Secondary lung lesions after head and neck cancer: Diagnosis, differentiation, screening, survival
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Chapter 6

The psychological impact of annual chest X-ray follow-up in head and neck cancer

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Abstract

Objective:
To assess the psychological impact of annual post-treatment screening for second primary lung cancer and metastases in HNSCC patients.

Patients and methods:
In a cohort of 106 patients, 68 men and 38 women, with a mean age of 56, the impact of the yearly chest radiograph was evaluated by means of a nine-item questionnaire.

Results:
In all, 90% of the patients were in favor of annual post-treatment screening, 2% would not like to receive this screening, and 8% had no preference. A majority (98%) considered the screening as an extra medical check and 76% felt reassured. Although 21% of the patients were very nervous about the outcome of the screening, only 3% wanted to avoid the yearly chest X-ray for this reason.

Conclusion:
Annual post-treatment screening of head and neck squamous cell carcinoma (HNSCC) patients for second primary lung cancer and metastatic recurrence appeared to form no major burden for head and neck cancer patients. A majority of patients regard the annual chest X-ray as a reassurance. Given these results a more intensive screening program seems psychologically justifiable for this group.
Introduction

Patients curatively treated for head and neck squamous cell carcinoma (HNSCC) are at high risk for developing second primary tumors or metastatic recurrence in the lungs.\textsuperscript{1,2} The differentiation between second primary lung carcinoma and metastasis is not easily made on clinical grounds. In a recent study from our institute it was shown that lesions, clinically diagnosed as metastases, frequently appear to be second primary tumors based on ‘loss of heterozygosity’ analysis.\textsuperscript{3} Per follow-up year, 3–7\% of patients surviving HNSCC develop a second malignancy in the upper aero-digestive tract.\textsuperscript{1} The relative risk of developing lung cancer after curative treatment for HNSCC is three to six times higher than in the normal population.\textsuperscript{2} In HNSCC patients, pulmonary metastases account for 66\% of distant metastases\textsuperscript{4} and the incidence of pulmonary metastases in curatively treated HNSCC patients ranges from 1.6\% to 23\% depending on the tumor stage.\textsuperscript{5,6}

The issue of screening for lung cancer during follow-up for a previous head and neck cancer is still under discussion. Based on retrospective analyses some groups have abandoned lung cancer screening for second primary lung carcinoma, since no survival benefit seemed to be associated with an annual follow-up chest X-ray.\textsuperscript{7,8} However, the final verdict on the value of lung cancer screening is still unknown.\textsuperscript{9–12} Some authors assume that a more intensive screening program using pulmonary spiral CT scan in combination with PET may result in earlier detection of malignant lung lesions, possibly contributing to a better survival.\textsuperscript{13–15}

Besides the argument of a potential limited improvement of overall survival, the issue of psychological distress for the individual patient has also been used to argue against routine radiological follow-up. To substantiate this assumption we have investigated the (psychological) distress in a cohort of 106 patients curatively treated for HNSCC in our clinic, undergoing annual lung cancer chest X-ray screening.

Patients and methods

Between March and November 2004 every patient visiting our outpatient clinic for a routine check-up of their HNSCC, being in complete remission and recommended to have an annual chest X-ray, was asked to participate in the study. A total of 121 patients was accrued, of whom 14 were excluded because
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the histology of their cancer was different from squamous cell carcinoma (e.g.
adencarcinoma, salivary gland carcinoma). Another patient, who filled in the
questionnaire, but failed to show up for his chest X-ray, was also excluded. This
resulted in a study group of 106 patients (68 men and 38 women), with a mean
age of 56 years (range 37–83). Median follow-up (months from end of treatment
until date of chest X-ray) was 33 months, with a mean number of X-rays of 3.6.
Primary tumor sites were as follows: larynx (n=33), oral cavity (25), oropharynx
(25), hypopharynx (11), skin (4), nasopharynx (3), maxillary sinus (1), unknown
primary tumor site (4). The following stages (UICC TNM class of malignant
tumours 2002\(^\text{16}\) were included: stage I (n=27), stage II (31), stage III (18), and
stage IV (30) (Table 1).

Participating individuals received a nine-item study-specific questionnaire. All
patients were informed about the value of chest X-ray for the early detection of
lung cancer. Besides the nine study-specific items, the questionnaire also
contained items on sociodemographic characteristics (including age, marital
status, living status (single or together), educational level, and cancer-related
characteristics (years of chest X-ray adherence, site, TNM stage) (see also Figure
1). Stress-related items were evaluated on a four-point scale: ‘not at all’, ‘a little’,
‘quite a bit’, and ‘very much’. The questionnaire was made concise to maximize
compliance. All patients filled in the questionnaire at the time of visiting the
outpatient clinic and before the outcome of the chest X-ray was known.
Statistical analyses mainly included descriptive analyses and, if appropriate,
correlations were measured by Spearman’s correlation coefficient. A two-tailed p
value<0.05 was taken to indicate statistical significance.

Table 1. Localization of primary tumor

<table>
<thead>
<tr>
<th>Primary HNSCC</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharynx</td>
<td>3</td>
<td>2.8</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>25</td>
<td>23.6</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>11</td>
<td>10.4</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>25</td>
<td>23.6</td>
</tr>
<tr>
<td>Larynx</td>
<td>33</td>
<td>31.1</td>
</tr>
<tr>
<td>Skin</td>
<td>4</td>
<td>3.8</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
<td>3.8</td>
</tr>
<tr>
<td>Sinus</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>Total</td>
<td>106</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Results

The number of previous annual X-rays ranged from none to more than eight. Seventy-nine patients (74%) had 0–4 X-rays, 21% had 5–8 and 5% had >8. The mean number of X-rays was 3.6, during a median follow-up of 33 months. The great majority of patients (86%) received the result of screening within 1 week after the X-ray was carried out. In this series four positive X-rays were found. Eighty-four patients (79%) reported that they were ‘not’ or just ‘a little nervous’ in awaiting the report on the chest X-ray. This means that 22 patients (21%) were ‘quite a bit’ to ‘very’ insecure or nervous (Table 2).
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Table 2. Nervousness in the waiting period for the result of the X-ray.

<table>
<thead>
<tr>
<th>Nervous</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>41</td>
<td>38.7</td>
</tr>
<tr>
<td>A little</td>
<td>43</td>
<td>40.6</td>
</tr>
<tr>
<td>Quite a bit</td>
<td>15</td>
<td>14.2</td>
</tr>
<tr>
<td>Very much</td>
<td>7</td>
<td>6.6</td>
</tr>
<tr>
<td>Total</td>
<td>106</td>
<td>100.0</td>
</tr>
</tbody>
</table>

For almost all patients (97.2%) feelings of anxiety never were a reason to abandon the routine follow-up chest X-ray. Only three patients (2.8%) wanted to skip their routine follow-up chest X-ray to avoid those feelings, but of these three patients, two stated that they were just a little nervous and the other one reported no nervousness during the waiting period. Of these three patients, only one felt reassured by the yearly chest X-ray. As a result, two of them preferred to have no yearly chest X-ray at all (see also below).

When asked how the annual chest X-ray was experienced, all but two patients (98.1%) considered the X-ray as an extra medical check up. The majority of them (76.5%) felt reassured by the yearly lung check, 19 patients (18%) only a little, and 5 patients (4.5%) did not feel reassured at all (Table 3). Twenty-seven of the 106 patients (25.5%) asked for a chest X-ray themselves during follow-up. For 22 patients this was not related to any symptoms; however, for 5 patients this was related to pulmonary complaints. Of the total study population (n=106), eight patients (7.8%) reported having pulmonary problems at the time of undergoing the chest X-ray.

Table 3. Reassurance provided by annual chest X-ray.

<table>
<thead>
<tr>
<th>Reassurance</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>5</td>
<td>4.7</td>
</tr>
<tr>
<td>A little</td>
<td>19</td>
<td>17.9</td>
</tr>
<tr>
<td>Quite a bit</td>
<td>38</td>
<td>35.8</td>
</tr>
<tr>
<td>Very much</td>
<td>43</td>
<td>40.6</td>
</tr>
<tr>
<td>Total</td>
<td>105</td>
<td>99.1</td>
</tr>
<tr>
<td>Missing</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>Total</td>
<td>106</td>
<td>100.0</td>
</tr>
</tbody>
</table>
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The last item, concerning the preference for a yearly chest X-ray, was answered as follows: 95 (90%) patients preferred an annual chest X-ray, 2 patients did not want a yearly chest X-ray (remarkably both of them being ‘not at all’ nervous in the waiting period for the result), and 8 patients (7.5%) had no preference (Table 4). Responses were related to the number of previous follow-up chest X-rays. The more previous examinations, the higher the acceptability (Spearman’s rho test; $p=0.007$).

Table 4. Preference for annual chest X-ray.

<table>
<thead>
<tr>
<th>Preference</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yearly X-ray</td>
<td>95</td>
<td>89.6</td>
</tr>
<tr>
<td>No yearly X-ray</td>
<td>2</td>
<td>1.9</td>
</tr>
<tr>
<td>No preference</td>
<td>8</td>
<td>7.5</td>
</tr>
<tr>
<td>Total</td>
<td>105</td>
<td>99.1</td>
</tr>
<tr>
<td>Missing</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>Total</td>
<td>106</td>
<td>100.1</td>
</tr>
</tbody>
</table>

No statistically significant correlation between the level of education (elementary school, $n=25$; advanced elementary school, $n=47$; college, $n=20$; and university, $n=11$; 3 patients provided no information on their educational level), age and gender, and feelings of distress/nervousness and/or preference could be found.

Discussion

Screening of head and neck cancer patients, at risk of developing second primary lung cancer, is still a matter of debate. Apart from the cost-benefit discussions on radiological screening, causing lung cancer-specific distress is often put forward as an argument against post-treatment lung cancer screening. In the literature no data are available which address the issue of psychological distress in high risk head and neck cancer patients adhering to chest X-ray surveillance. The impact of screening on health-related quality of life has been studied more extensively in breast, prostate, and pulmonary cancer patients. Recent literature data on psychological distress around two consecutive screening visits in 357 women with a hereditary risk of developing breast cancer showed that general distress remained within normal limits during surveillance, consisting of self breast examination, biannual physical examination, and annual mammography, and that
pre-visit stress levels were considerably lower before the second surveillance appointment.\textsuperscript{17,18} This fits with our observation of a higher acceptability of post-treatment screening after previous chest X-ray examinations. This effect was confirmed by Sutton et al., who did not find anxiety-raising effects of breast cancer screening.\textsuperscript{19} Rijnsburger et al. demonstrated that 37\% of the women experienced some degree of anxiety when undergoing magnetic resonance imaging (MRI), versus 27\% of women undergoing mammography and 22\% undergoing clinical breast examination.\textsuperscript{18} An explanation for this could be that patients assume that MRI is a more sensitive screening modality compared with mammography and clinical breast examination, and thus has a higher chance of tumor detection. Patients with a hereditary risk for breast cancer and HNSCC patients share the high risk of developing second cancer and the no-distress raising screening appointments are probably experienced as a routine check-up, thereby finding a way of coping with their high risk status. The search for reassurance afterwards is probably of most importance, since the breast cancer screening study indicates that general distress significantly decreases after the screening appointment.\textsuperscript{17}

Although screening for prostate cancer is obviously more aggravating, physical discomfort was only reported by 37\% of 491 men during digital rectal examination and by 29\% of 487 men during transrectal ultrasound.\textsuperscript{20} It is therefore striking that mean scores for health status and anxiety in this group did not indicate relevant changes in physical, psychological, and social functioning during this screening procedure.\textsuperscript{20} Reasons for refusing screening for prostate cancer were mainly absence of urological complaints and to a lesser degree anticipated pain or discomfort.\textsuperscript{21} In the prostate screening study group no empirical support was found for the objection that the availability of a screening program elicits emotional stress among large population groups. If one could prove that mortality rates will be reduced by early detection programs, negative effects on the psychological condition of patients will be neutralized.

A large proportion of distress may be related to being informed about a positive chest X-ray screening result and false positive results will certainly have consequences for future screening adherence.\textsuperscript{22} Non-adherence to lung cancer screening increased >50\% in 4705 patients with false positive results at the previous screening.\textsuperscript{22} It is therefore extremely important to minimize false positive results in pulmonary carcinoma surveillance in HNSCC patients. The combination of spiral CT and PET is more sensitive than chest X-ray and will probably diminish the negative effects on the health status. However, since more suspicious lesions are detected early by CT and PET, recalls for additional work-up (bronchoscopy), which later prove to be false positive, will induce substantial distress.
Nevertheless, the high sensitivity of PET/CT in lung cancer screening seems to outweigh the risk of distress in the subgroup of patients receiving additional examinations. Interestingly, in a group of breast cancer patients undergoing further work-up (biopsies) after a false positive mammography, 6 months later no excess distress was demonstrated.\textsuperscript{18}

The available literature on the impact of cancer screening for breast, prostate, and lung cancer showed that psychological distress was not increased by screening procedures, even when the screening was accompanied by considerable physical or psychological discomfort. This is in concordance with our results in which 79\% of the patients reported to be 'not' or 'just a little' nervous before the screening. It is remarkable that the great majority (90\%) of our patient group prefers to undergo the screening despite the distress it might bring. It seems therefore psychologically justified to extend our current screening with PET/CT.

Another source of distress related to screening can be a long period of time between the examination and the result. To minimize this, our intention to inform the patient within 1 week was successful: 86\% received the result of screening within 1 week after the X-ray was carried out. Solitary lung carcinoma detected by chest X-ray screening in our HNSCC patient group is in principle treated by resection unless contraindicated by signs of metastases to multiple organs or by poor general condition (e.g. ASA status). This approach is based on the fact that resection of pulmonary carcinoma is generally proven to be the most important modality for cure.\textsuperscript{6} Pulmonary lesions found by chest X-ray can be either metastases or second primary lung carcinoma. Since clinical criteria are not reliable enough to differentiate between second primary lung carcinoma and metastases in HNSCC, and clinically diagnosed metastases frequently appear to be second primary tumors\textsuperscript{3}, we prefer to choose the curative surgical option in case of resectable lung lesions. However, the interval of 12 months for carrying out the chest X-ray remains arbitrary. It may be expected that more sensitive advanced screening programs with spiral CT scan in combination with PET will dictate shorter screening intervals. This is supported by the finding that 85\% of stage 1 lesions are detected by CT scan, in contrast to 30\% by chest X-ray.\textsuperscript{23} Early detection programs are therefore very important, because presentation of pulmonary carcinoma by clinical symptoms limits the curability significantly.\textsuperscript{11,12,23} Overall 5-year survival of >80\% can be achieved if lung lesions <2 cm\textsuperscript{2} are resected.\textsuperscript{24} Others confirm these survival improvements after resection of early staged lung lesions as well.\textsuperscript{11,14,15}

In conclusion, this is the first survey on the burden of lung cancer screening in curatively treated HNSCC patients. Our data demonstrate in a prospective setting
that the vast majority of the patients (90%) prefer annual post-treatment screening. Although 21% of the patients were very nervous about the outcome of screening, only 3% wanted to abandon surveillance for this reason. These figures in combination with literature data on the impact of screening in breast, lung, and prostate cancer patients give us enough confidence to start screening for second primary lung carcinoma in curatively treated HNSCC patients by spiral CT scan in combination with PET, which is also attractive from a cost-effective point of view.25

References