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Fixed, bilateral cervical nodes

by

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Introduction

It has long been known that the outlook is poor for a patient who has palpable nodes on both sides of the neck or nodes that are fixed due to invasion by a Head and Neck cancer. Attempts have now been made for over 20 years to classify Head and Neck cancers by the TNM system, the two international systems being that of the American Joint Committee (AJC) for North America, and that of the Union Internationale Contre le Cancer (UICC) for Europe. The M. D. Anderson Hospital of Houston, Texas has its own system.

The AJC brought out its classification for the larynx in 1961 (Smith *et al.*, 1961) and for the pharynx in 1963 (Smith *et al.*, 1963). Patients with mobile nodes on *one* or *both* sides of the neck were classified as N_1 and all those with fixed nodes, also on one or both sides, were included in category N_2. A later revision in 1967 (Smith *et al.*, 1967) added a third category of N_3 for fixed or bilateral nodes.

Because of wide variation in individual interpretation of the word 'fixed', the AJC changed in 1976 to a system based on size (Chandler *et al.*, 1976) shown in Table I.

The UICC classification since its inception has had four categories: N_0–N_3 (UICC, 1978), N_2 has always been used for bilateral mobile nodes, and N_3 for fixed nodes on one or both sides of the neck (Table II). The staff of the M. D. Anderson Hospital in Houston (Texas) have used their own scheme (Table III) since the late 1950s (Barkley *et al.*, 1972), N_{3b} also covers two categories; nodes on both sides of the neck which may be fixed or mobile.

Thus, whatever system is used, there are only two categories to cover three different possible combinations of side and fixation: mobile nodes on both sides of the neck; nodes on both sides, one or more being fixed; and fixed nodes on one side of the neck.

Patients with nodes on both sides of the neck, one of which is fixed, have not been discussed separately in the literature, probably because such patients cannot be classified separately. Indeed the only reference is that by Smith and his colleques (1961) when they defined the first AJC classification for pharyngeal carcinoma in 1963. They described 1320 such patients and stated that 'in a few instances of bilateral fixed nodes in oro and hypopharynx cancer patients, there were no 5 year survivals'.

The latest AJC classification (Chandler *et al.*, 1976) states that each side of the neck should be classified separately if both sides are invaded. An alternative would be a fourth category which might, on arithmetical grounds be called N_4 (ie. $N_3 + N_1$) to cover the patient with bilateral nodes, one of which is fixed.

The present paper compares three groups of patients classified N_2 and N_3 under the UICC system and 'N_4' as suggested above. The following characteristics of the three groups will be described: age and sex, site

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TABLE I
AJC CERVICAL LYMPH NODE CLASSIFICATION

N_0	No clinically positive node.
N_1	Single clinically positive homolateral node less than 3 cm in diameter.
N_2	Single clinically positive homolateral node 3 to 6 cm in diameter, or multiple clinically positive homolateral nodes, none greater than 6 cm in diameter.
N_{2a}	Single clinically positive homolateral node 3 to 6 cm in diameter.
N_{2b}	Multiple clincially positive homolateral nodes, none greater than 6 cm in diameter.
N_3	Massive homolateral node(s), bilateral nodes, or contralateral node(s).
N_{3a}	Clinically positive homolateral node(s), one greater than 6 cm in diameter.
N_{3b}	Bilateral clinically positive nodes (in this situation each side of the neck should be staged separately, that is N_{3b}-right N_{2a}, left N_1).
N_{3c}	Contralateral clinically positive node(s) only.

TABLE II
UICC CLASSIFICATION

N_0	No evidence of regional lymph node involvement.
N_1	Evidence of involvement of movable homolateral regional lymph nodes.
N_2	Evidence of involvement of movable contralateral or bilateral regional lymph nodes.
N_3	Evidence of involvement of fixed regional lymph nodes.
N_x	The minimum requirements to assess the regional lymph nodes cannot be met.

TABLE III
M. D. ANDERSON HOSPITAL NODAL STAGING SYSTEM

N_0	No clinically positive node.
N_1	Single clinically positive node $\leqslant$ 3 cm in diameter.
N_{2a}	Single clinically positive node $>$ 3 cm in diameter.
N_{3a}	Unilateral fixed node(s), clinically positive.
N_{3b}	Clinically positive bilateral nodes, fixed or not fixed.

and stage of the primary tumour, the level of the lymph nodes, the patient's general health, the proportion of patients treated, and the survival.

Patients and Methods

This report is based on a series of 1963 patients with squamous carcinoma of the Head and Neck seen at the Liverpool ENT Hospital from October 1965 to October 1978, and the Royal Liverpool Hospital from October 1978 to October 1981. 237 patients had been treated elsewhere before, and the report is based on the remaining 1,726 patients.

64 patients had mobile nodes (N_2) on both sides of the neck at presentation; 128 had fixed nodes (N_3) on one side of the neck; and 24 patients had nodes on both sides of the neck, one or more of which were fixed (N_4). The proportion of the whole group formed by these three sub-groups was: N_2 3.7 per cent; N_3 7.4 per cent; and N_4 1.4 per cent. The patients' age and sex are shown in Table IV. 2 patients in the N_3 group and 1 in the N_4 were too unfit to allow a specimen to be obtained for histology.

The site and stage of the primary tumour can be seen in Tables V and VI, and the level of lymph nodes in the neck, using the New York Memorial Hospital's Scheme (Barrie *et al.*, 1970) Fig. 1) is shown in Table VII.

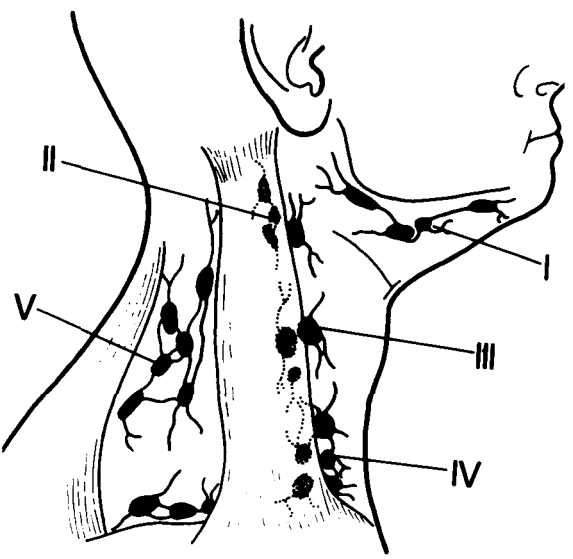


FIG. 1
Level of lymph nodes in the neck (Redrawn from Batsakis).

Finally, the patients' general condition is shown in Table VIII, using one of the following three categories:

I Patients with no serious systemic illness and fully active.

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II Patients with a serious systemic illness, eg. chronic bronchitis, heart failure, and fully active.

III Patients in poor general health, and seriously incapacitated.

Treatment

Some patients were not treated, some were treated by surgery, some by radiotherapy, and some by a combination of the latter two. The proportion of patients who were offered treatment is shown in Table IX.

Follow-up and analysis of the data

Most patients were followed up personally. The date of death of other patients was obtained from the Mersey Regional Clinical Registry or from the Office of Population Censuses and Statistics. Four patients (1.8 per cent) could not be traced, two because they had emigrated.

Survival curves were drawn up using the cumulative method (Armitage, 1971) and were analyzed by Peto's log rank method. (Peto *et al.*, 1977). Confidence intervals shown on the graphs are the standard error of the proportion surviving (Greenwood, 1926). Survivals are also quoted by the 'half-life' method; that is, the time interval at which the survival rate has dropped to 50 per cent.

Contigency tables were analyzed by χ^2.

Results

Age and Sex (Table IV)

Women in the N_3 group were about 5 years older than those in the N_2 and N_4 groups, but these differences were not statistically significant ($F_{2,\ 66} = 1.78$). The men's ages were similar. The sex distribution of all three groups was similar, with about 2 men to 1 woman.

Site of the Primary Tumour (Table V)

Nearly all the patients with no known primary tumour fell into the N_3 category. There was a highly significant difference in the proportion of the three N stages at the different primary sites.

TABLE V
SITE OF PRIMARY

	N_2	N_3	N_4
Oral cavity	6 (9%)	20 (16%)	3 (13%)
Larynx	21 (33%)	20 (16%)	5 (21%)
Nasopharynx	4 (6%)	1 (1%)	3 (13%)
Oropharynx	14 (22%)	24 (19%)	6 (25%)
Hypopharynx	15 (23%)	37 (29%)	6 (25%)
No known primary	4 (6%)	26 (20%)	1 (4%)

($\chi^2_{10} = 25.09$, $p < 0.01$)

The differences between the three groups are entirely due to the N_3 group—there were no statistically significant differences between groups N_2 and N_4 ($X^2_5 = 2.10$, N.S.).

Stage of the Primary Tumour (Table VI)

Although there was a greater proportion of T_4 lesions in group N_4 than in group N_2, the difference between all the groups was not significant ($X^2_6 = 9.68$).

TABLE VI
T STAGE OF PRIMARY TUMOUR

	N_2	N_3	N_4
T_1	17 (27%)	15 (12%)	5 (21%)
T_2	8 (13%)	14 (11%)	1 (4%)
T_3	24 (38%)	44 (34%)	8 (33%)
T_4	15 (23%)	55 (43%)	10 (42%)

($\chi^2_6 = 11.56$ N.S.)

Level of Nodes (Table VII)

The N_3 group had a much greater proportion of patients with nodes at level 1

TABLE IV
AGE AND SEX INCIDENCE

	N_2	N_3	N_4	Whole group
MEN – Number	41	88	18	1176
Age (mean and SD)	59.17 (10.60)	62.94 (11.60)	58.22 (13.42)	62.41 (10.86)
WOMEN – Number	23	40	6	550
Age (mean and SD)	59.00 (11.70)	64.07 (11.57)	58.16 (9.23)	62.52 (11.33)

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TABLE VII
LEVEL OF LOWEST LYMPH NODE

	N_2	N_3	N_4
1	2 (3%)	20 (16%)	0 (0%)
2	39 (61%)	52 (41%)	13 (54%)
3	6 (9%)	12 (9%)	2 (8%)
4	5 (8%)	16 (13%)	5 (21%)
5	1 (2%)	18 (14%)	3 (13%)
Not recorded	11	10	1

($\chi^2_8 = 22.30$, $p < 0.01$)

(the submandibular triangle) and this difference was significant. Again, the N_2 and N_4 groups were similar.

General Condition (Table VIII)

There was a lower proportion of patients in the N_3 group in good health, and the difference was statistically significant. Once more there were no significant differences between groups N_2 and N_4 ($\chi^2_2 = 5.62$).

TABLE VIII
GENERAL HEALTH

	N_2	N_3	N_4
I	45 (70%)	74 (58%)	19 (79%)
II	12 (19%)	34 (27%)	1 (4%)
III	3 (5%)	12 (9%)	4 (17%)
Not recorded	4	8	0

($\chi^2_4 = 9.65$, $p < 0.05$)

Proportion of Patients Treated (Table IX)

The proportion of patients treated was 75 per cent for the N_2 group, 46.8 per cent for N_3, and only 25 per cent for the N_4 group. These differences were statistically very highly significant. The trend of decreasing proportion of patients treated with increasing N stage was also very highly significant.

TABLE IX
PROPORTION OF PATIENTS TREATED

N_2	N_3	N_4
48/64	60/128	6/24

($\chi^2_2 = 21.90$, $p < 0.001$)
(For trend $\chi^2_1 = 21.72$, $p < 0.001$)

Survival

The survival rate fell progressively from N_2 to N_4 and the patients in the N_4 group were almost all dead within one year (Fig. 2). Peto's (Peto *et al.*, 1977) test for trend in prognosis showed that the trend of decreasing survival with increasing N stage was highly significant ($\chi^2_1 = 12.67$, $p<0.001$). The 'half-life', that is the time elapsing until the survival rate had fallen to 50 per cent, was 337 days, 200 days and 125 days for N_2, N_3 and N_4 respectively.

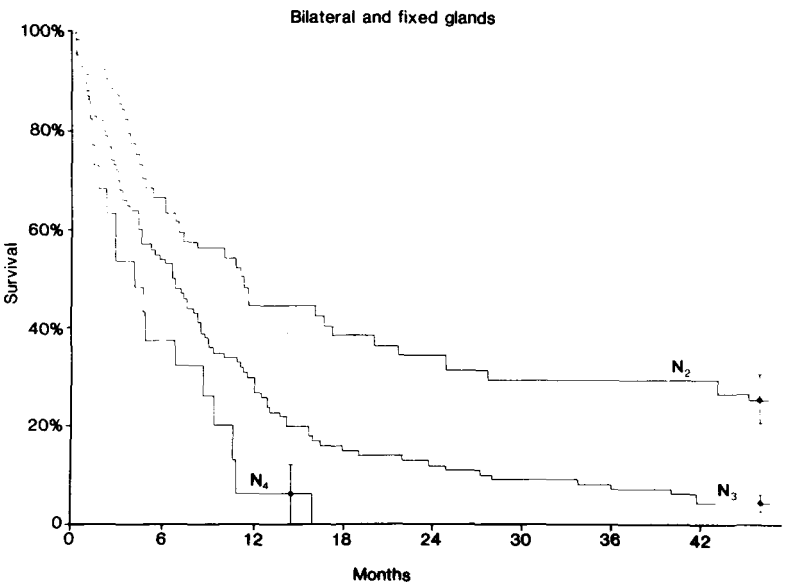


FIG. 2
Cumulative survival rate.

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Discussion

The above results show that, except for age and sex, the three groups differ markedly with respect to site of the primary tumour, the level of lymph nodes in the neck, and general health. On each occasion it was the N_3 group which was the 'odd man out'. This group had almost all the patients with no known primary, a higher incidence of patients with mouth and hypopharyngeal cancer, a higher incidence of patients with nodes at the submandibular level, and a higher proportion of patients in poor general health. The findings with respect to patients with no known primary tumour emphasize the statement of Batsakis that patients with an unknown primary tumour have a node in the neck which is single, unilateral and fixed.

There was a highly significant fall in the proportion of patients who could be offered treatment as N stage increased. Only one quarter of patients in the N4 group were treated.

The survival rate also fell with increasing N stage. A few patients in the N_2 and N_3 groups survived 5 years, but the longest survival in the N_4 group was only just greater than one year.

The above findings provide good evidence that patients with bilateral nodes, one of which is fixed, constitute a separate group. Few of them can be treated, and their prognosis is significantly worse than patients with bilateral mobile nodes or unilateral fixed nodes. Indeed it is doubtful if it is worth treating patients in this group at all.

The N_4 group resembled the N_2 group in respect to parameters such as age and general health of the patient, the site and stage of the primary tumour, and the level of lymph nodes in the neck. If this group is not to have a separate category it should logically be included with bilateral nodes, as is done in the AJC system (N_{3b}) and in the M. D. Anderson system (N_{3b}), but not in the UICC system.

Summary

A series of 1,726 previously untreated patients with squamous carcinoma of the Head and Neck is presented. 64 patients (3.7 per cent) had bilateral mobile nodes in the neck (N_2). 128 (7.4 per cent) had unilateral fixed nodes (N_3) and 24 (1.4 per cent) had bilateral nodes, one or more of which were fixed ('N_4').

The N_2 and N_4 groups were similar with respect to the characteristics of the patient and his tumour such as primary site, etc., but the N_3 group differed significantly: more patients were in poor general health and this group contained almost all the patients with no known primary tumour.

The proportion of patients treated fell from 75 per cent for N_2 to 47 per cent for N_3 and 25 per cent for N_4.

The survival fell significantly with N stage: at one year the survivals were respectively 44 per cent, 30 per cent and 6 per cent. Very few patients in the N_4 group survive to one year, and it is doubtful if this group should be treated at all.

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