ORIGINAL ARTICLE

ELECTIVE NECK DISSECTION IN EARLY-STAGE ORAL SQUAMOUS CELL CARCINOMA—DOES IT INFLUENCE RECURRENCE AND SURVIVAL?

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Abstract: *Background.* This study investigates the influence on survival and regional control rates of neck dissection therapy at the time of surgery of the primary tumor in early stages of squamous cell carcinoma (SCC) of the oral cavity.

Methods. A series of 154 patients with pT1N0M0 and pT2N0M0 intraoral carcinomas was analyzed retrospectively. Neck dissection was associated with tumor ablation in 87 patients (56.5%), although 67 patients (43.5%) were treated with local resection exclusively. Survival and relapse rates were studied with the Kaplan–Meier curves and the log-rank test for univariate analysis and Cox proportional model for multivariate analysis ($p < .05$).

Results. Regional recurrences occurred in 25 cases (16.2%), 7 cases (8%) with primary neck dissection and 18 cases (26.8%) with local excision alone. Neck dissection therapy was a significant prognostic factor for recurrences and survival ($p < .05$). The 5-year regional control rate was of 92.5% for patients with elective lymph node ablation versus 71.2% for patients without primary neck dissection. Neck dissection was also significant for recurrences in stage I and for survival and recurrences in stage II. Neck dissection therapy also showed independent prognostic value in the Cox analysis.

Conclusions. In patients with intraoral carcinomas, elective neck treatment should be considered even in cases with a small primary tumor and negative clinical examination because of the high incidence of occult nodal metastases and the tendency to regional recurrences. © 2006 Wiley Periodicals, Inc. *Head Neck* **29:** 3–11, 2007

Keywords: elective neck dissection; early stages; oral carcinoma; neck recurrences; occult metastases; survival

The most important prognostic factor for tumor behavior and outcome in squamous cell carcinoma (SCC) of the oral cavity is the presence of neck lymph node metastases at diagnosis, which can decrease the 5-year survival rates to lower than 50%.[1–5] In patients with small tumors without clinical neck involvement, local excision alone with wide margins is the treatment modality of choice suggested classically in literature. However, treatment of the clinically negative neck in patients with early-stage oral carcinoma is still controversial. Some surgeons advocate for elective neck dissection because of the high incidence of occult metastases, which varies from 6% to 46% between different series.[1,4,6–8] Both elective neck dissection and a "watchful-waiting" policy of the neck have their

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supporters among head and neck surgeons. Recently, some studies have indicated that this watchful-waiting policy may not be safe, because delayed cervical metastases have an increased incidence of extracapsular spread, involvement of multiple node levels, and reduced survival.[9,10]

The presence of regional recurrences in the follow-up period is the most common cause of failure after surgical treatment for early-stage carcinomas.[11,12] Furthermore, the salvage rates for patients that develop neck recurrences are reported to be less than 40%, even with combined therapies with chemotherapy or radiotherapy.[1,6] These issues and the risk of occult metastases may also support elective treatment of the neck even in early oral carcinomas.

This study reviews the outcome of a series of 154 patients with early-stage oral SCC and determines the indication of elective neck dissection at the time of primary tumor surgery as well as its effect in preventing regional recurrence and improving survival.

MATERIALS AND METHODS

A series of 154 patients, 113 men (73.4%) and 41 women (26.6%), was analyzed retrospectively. The mean age of the group was 58 years (range, 18 to 88 years). All the patients received primary surgical resection of the oral tumor, excluding those treated with preoperative radiation therapy or chemotherapy. Disease in the 154 selected cases was classified postoperatively as early stage (stages I and II) according to the TNM classification of the American Joint Committee on Cancer[13]: 81 cases (52.6%) were stage I (pT1N0M0) and 73 cases (47.4%) were stage II (pT2N0M0). Eighty-seven patients (56.5%) underwent elective neck dissection at the time of local surgery, whereas 67 patients (43.5%) were treated with local resection exclusively and a watchful-waiting policy on the neck. Patients with positive nodes on histologic examination of the neck dissection specimen were excluded. The patients were classified into 2 groups based on the primary neck therapy: primary neck dissection group and no primary neck dissection group. The minimum follow-up period was 2 years.

Eighteen patients (11.7%) received adjuvant postsurgical radiotherapy under the protocol of the Head and Neck Tumor Committee of the Hospital La Princesa of Madrid; these patients had poorly differentiated tumors, involved surgical margins, and perineural spread. Postoperative radiation therapy was indicated in 12 cases (7.8%) with primary neck dissection and in 6 cases (3.9%) with no primary neck dissection.

Surgical margins were considered involved when the presence of invasive carcinoma and/or carcinoma "in situ" on the margins of the mucosa was identified or the distance to normal mucosa margin was less than 5 mm. The histological grading system employed to analyze the series was described previously by Broders[14]: well-differentiated tumors, moderately differentiated tumors, and poorly differentiated tumors. Perineural spread was also evaluated on histologic examination of the tumor specimens.

Regional recurrences were recorded during follow-up. Disease-free survival was calculated from the date of initial surgical treatment to the date of diagnosis of the recurrence. Distant metastases were excluded as regional recurrences. Kaplan–Meier curves were used for statistical analysis of overall and cause-specific survival as well as disease-free survival. Patient outcome, regardless of the type of neck therapy, was also analyzed to study the influence of cervical lymph node ablation on the survival and recurrence in early stages of oral carcinomas. The log-rank test was used to assess this association and the correlation of other classic factors with survival and regional relapse rates. Multivariate analysis with Cox proportional model (hazard ratio) was used to study the independent prognostic significance of neck therapy and other variables. A p value less than .05 was considered significant. All the statistical studies were performed with the SPSS 8.0 program.

RESULTS

Eighty-seven patients underwent neck dissection as initial treatment; 59 patients (67.8%) under-

Table 1. Location of the primary tumor.

	No. of patients (%)	
Location	PND	NPND
Mobile tongue	46 (52.9)	38 (56.7)
Floor of the mouth	25 (28.7)	11 (16.4)
Buccal mucosa	0 (0)	7 (10.4)
Gingiva	3 (3.4)	1 (1.5)
Base of tongue	4 (4.6)	0 (0)
Retromolar trigone	3 (3.4)	1 (1.5)
Oropharynx	0 (0)	2 (3)
Soft palate	3 (3.4)	6 (9)
Hard palate	0 (0)	1 (1.5)

Abbreviations: PND, primary neck dissection group; NPND, no primary neck dissection group.

Table 2. Treatment modalities employed for patients with neck recurrences.

Treatment	No. of patients ($n = 25$)
Surgery	8
Radiotherapy	1
Chemotherapy	2
Surgery + radiotherapy	10
Chemotherapy + radiotherapy	1
Palliative	3

went unilateral neck dissections and 28 patients (32.2%) underwent bilateral neck dissections. The location of the primary tumor in each study group (primary neck dissection and no primary neck dissection) is shown in Table 1. Surgical margin status was described as free in 113 cases (86.7%) and involved in 19 cases (12.3%) in the entire study group. Perineural spread was detected in 17 patients (11%). Sixty-four patients (41.6%) presented with well-differentiated carcinomas, 74 patients (48.1%) with moderately differentiated carcinomas, and 16 patients (10.4%) with poorly differentiated carcinomas.

The rate of regional recurrences in the series was of 16.2% (25 cases). These recurrences were as follows: homolateral neck recurrences in 14 cases (56%), contralateral neck recurrences in 4 cases (16%), and lococervical recurrences in 7 cases (28%). Treatment modalities for neck recurrences are shown in Table 2. Seven patients (8%) in the primary neck dissection group presented with regional recurrences versus 18 cases (26.8%) in the no primary neck dissection group. Moreover, 25 patients (16.2%) presented with local recurrences alone in the follow-up period; 4 of these 25 patients developed both local and regional relapses at different times. A local control rate of 83.8% was observed in the global group. Patient outcomes in the 2 groups are shown in Table 3. The 2-year, 5-year, and 10-year regional disease–free survival rates of the global group in the Kaplan–Meier Curves were 87.9, 83.4, and 80.6%, respectively. Most of the neck relapses (18 patients; 72%) occurred in the first 2 years of the follow-up period.

The log-rank test for regional disease-free survival demonstrated that the type of neck therapy was highly correlated with regional recurrences ($p = .001$). Patients treated without neck dissection had a significantly higher risk for the development of a neck recurrence than did those treated with cervical lymph node resection. The 5-year disease-free survival rate was 92.5% for patients with elective lymph node ablation versus 71.2% for patients with local excision alone (Figure 1). The differences between these groups were also studied with regard to tumor stage. Fourteen patients (17.2%) with stage I disease had neck recurrences (2 in the primary neck dissection group and 12 in the no primary neck dissection group); 11 patients (15%) with stage II disease had neck recurrence (5 in the primary neck dissection group and 6 in the no primary neck dissection group). The type of neck therapy significantly affected disease-free survival in both stage I ($p = .01$) (Figure 2) and stage II ($p = .01$) cases (Figure 3). Other classic factors analyzed were as follows: age (<40 years vs ≥40 years), sex,

Table 3. Outcome of patients of primary neck dissection and no primary neck dissection groups.

	No. of patients (%)					
	Recurrences			Survival		
				Death from tumor		
Patients	Regional recurrences	Local recurrences		Regional recurrence	No regional recurrence	Death from other causes
Primary neck dissection group (n = 87)	7 (8)	8 (9.2)	15 (17.2)	5 (5.7)	4 (4.6)	11 (12.6)
				9 (10.3)		
No primary neck dissection group ($n = 67$)	18 (26.8)	17 (25.4)	35 (52.2)	12 (18)	5 (7.4)	6 (9)
				17 (25.4)		
Total	*25 (16.2)*	*25 (16.2)*	*50 (32.4)*	*17 (68)*	*9 (32)*	*17 (11)*
				26 (16.9)		
						43 (27.9)

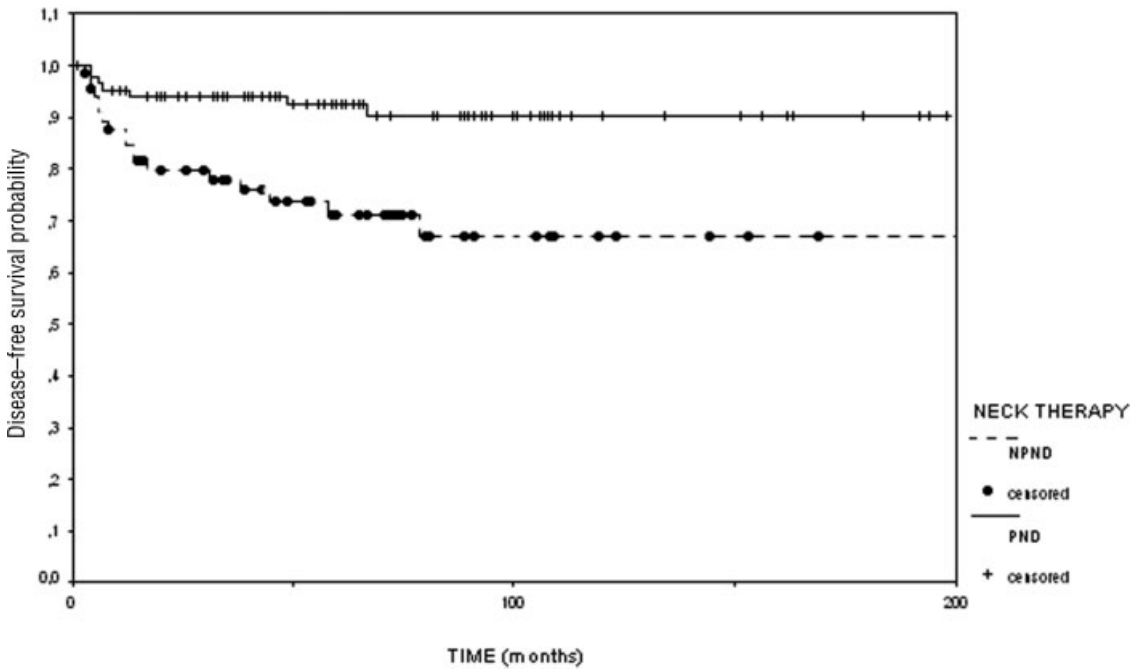

FIGURE 1. Regional disease-free survival for neck therapy groups: primary neck dissection (PND) group compared with no primary neck dissection (NPND) group ($p < .05$).

stage, location (free tongue vs floor of the mouth), histologic grade, surgical margins, perineural spread, and postoperative radiotherapy; these showed no significant differences in regional recurrence rates ($p > .05$). In the multivariate analysis with Cox proportional model, neck dissection therapy showed an independent prognostic value for regional recurrences (Table 4).

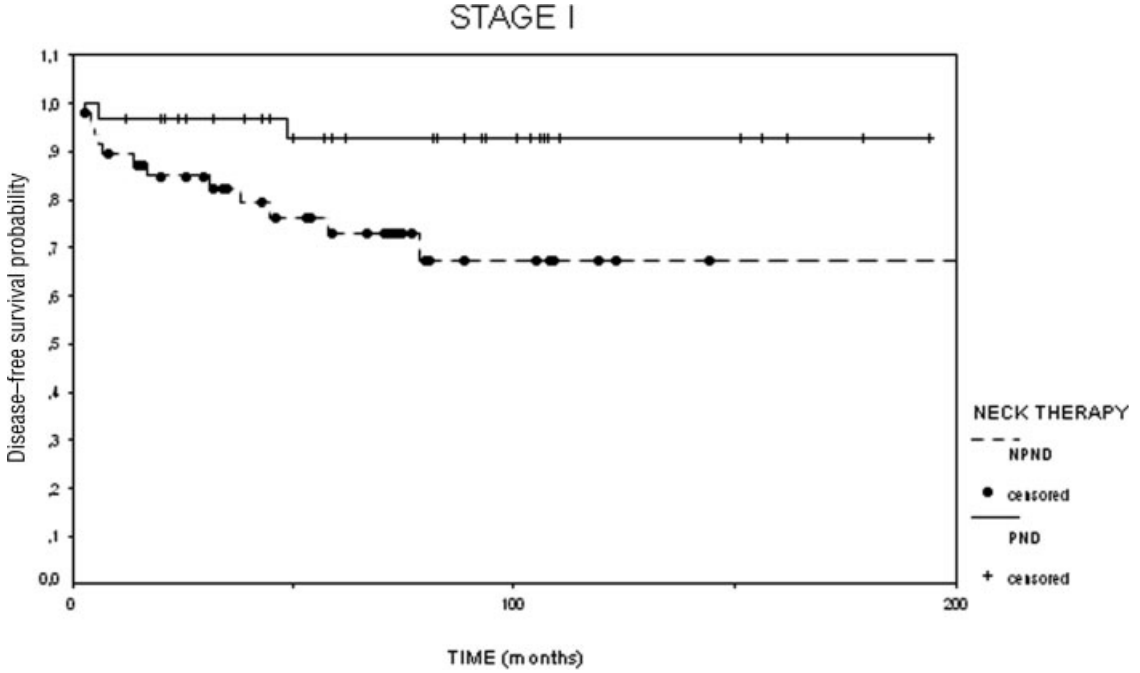

FIGURE 2. Regional disease-free survival for neck therapy groups in stage I: primary neck dissection (PND) group compared with no primary neck dissection (NPND) group ($p < .05$).

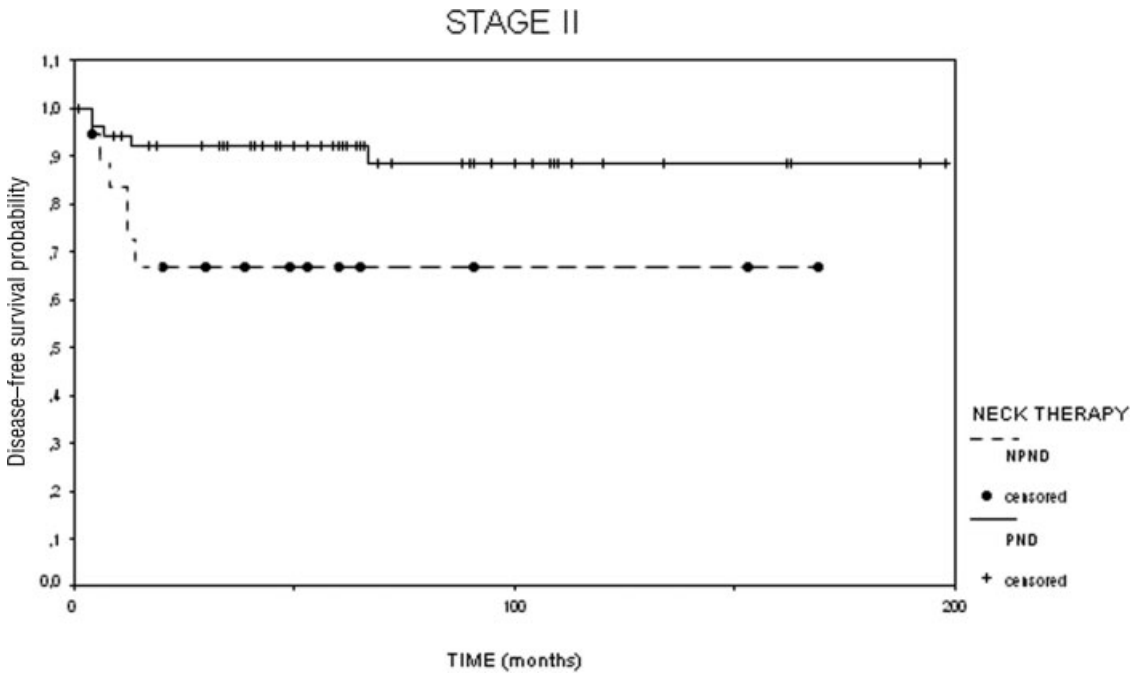

FIGURE 3. Regional disease-free survival for neck therapy groups in stage II: primary neck dissection (PND) group compared with no primary neck dissection group (NPND) ($p < .05$).

During follow-up, 26 patients (16.9%) died from disease (9 patients in the primary neck dissection group and 17 patients in the no primary neck dissection group), and 17 patients (11%) died from other causes. The 5-year and 10-year overall survival rates were 79.3% and 61%, respectively. The 5-year and 10-year cause-specific survival rates were 85.4% and 80.1%. In the group of 25 patients that developed neck nodal recurrences, the salvage rate after neck failure was 32% (8 cases). Seventeen (68%) of these 25 patients died from the tumor after treatment of the recurrence: 5 patients with primary neck dissection versus 12 patients with no primary neck dissection (Table 3). The log-rank test for cause-specific survival showed that neck therapy had a significant prognostic influence in predicting patient outcome ($p < .01$), with the no primary neck dissection group showing a higher probability of death from disease (5-year cause-specific survival rate of 91.7% in the primary neck dissection group vs 77% in the no primary neck dissection group) (Figure 4). In patients with stage II disease, these differences were also observed between the 2 groups ($p = .006$) (Figure 5). In patients with stage I disease, the no primary neck dissection group showed a low cause-specific survival curve compared with primary neck dissection group, although these differences were not statistically significant ($p = .17$) (Figure 6). No other factors analyzed with this test showed a significant association with survival. The Cox analysis suggested that neck therapy also influences survival as an independent factor in early-stage intraoral carcinomas (Table 4).

Table 4. Multivariate analysis of regional disease–free survival and cause-specific survival (Cox-regression).

	p value	
	Recurrences	Survival
Age	.63	.45
Sex	.09	.13
Histologic grading	.14	.12
Tumor thickness	.07	.26
pT classification	.84	.36
Surgical margin	.35	.93
Perineural spread	.52	.79
Postsurgical radiotherapy	.96	.08
Neck dissection modality	.001*	.005**

**Relative risk: 3.9; 95% CI: 2.1–6.9.*
***Relative risk : 4.2; 95% CI: 2.3–7.8.*

DISCUSSION

The biological aggressiveness of oral SCC is reflected by the capability of tumor cells to metastasize to neck lymph nodes, even in early stages with small tumors that are considered to have a good prognosis. Neck micrometastasis may be established in these cases in first steps of tumor

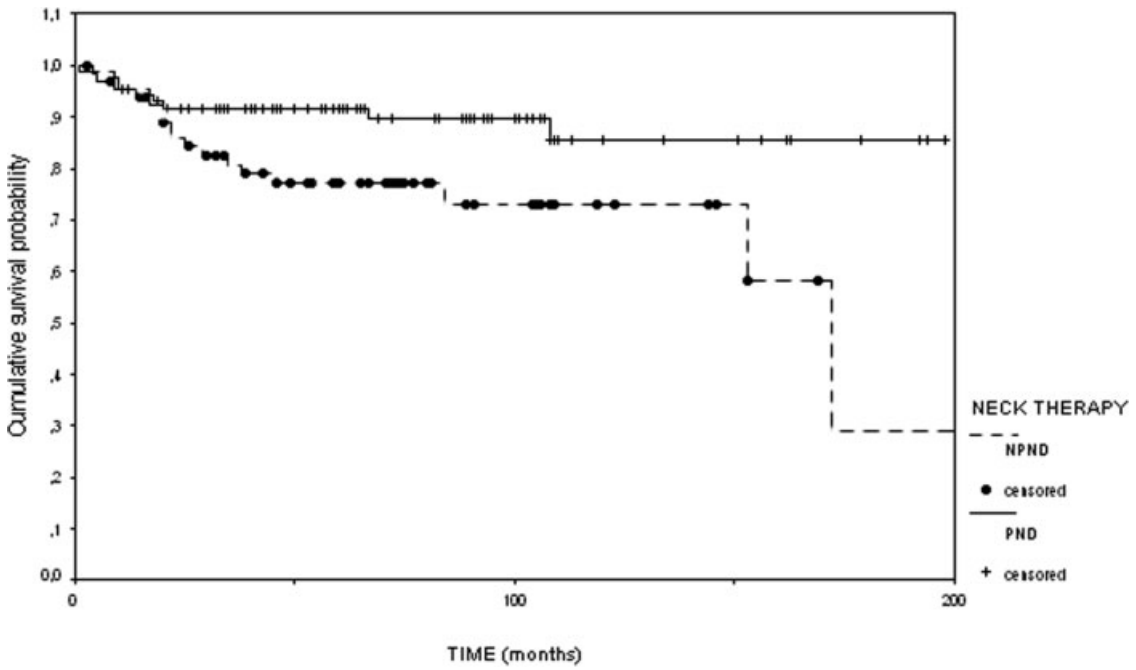

FIGURE 4. Cause-specific survival for neck therapy groups: primary neck dissection (PND) group compared with no primary neck dissection (NPND) group ($p < .05$).

progression and escape clinical examination and conventional imaging techniques.[8,10,15,16] This contributes to controversy regarding the indication of elective neck dissection in stages I and II SCC. Kaya et al[7] presented an incidence of occult metastases of 21.7% for T1-T2 tongue tumors, recommending elective neck therapy in these stages. Therefore, Ho et al[6] obtained a rate of occult metastases of 42% in early stages in which the neck was only observed closely in the follow-up period.

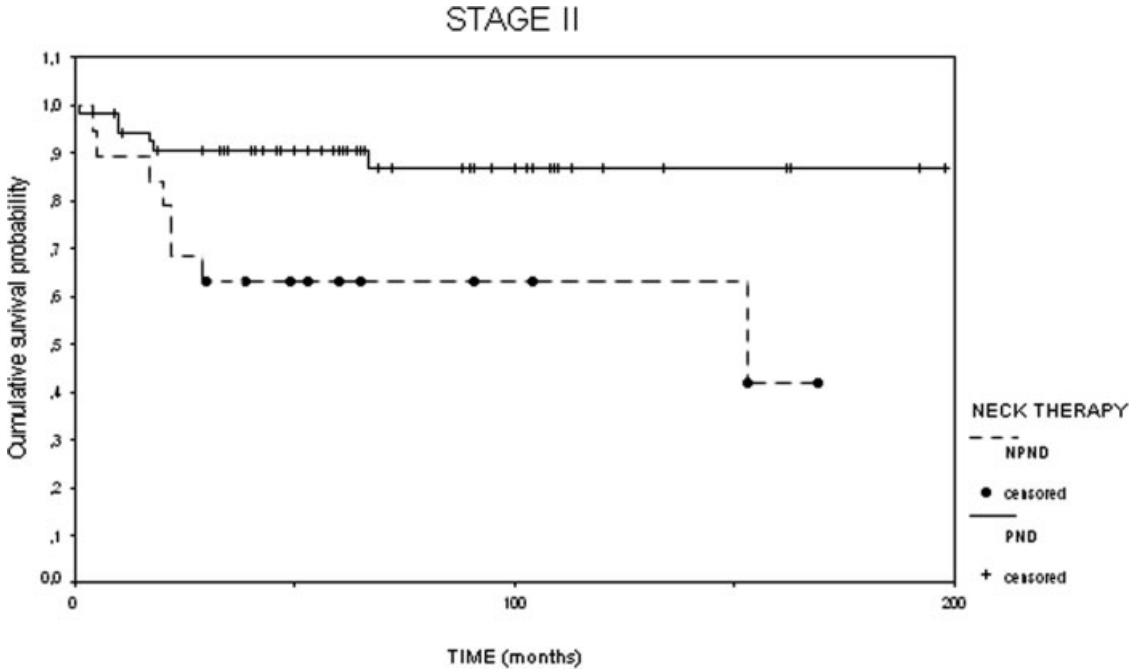

FIGURE 5. Cause-specific survival for neck therapy groups in stage II: primary neck dissection (PND) group compared with no primary neck dissection (NPND) group ($p < .05$).

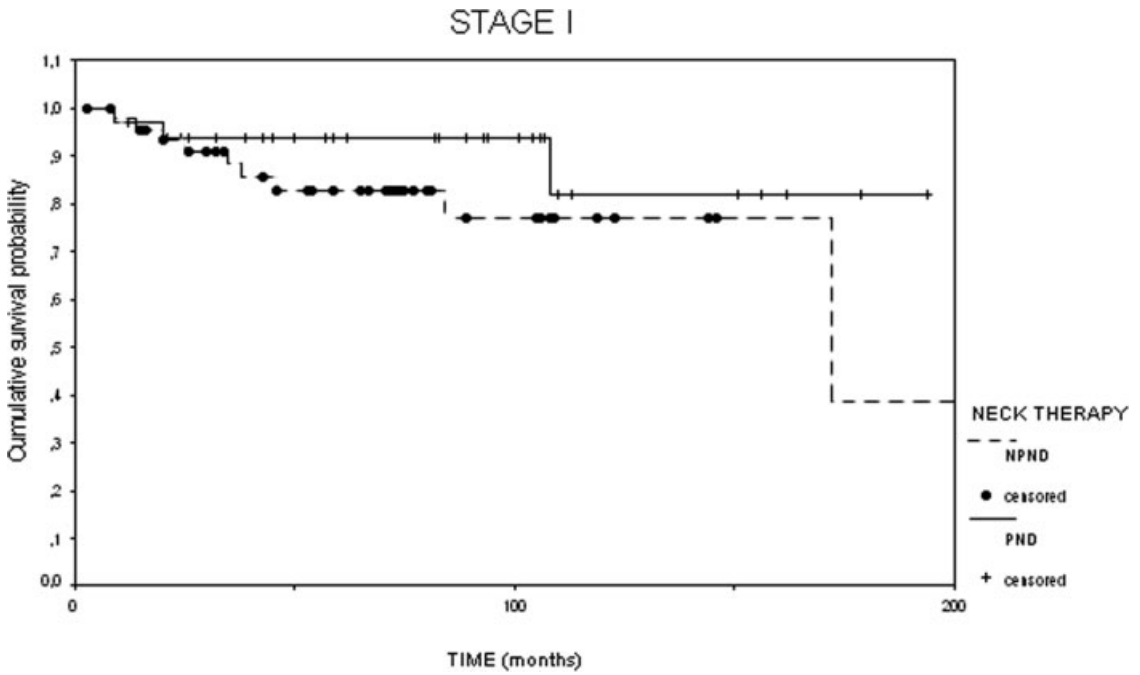

FIGURE 6. Cause-specific survival for neck therapy groups in stage I: primary neck dissection (PND) group compared with no primary neck dissection (NPND) group ($p = .17$).

In our series, we could infer that our rate of occult lymph node metastases was 26.8%, because it was the incidence of neck recurrences in the group of watchful-waiting policy of the neck. When the risk of occult metastases is higher than 20%, authors consider the need for elective neck treatment.

Regional recurrences are the most common cause of failure in the follow-up period, although high local control rates are approximately 85% to 90%.[6,11,12] This study has demonstrated that the type of neck treatment influences the outcome of patients with early-stage oral carcinomas. The rate of neck relapse in our series (16.2%) is similar to that in other series (14%–46%).[1,6,7] The incidence of recurrences was higher in the no primary neck dissection group (26.8%) than in the primary neck dissection group (8%); these differences were statistically significant. This significant association was also confirmed in both the stage I and stage II groups, with a high probability of recurrence in those patients without elective neck dissection. Other authors have noted the positive effect of elective neck dissection on regional control rates and survival.[1,11,17–19] Dias et al[1] has observed differences in neck relapse between different groups with stage I oral carcinomas, with a rate of 4% in patients with local resection plus neck dissection versus a 24% in patients with local resection alone. Yuen et al[11] also found that elective neck dissection significantly reduced mortality from regional recurrences and increased overall survival, whereas Yii et al[17] found a lower recurrence rate with elective neck treatment, although elective neck dissection did not improve 5-year survival in patients with early-stage tongue cancers. On the other hand, Franceschi et al,[20] in a study of stage I–II tongue cancers, found no difference in the 5-year survival rates between patients with elective neck dissection and patients with N0 disease who had a neck recurrence development and underwent a delayed therapeutic neck dissection. Khafif et al,[21] in their retrospective review, also found no differences between elective and delayed radical neck dissection in head and neck carcinomas.

Despite controversies between studies, most authors support the role of elective neck dissection in early-stage oral carcinomas to prevent late lymph node metastases. This technique allows correct neck staging and determination of the need of other adjuvant therapies.[3,7,10] Our study showed primary neck dissection therapy to be an important independent prognostic factor for regional recurrences in the Cox model. This relationship has not been previously reported, as most analyses in the literature are univariant and with contradictory results. As documented by other studies, we observed that most of the neck failures occurred within the first 24 months,

which supports the need of close monitoring of these patients during the first years.[1,22]

Salvage rates after regional recurrence are poor. In our series, only 8 patients (32%) of 25 who developed neck failure were alive at the end of the follow-up period, similar to reported salvage rates of less than 40%.[1,2,6] Survival decreases considerably when neck relapse occurs. The presence of late cervical lymph node metastases in an undissected neck has been associated independently with a poor cause-specific survival.[5,23] Five-year cause-specific survival rates were 91.7% and 77% in the primary neck dissection and no primary neck dissection groups, respectively; this difference was significant. This survival difference was conserved when analyzing the patients with stage II disease. In patients with stage I disease, although the difference was not statistically significant, we observed a tendency to high survival curves for patients with primary neck dissection. Neck treatment modality was also shown to be an independent prognostic factor for survival in this study.

The incidence of occult metastasis is associated with primary tumor size, perineural invasion, sex, tumor thickness, and location.[4,8,24–26] Moreover, different histologic factors may be implicated in regional recurrences and tumor aggressiveness.[4,5,22,27–29] Jones et al[12] suggested that tumor thickness more than 5 mm and positive surgical margins correlated with regional recurrences and recommend elective neck dissection in early-stage oral carcinomas. O-charoenrat et al[26] showed that tumor thickness was an independent predictor for neck recurrences. The tongue carries the highest incidence of delayed nodal disease even in small tumors.[6,7] We did not observe any difference in regional control rates and survival related to tumor location and other factors.

Different authors have proposed the role of selective neck dissection in elective treatment of N0 oral carcinomas.[3,10,30,31] This neck dissection modality had less morbidity but showed controversial results in recurrence and survival rates compared with other techniques.[3,31] We did not include the analysis of different neck dissection modalities in this study. The indications for selective neck dissection in N0 disease have yet to be established.[31,32]

In conclusion, we have shown in this study that elective neck dissection influences the outcome in patients with stages I and II oral SCC because it lowers the probability of regional recurrence and improves cause-specific survival. Salvage rates after neck relapse are poor despite aggressive therapies in these stages. Elective neck treatment should be considered also in patients with early-stage disease, even those with a small primary tumor and negative clinical examination, because of the high incidence of occult nodal metastases and the tendency to regional recurrences.

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