

# Head and Neck Squamous Cell Carcinoma in Elderly Patients

## A Long-term Retrospective Review of 273 Cases

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**Background:** The prolongation of life expectancy results in an increasing number of malignant neoplasms occurring in the elderly population. For a long time these patients were not considered good candidates to receive aggressive therapy and probably were inadequately treated in many instances.

**Objective:** To assess the outcome of patients older than 74 years who had had head and neck squamous cell carcinoma.

**Materials and Methods:** In our database of 4610 consecutive patients with head and neck squamous cell carcinomas who were evaluated and treated at the Centre Oscar Lambret, Northern France Comprehensive Cancer Center, Lille, over a 10-year period (1974-1983), we identified 273 patients who were 75 years or older. The outcome was updated for all patients included in the database.

**Results:** A significantly higher proportion of females were noted in the older patient group (43/273, 15.8%) than in younger patient group (192/4337, 4.4%,  $P < .001$ ). There were no differences for primary site except for hypopharyngeal squamous cell carcinoma that occurred less frequently in the elderly patients (8.8% vs 14.5%, borderline significance  $P = .02$ ). There were no differences for TNM stage grouping, histological classification, incidences of previous cancer, and comorbidities. Surgery was performed in a smaller proportion of older patients (13.9% vs 27.4%,

$P < .001$ , for the primary site and 15.4% vs 35.6%,  $P < .001$ , for those occurring in the neck) as well as chemotherapy that was delivered in 5.5% vs 17.7% ( $P < .001$ ). On the contrary, there was no difference in radiotherapeutic treatments. Tolerance to treatment was similar and there was the same proportion of persistent diseases 2 months after completion of the overall treatment (27.8% vs 25.4%,  $P = .94$ ). Pooling local, regional, and distant failures and metachronous cancers, there was a borderline lower incidence in older patients (57.1% vs 64.2%,  $P = .02$ ), which is explained by an obvious shorter life expectancy. If survival is not meaningful in such a comparison (5-year survival 23.8% vs 36.4%), then the causes of deaths may be compared. Among the 4067 patients who were dead at the last update, index tumor evolution-related deaths numbered 130 (48.1% of dead patients in this cohort) in older patients compared with 2045 (53.9% of dead patients in this cohort), which was not significantly different. There was no difference in treatment-related deaths (11.1% vs 9.3%). Fewer intercurrent disease-related deaths occurred in the older patients (19.7% vs 11.8%).

**Conclusions:** Head and neck squamous cell carcinoma in elderly patients did not seem to have a significantly different outcome when compared with head and neck squamous cell carcinoma occurring in younger patients. When properly monitored, conventional therapies seem feasible in older patients.

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**I**N DEVELOPED countries, the prolongation of life expectancy results in an increasing number of patients older than 75 years who have cancer.<sup>1,2</sup> Most head and neck squamous cell carcinomas (HNSCCs) commonly arise between the fifth to seventh decades of life, but their occurrence in the elderly population is not rare. Because morbidity rates often increase with age, therapeutic selection is more difficult. For a long time surgical procedures were available for cancer treatment but anaesthetic risks and functional conse-

quences were unacceptable. Currently, progress in anesthetic risks and reanimation and improvements in surgical reconstruction allow an increased choice of surgery during decision making especially in the older population.

There are few publications in the literature concerning HNSCC outcome in the older population. This part of the population is never included in randomized trials. Thus, to our knowledge, the outcome of HNSCC in older persons has never been evaluated using scientific methods.

## PATIENTS, MATERIALS, AND METHODS

From 1974 to 1983, 4610 new patients with HNSCC were evaluated, treated, and followed up at the Centre Oscar Lambret, Northern France Comprehensive Cancer Center, Lille, for tumors of the oral cavity, oropharynx, hypopharynx, or larynx. At admission the patients' ages ranged between 18 and 98 years. Ninety percent of the patients were aged from 41 to 74 years. As a result, we selected 40 years and 75 years as the cutoff points to define the patient age groups on a chronological basis rather than an epidemiological basis.

Two hundred seventy-three patients fulfilled the criteria to be considered in the so-called older patients group, presenting with a squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, or larynx. The rest of the database was the control group. We compared demographics, treatments, and outcomes (ie, disease control, causes of death, and survival).

Tumors were classified according to the American Joint Committee on Cancer/Union Internationale Contre le Cancer 1997 recommendations. Clinical staging was assessed at the time of decision making by the multidisciplinary team. Those patients who had had undergone an excisional biopsy for pathologic diagnosis and had no visible disease at admission were classified as TX. Immediate response to initial treatment was assessed 2 months after completion of the overall planned treatment.

All patients were followed up until death or at least 5 years after treatment. In the absence of information on the precise cause of death, all patients with confirmed or suspected disease evolution at the last examination were considered dead of cancer. In the absence of any information on the cause of death, patients were considered dead of unknown causes only if they had been examined and considered free of disease at Centre Oscar Lambret within a period of 3 months before their deaths. All patients dead of intercurrent disease were not considered dead of cancer if they had no suggestion of cancer evolution at the last examination and if the nature of the intercurrent disease had been well documented.

The database was divided into 2 (273 patients aged  $\geq 75$  years; and 4337 other patients aged  $\leq 74$  years) or 3 groups (194 young patients aged  $\leq 40$  years; 4143 middle-aged patients aged  $>40$  years but  $<75$  years; and 273 older patients aged  $\geq 75$  years).

Percentages were compared using the  $\chi^2$  test with optional Yates correction. Survival rates were assessed using the nonparametric Kaplan-Meier method. The log rank test was used for survival comparisons.

All studies in the elderly population were retrospective. We found in each study some interesting results that were globally found in our study.

Table 1. Primary Site Distribution

Primary Site	No. (%) of Patients	
	$<75$ y (n = 4337)	$\geq 75$ y (n = 273)
Oral cavity	1466 (33.8)	109 (39.9)
Oropharynx	1274 (29.4)	73 (26.7)
Hypopharynx	628 (14.5)	24 (8.8)
Larynx	969 (22.3)	67 (24.6)

## RESULTS

### DEMOGRAPHICS

Comparisons were made on 2 patient groups. The sex ratio differs significantly between the older and the other patients (female-male ratio, 6:1 vs 1:25,  $P < .001$ ). Primary site distribution seemed to be similar in both patient groups, even if there was a trend toward fewer patients with cancer of the hypopharynx and more patients with cancer of the oral cavity in the older patient group (**Table 1**). Cancer stage grouping was equally distributed between the older patients and the other patients regardless of age—31.1% vs 29.8% for those with stages I and II, 37.9% vs 37% for those with stage III, and 31% vs 33.2% for those with stage IV, respectively. More precisely the following breakdown was noted for the TNM stages in older patients and other patients: T3, 48.5% vs 51.1%; T4, 11% vs 7.2%; N0, 59.7% vs 52.1%; and M+, 0.7% vs 2.8%, respectively ( $P = .09$ ).

Despite a longer duration of life before diagnosis, there was no significant difference in previous cancers (10.3% vs 9.1%). There were fewer simultaneous cancers in older patients than in the other patients (7.3% vs 11.3%) with borderline significance ( $P = .06$ ). Finally, there was no difference for comorbid conditions between the 2 groups.

### TREATMENT

Decision making varied according to the patient's age. Surgery was less often used for older patients than for the other patients: 13.9% vs 27.4% ( $P < .001$ ) for the primary site and 15.4% vs 35.6% ( $P < .001$ ) for cancers of the neck. Irradiation was equally used in both groups but the combination of surgery and irradiation or chemoradiotherapy was less frequently used in older patients than in the other patients: 22.3% vs 9.7% and 14.1% vs 0.2%, respectively. Chemotherapy was less frequently used for older patients than for the other patients: 5.5% vs 17.6% ( $P < .001$ ), and chemotherapy was mainly used for palliative treatment in the older patients.

### OUTCOME

There was no significant difference for immediate response to treatment: complete response rates 2 months after completion of the overall planned treatment numbered 76.6% in young patients vs 71.7% in middle-aged patients vs 72.2% in older patients. Treatment-

related deaths progressively increased according to the patient's age, 4.6% vs 9.5% vs 11.1%, respectively ( $P = .04$ ). As expected because of a shorter life expectancy after treatment, metachronous cancers appeared less frequently in older patients than in younger and middle-aged patients—8% vs 17.5% and 17.6%, respectively.

Causes of death are given in **Table 2**. At last information, 270 older patients (98.9%) had died while 173 younger patients (89%) and 3624 middle-aged patients (87.5%) had died. As far as index tumor progression-related deaths were concerned, there was no statistical difference between the 2 first groups with deaths in approximately 55% (57.9% in the younger patients and 53.7% in the middle-aged patients) but a notable difference with older patients for whom the evolution of the index tumor was the cause of only 48.1% of the deaths. This may be explained by a bias caused by the observed increase in deaths of intercurrent disease or an unknown cause (most probably death caused by the effects of aging) in the older population (19.7% and 14.1% of deaths, respectively) when compared with the younger groups (11.7% and 11.1% of deaths, respectively). If the comparison was made only between patients younger than 75 years and those older than 75 years, the ultimate control disease was statistically better in the older group (31.8% vs 22.8%,  $P = .02$ ).

If as foreseeable, the median survival was shorter in older patients (14 months), there was no major difference between younger patients and middle-aged patients (21 vs 19 months) (**Table 3**). When considering overall survival, older patients had a significantly worse 5-year survival than either younger or middle-aged patients (16.5% vs 30.1% vs 25.1%, respectively,  $P < .001$ ).

#### COMMENT

The incidence of cancer of the head and neck in older patients is difficult to establish since few reports have been published. The definition itself of the so-called older population is somewhat controversial. We have selected 75 years as the cutoff point because 90% of the patients with HNSCC were aged between 41 and 74 years. This age seems to be considered by many authors<sup>2-4</sup> as appropriate, even if some of authors selected a younger age limit<sup>5</sup> and others an older one.<sup>6-8</sup> In addition, some articles focused on only 1 therapeutic method, that is, either radiotherapy<sup>7-9</sup> or surgery.<sup>3,5,6</sup> The evolution of the occurrence of cancer of the head and neck in older patients is also difficult to predict.

Some articles reported an increased rate of the older population in general<sup>1</sup> or specifically in the population with HNSCC.<sup>2</sup> In the Northern France Head and Neck Cancer Registry, there was a trend for stability in older patients with HNSCC from 6.2% in 1987 to 7% in 1997.

In our experience, we have found some differences between the populations of patients younger than or older than 75 years at the time of diagnosis. In our experience, the sex ratio, rarely mentioned in reports, showed a higher proportion of females in the group of older patients compared with the younger patients (female-male ratio, 1:6 vs 1:23,  $P < .001$ ).

**Table 2. Causes of Death**

Variable	% of Dead Patients		
	≤40 y (n = 173)	41-74 y (n = 3624)	≥75 y (n = 270)
Primary tumor	54.4	50.3	47.0
Both	3.5	3.4	1.1
2nd Primary	15.0	13.9	7.0
Treatment related	4.6	9.5	11.1
Intercurrent	13.3	11.7	19.7
Unknown	9.2	11.1	14.1

**Table 3. Overall and Median Survival**

Survival	% of Dead Patients		
	≤40 y	41-74 y	≥75 y
6 mo	85.5	82.9	70
1 y	62.8	62.8	52.7
2 y	44.6	43.2	31.9
3 y	38.4	35.4	23.8
5 y	30.1	25.1	16.5
Median, mo	21	19	14

This sex ratio change in the older population is explained by a longer life expectancy for females. Rew<sup>10</sup> considers cancer in old patients as a degenerative disease. This theory too could explain the higher rate of females in older patients. Currently, HNSCCs are alcohol- and tobacco-related cancers. But older patients with HNSCC seemed less likely to be smokers.<sup>11</sup> In older patients, we observed less simultaneous cancers when compared with younger patients (7.3% and 11.3%, respectively, with a borderline significance  $P = .06$ ). Other characteristics were similar (tumor extension, comorbidities, or previous cancer), but there were fewer cases of cancer of the hypopharynx and more cases of cancer of the oral cavity in older patients than in younger patients (8.8% vs 14.5% and 39.9% vs 33.8%, respectively) that were particularly frequent in females (and rarely associated to tobacco and alcohol abuse).

For a long time it has been anticipated that poor tolerance to treatment in older patients led to undertreatment.<sup>2</sup> This is obvious in our report; although there were not more comorbidities, these patients underwent fewer combined treatments. Surprisingly, they did not do worse after these suboptimal treatments. There is a consensus to consider as often as possible these older patients as candidates for conventional protocols even if there are conflicting data in the literature on the incidence of treatment-related deaths.<sup>3,6</sup> In addition, in reported series there are confusing data about the real cause of posttreatment deaths (either directly linked to the treatment or caused by a preexisting intercurrent disease).<sup>5</sup> Age by itself is an unreliable parameter for decision making. Obviously, the psychological profile is important.<sup>12</sup> Linn et al<sup>13</sup> reported that the nutritional profile was a definitive and relevant indicator for older patient selection.

For many authors,<sup>7-9,11</sup> radiotherapy is usually available in the elderly population for HNSCC treatment. Older patients were able to tolerate radical courses of radiotherapy as well as younger patients<sup>11</sup> except for severe functional acute toxic reaction.<sup>9</sup> It explains the large number of older patients treated with radiotherapy in our experience (227/273). A subset of them (21/227) had had radiotherapy carried out with palliative intent (exclusive treatment with a total dose delivered of <4500 rad).

Finally, survival is not easy to assess in a population that has, by definition, a rather short life expectancy whether or not they present with a malignant neoplasm. Even cause-specific survival does not seem relevant.<sup>6</sup>

## CONCLUSION

Each time the patient's psychological and biological profile allows it, HNSCCs occurring in the elderly population should be treated with conventional protocols.

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