PRIMARY NECK MANAGEMENT AMONG PATIENTS WITH CANCER OF THE ORAL CAVITY WITHOUT CLINICAL NODAL METASTASES: A DECISION AND SENSITIVITY ANALYSIS

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Abstract: *Background.* A standardized neck management strategy for oral cancer patients without clinical nodal metastases remains to be established. Consequently, a decision and sensitivity analysis of two neck management protocols, involving either prophylactic neck dissection or careful observation, was conducted using the Oral Cancer Registry of Kyushu, Japan.

Methods. We calculated probabilities of subclinical nodal metastases and 5-year survival using the registry data. A two-way sensitive analysis was conducted using the probabilities and parameters of the complete nodal metastasis resection rate (x) and a utility rating that describes the health state induced by dissection (y) compared with the neck condition in a careful-observation group.

Results. We solved the threshold curve for y and x for the expected utility between the two groups. The results showed that prophylactic neck dissection must guarantee a complete resection of subclinical nodal metastases with no disadvantage to health state to be evaluated as equally satisfactory as careful observation.

Conclusions. Careful observation involving standardized systematic preoperative and postoperative screening of the neck seems preferable to prophylactic neck dissection for oral cancer patients without subclinical nodal metastases. © 2002 Wiley Periodicals, Inc. *Head Neck* **24:** 582–590, 2002

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A standard strategy for the primary management of the neck among patients with cancer of the oral cavity without clinical nodal metastases remains to be established. The neck of these patients has been managed primarily by the following three strategies: (1) prophylactic neck dissection at the same time as surgical resection of a primacy cancer; (2) careful observation after surgical resection of a primary cancer; and (3) prophylactic neck irradiation. From the viewpoint of patients' quality of life (QOL) after the primary treatment, selection of management strategies is a critical issue.

Management by prophylactic neck dissection and irradiation is used when there is an assumption of difficulty in diagnosing subclinical nodal metastases in the neck and when early dissection or radiation allows better prognosis if nodal metastases actually exist.[1–5] In other words, these strategies primarily aim to benefit patients with subclinical nodal metastases while disregarding those with no nodal metastases. On the other hand, management by careful observation can reduce the extent of unnecessary surgical invasion of the neck to offer better QOL for patients who do not actually have nodal metastases and attempts to save patients who do have subclinical nodal metastases by early detection of metastatic nodes and salvage treatment of the neck. Thus, the decision regarding primary management of the neck in clinically N0 patients is a tradeoff in the benefit gained between those who do and those who do not have nodal metastases. In particular, the decision to manage by either prophylactic neck dissection or careful observation is critical, because these are the two most common strategies used, and the difference in QOL offered by them is not negligible or inconsequential.

However, previous studies have focused only on the benefit for patients who have subclinical nodal metastases by comparing the survival rates between those who received prophylactic neck dissection and those who were followed up by careful observation/salvage treatment. In this study, using the Oral Cancer Registry in Kyushu, Japan, we conducted a decision and sensitivity analysis to examine the decision regarding primary management of the neck among clinically N0 oral cancer patients, considering equal assignment of benefits for all patents.

METHODS

The Oral Cancer Registry in Kyushu produced by the Kyushu Working Group for Oral Cancer. The Oral Cancer Registry in Kyushu was founded in 1985 to investigate the diagnosis, treatment, and prognosis of patients with cancer of the oral cavity. From 16 oral and maxillofacial surgery units of the university hospitals in Kyushu area, information regarding the following items is provided using the same registration form:

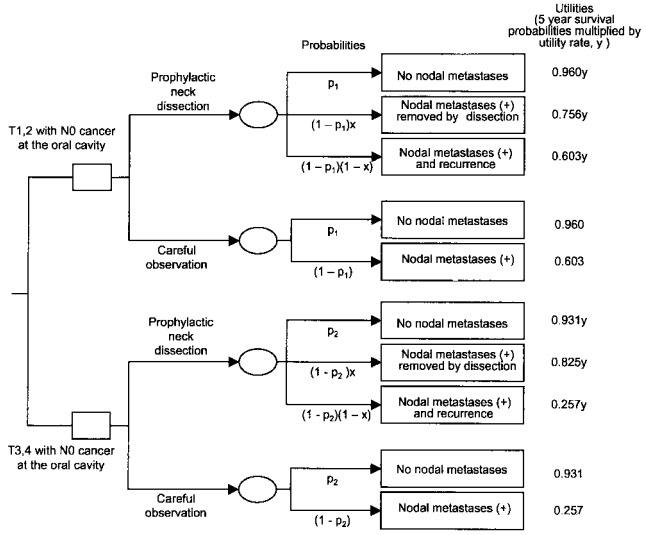

FIGURE 1. Schematic description of the probabilities of subclinical nodal metastases at the neck among oral cancer patients with N0 stage neck. Probability of complete removal by prophylactic neck dissection (x), and utility rating value for decision analysis (y); where p_1 and p_2 (probability of no nodal metastasis) are 0.946 for p_1 and 0.907 for p_2 using the probability of the careful-observation group and 0.708 for p_1 and 0.632 for p_2 using the prophylactic neck dissection group.

gender, age, date of diagnosis, histopathologic diagnosis, site of the primary cancer, TNM stage, treatment methods, and vital status of each patient supplemented by the periodic surveys conducted by each unit. The accumulated data are transformed into an electronic file and managed by the Registry secretariat. From 1985 to 1996, 2424 patients with previously untreated squamous cell carcinoma of the oral cavity were listed in the Registry.[6]

Definition of Subclinical Nodal Metastases at the Neck and Calculation of Probabilities of Subclinical Nodal Metastases. From all the registered cases, we retrieved 868 patients diagnosed between 1985 and 1996 who fulfilled all the following retrieval criteria: (1) patient diagnosed as N0 at the time of treatment for the primary cancer, the pathologic diagnosis of which was squamous cell carcinoma of the oral cavity, including buccal mucosa, upper and lower gingiva, hard palate, oral tongue, and floor of the mouth; (2) patient's primary cancer had not recurred during the follow-up period; (3) either the patient's neck nodal metastases had *not* been identified at least 2 years after surgery for the primary cancer,[7,8] or the patient was diagnosed as having nodal metastases in dissected materials or by postoperative clinical examination. Using the third retrieval criterion, we excluded patients who might have had subclinical nodal metastases that were not identified in the short follow-up period. Patients without pathologic records of the dissected lymph nodes were also excluded from the analysis.

The status of nodal metastasis at the time of treatment for the primary cancer was retrospectively decided by the results of histopathologic diagnosis of the dissected materials and/or postoperative clinical examinations; when histopathologic diagnosis of dissected materials and postoperative clinical examinations of the dissection and carefully observed patients did not reveal evidence of nodal metastasis, we decided that the patients had no nodal metastases; when histopathologic diagnosis and/or postoperative clinical examinations detected evidence or signs of nodal metastasis in the neck in any patient, we decided that the patient had nodal metastases. According to the status of nodal metastasis and the results of postoperative examinations, we categorized the retrieved patients into three groups: patients who had no nodal metastases (group 1), patients who had subclinical nodal metastases at the time of operation for the primary cancer and no nodal recurrence afterwards because of prophylactic neck dissection (group 2), and patients who had subclinical nodal metastases and afterwards nodal recurrence (group 3).

To evaluate the effect of the neck dissection on postoperative survival, Kaplan-Meier survival curves were produced, and log rank tests were performed to compare patients managed by neck dissection with those managed by careful observation.

Decision Analysis and Two-Way Sensitive Analysis to Assign Equal Benefit to Each Patient. To assign an equal benefit for each patient, the following factors were considered: (1) prognosis or survival of patients after treatment for the primary cancer, (2) probability of subclinical nodal metastasis, (3) probability of complete removal of subclinical nodal metastases by prophylactic neck dissection, (4) disadvantages to QOL caused by prophylactic neck dissection. The first and second factors can be estimated using the registry data. We used

Table 1. Distribution of primary cancer sites and the T classification and subclinical nodal metastasis of the retrieved patients.

	T classification				
Primary cancer site	1	2	3	4	Total
Buccal mucosa	30 (5)	46 (9)	11 (1)	4 (0)	91 (15)
Upper gingiva	40 (6)	66 (10)	12 (1)	32 (9)	150 (26)
Lower gingiva	21 (4)	38 (6)	13 (3)	18 (5)	90 (18)
Hard palate	10 (0)	12 (0)	3 (1)	1 (0)	26 (1)
Oral tongue	201 (29)	167 (34)	25 (7)	15 (7)	408 (77)
Floor of mouth	31 (1)	57 (4)	3 (2)	12 (4)	103 (11)
Total	333 (45)	386 (63)	67 (15)	82 (25)	868 (148)

Numbers in parentheses mean that number of patients who were diagnosed as N0 but retrospectively had nodal metastasis.
There was no association of distribution between primary cancer site and presence of subclinical nodal metastasis for each T stage; the p values of Pearson chi square test (df = 5) were .37, .14, .26, and .52 for T1, T2, T3, and T4, respectively.

Table 2. Comparison of the follow-up periods of survivors who received prophylactic neck dissection and managed by careful observations.

Management strategies	Number of patients	Number of deaths during follow-up	Mean age ± SD	Mean follow-up (*y*)
T1,2				
Careful observation	428	39	61.5 ± 12.7	4.8 ± 2.0
Prophylactic neck dissection	299	52	60.6 ± 12.1	4.7 ± 2.5
p value			0.26	0.42
T3,4				
Careful observation	54	8	67.5 ± 12.6	4.5 ± 2.0
Prophylactic neck dissection	95	39	63.5 ± 10.8	4.3 ± 2.2
p value			0.043	0.47

Two-sample t test with equal variances was used to test the equality of means of age and follow-up period. According to the F tests on the equality of variances, two-sample t test with unequal variances was used for test on the equality of means of follow-up period of T1,2 patients.

5-year survival probabilities during the follow-up period obtained by survivor functions of the Kaplan-Meier method and probabilities of subclinical nodal metastases among patients in each group. To determine the probability of subclinical nodal metastases, those managed by careful observation were used to calculate expected utilities for each group, because patients in the group managed by careful observation would have undergone preoperative screening of the neck using diagnostic imaging to detect nodal metastases. The third and fourth factors cannot be obtained from the registry data, and thus they were defined as variables x and y according to the following:

$x =$ Probability of completely removing subclinical nodal metastases by neck dissection

$y =$ Utility rating of health state caused by prophylactic neck dissection compared with that caused by careful observation. If neck dissection has no disadvantages at all for the oral cancer patients with stage N0, the value of y equals 1. As the degree of disadvantage increases, y decreases, with 0 being the lowest possible value.

Table 3. Distribution of oral cancer patients in this study who had no recurrence of primary cancer according to status of subclinical nodal metastases.

	No nodal metastasis	Nodal metastasis positive		
	Group 1*	Group 2†	Group3‡	Total
T1,2 cancer				
Prophylactic neck dissection	206	27	58	291
	(70.8%)	(29.2%)		(100.0%)
Careful observation	405	—	23	428
	(94.6%)	(5.4%)		(100.0%)
Total	611	27	81	719
	(84.5%)	(15.0%)		(100.0%)
T3,4 cancer				
Prophylactic neck dissection	60	15	20	95
	(63.2%)	(36.8%)		(100.0%)
Careful observation	49	—	5	54
	(90.7%)	(9.3%)		(100.0%)
Total	109	15	25	149
	(73.2%)	(26.8%)		(100.0%)
Total	720	42	106	868
	(82.9%)	(17.1%)		(100.0%)

**Group 1: patients who had no nodal metastases.*
†Group 2: patients who had subclinical nodal metastases at the time of surgery for the primary site and afterward nodal recurrence.
‡Group 3: patients who had subclinical nodal metastases and no nodal recurrence afterwards.

Using the 5-year survival data, the probability of subclinical nodal metastases (x) and the expected utility value (y) were calculated using the folding back method.[9] A two-way sensitive analysis was conducted to solve the threshold curve of y and x on the expected utility between the prophylactic neck dissection group and the careful-observation group.

In addition, to evaluate the influence of differences between the two neck management strategies on our results, we also used the probabilities of the prophylactic neck dissection group to solve the threshold curve. A schematic description of the system is presented in Figure 1. The STATA statistical package (version 6.0) was used for data cleaning, calculation of survival functions, and data analysis.[10]

RESULTS

Distribution of site, T stage, and number of subclinical nodal metastasis cases among the patients retrieved is presented in Table 1. No association in distribution was observed between primary cancer site and presence of subclinical nodal metastasis for each T stage; the p values of the Pearson chi square test (df = 5) were .37, .14, .26, and .52 for T1, T2, T3, and T4, respectively. The number of deaths, mean age at the time of diagnosis, and mean follow-up periods are shown in Table 2 according to T stage and neck management strategy. The mean age at the time of diagnosis was slightly higher in prophylactic neck dissection group for T3,T4 patients, although the mean follow-up periods between these two groups of patients did not differ significantly.

The probability of not having subclinical nodal metastases at the time of treatment for the primary cancer in patients with clinical N0 was .946 for T1,T2 patients and .907 for T3,T4 patients who had been followed up by careful observation. The probability of not having subclinical nodal metastases was .708 for T1,T2 patients and .632 for T3,T4 patients among those who had been managed by prophylactic neck dissection (Table 3).

Kaplan-Meier survival curves by treatment strategy are shown in Figures 2 and 3. Survival of patients managed by the different strategies for the neck in the same group (group 1 and group 3) were not significantly different according to log rank tests (p = .40, p = .96 for group 1 and group 3, respectively, in T1,T2 patients, and p = .92, p = .84 for group 1 and group 3, respectively, in T3,T4 patients). Therefore, 5-year survival probabilities were calculated according to the group and T stage regardless of treatment strategy. The 5-year survival probabilities are shown in Figure 1 along with the probabilities of having subclinical nodal metastases.

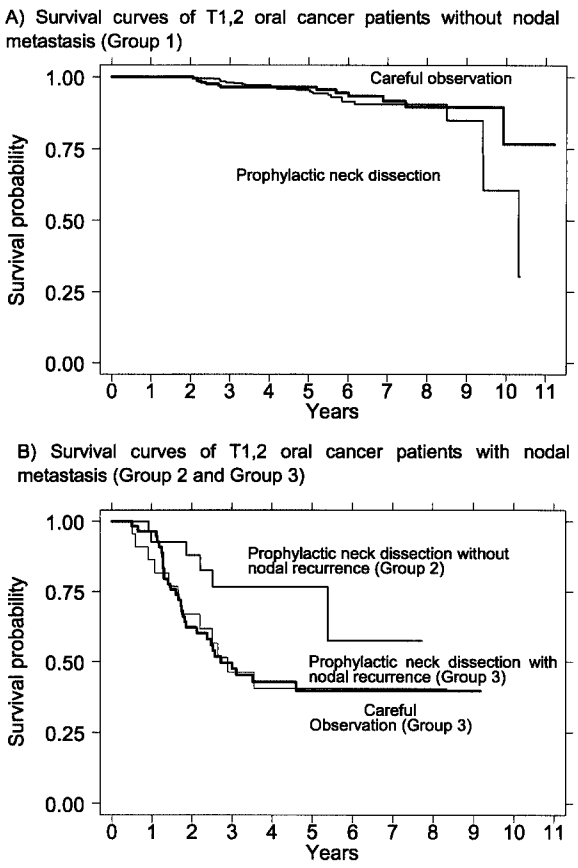

FIGURE 2. Comparison of survival of T1, T2 oral cancer patients with N0 stage neck between the prophylactic neck dissection and careful-observation treatment strategies (log rank test for group 1: p value = .40; for group 3: p value = .96). Bold line, prophylactic neck dissection; thin line, careful observation in (**B**).

Using the 5-year survival probabilities, the probabilities of having subclinical nodal metastases at the time of treatment for the primary cancer and value x; the complete resection rate of subclinical nodal metastases by prophylactic neck dissection and value y; the utility rating for the dissection, and threshold curves were obtained. The curves according to T1,T2 and T3,T4 were $y = 0.94/(0.94 + 0.008x)$, and $y = 0.86/(0.86 + 0.04x)$, when we used the low probability of nodal metastasis in the careful-observation group. The threshold curves were expressed as $y = 0.86/(0.86 + 0.05x)$, and $y = 0.68/(0.68 + 0.21x)$ for T1,T2 and T3,T4, respectively, when we applied the high

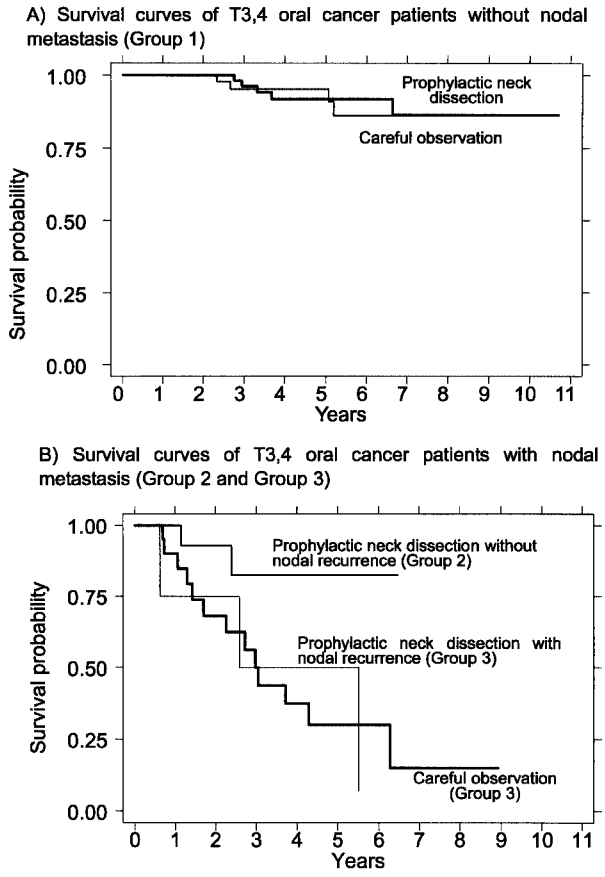

FIGURE 3. Comparison of survival of T3, T4 oral cancer patients with N0 stage neck between the prophylactic neck dissection and careful-observation treatment strategies (log rank test for group 1: p value = .92; for group 3; p value = .84). Bold line, prophylactic neck dissection; thin line, careful observation in (**B**).

nodal metastasis probability obtained from the prophylactic neck dissection group. When x and y cross in the area above the curve, prophylactic neck dissection is preferred as the standard treatment for all oral cancer patients without clinical nodal metastasis. On the other hand, if they cross under the curve, careful observation is preferred as the standard treatment for those patients.

DISCUSSION

The validity of prophylactic neck dissection for oral cancer patients who have no clinically obvious nodal metastases at the time of treatment of the primary cancer has been discussed primarily on the basis of survival comparisons between those who were managed with prophylactic neck dissection and those managed with careful observation/salvage treatment.[1–5] However, the better survival observed in this study among the prophylactic neck dissection group is to be expected compared with the careful-observation group, because the former group includes patients whose subclinical nodal metastases, which would have been clinically found at an advanced stage if they had not been dissected at the same time as the primary cancer, had been removed in advance. Furthermore, a high probability of nodal metastases among patients diagnosed clinically as N0 because of the low detection rate clearly indicated better survival among the prophylactic neck dissection group.

However, improvements in diagnostic accuracy for nodal metastases in the neck during recent years, brought about by ultrasonography and fine-needle aspiration cytology, enables highly accurate detection of nodal metastases that would have been diagnosed as N0 in preoperative screening in the past.[11–14] These improvements in diagnostic accuracy have reduced the probability of subclinical nodal metastases among patients clinically diagnosed as N0 in preoperative examinations. Therefore, we should also consider the benefits of each management strategy for oral cancer patients with no nodal metastases at the neck (ie, most N0 patients).

Assuming that a high and accurate detection rate of nodal metastasis can be achieved using new technology and devices, our results show that the preference and choice of one treatment strategy over another depends on the values of x and y (Figure 4). If y were quite close to 1; that is, neck dissection does not cause any disadvantage or damage to patients, prophylactic neck dissection should be chosen as the standard for oral cancer patients with no clinical nodal metastases. However, according to reductions in the value of y; that is, as neck dissection becomes more and more disadvantageous, higher complete resection rates of subclinical nodal metastases, value x is required to yield equal benefits for all patients. When y is lower than 0.95, even though the resection rate is 1, that is, complete resection rate is 100%, prophylactic neck dissection is not accepted as the standard strategy. When we assume the low detection rate of nodal metastasis (high subclinical nodal metastasis rate) observed in the prophylactic neck dissection group (Figure 5), a similar conclusion can be reached by applying the complete resection rate obtained from Table 3; 0.32 (95% CI, 0.22–0.43) for T1,T2 cases; group 2/(group 2 + group 3) = 27/(27 + 58), and 0.43 (95% CI, 0.26–0.61) for T3,T4 cases.

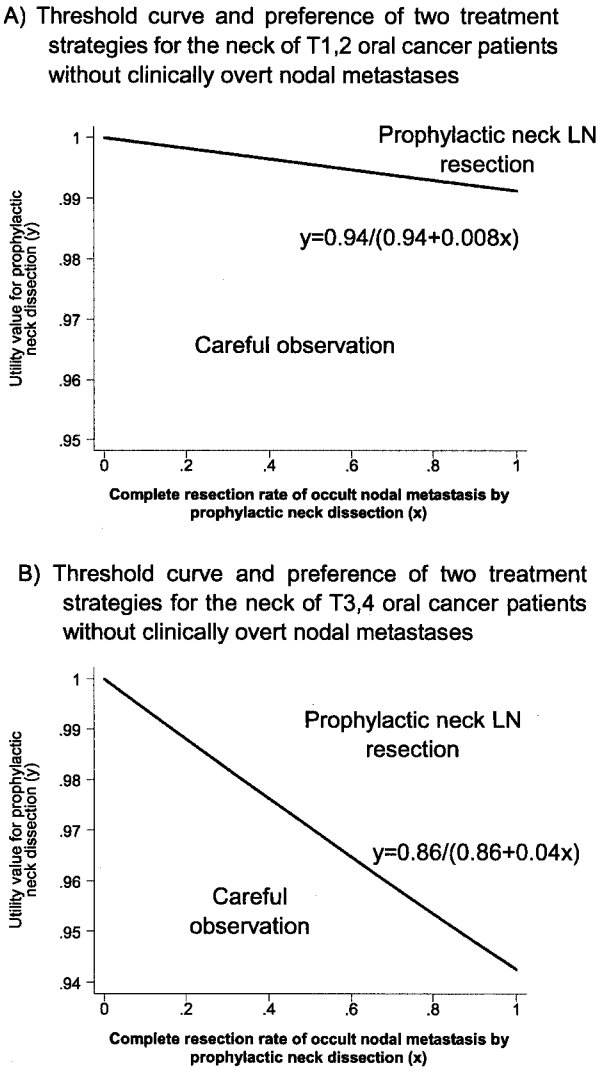

FIGURE 4. Threshold curve and preferences of the prophylactic neck dissection and careful-observation treatment strategies obtained from two-way sensitivity analysis; y = utility rating value; x = probability of complete resection of subclinical nodal metastases by prophylactic neck dissection, where the probability of subclinical nodal metastases was that of the careful-observation group.

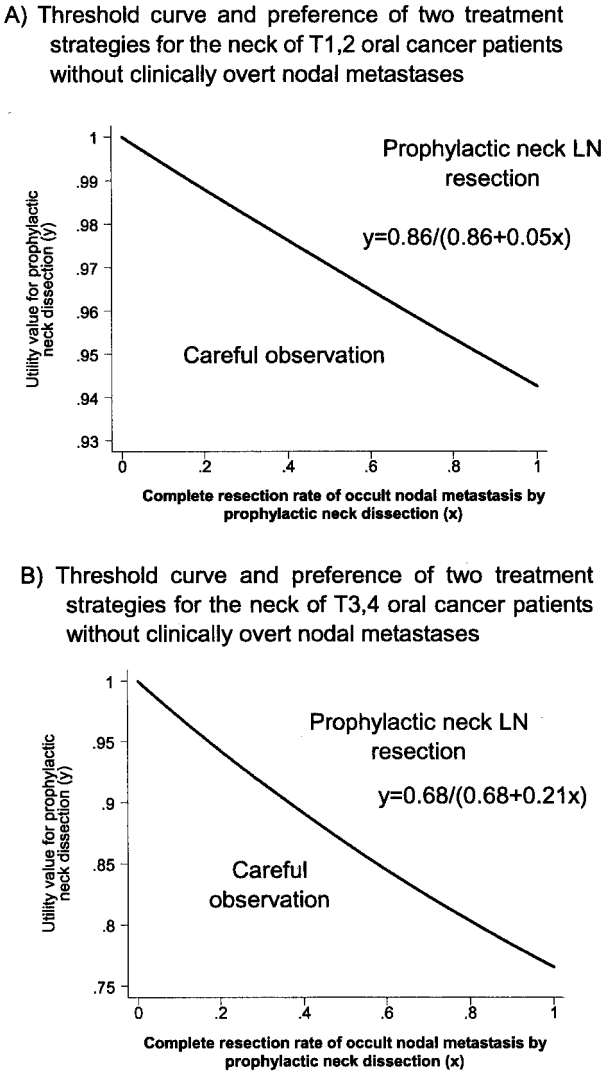

FIGURE 5. Threshold curve and preferences of the prophylactic neck dissection and careful-observation treatment strategies obtained from two-way sensitivity analysis: y = utility rating value; x = probability of complete resection of subclinical nodal metastases by prophylactic neck dissection, where the probability of subclinical nodal metastases was that of the prophylactic dissection group.

There are several limitations to this study. The management strategy for the neck of each patient was not randomly assigned in this study. However, we calculated the survival rates using the status of nodal metastasis retrospectively determined using surgically removed tissue and follow-up data. Because the status of nodal metastasis is not subject to any confounding factors in the preoperative procedures, the survival data represent unbiased values, as proven by the fact that survival rates between the same groups were not statistically different (Figures 2 and 3).

Furthermore, y should be decided by simultaneously assessing physical, social, and emotional aspects of neck dissection.[9,15] However, even only a 5% disadvantage from neck dissection is unacceptable. Thus, our result suggests that the careful-observation strategy involving strict intensive preoperative examination of the neck should be applied for oral cancer patients with no clinical nodal metastases. This suggestion is consistent with previous decision analyses of planning a management strategy for the N0 stage neck of oral cancer patients.[16,17]

The subclinical nodal metastasis rate is quite different between the prophylactic neck dissection and the careful-observation groups. The probability of subclinical nodal metastases in the prophylactic neck dissection group is almost the same as in previous reports.[2–4] Because the follow-up periods and survival between the prophylactic neck dissection and careful-observation groups were not statistically different, the difference probability of subclinical nodal metastases might not be due to different quality of postoperative follow-up between the two neck management strategies. Strict preoperative examination by ultrasonography and fine-needle aspiration cytology may have contributed to the low rate of subclinical nodal metastasis in the careful-observation group. Standardized preoperative examination is required to explain the difference in the subclinical nodal metastasis rate between the prophylactic neck dissection and careful-observation groups.

Neck management by prophylactic neck irradiation was not considered in this study. The irradiation rates are relatively low in this series: 2.8% for T1,T2 patients and 7.4% for T3,T4 patients, and thus we believe that the irradiation data would not affect these results.

In summary, our results suggest that the careful observation strategy is preferable for all oral cancer patients with no clinical nodal metastases. However, to reduce the number of patients who have subclinical nodal metastases at the time of the primary treatment, an intensive preoperative clinical examination of the neck needs to be standardized, and a standardized systematic postoperative screening program of the neck should be arranged for all patients.

Notes. Institutions involved in the Kyushu Working Group for Oral Cancer, are as follows: Department of Oral and Maxillofacial Surgery, School of Medicine, University of Occupational and Environmental Health, Japan (Dr. Kunio Ikemura); Department of Oral and Maxillofacial Surgery, Graduate School of Dental Science, Kyushu University (Dr. Kanemitsu Shirasuna); Department of Oral and Maxillofacial Surgery, Kurume University School of Medicine (Dr. Jingo Kusukawa); Department of Oral and Maxillofacial Oncology, Division of Maxillofacial Diagnostic and Surgical Sciences, Faculty of Dental Science, Kyushu University (Dr. Masamichi Ohishi); Department of Oral and Maxillofacial Surgery, Miyazaki Medical College (Dr. Ryosuke Shiba); Department of Oral and Maxillofacial Surgery, School of Medicine, University of the Ryukyus (Dr. Hajime Sunakawa); First Department of Oral and Maxillofacial Surgery, Kyushu Dental College (Dr. Kazuhiro Tominaga); First Department of Oral and Maxillofacial Surgery, Kagoshima University, Dental School (Dr. Kazumasa Sugihara); Department of Oral and Maxillofacial Surgery, Kumamoto University School of Medicine (Dr. Masanori Shinohara); Department of Oral and Maxillofacial Surgery, Saga Medical School (Dr. Takeshi Katsuki); Department of Oral and Maxillofacial Surgery, School of Medicine, Oita Medical University (Dr. Shigetaka Yanagisawa); Second Department of Oral and Maxillofacial Surgery, Kyushu Dental College (Dr. Hideo Kurokawa); Second Department of Oral and Maxillofacial Surgery, Kagoshima University, Dental School (Dr. Tamotsu Mimura); Second Department of Oral and Maxillofacial Surgery, Nagasaki University School of Dentistry (Dr. Hisazumi Ikeda); First Department of Oral and Maxillofacial Surgery, Nagasaki University School of Dentistry (Dr. Shigeru Yamabe); and the Department of Oral and Maxillofacial Surgery, Fukuoka Dental College (Dr. Satoru Ozeki).

REFERENCES

1. Davidson J, Biem J, Detsky A. The clinically negative neck in patients with early oral cavity carcinoma: a decision-analysis approach to management. J Otolaryngol 1995;24:323–329.
2. Haddadin KJ, Soutar DS, Oliver RJ, Webster MH, Robertson AG, MacDonald DG. Improved survival for patients with clinically T1/T2, N0 tongue tumors undergoing a prophylactic neck dissection. Head Neck 1999;21:517–525.
3. Ho CM, Lam KH, Wei WI, Lau SK, Lam LK. Occult lymph node metastasis in small oral tongue cancers. Head Neck 1992;14:359–363.
4. Hughes CJ, Gallo O, Spiro RH, Shah JP. Management of occult neck metastases in oral cavity squamous carcinoma. Am J Surg 1993;166:380–383.
5. Lydiatt DD, Robbins KT, Byers RM, Wolf PF. Treatment of stage I and II oral tongue cancer. Head Neck 1993;15: 308–312.
6. Ikemura K, Yanagisawa S, Ozeki S, et al. Multi-institutional cooperative study on malignant tumors of oral cavity and its adjacent regions–1. documentation sheets for patients data. J Jpn Soc Oral Tumor 1998;10:71–85.
7. August M, Gianetti K. Elective neck irradiation versus observation of the clinically negative neck of patients with oral cancer. J Oral Maxillofac Surg 1996;54:1050–1055.
8. Leon X, Quer M, Orus C, Sancho FJ, de Juan M, Lopez-Pousa A. Histologically negative specimens after induction therapy: frequency and impact on survival. Head Neck 2000;22:808–813.
9. Petitti DB. Meta-analysis, decision analysis, and cost-effectiveness analysis: methods for quantitative synthesis in medicine. New York: Oxford University Press; 2000. 24 p.

10. STATA Corp. STATA Reference Manual Release 6. Texas: Stata Press; 1999. p.
11. O'Brien CJ, Traynor SJ, McNeil E, McMahon JD, Chaplin JM. The use of clinical criteria alone in the management of the clinically negative neck among patients with squamous cell carcinoma of the oral cavity and oropharynx. Arch Otolaryngol Head Neck Surg 2000;126:360–365.
12. Oyafuso MS, Longatto Filho A, Ikeda MK. The role of fine needle aspiration cytology in the diagnosis of lesions of the head and neck excluding the thyroid and salivary glands. Tumori 1992;78:134–136.
13. Beissert M, Jenett M, Wetzler T, Hinterseher I, Kessler C, Hahn D. Enlarged lymph nodes of the neck: evaluation with parallel extended field-of-view sonographic sequences. J Ultrasound Med 2000;19:195–200.
14. Jandu M, Webster K. The role of operator experience in fine needle aspiration cytology of head and neck masses. Int J Oral Maxillofac Surg 1999;28:441–444.
15. Bjordal K, Hammerlid E, Ahlner Elmqvist M, et al. Quality of life in head and neck cancer patients: validation of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-H&N35. J Clin Oncol 1999;17:1008–1019.
16. Weiss MH, Harrison LB, Isaacs RS. Use of decision analysis in planning a management strategy for the stage No neck. Arch Otolaryngol Head Neck Surg 1994;120: 699–702.
17. van den Brekel MW, Castelijns JA, Reitsma LC, Leemans CR, van der Waal I, Snow GB. Outcome of observing the N0 neck using ultrasonographic-guided cytology for follow-up. Arch Otolaryngol Head Neck Surg 1999;125: 153–156.