, and the type of treatment instituted, may be attached greater significance in larger series and prospective studies. We must stress that no prospective randomized study has been found in the literature consulted. Therefore, the information contained herein may contribute to treatment when dealing with borderline cases.

The anatomopathological studies mentioned must be considered as microscopic help for clinical TNM classification in the choice of more effective treatment. An ever-increasing number of studies have tried to analyze prognostic factors for tumors in several sites.

Lower lip cancer is an easily diagnosed tumor which generally strikes light-skinned males in their 60's or 70's, particularly those who are smokers and have been excessively exposed to the sun. Tumors less than 4cm with no suspected lymph node involvement can be successfully treated by resection and surgical reconstruction, with cures being obtained in 90 percent of cases.

A minimum follow-up of 5 years would be desirable, with appointments every 3 or 6 months. For patients with tumors >4cm, or for those with suspected cervical lymph nodes, resection must be combined with modified neck dissection. Such dissection should be ipsilateral for tumors predominant on one side, and bilateral for median tumors.³⁰

Recurrent tumors, whether on the lip or neck, should be treated more aggressively, with wider resections and modified⁶ or radical¹⁴ neck dissections. Radiotherapy may be used as combined postoperative treatment.

RESUMO

Entre os pacientes portadores de carcinoma espinocelular do lábio inferior, atendidos no período de janeiro de 1980 a dezembro de 1989, no Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, analisamos, retrospectivamente, 58 prontuários. Além dos dados demográficos, as informações relativas aos pacientes foram completadas com anotações sobre o uso de álcool, fumo e exposição solar. O estadiamento clínico na época da cirurgia, bem como as características macroscópicas dos tumores, o tipo de tratamento instituído e as observações do seguimento pós-operatório também foram anotados. Foi, então, realizada uma minuciosa revisão anatomopatológica dos espécimes cirúrgicos, analisando o grau de diferenciação histológica, espessura, máxima tumoral, elastose solar, invasão perineural, invasão vascular, invasão muscular, margens cirúrgicas, infiltrado inflamatório peritumoral e acometimento ganglionar, com ou sem rotura capsular. A análise da sobrevida global a 5 anos demonstrou diferenças estatisticamente significativas para as variáveis *espessura tumoral*, *tamanho do tumor (T)* e *acometimento ganglionar*.

REFERENCES

1. Bailey BJ. Management of carcinoma of the lip. *Laryngoscope* 1977;87:250-60.
2. Baker SR, KRAUSE CJ. Carcinoma of the lip. *Laryngoscope* 1980;90:19-27.
3. Beckman JS, Westbrook KC, Thompson BW. Lip cancer: surgical management. *Am J Surg* 1974;128:732-4.
4. Bernier JL. Carcinoma of the lip: preliminary statistical analysis of 827 cases. *J Am Dent Assoc* 1948;36:262-70.
5. Bernier JL, Clark M. Squamous-cell carcinoma of the lip: a critical, statistical and morphological analysis of 835 cases. *Mil Surgeon* 1951;109:379-405.
6. Bocca E. Conservative neck dissection. *Laryngoscope* 1975;85:1511-15.
7. Broders AC. Carcinoma: grading and practical application. *Arch Pathol* 1926;2:376-381.
8. Broders AC. Squamous-cell carcinoma of the lip: a study of 537 cases. *JAMA* 1920;74:656-664.
9. Brown RG, Poole MD, Calamel PM, Bakamjian VY. Advanced and recurrent squamous carcinoma of the lower lip. *Am J Surg* 1976;132:492-7.
10. Burke RH. Squamous-cell carcinoma of the lower lip. *Ear, Nose Throat J* 1987;66:60.
11. Byers RM, O'Brien J, Waxler J. The therapeutic and prognostic implications of nerve invasion in cancer of the lower lip. *Int J Rad Oncol Biol Phys* 1978;4:215-17.
12. Campos-Filho N, Franco ELF. Microcomputer-assisted univariate survival data analysis using Kaplan-Meier life table estimators. *Comput Methods Programs Biomed* 1988;27:223-8.
13. Creely JJ Jr, Peterson HD. Carcinoma of the lip. *South Med J* 1974;67:779-84.
14. Crile G. Excision of cancer of the head and neck, with special reference to the plan of dissection based on 132 operations. *JAMA* 1906;22:1780-6.
15. Cruse CW, Radocha RF. Squamous-cell carcinoma of the lip. *Plast Reconstr Surg* 1987;80:787-91.
16. Dargent M, Gignoux B, Mayer M, Colon J. Le problème ganglionnaire dans le traitement des cancers de la lèvre inférieure. *Ann Oto-Laryngol Chir Cervicofac* 1973;90:609-22.
17. Decker J, Goldstein JC. Risk factors in head and neck cancer. *N Engl J Med* 1982;306:1151-5.
18. Eggert JH, Dumbach J, Steinhauser EW. Operative therapie der regionaren lymphknoten bei unterlippenkarzinomen. *Hautartz* 1986;37:444-9.
19. Elfenbaum A. Cancer of the lower lip. *Dental Digest* 1965;71:550-3.
20. Fitzpatrick PJ. Cancer of the lip. *J Otolaryngol* 1984;13:32-6.
21. Franco EL, Kowalski LP, Oliveira BV, et al. Risk factors for oral cancer in Brazil: a case-control study. *Int J Cancer* 1989;43:992-1000.
22. Frierson HF Jr, Cooper PH. Prognostic factors in squamous-cell carcinoma of the lower lip. *Human Pathol* 1986;17:346-54.
23. Giuliani M, D'Amore L, Giuliani L, Tordiglione P. Revisione critica su 121 epiteliomi spinocellulari del labbro. *Minerva Chir* 1989;44:1745-9.
24. Grover R, Douglas RG, Shaw JHF. Carcinoma of the lip in Auckland, New Zealand, 1969-1987. *Head & Neck* 1989;11:264-8.
25. Harris TJ. Squamous carcinoma of the lip in Queensland: a relatively benign lesion. *Br J Plast Surg* 1976;29:68-9.
26. Heller KS, Shah JP. Carcinoma of the lip. *Am J Surg* 1979;138:600-3.
27. Hendricks JL, Mendelson BC, Woods JE. Invasive carcinoma of the lower lip. *Surg Clin North Am* 1977;57:837-844.
28. Hornback NB, Shidnia H. Carcinoma of the lower lip: treatment results at Indiana University Hospital. *Cancer* 1978;41:352-7.
29. Ju DMC. On the etiology of cancer of the lower lip. *Plast Reconstr Surg* 1973;52:151-4.
30. Khafif RA, Gelbfish GA, Attie JN, Tepper P, Zingale R. Thirty-years experience with 457 radical neck dissections in cancer of the mouth, pharynx and larynx. *Am J Surg* 1989;158:303-8.
31. Klein AW, Weikel AM, Bingham HG. Cancer of the lip. *J Fla Med Assoc* 1975;62:31-3.
32. Landais H. Technique chirurgiccale identique dans dix cas de cancers des lèvres: resultats éloignés. *Rev Stomatol* 1968;69:251-9.
33. Lewis GK. Carcinoma of the lip. *J Int Coll Surg* 1965;44:618-631.
34. Lindqvist C. Risk factors in lip cancer: a questionnaire survey. *Am J Epidemiol* 1979;109:521-30.
35. Luce EA. Carcinoma of the lower lip. *Surg Clin North Am* 1986;66:3-11.
36. Lund C, Sogaard H, Elbrond O, Jorgensen K, Andersen AP. Epidermoid carcinoma of the lip: histologic grading in the clinical evaluation. *Acta Radiol Therapy Physics Biology* 1975;14:465-74.
37. Mahoney LJ. Resection of cervical lymph nodes in cancer of the lip: results in 123 patients. *Can J Surg* 1969;12:40-2.
38. Marshall DR, Bennett CS. Surgical treatment of lip cancer: the long term prognosis and functional results. *Aust N Z J Surg* 1982;52:525-30.
39. Marshall KA, Edgerton MT. Indications for neck dissection in carcinoma of the lip. *Am J Surg* 1977;133:216-7.
40. Martin H. The case for prophylactic neck dissection. *Cancer* 1951;4:92-7.
41. Mehregan DA, Roenigk RK. Management of superficial squamous-cell carcinoma of the lip with Mohs micrographic surgery. *Cancer* 1990;66:463-8.
42. Mickalites CJ, Rappaport, I. Perineural invasion by squamous-cell carcinoma of the lower lip: review of the literature and report of a case. *Oral Surg* 1978;46:74-8.
43. Mirra AP, Franco EL. Cancer mortality in São Paulo, Brazil. Ludwig Institute for Cancer Research, São Paulo, 1985.
44. Mirra Ap, Franco EL. Incidência de câncer no Município de São Paulo, Brasil. Ludwig Institute for Cancer Research Epidemiology Monographs, São Paulo Series-1, 1985.

45. Mohs FE, Snow SN. Microscopically controlled surgical treatment for squamous-cell carcinoma of the lower lip. *Surg Gynecol Obstet* 1985;160:37-41.
46. Mora RG, Perniciaro C. Cancer of the skin in blacks. II. A review of 36 black patients with squamous-cell carcinoma of the lower lip. *J Am Acad Dermatol* 1982;6:1005-9.
47. Noone RB, Bonner H Jr, Raymond S, Brown AS, Graham WP, Lehr HB. Lymph node metastasis in oral carcinoma: a correlation of histopathology with survival. *Plast Reconstr Surg* 1974;53:158-66.
48. Petrovich Z, Kuisk H, Tobochnik N, Hittle RE, Barton R, Jose L. Carcinoma of the lip. *Arch Otolaryngol* 1979;105:187-91.
49. Petrovich Z, Parker RG, Luxton G, Kuisk H, Jepson J. Carcinoma of the lip and selected sites of head and neck skin. A clinical study of 896 patients. *Radiother Oncol* 1987;8:11-7.
50. Pitkanen J, Lahti A, Sundell B. Carcinoma of the lip: a retrospective review of 70 patients. *Scand J Plast Reconstr Surg* 1985;19:289-94.
51. Ratzkowski E, Hochman A, Buchner A, Michman J. Cancer of the lip: a review of 167 cases. *Oncology* 1966;20:129-44.
52. Sack JG, Ford CH. Metastatic squamous-cell carcinoma of the lip. *Arch Otolaryngol* 1978;104:282-5.
53. Schmidseider R, Dick H. Spread of epidermoid carcinoma of the lip along the inferior alveolar nerve. *Oral Surg* 1977;43:517-20.
54. Scopp IW. Carcinoma of the lower lip. *N Y J Dent* 1977;47:243-4.
55. Shah JP, Candela FC, Poddar AK. The patterns of cervical lymph node metastases from squamous carcinoma of the oral cavity. *Cancer* 1990;66:109-13.
56. Silla M, Scarpa C, Torretta A. I tumori primitivi del labbro inferiore. *Riv Ital Stomatol* 1976;46:4-59.
57. Spitzer WO, Hill GB, Chambers LW, Helliwell BE, Murphy HB. The occupation of fishing as a risk factor for cancer of the lip. *N Engl J Med* 1975;293:419-24.
58. Stephens FO, Harker GJS, Hambly CK. Treatment of advanced cancer of the lower lip - the use of intraarterial or intravenous chemotherapy as basal treatment. *Cancer* 1981;48:1309-14.
59. Stoddart TG. Conference on cancer of the lip (based on a series of 3166 cases). *Can Med Assc J* 1964;90:666-72.
60. Suen JY, Goepfert H. Standardization of neck dissection nomenclature. *Head Neck Surg* 1987; 9:75-7.
61. Syrjanen K, Nuutinen J, Karja J. Tumor differentiation and tumor-host interactions as prognostic determinants in squamous-cell carcinoma of the lip. *Acta Otolaryngol (Stockholm)* 1986;101:152-60.
62. Tan KN. Cancer of the lip in Australia. *Aust Dent J* 1970;15:179-84.
63. Ūrmosi J, Szab I. Lip cancer in our five-year patient material. *Fogorv Sz* 1982;75:278-81.
64. Wurman LH, Adams GL, Meyerhoff WL. Carcinoma of the lip. *Am J Surg* 1975;130:470-4.
65. Zurrada S, Bartoli C, Bono A, Chiesa F. Outpatient surgical treatment of lip carcinomas: immediate and long-term results. *Tumori* 1989;75:263-5.