Factors influencing early diagnosis of cancer of the oral cavity

Original Research

J. Mark Elwood,* MD, FRCPC
Richard P. Gallagher,† MA

Factors associated with stage at time of diagnosis and with interval between recognition of the first symptom and histologic diagnosis were assessed in a consecutive series of patients with primary epithelial tumours of the oral cavity. Of the 160 patients 55% had stage I or II disease. The proportion was significantly higher among patients with a high socioeconomic status, those with low levels of alcohol consumption and those who regularly received dental care. The interval between recognition of the first symptom and diagnosis was not significantly related to these factors, but it was shorter for the men. These relations were specific to the patients with cancer of the oral cavity, not being seen in those with other head and neck tumours. Dental practitioners are an important source of early diagnosis of oral cavity cancers. The impact of the disease might thus be lessened by more regular dental care.

Dans une série consécutive de 160 malades présentant un épithélioma primitif de la bouche, on a étudié les facteurs reliés au stade de la tumeur au moment du diagnostic et au délai entre la survenue du symptôme d'appel et le diagnostic histologique. Dans 55% des cas il s'agit de tumeurs au stade I ou II. La proportion est significativement plus élevée chez les malades de haut statut socio-économique, ceux qui consomment peu d'alcool et ceux qui ont visité régulièrement leur dentiste. Mais ces facteurs n'influencent pas de façon significative le délai entre la survenue du symptôme d'appel et le diagnostic; ce délai est plus court chez les hommes. Ces trouvailles sont particulières aux cancers de la bouche et ne s'appliquent pas aux autres tumeurs de la tête et du cou. Le dentiste est très bien placé pour porter le diagnostic précoce de cancer de la bouche; la visite régulière chez lui pourrait en abaisser la gravité et la mortalité.

From *the Department of Community Health, University of Nottingham, Queen's Medical Centre, Nottingham, England, and †the Division of Epidemiology, Biometry and Occupational Oncology, Cancer Control Agency of British Columbia, Vancouver

Reprint requests to: Professor J. Mark Elwood, Department of Community Health, University of Nottingham, Queen's Medical Centre, Nottingham NG7 2UH, England

As tumours of the oral cavity arise on an accessible and partially visible epithelial surface, they should, in principle, be diagnosed early. However, many of these tumours are diagnosed only when they are at an advanced stage, and the 5-year relative survival rate from the time of diagnosis is around 40%.[1] We describe the presentation of primary epithelial tumours of the oral cavity in patients seen at one major referral centre and compare it with that of other tumours of the head and neck.

Patients and methods

Our study was of a consecutive series of patients with newly diagnosed cancer of the oral cavity seen at the A. Maxwell Evans Clinic, Vancouver, the main referral centre for patients with cancer and the only radiotherapy centre on the mainland of British Columbia. The patients had primary epithelial tumours of the tongue and oral cavity ("International Classification of Disease for Oncology" [ICDO] 141, 143, 144 and 145[2]) that were first diagnosed between Jan. 1, 1977 and Jan. 31, 1980. A standardized abstract of the medical record of each patient was prepared by an experienced medical records technician employed solely for research, and all tumour specimens were reviewed by the clinic's pathologists, who deal almost exclusively with malignant disease.

During the study period 178 patients with newly diagnosed tumours of the oral cavity were identified. A comparison of this figure with those from the British Columbia Cancer Registry showed that some 88% of patients with cancer of the oral cavity who were residents on the mainland of British Columbia were seen at the clinic.

The stage of disease at the time of diagnosis was categorized according to the criteria of the American Joint Committee for Cancer Staging and End Results Reporting.[3] Information on the first symptom and the interval between recognition of this symptom and diagnosis was assessed from the standardized admission history. This information

← For prescribing information see page 701

has been a part of the routine admission history since the inception of the clinic. The histories are taken in uncrowded and relatively relaxed surroundings by physicians who are employed specifically to interview and examine new patients before they are seen by an oncologist. In a previous study we demonstrated the prognostic value of the interval between recognition of the first symptom and histologic diagnosis recorded in this way in patients with breast cancer.[4] A later, independent review of the records of the patients with cancer of the oral cavity was done to determine whether the initial referral had been by a dental practitioner.

The staging classification was as follows: stage I, tumour 2 cm or less in diameter; stage II, tumour greater than 2 but less than 4 cm in diameter; stage III, tumour greater than 4 cm in diameter or single homolateral node less than 3 cm in diameter; and stage IV, tumour greater than 4 cm in diameter with deep invasion or single node greater than 3 cm in diameter, multiple nodes or distant metastases.

Patients were interviewed by one of four full-time interviewers, who used a structured questionnaire that had been designed primarily for an etiologic study comparing patients with head and neck tumours with control subjects.[5] This questionnaire has been extensively tested, and its results in terms of measuring the alcohol and tobacco consumption of different patient groups are consistent with those in the literature. The questionnaire includes a detailed history of alcohol consumption and smoking, and a life-time occupational history, from which a socioeconomic classification based on the "highest" job categorization obtained was developed.[5] The patients in this series were asked if they had made regular visits to the dentist — that is, at least one visit per year in the past 5 years. A number of other questions related to dental care and the use of dentures were also asked.

Questionnaires were completed for 160 patients, 90% of those eligible for the study. The series in this paper is thus slightly larger than that in the etiologic study.[4] Data were also collected in the same manner over the same period for patients with primary epithelial tumours in the oro- and hypopharynx (ICDO 146, 148 and 149), nasopharynx (147), extrinsic larynx (161.1) and intrinsic larynx (other 161 categories).[5]

We analysed the data with cross-tabulations and the chi-square test with continuity correction. To assess the associations after controlling for confounding variables we used Mantel's method.[6]

Results

Stage distribution

Of the 160 patients with tumours of the oral cavity 100 were men, and the average age of the patients was 61.5 (extremes, 20 and 92) years. The proportion of patients with stage I to IV disease was 26%, 29%, 10% and 35% respectively (Table I); the information was incomplete for two patients. This distribution — that is, 55% of the patients had stage I or II tumours — was considerably more favourable than that of all the patients with stage I or II tumours of the oro- and hypopharynx, of whom 13% had stage I or II tumours, and all the patients with nasopharyngeal tumours, of whom 15% had stage I or II tumours. The proportion of the patients with stage I or II extrinsic laryngeal tumours (29%) was also poor; that of the patients with stage I or II intrinsic laryngeal tumours was much more favourable (79%).

As shown in Table II the age distribution of the patients with cancer of the oral cavity varied little by stage of disease, and the stage distribution was similar in the two sexes. The factor most strongly associated with differences in stage distribution was regular dental care: of the 41 patients who reported having had regular dental care 70% had stage I or II tumours, compared with 40% of those who did not have regular dental care ($p = 0.0002$). Socioeconomic status, as assessed by occupational classification, was also related, although less strongly, to differences in stage distribution: 60% of the patients with relatively high socioeconomic status had stage I or II tumours, compared with 51% of those with lower socioeconomic status ($p = 0.04$). The third significant factor was alcohol consumption. The stage distribution was very similar in the patients who drank up to 9 oz (320 mL) of alcohol per week, with 65% having stage I or II tumours; of the patients who drank 10 oz (321 mL) or more of alcohol (i.e., 17 or more drinks) per week only 34% had stage I or II tumours ($\chi^2 = 13.9$, 6 degrees of freedom, $p = 0.03$).

The associations between stage distribution and regular dental care, socioeconomic status and alcohol consumption were each assessed after controlling for the effects of the other two variables by cross-tabulation and the application of Mantel's method of assessing the unconfounded associations. The associations of stage of disease with dental care and alcohol consumption remained statistically significant; however, that of stage of disease and socioeconomic status became weaker and nonsignificant, which indicates that most of

Table I—Distribution of stage of head and neck cancer, according to site of primary tumour

Site of tumour	No. of patients	Stage; % of patients			
		I	II	III	IV
Oral cavity*	158	26	29	10	35
Oro- and hypopharynx	100	4	9	12	75
Nasopharynx	47	4	11	11	72
Extrinsic larynx	53	6	23	8	64
Intrinsic larynx	123	46	33	2	19

*Information was incomplete for two patients (1%).

the observed association with low socioeconomic status may have been due to differences in dental care and alcohol consumption.

Other factors that were assessed but that showed no significant relation to stage of disease included smoking history, marital status, diet and religion.

Interval between recognition of first symptom and histologic diagnosis

The diagnosis of a cancer at an advanced stage may indicate either late recognition of the first symptom of disease or a longer interval between the recognition of the first symptom and histologic diagnosis. Fig. 1 shows the distribution of 134 patients with cancer of the oral cavity according to the interval between the recognition of the first symptom and the histologic diagnosis of the tumour. This information was not available for the other 26 patients. The median interval was 3 months; in 36% of the patients it was less than 2 months, in 25% it was 6 months or longer, and in 10% it was 1 year or longer.

In contrast to stage distribution, the interval between recognition of the first symptom and diagnosis did not differ significantly between the patients with oral cavity tumours and those with pharyngeal or laryngeal tumours. The factors that were significantly related to stage distribution in the patients with oral cavity tumours (dental care, socioeconomic status and alcohol consumption) were not significantly related to the interval between recognition and diagnosis (Table III). In fact, for alcohol consumption this association, while nonsignificant, was the opposite of that between stage distribution and alcohol consumption, the interval tending to be longer in the patients with low levels of or no alcohol consumption. The only factor that was significantly related to interval was

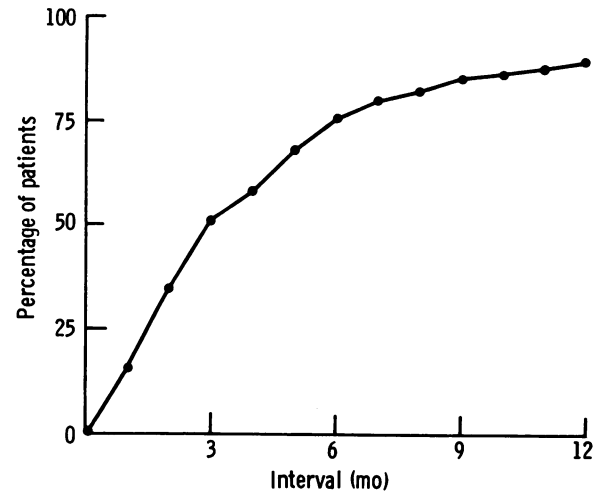

Fig. 1—Distribution of 134 patients with cancer of oral cavity according to interval between recognition of first symptom and histologic diagnosis.

Table II—Factors associated with stage of disease in patients with cancer of the oral cavity

Variable	No. of patients (n = 158)	Stage; mean or % of patients I (n = 9)	II (n = 19)	III (n = 10)	IV (n = 35)	p value*
Mean age (yr)	158	60.5	62.3	60.3	61.9	NS
Sex						
Male	99	27	27	12	33	NS
Female	59	24	32	7	37	
Dental care						
Regular†	41	46	24	17	12	0.0002
Not regular	117	19	31	8	43	
Socioeconomic status‡						
Relatively high	85	35	25	12	28	0.04
Relatively low	64	16	35	9	41	
Alcohol consumption, oz (mL)/wk						
< 1 (34)	49	27	39	6	27	
1–9 (34–320)	60	33	32	7	28	0.03
≥ 10 (321)	49	16	18	18	47	
Smoking history, no. of cigarettes per day						
0–9	45	31	33	7	29	
10–29	74	26	24	10	41	NS
30+	39	21	33	15	31	
Marital status						
Married	93	26	30	12	32	NS
Unmarried	65	26	28	8	39	

*NS = not significant, $p > 0.05$.
†At least one visit per year in the past 5 years.
‡Information was inadequate for nine patients (6%).

sex, the interval being significantly shorter in the men ($p = 0.05$). There was no association between this interval and age, marital status, smoking history, diet or religion.

First symptoms

The most common first symptom was a visible sore, occurring in 81% of the patients with stage I or II disease but in only 54% of those with stage III or IV disease. Dental problems constituted the first symptom in 8% of the former and 9% of the latter patients. Sore throat and various other symptoms were significantly more common in the patients whose cancer was diagnosed late, accounting for 42% of those with stage III or IV disease, compared with only 12% of those with stage I or II disease.

Site of tumour

The sites of the primary epithelial tumours, according to stage of disease, are shown in Table IV. There was a tendency for the tumours on more easily visible surfaces to be diagnosed earlier. The interval between recognition of the first symptom and histologic diagnosis did not differ significantly with the site of the tumour, although it tended to be slightly shorter with tumours of the palate than with other tumours.

Dental care

The relation between stage of disease at the time of presentation of the patients with cancer of the oral cavity and regular dental care was examined in more detail. The patients who had regular dental care were more likely to have stage I or II disease, although the intervals between recognition of the first symptom and diagnosis in this group were similar to those in the patients who did not have regular dental care. The former group more often presented with a visible sore or a dental problem than with a sore throat or other symptoms (Table V). Of these patients 34% had been referred for further investigation by a dentist, compared with only 13% of those who did not have regular dental care. Further analysis showed that referral by a dentist was not associated with earlier presentation or a shorter interval between recognition of the first symptom and diagnosis independently from the factor of regular dental care.

Discussion

Only 26% of the patients with primary tumours of the oral cavity in this series presented with localized stage I disease, whereas 35% presented with frank metastases and thus a poor prognosis. The most common first symptom was a visible sore; the diagnostic process must be started by someone noticing that sore, most likely the patient

Table III—Factors associated with the interval between recognition of the first symptom and histologic diagnosis in patients with cancer of the oral cavity

Variable	No. of patients (n = 134)	Interval (mo);* mean or % of patients				p value
		< 2 (n = 36)	2–3.9 (n = 23)	4–6.9 (n = 22)	≥ 7 (n = 20)	
Mean age (yr)	134	62.0	57.4	62.0	61.7	NS
Sex						
Male	87	41	25	16	17	0.05
Female	47	26	17	32	26	
Dental care						
Regular	34	44	18	12	27	NS
Not regular	100	33	24	25	18	
Socioeconomic status†						
Relatively high	72	38	22	24	17	NS
Relatively low	54	37	19	19	26	
Alcohol consumption, oz (mL)/wk						
< 1 (34)	39	23	26	23	28	
1–9 (34–320)	47	38	21	23	17	NS
≥ 10 (321)	48	44	21	19	17	
Smoking history, no. of cigarettes per day						
0–9	35	23	26	20	31	
10–29	67	36	22	24	18	NS
30+	32	50	19	19	13	
Marital status						
Married	78	36	24	18	22	NS
Unmarried	56	36	20	27	18	

*Information was inadequate for 26 patients (16%).
†Information was inadequate for 34 patients (21%).

or his or her physician or dentist. The stage distribution of cancers of the oral cavity was somewhat more favourable than that of cancers of the pharynx or extrinsic larynx, which are less accessible to inspection and usually present with pain, dysphagia or swelling; however, the distribution was not as favourable as that of internal laryngeal cancers, which present most often with hoarseness. That a visible sore was the most common first symptom of cancer of the oral cavity demonstrates the potential for earlier diagnosis.

Another factor that was strongly associated with earlier diagnosis was regular dental care (i.e., at least one visit per year in the past 5 years). Of the patients in our series who were receiving such care 34% had been referred for further investigation by their dentist. The true figure was probably higher, since our estimate was based only on the assessment of medical records; if the patient had been referred by the dentist to a family doctor and then referred by the family doctor to the clinic the role of the dentist might not have been recorded in the medical notes. Referrals by a dentist were also noted for the patients who were receiving less regular dental care, accounting for 13%. As would be expected, regular dental care was strongly associated with higher socioeconomic status and less strongly with relatively low levels of alcohol and cigarette consumption.

However, the association between regular dental care and earlier diagnosis of cancer of the oral cavity was specific. No association was seen between regular dental care and stage distribution of pharyngeal or laryngeal cancers, whereas for the other cancers, as with cancer of the oral cavity, there was a rather weak tendency for stage I and II disease to be associated with higher socioeconomic status. The third factor associated with stage distribution was alcohol consumption: the patients who regularly drank 10 oz (321 mL) or more (i.e., 17 drinks) a week had a less favourable stage distribution.

There was no association between any of these three factors and the interval between recognition of the first symptom and histologic diagnosis. Therefore, these factors were not associated with a longer delay in reaction to symptoms on the part of either the patient or the referring dentist or physician. These associations may reflect later recognition of the first symptom, which implies that a visible sore may go unrecognized longer in patients without regular dental care, those with a lower socioeconomic status and those with high levels of alcohol consumption. It is also possible that tumours in these three groups of patients are inherently more biologically aggressive and thus spread further over a similar interval, but there is no evidence to support this theory. A third possibility, also without supporting evidence, is that stage III and IV disease is, in fact, a consequence of a longer interval between recognition and diagnosis, but because the interval is difficult to measure accurately the true associations are not apparent.

The interval between recognition of the first symptom and definitive diagnosis was significantly longer in the women in our series. Although the trend was not significant, the interval also tended to be longer in the patients with low levels of or no alcohol consumption. Cancer of the oral cavity is more common in men than women, and the risk of this disease is very strongly related to high levels of alcohol consumption.[4] The characteristics of the patients in our series in whom the interval be-

Table IV—Distribution of stage of cancer of the oral cavity according to site of primary tumour

Site of tumour*	Stage; no. of patients		% of stage I or II disease
	I or II	III or IV	
Hard palate	4	0	100
Lateral tip of tongue	12	1	92
Cheek mucosa	6	1	86
Anterior floor of mouth	5	1	83
Dorsal tongue	7	3	70
Ventral tongue	9	4	69
Upper gum	4	2	67
Unspecified area on floor of mouth	12	6	67
Anterior two thirds of tongue	3	2	60
Vestibule	3	2	60
Lateral floor of mouth	4	3	57
Retromolar	8	8	50
Soft palate, uvula	4	7	36
Lower gum	3	9	25
Base of tongue	3	19	14
Unspecified	0	3	0
Total	87	71	55

*Information was incomplete for two patients (1%).

Table V—Association between regular dental care* and stage of disease, first symptom and referral pattern in patients with cancer of the oral cavity

Variable	% of patients†	
	Receiving regular dental care (n = 41)	Not receiving regular dental care (n = 117)
Stage		
I	46	19
II	24	31
III	17	8
IV	12	43
First symptom		
Visible sore	73	64
Dental problem	15	6
Sore throat	2	14
Other	10	16
Referred by		
Physician	66	87
Dentist	34	13

*At least one visit per year in the past 5 years.
†Information was incomplete for two patients (1%).

tween recognition and diagnosis was long were therefore representative of population groups at relatively low risk of disease. This suggests that the longer interval preceding diagnosis may reflect a delay in diagnosis in patients who do not have the characteristics of high-risk groups, in whom the disease might be more readily considered.

Few other studies have systematically examined factors affecting the timing of diagnosis of cancer of the oral cavity, although clinical reviews have stressed the need for vigilance by both physicians and dentists.[7-9]

Kaufman and associates[10] reported that later stages of head and neck cancer were associated, though not significantly, with shorter intervals between recognition of the first symptom and diagnosis. We found no association between the stage of the disease and this interval for either cancer of the oral cavity or other head and neck cancers; our results do suggest, however, that variations in the promptness of recognition of the first symptom or in the speed of tumour growth determine the stage of the tumour at the time of diagnosis.

The role of the dentist in the detection of cancer of the oral cavity was assessed some 10 years ago in both the United States and Scotland.[11,12] More recently Amsel and colleagues[13] studied 231 patients with head and neck cancers, including 193 with cancer of the oral cavity, as defined in our study, seen at a referral centre in the United States. Of the 193 patients, 41% had been referred by a dentist only, compared with 30% in our study. These proportions are not directly comparable, as the methods of documenting the referral source were different. However, Amsel and colleagues found, as we did, that patients referred by dentists had a more favourable stage distribution.

Conclusion

In summary, our study has shown that patients with lower socioeconomic status and those with high levels of alcohol consumption are more likely to present with less favourable stages of oral cavity cancer. This may indicate a lesser awareness of abnormalities and a greater tolerance of symptoms, such as dental problems or a visible lesion, among these patients. The association between stage III and IV tumours and a lack of regular dental care suggests the importance of the dentist's role in first recognizing the symptoms of cancer of the oral cavity. This hypothesis is supported by the more frequent involvement of the dentist in the referral of patients receiving regular dental care.

Published statistics for white patients with cancer of the oral cavity in the United States, adjusted to the distribution by subsite in our study, give relative survival rates 5 years after diagnosis of 63% for those with localized tumours, 30% for those with regional metastatic spread and 17% for those with distant metastatic spread. Application of these figures to the stage distribution of oral cavity tumours in our study shows that the 5-year relative survival rate in patients receiving regular dental care would be expected to be 51%, compared with 41% in those not receiving regular dental care. This calculation assumes that the prognosis for each stage of disease is the same in both groups of patients, thus ignoring any effects of lead time or differences in the speed of tumour growth, and is based on rather dated survival data. While it is obviously an approximation, it does suggest that the prognosis is substantially better in patients who receive regular dental care. Thus, with cancer of the oral cavity, for which there is no effective therapy except at the localized stage, earlier diagnosis through regular dental care should be encouraged.

We thank the patients in our series for their cooperation, the staff of the admitting and medical records departments of the A. Maxwell Evans Clinic, Mrs. Judy Carle and Miss Diane Skippen for performing the interviews, and Mr. Patrick Stapleton for his assistance with the analysis. We are also grateful to Mr. Peter Stevenson-Moore, head, Division of Dental Oncology, Cancer Control Agency of British Columbia, who gave valuable advice on the design of the questionnaire. This study was supported by project grant 6610-1134-44 from the Department of National Health and Welfare.

References

1. *Cancer Patient Survival* (publ no [NIH] 77-992), US Dept of Health, Education, and Welfare, Washington, 1976: 18–22, 29–38
2. *International Classification of Diseases for Oncology*, 1st ed, WHO, Geneva, 1976
3. American Joint Committee for Cancer Staging and End Results Reporting: *Manual of Staging for Cancer*, Whiting Pr, Chicago, 1978: 27–48
4. Elwood JM, Moorehead WP: Delay in diagnosis and long-term survival in breast cancer. *Br Med J* 1980; 280: 1291–1294
5. Elwood JM, Pearson JCG, Skippen DH et al: Alcohol, smoking, social and occupational factors in the aetiology of cancer of the oral cavity, pharynx and larynx. *Int J Cancer* 1984; 34: 603–612
6. Mantel N: Chi-square tests with one degree of freedom: extensions of the Mantel-Haenszel procedure. *J Am Stat Assoc* 1963; 58: 690–700
7. Shaw HJ: Early diagnosis of cancer in the head and neck. *Br Med J* 1976; 1: 379–383
8. Southwick HW: Head and neck cancer: early detection. *Cancer* 1981; 47: 1188–1192
9. Robertson MS, Hornibrook J: The presenting symptoms of head and neck cancer. *NZ Med J* 1982; 95: 337–341
10. Kaufman S, Grabau JC, Lore JM: Symptomatology in head and neck cancer: a quantitative review of 385 cases. *Am J Public Health* 1980; 70: 520–522
11. Adams RJ, Pullon PA, Lee FL: Expanding the role of the dentist in the detection of oral and laryngeal cancer. *J Am Dent Assoc* 1974; 89: 607–610
12. Pogrel MA: The dentist and oral cancer in the north east of Scotland. *Br Dent J* 1974; 137: 15–20
13. Amsel Z, Engstrom PF, Strawitz JG: The dentist as a referral source of first episode head and neck cancer patients. *J Am Dent Assoc* 1983; 106: 195–197

For prescribing information see page 698 →