Squamous Cell Carcinoma of the Head and Neck in the Elderly

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Abstract: Background: Increasing life expectancy and incidence of head and neck carcinomas, including some types of head and neck malignancies, lead to a constantly higher proportion of old oncologic patients. Previous reports regarding the outcome for elderly patients with head and neck carcinomas squamous cell carcinoma (HNSCC) are controversial. For further insight, a large single-institution material has been analysed.

Material: Prospective recording of demographic details, continuous follow-up and determining exact cause of deaths of patients with carcinoma of the head and neck have been in progress over a period of 14 years. Having excluded 154 patients (7.3%), who did not follow-up, who had distant metastases at diagnosis, or who had received extensive treatment for a previous head and neck carcinoma or who refused treatment, or for medical or mental reasons, were unable to receive curative treatments. The material includes 1944 patients, of whom 37% received combined treatment, 58% radiotherapy alone and 6% surgery alone. The mean age was 65 years with a mean follow-up of 3.8 years. The material was divided into two groups; ≤65 and >65 years of age and analysed by means of X² tests and log-rank X² tests.

Results: Early stage primary tumours and a more advantageous N-classification were more conspicuous among the older patients (p = 0.2406 and p<0.0002). The group of patients ≤65 years had a significantly better disease-specific survival rate compared to the older patients (p = 0.145). However, 40% of the older patients were alive with no evidence of disease. By comparing 65-74 patients with patients ≥76 years of age, a p-value of 0.0105 was obtained in favour of the younger group, but still an appreciable number of the older patients escaped their HNSCC.

Conclusion: Given a satisfactory mental and physical condition, patients older than 65 years had a reasonable disease-specific survival. It is therefore no reason to withhold appropriate treatment for the elderly, fit patients which could prevent or delay the misery and devastating situation, as well as a reduction in the heavy expenditures that patients with persistent or recurrent head and neck tumours represent.

Keywords: Head and neck carcinoma, geriatrics, oncology prognosis, survival, treatment.

INTRODUCTION

Squamous cell carcinoma of the head and neck (SCCHN) is generally considered a disease of the late middle-aged and elderly people. The literature abounds with bewildering reports of the effect of advanced age on survival and other tumour parameters [1]. Because this group of people is the fastest growing population segment in Europe and North America, a steadily increasing incidence of malignant tumours, including in some sites within the head and neck region, an increasing number of older patients with SCCHN is anticipated. In light of this and the escalating expenditures connected to medical care, it is important to determine the impact of appropriate treatment on the disease-specific survival in elderly patients.

Based on continuous prospective recording of relevant clinical information and complete follow-up collected over a period of 14 years, the disease specific survival for SCCHN of the upper aero-digestive tract was analysed in relation to age at the diagnosis.

PATIENTS AND METHODS

From 1983 through 1997, the author has, in prospective manner, collected relevant clinical information, follow-up and the exact cause of death for all patients with malignant disease of the head and neck admitted to our institution. Classification was initially performed according to the 3rd edition (1982) of the International Union against Cancer (UICC). The database has recently been updated to the 1997 (4th) edition of UICC. The registration has through the years been equivalent to certainty factor 2 (UICC, 6th Ed).

The database comprises of a total of 2096 patients with histologically verified squamous cell carcinoma of the upper aero-digestive tract (lips and salivary glands not included) treated at the Department of Otolaryngology, Rikshospitalet, in close collaboration with the Norwegian Radiumhospital, a tertiary referral centre that recruits patients from the South-Eastern part of Norway, with approximately 1.5 million people. Excluded from this evaluation were 154 patients (7.3%) who did not receive any treatment with curative intent. The reasons for abstaining from treatment were either distant metastases of the actual tumour, a refusal of treatment, or other serious diseases corresponding to the ASA physical indexing (American Society of Anaesthesiology), an ASA index exceeding ≥4 (life threatening diseases, not necessarily related to the primary disease) [2], or mental disorders that
made curative treatment impossible, previous extensive
treatment for a malignant head and neck tumour, for whom
the treatment options were exhausted and one patient lost to
follow-up. Age alone has never been a reason to abstain
from treatment. For obvious reasons, the number of patients
not receiving treatment was highest in the group of patients
older than 65 years (Table 1). Some of the patients excluded
received some kind of palliative treatment. All these patients
died either from their HNSCC or co-morbidity within 2
years. The material (Table 1) thus comprises of 1944 eligible
patients with squamous cell carcinoma of the oral cavity,
oro-, epi- and hypopharynx, sino-nasal cavity, larynx and
neck metastases with unknown primary tumour (ICD9; 141,143,144 146 147, 148, 149,160, 161 and 196).

Table 1. Material According to Age Groups

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age Groups</th>
<th>Total Sum</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of pat. with HNSCC</td>
<td>≤65 y</td>
<td>&gt;65 y</td>
<td>2096</td>
</tr>
<tr>
<td>M+ at diagnosis</td>
<td>1087</td>
<td>1009</td>
<td>1</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>previous head and neck carcinoma; no treatment</td>
<td>15</td>
<td>55</td>
<td>70</td>
</tr>
<tr>
<td>Unfit for treatment; (ASA≥3)</td>
<td>30</td>
<td>51</td>
<td>81</td>
</tr>
<tr>
<td>No. of pat. excluded</td>
<td>46</td>
<td>108</td>
<td>154</td>
</tr>
<tr>
<td>No. of pat. treated with curative intent</td>
<td>1043</td>
<td>901</td>
<td>1944</td>
</tr>
</tbody>
</table>

The mean age was 65 years (from 20 to 92 years). A cut-off
age of 65 years was therefore chosen, resulting in two
age groups of approximately equal size (≤65 and >65 years),

enabling comparison and statistical analysis. Information
regarding tobacco and alcohol abuse has not been recorded.

Complete follow-up and accurate cause of death were
obtained by, review of outpatient and hospital charts,
autopsy findings (when performed), direct contact with the
local hospitals, family physicians, direct contact with
patients or next to kin. The mean follow-up time was 3.8
years, but never less than 3 years [3].

Since 1983 the author holds an authorization from the
Norwegian Data Inspectorate to collect and evaluate data
from patients admitted to our department. The local Ethical
Committee and the Ministry of Health and Welfare have
approved the study. There is no conflict of interest.

Treatment was planned in a joint, clinical meeting with
radiation oncologist, head and neck surgeons, pathologists
and a nurse specialized in oncology. Initially the patients
were treated with radiotherapy alone, or radiotherapy
followed by surgery, when this was planned, or in cases of
residual loco-regional tumor manifestations 6 weeks after
completion of radiotherapy. In 1991 we revised our
treatment policy, and since then surgery has played an
increasingly grater role. Whenever possible, we now prefer
surgery, followed by radiotherapy, for most tumours,
decided by primary tumour size, unfavourable histological
spread, such as violated resection margins or an infiltration
depth of the primary tumour exceeding 3 mm or a spread to
cervical glands. The neck has, as a rule, been treated together
with the primary tumour. Neo-adjuvant chemotherapy with
cisplatin and 5-fluorouracil, according to a Nordic protocol
[4] was administered to 53 patients. Tumours of advanced
stage were otherwise treated by radiotherapy alone.
Radiotherapy was generally given in fractions of 2 Gy/day 5
days a week from a high voltage source. The primary site
received 60-70 Gy and the neck 50-60 Gy over a period of 5-
7 weeks.

Statistics

The data were stored and analysed by means of SAS
software (SAS Institute, Cary, NC). X² tests were performed
for categorical data. Kaplan-Meyer plots were used to
illustrate the disease-specific survival and the log-rank
procedure, to test the effect of age on the disease-specific
survival. A case was censored if death resulted from diseases
other than the original tumour, or if the patient was alive
with no evidence of the original tumour at the last follow-up
contact/consultation. P-values <0.05 were considered
statistically significant.

RESULTS

Table 2 presents the clinical data and treatment. Men
outnumbered women in both age groups (p<0.001).

There was no evident difference in the T-classification.
An advantageous N-classification favouring the older
patients resulted in a significant stage distribution. It should,
however, be noted that the material includes 145 patients
with T1a glottic carcinoma (all N0), who since 1996 have
preferably were treated with CO2 laser surgery. As T1a
with curative intent.

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with curative intent.
Table 2. Clinical Data According to Age Groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Age Groups</th>
<th>Sum</th>
<th>Statistics(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(\leq 65)</td>
<td>(&gt;65)</td>
<td></td>
</tr>
<tr>
<td>Gender Male</td>
<td>832</td>
<td>678</td>
<td>1510</td>
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<tr>
<td>Female</td>
<td>211</td>
<td>223</td>
<td>434</td>
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<tr>
<td>Eligible patients</td>
<td>1043</td>
<td>901</td>
<td>901</td>
</tr>
<tr>
<td>Tumor sites(^1)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Sino-nasal (160)</td>
<td>40</td>
<td>43</td>
<td>83</td>
</tr>
<tr>
<td>Larynx (161)</td>
<td>373</td>
<td>359</td>
<td>661</td>
</tr>
<tr>
<td>Oral cavity (141)</td>
<td>332</td>
<td>318</td>
<td>650</td>
</tr>
<tr>
<td>Oropharynx (146)</td>
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<td>246</td>
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<tr>
<td>Nasopharynx (147)</td>
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<td>38</td>
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<tr>
<td>Hypopharynx (148)</td>
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<td>73</td>
<td>147</td>
</tr>
<tr>
<td>Unknown primary (196)</td>
<td>33</td>
<td>15</td>
<td>48</td>
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<td>Primary tumor classification</td>
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<tr>
<td>T1</td>
<td>306</td>
<td>246</td>
<td>552</td>
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<tr>
<td>T2</td>
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<td>230</td>
<td>502</td>
</tr>
<tr>
<td>T3</td>
<td>113</td>
<td>108</td>
<td>221</td>
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<tr>
<td>T4</td>
<td>319</td>
<td>302</td>
<td>621</td>
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<td>Tx</td>
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<td>Neck node classification</td>
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<td>636</td>
<td>1286</td>
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<tr>
<td>N1</td>
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<tr>
<td>N2</td>
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<td>N3</td>
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<td>38</td>
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<td>Stage distribution</td>
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<td>234</td>
<td>485</td>
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<tr>
<td>II</td>
<td>212</td>
<td>173</td>
<td>385</td>
</tr>
<tr>
<td>III</td>
<td>123</td>
<td>113</td>
<td>236</td>
</tr>
<tr>
<td>IV</td>
<td>457</td>
<td>381</td>
<td>838</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery alone</td>
<td>74</td>
<td>83</td>
<td>157</td>
</tr>
<tr>
<td>Surgery + irradiation</td>
<td>172</td>
<td>135</td>
<td>307</td>
</tr>
<tr>
<td>Irradiation + surgery</td>
<td>154</td>
<td>101</td>
<td>255</td>
</tr>
<tr>
<td>Chemotherapy + irradiation</td>
<td>85</td>
<td>45</td>
<td>130</td>
</tr>
<tr>
<td>Chemotherapy + irradiation + surgery</td>
<td>15</td>
<td>8</td>
<td>23</td>
</tr>
<tr>
<td>Irradiation alone</td>
<td>543</td>
<td>529</td>
<td>1072</td>
</tr>
</tbody>
</table>

1. \(^1\) ICD9 classification
2. Chemotherapy with cisplatin + 5-Fluorouracil[4].
3. \(^3\) \(p\)-values where T1a glottic laryngeal carcinoma are left out.

Table 3. Failures (Residual Disease Following Treatment and Recurrences) According to Age Groups

<table>
<thead>
<tr>
<th>Failures</th>
<th>Age Groups</th>
<th>Sum</th>
<th>Statistics(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(\leq 65)</td>
<td>(&gt;65)</td>
<td></td>
</tr>
<tr>
<td>Residual tumor(^1)</td>
<td>100</td>
<td>265</td>
<td>365</td>
</tr>
<tr>
<td>Locally</td>
<td>121</td>
<td>144</td>
<td>265</td>
</tr>
<tr>
<td>Regionally</td>
<td>66</td>
<td>70</td>
<td>136</td>
</tr>
<tr>
<td>Recurrences(^2)</td>
<td>324(321)</td>
<td>208(205)</td>
<td>0</td>
</tr>
<tr>
<td>Locally</td>
<td>212(210)</td>
<td>1338(131)</td>
<td>0</td>
</tr>
<tr>
<td>Regionally</td>
<td>72(79)</td>
<td>54(53)</td>
<td>0</td>
</tr>
<tr>
<td>Distant</td>
<td>45</td>
<td>36</td>
<td>81</td>
</tr>
<tr>
<td>Salvage(^3)</td>
<td>73(71)</td>
<td>22(22)</td>
<td>94(94)</td>
</tr>
<tr>
<td>Locally</td>
<td>61(60)</td>
<td>17(17)</td>
<td>78(77)</td>
</tr>
<tr>
<td>Regionally</td>
<td>10(10)</td>
<td>4(4)</td>
<td>14(14)</td>
</tr>
<tr>
<td>Distant</td>
<td>2(2)</td>
<td>1(1)</td>
<td>3(3)</td>
</tr>
</tbody>
</table>

1. \(^1\) 13 patients had residual disease both locally and regionally
2. 11 patients had recurrences at more than one site simultaneously
3. Alive with no evidence of disease.
4. \(^3\) \(p\)-values where T1a glottic squamous cell carcinoma are left out.

A total of 199 secondary primary tumours (including 9 synchronous tumours) within the aero-digestive tract were observed (Table 4). The upper aero-digestive tract, especially the oral cavity, was the dominant site of a secondary primary tumour. The annual incidence of such tumours was 2.3 and 4.3 for patients \(\leq 65\) years and \(>65\) years, respectively. Secondary lung carcinomas increased to 66 with approximately equal annual incidence. A majority of the secondary lung carcinomas was diagnosed after the 70th birthday. Secondary tumours as cause of death were equal when comparing the two age groups.

Table 5 presents the outcome, according to site and age. Patients with laryngeal cancer represents the largest group of patients, and these patients experienced the most advantageous course, which might be an effect of likely is a relatively high number of T1 tumours. For pharyngeal tumours, the older patients were in the worst situation. Fig. (1) shows that patients \(\leq 65\) had a significantly better disease-free survival than the group with the older patients \((p=0.105)\). When comparing the outcome for patients 65-75
years of age with those older than 76, the older had the poorest survival (Fig. 2), but still there was an appreciable number of the older patients who escaped their HNCC.

Combined treatment, irrespectively of whether radiotherapy was given pre- or postoperatively, showed the best results, when compared to monotherapy, principally radiotherapy. For radiotherapy alone, the disease-specific survival was 44% and 28% for patients ≤65 and >65 years respectively. The disease-specific survival was independent of gender.

DISCUSSION

This study focuses on the disease-specific survival of elderly patients with SCCHN, considered physically and mentally fit for the treatment with curative intent. Several recent studies have established co-morbidity as an independent predictor of survival in elderly patients (age ≥65 years) [5, 6] A malignant disease may aggravate co-morbidity illnesses or vice versa. There are certainly in this, as in comparable materials, patients with significant concomitant illnesses who did not preclude treatment, but that might have affected survival unfavourably. There is, however, no way to identify these patients with certainty, and/or to judge the impact of their comorbidity on survival. As most patients in this study had surgery as part of the treatment, the ASA index, which since the 1960s has been used as a simple prognostical description of a patient’s physical state as an exclusion criterion, has been used [2]. Patients with an ASA index of ≥ 4 (life threatening diseases, not necessarily related to the primary disease) were considered unfit for the treatment and consequently were excluded from this study. Roughly seen, the ASA classification emphasizes the same disadvantageous conditions as does the co-morbidity indices in use [6]. Likewise, treatment was withheld when patients were considered mentally unfit for treatment. The percentage of patients excluded (7.9%) from treatment in this study is similar to that previously reported from a comparable institution in Canada [7].

Table 4. Second Primary Tumors According to Age Groups

<table>
<thead>
<tr>
<th>Site/second. prim.</th>
<th>≤65 y</th>
<th>&gt;65 y</th>
<th>Sum/Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Mean No./Year (Range)</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Head and Neck</td>
<td>78</td>
<td>2,3 (0-17.8)</td>
<td>37</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>12</td>
<td>3,3 (0-10.7)</td>
<td>6</td>
</tr>
<tr>
<td>Lung</td>
<td>45</td>
<td>2,3 (0,1-12,5)</td>
<td>21</td>
</tr>
<tr>
<td>No., mean/year (range)</td>
<td>135</td>
<td>2,6 (0-17.8)</td>
<td>64</td>
</tr>
<tr>
<td>Patients dead sec. prim. (%)</td>
<td>89</td>
<td>(6.6)</td>
<td>41</td>
</tr>
</tbody>
</table>

Table 5. Outcome According to Age Groups

<table>
<thead>
<tr>
<th>Site</th>
<th>≤65 y</th>
<th>&gt;65 y</th>
<th>Total No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sino-nasal</td>
<td>13</td>
<td>6</td>
<td>43</td>
</tr>
<tr>
<td>Larynx</td>
<td>181</td>
<td>142</td>
<td>359</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>132</td>
<td>79</td>
<td>113</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>8</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>60</td>
<td>13</td>
<td>27</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>14</td>
<td>8</td>
<td>21</td>
</tr>
<tr>
<td>Unknown primary</td>
<td>13</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>All</td>
<td>421</td>
<td>254</td>
<td>901</td>
</tr>
</tbody>
</table>

Abbrevations: Aned: Alive no evidence of disease, Dfd: Dead from disease, Dod: Dead other disease.
As life expectancy increases, clinicians increasingly face the challenge of treating elderly patients with cancer, including some types of head and neck carcinomas [8]. It has been estimated that in Norway the number of persons older than 70 will be increased by 40% by 2020 (Source: Ministry of Health and Welfare). This increase in the number of old patients with cancer, combined with increasing costs related to medical management, force clinicians to concern themselves with the effect of age on survival.

Paucity of well controlled materials and conflicting reports limit our knowledge of the disease-specific survival of the older patients with SCCHN [1, 8]. Several factors may

Fig. (1). Disease-specific survival for patients ≤65 vs >65 years of age (failed/total: 330/1049 vs 303/901; p<0.143).

Fig. (2). Disease-specific survival for patients 65-75 vs ≥76 years of age (failed/total: 192/603 vs 111/603; p<0.105).
explain the lack of attention to this topic and the
contradicting results, the major limitations probably being
that it has been difficult to accumulate a sufficiently large
number of patients with long follow-up, and that most
studies presented are retrospective [9,10]. Other
methodological issues, such as unequivocal criteria for
tumour sites, stage, histology, inclusion and exclusion, are
also some features that should be accurately accounted for.

The classification of age, with a cut-off at 65 years that
coincides with the average age is similar to that used in
several other studies [5-7]. This age cut-off might also
contribute to a reduction of the impact of co-morbidity in the
group of the older patients. This material thus satisfies the
strict and compulsory criteria for evaluation, proposed by
Lacy and co-workers for this kind of studies [9].

In contrast to some reports [9-11], it was our observation,
as well as that of others [12, 13] that the older patients in
general had less advanced disease. This distribution of stage
in favour of the older patients was accentuated after
exclusion of the early stage glottic carcinomas. There was no
difference in extent of the disease, when comparing those
excluded from the treatment with those included and thus no
selection bias.

Clinicians may be inclined to treat older patients less
aggressively than younger. This reluctance toward treating
elderly patients may be attributed to a presumed lower
tolerance of radiation toxicity and fear of postoperative
complications and morbidity in these patients [14]. Although
the group of patients older than 65 had the poorest survival
rate, the fact that 40% of the patients older than 65 were
alive and free of disease at the closure of this study, strongly
suggests that treatment is worthwhile in patients at an
advanced age, regarding the disease-free survival for
SCCHN. This observation concurs with observations in
materials similar to the present study [1, 13]. Other reports
further substantiate the opinion that age in itself is not an
independent prognostic factor, neither is it in itself a decisive
factor for survival of SCCHN [9,11,15-17]. On the other
hand, Davidson and co-workers [18] showed in a material of
oral tongue squamous cell carcinoma matched for age,
gender, site, stage and treatment that an increase of 10 years
in age was associated with an 18% increase in disease-
specific mortality. Both surgery [17, 19, 20], even when
combined with free-tissue graft reconstruction [19], and
radiotherapy [10, 20-22] offer commendable results in older
patients. Moreover, the incidence of peri- and postoperative
complications has been reported to be independent of age
[14, 20]. Radiotherapy appears to be well tolerated by elderly
patients and does not generate drastically different side
effects when compared to that experienced by younger
patients [14, 21]. Cisplatin based regiments have been
widely employed in primary and recurrent treatment of
SCCHN. Argiris and co-workers [22] report that elderly fit
patients (>70 years) with metastatic or recurrent disease had
response rates similar to younger patients, but the older
patients suffered a higher rate of toxicity. These authors
strongly warn against a therapeutic nihilistic attitude towards
chemotherapy in the treatment of elderly patients. Novel
chemo-radiation treatment schemes [23] might also become
a useful treatment option for elderly patients.

A recent prospective study shows that the impact of
treatment on quality of life after one year did not differ when
elderly and younger patients with head and neck cancer were
compared [14]. However, a large longitudinally prospectively recorded study from Sweden and Norway
reveals that the quality of life in patients older than 65 with
cancer of the head and neck continue to deteriorate up to 5
years following treatment [24]. The adverse effect of
treatment on quality of life varies with the site of the primary
tumours, being least pronounced for patients treated for
laryngeal carcinoma and worst for those with pharyngeal
carcinoma [25, 26].

Contrary to others [10, 11] this study showed the highest
incidence of secondary malignancies of the aero-
digestive tract among the group with the older patients. This may, to
some extent, be an effect of insufficient observation time.
Whether the same factors causing the initial tumour,
principally alcohol and tobacco consumption [27], are also
accountable for the secondary tumours in older patients, is
debatable. It has recently been shown that P53 mutations are
less common in older patients, and based on this observation,
it has been suggested that accumulation of spontaneous
mutations during lifetime and defective DNA repair
mechanisms may play an important role in the
carcinogenesis in elderly patients [10]. In addition to faulty
DNA repair, an aging immune surveillance [1] and previous
radiotherapy [28] might partly to some extent explain the
reduced incidence of secondary malignancies among older
patients.

SUMMARY

An assumed prejudiced and erroneous conception of a
poor tolerance to treatment of older patients may lead to
undertreatment. This should no longer be the case. When
properly monitored, conventional therapies seem feasible for
elderly patients.

Although co-morbidity may play an important role
regarding the disease-free survival age at diagnosis, is in
itself no contraindication for treatment. The site, stage or
intrinsic characteristics of the tumour appear to be equally
important determinants of the prognosis. Radiotherapy,
surgery and chemotherapy have been reported to be well
tolerated and with encouraging results in aged patients.
Granted a satisfactory physical and mental condition, there is
no reason why elderly people should be withheld appropriate
treatment that could delay or prevent the misery, suffering
and disability that a persistent or progressive head and neck
cancer entail. Most likely, treatment of elderly patients might
also prove cost favourable. This issue should be an object to
further analysis.

ACKNOWLEDGEMENTS

My sincere thanks to Dr. Terje Osnes, M.D., Ph.D. for
the advice regarding the presentation and to Maj Boysen for
linguistic advice.

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