

## Prognosis in mouth cancer: host factors

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### Abstract

A personal series of 842 patients with a tumour of the oral cavity is presented. Five hundred and twelve of these patients had a histologically proven squamous cell carcinoma, and were previously untreated.

Increasing age was associated with worsening performance status. Women were older at presentation than men, and tumours of the upper part of the mouth were more common in the elderly, but there was no relation between age and histological grade or stage grouping.

Sex had no correlation with performance status or histological grade. However, men were more likely to have an advanced tumour, and tumours of the floor of the mouth and alveolus were much commoner in men.

There was no correlation between performance status and site or histological grade, but patients in poor general condition were more likely to have stage III-IV tumours.

Multivariate analysis showed that sex had no impact whatever on survival, but survival fell with increasing age and worsening performance status. The effect of age and performance status disappeared when the survival of treated patients was adjusted for deaths due to other causes.

### Introduction

The survival of patients with cancer is thought to be affected by host and tumour factors. Few previous papers have considered the impact of host factors on survival in mouth cancer.

#### Age

Henk and Langdon (1985) in a series of 194 cases reported a 59.5 per cent survival in patients under the age of sixty compared with a 22 per cent survival of patients over that age. Age was a significant factor even after taking account of deaths due to other causes (Evans *et al.*, 1982). However, the authors do not state whether the analysis included all patients, or whether it was restricted to treated patients only.

Easson and Palmer (1976) state that older patients are more likely to have a stage IV cancer but they do not submit their data to statistical analysis. Furthermore the graph which they call in evidence to support this point shows that men in stage IV are approximately three years older than those in stage III, but that those in stage III are approximately two years younger than those in stage II. The 'response to treatment' for carcinoma of the tongue in their series declines briskly with age, from 90 per cent for patients under the age of fifty to about 30 per cent in patients over eighty. However, these data were not subjected to multivariate analysis to correct for confounding between age and stage, nor was survival corrected for deaths due to other causes.

Tytor *et al.* (1990) found age to be a significant factor whose effect disappeared when the data were subjected to multivariate analysis. Hibbert *et al.* (1983) also found age to be a non-significant factor.

#### Sex

Some authors (Henk and Langdon, 1985) state that the survival of women with mouth cancer is better than that for men, and that this sex difference has been confirmed by 'many authors'. They quote three series (Smith, 1973; Easson and Palmer, 1976; Berthelsen *et al.* 1977): the last of these (Berthelsen *et al.*, 1977) did indeed state of carcinoma of the floor of the mouth 'here as usual concerning head and neck tumours the survival rate for women is better'. This statement is difficult to understand as their results show exactly the same five-year survival for men and women. Others state that men fare better than women (Binnie *et al.*, 1972; Farr and Arthur, 1972). Some women with stage I and II cancers had a better survival than men (Easson and Palmer, 1976), but there was no sex difference for patients with stages III and IV tumours, whereas exactly the opposite conclusion was found in another series (Shah *et al.*, 1976). Finally, sex was found to have no effect on survival in two other series (Hibbert *et al.*, 1983; Tytor *et al.*, 1990).

#### Performance status

No series has yet studied the relation of performance status with other factors, nor with survival.

A review is presented here of the relation of each of the host factors (age, sex and performance status) with each other, their relation with tumour factors (subsite within the mouth, histological grade, T and N stage), and their effect on survival.

#### Patients

This report is based on 842 patients with a tumour of the

TABLE I  
HOST FACTORS

Age	ECOG status				
	0	1	2	3	4
0-49 years	52	12	1	1	0
50-59 years	83	20	2	3	1
60-69 years	102	41	13	2	7
70+ years	87	41	16	4	7
		$(\chi^2_3 = 17.62, P < 0.0001)$			
<i>Sex</i>					
Men	223	82	23	7	9
Women	101	32	9	6	3
		$(\chi^2_3 = 0.8, N.S.)$			

oral cavity seen personally between 1963 and 1991. The relationship between the host and tumour factors, and between host factors and survival, was calculated on 512 of these patients who had a histologically proven squamous carcinoma which had not previously been treated.

These patients have been treated throughout by a uniform policy: radiotherapy for favourable lesions (*i.e.* T<sub>1-2</sub>), and surgery for patients with palpable lymph node metastases or advanced tumours. 213 patients (42 per cent) were treated initially by radiotherapy (27 with palliative intent) and 207 (40 per cent) by surgery. 92 patients (18 per cent) were not treated for a variety of reasons—usually a combination of advanced age, poor general condition and advanced tumour.

Seven patients (1.4 per cent) had a distant metastasis at the time of presentation, and 36 (7 per cent) had a previous tumour.

## Methods

### Storage of the data and follow-up

The data on all these patients have been recorded prospectively, initially on cards, and for the last 12 years on a microprocessor. Data have been kept up to date by personal contact, and by information from general practitioners, the Mersey Regional Cancer Registry and the National Health Service Register. Two patients (0.4 per cent) have been lost to follow-up. The median potential period of follow-up is eight years.

TABLE II  
SITE

Age	Buccal Mucosa +RMT	Tongue	Alveolus/Floor of Mouth	Palate/Upper Alveolus
	0-49 years	3	26	34
50-59 years	16	30	60	9
60-69 years	32	52	77	8
70+ years	24	57	58	23
		$(\chi^2_3 = 25.13, P < 0.01)$		
<i>Sex</i>				
Men	42	98	189	26
Women	33	67	40	17
		$(\chi^2_3 = 34.43, P < 0.0001)$		
<i>Performance status</i>				
0	49	97	146	32
I	14	40	52	8
II	8	11	12	1
III	2	9	12	2
		$(\chi^2_3 = 7.0, N.S.)$		

## Staging

All patients were staged by the latest UICC conventions (1987). The patient's general condition was recorded, and later assigned a code of 0-4 using the ECOG scale (Beahres *et al.*, 1988). The data on performance status of 17 patients were insufficient for classification using the ECOG system. The histological grade was that assigned by whichever pathologist originally saw the slides—no attempt was made to have all the slides reviewed by one pathologist.

## Analysis of the data

Qualitative data are displayed in contingency tables, and analyzed by  $\chi^2$ . Survival curves were drawn up by the life table method (Armitage and Berry, 1987). Differences between survival curves were analysed by the log rank test (Peto *et al.*, 1976), with analysis for trend where several groups fell into a natural order, *e.g.* stage group.

The effect of prognostic factors were then analysed by relative risk and confirmed by multivariate analysis using Cox's regression (1972).

## Results

### 1. Relation between host factors and between host and tumour factors

#### Age

The mean age at presentation in men was 62.2 compared with 65.3 years in women, a significant difference ( $t_{510} = 2.90, P < 0.001$ ).

Performance status fell with increasing age (Table I): 79 per cent of patients younger than 50 were in good general condition compared with only 56 per cent of patients over 70, and this age effect was highly significant.

There was a significant age effect for site: tumours of the upper part of the mouth were more frequent in those aged over 70, whereas all other tumours were commonest between the ages of 60 and 70 (Table II). This difference was highly significant. However there was no significant relationship between age and histological grade nor between age and stage grouping (Tables III and IV).

There is a decreasing observed survival rate for the

TABLE III  
HISTOLOGICAL GRADE

Age (years)	Well Differentiated	Moderately Differentiated	Poorly Differentiated	Ungraded
	0-49	30	17	6
50-59	44	35	14	22
60-69	69	61	15	24
70+	78	39	20	25
		$(\chi^2_3 = 9.16, N.S.)$		
<i>Sex</i>				
Men	153	110	38	54
Women	68	42	17	30
		$(\chi^2_3 = 1.66, N.S.)$		
<i>Performance status</i>				
0	142	94	35	53
1	52	36	12	14
2	9	13	4	6
3-4	12	5	3	5
		$(\chi^2_3 = 5.76, N.S.)$		

TABLE IV  
STAGE GROUP

Age	I	II	III	IV
0-49 years	20	5	17	24
50-59 years	28	32	18	37
60-69 years	39	34	33	63
70+	39	35	38	46
	$(\chi^2_9 = 14.46, N.S.)$			
<i>Sex</i>				
Men	73	75	71	136
Women	53	31	26	47
	$(\chi^2_3 = 10.6, P < 0.01)$			
<i>Performance status</i>				
0	79	75	60	110
1	38	19	20	37
2	2	7	8	15
3-4	3	2	4	16
	$(\chi^2_6 = 18.19, P < 0.01)$			

whole group of patients with increasing age, from 41 per cent to 19 per cent, and this is highly significant ( $\chi^2_3 = 30.9, P < 0.0001$ ) (Table V). Univariate analysis shows that this age effect persists even when treated patients only are considered and survival is adjusted for deaths due to intercurrent disease (Table V) ( $\chi^2_3 = 10.7, P < 0.025$ ).

*Sex*

There was no relation between sex and performance status, nor between sex and histological grade (Tables I and III). However, tumours of the floor of mouth and lower alveolus are much commoner in men (Table II) as are tumours in stage groups III and IV (Table IV). The survival of women was about 5 per cent better than that for men (Table V) but the difference was not significant either for crude survival or adjusted survival of treated patients ( $\chi^2_1 = 1.25, \chi^2 = 0.65, \text{ resp.}$ ).

*Performance status*

General condition correlated neither with histological grade (Table III), nor with site (Table II). However, the proportion of patients in good general condition fell with increasing stage and this difference was significant (Table IV).

Crude survival fell with worsening ECOG status (Table V) ( $\chi^2_2 = 7.2, P < 0.05$ ). However, this effect becomes non-significant when only the adjusted survival of treated patients is considered ( $\chi^2_2 = 2.47$ ).

TABLE V  
SURVIVAL (5 YEARS)

Age	Observed survival	Adjusted survival of treated patients
0-49 years	41%	63%
50-59 years	33%	57%
60-69 years	27%	57%
70+ years	19%	54%
<i>Sex</i>		
Men	34%	57%
women	39%	61%
<i>Performance status (survival at 2 years)</i>		
ECOG 0	58%	73%
ECOG I	47%	68%
ECOG II-IV	17%	56%

2. *Survival*

The relative risk of dying within five years, for those treated five years or more ago is shown in Table VI. Three types of death are recorded—death from any cause, death from the original cancer and death from the original in cancer in treated patients.

*Sex.* The relative risk of death was slightly lower in women for all these three types of death.

*Age.* The relative risk of all deaths increased continuously with increasing age but the adjusted survival, both of all patients and of treated patients only, did not vary with age.

*Performance status.* Both death from all causes and cancer deaths became commoner with worsening performance status. However, deaths from cancer did not increase with worsening performance status in treated patients only, indicating that the effect of reduced performance status is due to its effect on the ability to treat the patient and not to some biological effect on the cancer.

Multivariate analysis of survival confirmed that sex is a completely non-significant predictor of survival, that both age ( $P < 0.01$ ) and performance status ( $P < 0.001$ ) are highly significant predictors of (crude) survival, but that these effects become completely non-significant when adjusted survival of treated patients only is analysed.

**Discussion**

In brief, this paper shows that the only relationship between the three host factors was that between age and performance status—scarcely a surprising finding. As regards the tumour factors, patients with advanced tumours (stages III and IV) were more likely to be men in poor general condition.

The most important findings about survival were that sex is a completely unimportant prognostic factor, and that the highly significant effect of age and performance status disappears when analysis of survival is restricted to treated patients only. Age and general condition thus affect survival firstly by their influence on the ability to treat the patient, and secondly because of the increased risk of death from other causes with increasing age and worsening general condition. However there is no biological effect on the speed of growth of the tumour due to age.

These findings emphasize that survival in mouth cancer must be analysed by multivariate methods that take into

TABLE VI  
RELATIVE RISK OF DEATH AT 5 YEARS  
(WITH 95% CONFIDENCE INTERVAL)

	Observed survival	Adjusted survival	Adjusted survival of treated patients only
<i>Sex</i>			
Men			
Women	0.92 (0.82-1.04)	0.96 (0.79-1.17)	0.93 (0.70-1.23)
<i>Age</i>			
0-49	—	—	—
50-59	1.16 (0.88-1.51)	1.03 (0.73-1.45)	1.07 (0.69-1.67)
60-69	1.37 (1.07-1.75)	1.05 (0.75-1.45)	0.97 (0.63-1.5)
70+	1.49 (1.17-1.90)	1.17 (0.85-1.61)	0.93 (0.59-1.48)
<i>Performance status</i>			
0	—	—	—
1	1.19 (1.06-1.35)	1.18 (0.95-1.47)	1.19 (0.89-1.58)
2-4	1.33 (1.19-1.49)	1.56 (1.27-1.92)	0.97 (0.53-1.78)

account interrelationships between host and tumour factors and deaths from other causes.

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