Miss Rate of Lung Cancer on the Chest Radiograph in Clinical Practice*

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Study objectives: To investigate the miss rate of non-small cell lung cancer (NSCLC) on the chest radiograph. In addition, the characteristics, the delay in diagnosis, and the change in prognosis of the missed lesions were studied.

Design: A retrospective study on patients with histopathologically proven NSCLC during the years 1992 through 1995 in a large community hospital.

Setting: Department of Radiology, Atrium Medical Center, Heerlen, the Netherlands.

Patients: During the study period, 495 patients presented with NSCLC. Of these patients, the complete set of chest radiographs was available for analysis in 396; there were 300 men and 96 women, with a mean age of 68 years.

Main outcome measures: The main outcome measures included the miss rate of NSCLC presenting as nodular lesions. Location, diameter, superposing structures, and delay of missed and detected lesions and the change of prognosis as a consequence of the delay in diagnosis were other measures.

Results: In 49 (19%) of 259 patients with NSCLC presenting as a nodular lesion on the chest radiographs, the lesions were missed. The miss rate was not dependent on location. Superposing structures were more often present in the group of missed lesions than in the group of detected lesions, respectively, 71% and 2%. The median diameter of the missed lesions was 16 mm and of the detected lesions it was 40 mm. The median delay of the missed lesions was 472 days and of the detected lesions it was 29 days. Twenty-two (45%) patients with missed lesions remained in stage T1, 6 (12%) remained in stage T2 and in 21 patients (43%), the tumor stage changed from stage T1 into T2.

Conclusion: The miss rate of 19% in our study is low compared with the rate in the literature but it has a definitive impact on prognosis.

Key words: diagnostic errors; lung neoplasms; thoracic radiography

Abbreviation: NSCLC = non-small cell lung cancer

The diagnosis of early non-small cell lung cancer (NSCLC) on the chest radiograph may be troublesome. Many lung cancers present themselves as small solitary nodules. Failure to detect lung cancer on the chest radiograph, which has become one of the most frequent causes of missed diagnosis in radiology,1–3 is a major cause of medicolegal action.

Small pulmonary nodules are often missed because of poor lesion conspicuity caused by superimposition of hilar and mediastinal structures, blood vessels, clavicles, or ribs. Poor viewing conditions and poor technical quality of the images are also reasons why small lesions can be missed.4–9

In the literature, the proportion of missed lung cancers on chest radiographs varied between 25% and 90%.10–12 However, these studies differ largely in study design. Some were designed to measure the miss rate of solitary pulmonary nodules in general rather than lung cancer. Other studies were laboratory studies that investigated different parameters influencing failure to detect small pulmonary lesions. Other investigators studied small selected groups of patients. Furthermore, some studies presented data resulting from screening programs to detect early lung cancer in high-risk patients. Thus, the exact miss rate in the detection of early lung cancer on the chest radiograph is difficult to estimate.

The generally accepted error rate for the radiologic detection of early lung cancer is between 20% and 50%.13

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The purpose of the present investigation was to determine the miss rate of the detection of early lung cancer on the chest radiograph in the daily routine of a radiology department of a large community hospital. In addition, the characteristics and distribution of these missed cancers were compared with those of the detected cancers. Finally, the delay in diagnosis was determined as well as an estimate of the consequence for the prognosis thereof.

**Materials and Methods**

The study included all consecutive patients with pathologically proven NSCLC selected from the database of the Dutch National Pathologic Anatomic Cancer Registration System between 1992 and 1995 in a 700-bed community hospital. Patients with recurrent cancer after therapy were excluded. The chest radiographs were obtained in the 125- to 150-kVp range, grid ratio 12:1, focus film distance 150 cm, rare earth screen with speed class 400 (Agfa ortho regular or Agfa curix HT-U films; Agfa Gevaert; Mortsel, Belgium). All available chest radiographs (posterior-anterior and/or lateral) on the chest radiography were recorded on a prearranged checklist. Furthermore, each lung cancer visible on the chest radiography were recorded on a prearranged checklist. The pathologic diagnosis were included in the study.

Patients' age and gender as well as characteristics of the tumor on the chest radiography were recorded on a prearranged checklist. Furthermore, each lung cancer visible on the chest radiograph was classified as a nodular lesion, focal area of airspace disease (i.e., infiltrate), atelectasis, pleural fluid, or combinations of these characteristics.

The nodular lesions were localized as peripheral (≥ 3 cm distance from the hilus), parahilar (< 3 cm from the hilus), or hilar and were also localized in a specific lung lobe. The margins of the lesions were characterized as sharp, partly sharp, or entirely unsharp. The visibility of the lesion on the posterior-anterior and lateral chest radiograph was scored on a three-point scale and any superposing structures were recorded. The largest diameter of each carcinoma was measured on the posterior-anterior and/or lateral chest radiographs.

Whether a lesion was missed, was determined by the following procedure. Two radiologists independently scrutinized all available posterior-anterior and/or lateral chest radiographs of all patients for nodular lesions. The decision whether a lesion was visible was made by consensus between these two radiologists. The location of the lesion in the lung was confirmed by the histopathologic report, bronchoscopic finding, or surgical report. If a lesion was not mentioned in the original radiologic report, it was considered visible but not detected. A third radiologist from another institution who was aware of the study design but blinded for the location of the lesion reviewed all radiographs of the patients with visible but not detected lesions as selected by the first two observers. In case the third observer did not locate the tumor, consensus with the first two observers decided whether a lesion was definitely missed or not. It was also recorded whether a lesion was missed more than once.

The delay was defined as the span of time between the date of the histopathologic diagnosis and the date of the first radiograph on which the missed lesion was first detectable according to the consensus of the three radiologists. According to the revised American Joint Committee on Cancer staging system, we divided the missed tumors as stage T1 and T2: stage T1 includes tumors with a diameter ≤ 30 mm and stage T2 tumors with diameter > 30 mm.

**Results**

From the Dutch National Pathologic Anatomic Cancer Registration System database, 495 consecutive patients from 1992 through 1995 with histopathologic proven first detected NSCLCs were identified in our hospital. In 99 patients, the radiographs were not traceable. The characteristics of the remaining 396 patients are presented in Table 1. In 36 patients, more than one abnormality on the chest radiograph was visible.

Two radiologists preselected 259 patients with visible lesions on the chest radiographs. In 60 patients, the NSCLC was visible but not detected on one or more consecutive chest radiographs. These NSCLCs were verified by the histopathologic report. After examination by the third radiologist of the radiographs of these 60 patients, consensus among the three reviewers agreed that in 49 patients, the lesion was missed and in 11 patients, the lesion was visible but not detectable without additional information of the chest radiographs in an advanced stage of the tumor.

Thus, in 49 (19%) of the 259 patients with a nodular lesion, the lesion was definitely missed. In 16 (33%) of the 49 patients, the lesion was missed twice on consecutive chest radiographs and in 6 (12%) patients, the lesion was missed more than twice. Table 2 compares the demographic patient variables and the characteristics of the tumors between detected and missed lesions. Most of the lesions were located in the periphery of the lung (56%) and in the upper lobes (66%), but no significant difference in location between missed and detected lesions was found. Superposing structures were more frequently present in radiographs with missed lesions, the diameter of the lesion was smaller, and the clinical delay was longer. All these differences were statistically significant.

Compared with the detected tumors, the median
diameter of the missed tumors is significantly smaller in all three regions (Table 3). Thirty-six of the 49 missed lesions (73%) did not have sharp borders or only part of the border was sharp. Only 13 of the 49 missed lesions (27%) had sharp borders.

In one patient, the lesion was visible on the lateral chest radiograph only, but this lesion was missed. Figure 1 shows a histogram of the diameter of the missed and detected lesions. Of the lesions ≤10 mm, the miss rate was 71%; between 10 and 30 mm, 28%; and between 30 and 40 mm, 12%.

The explanation for missing the tumors was diverse. Ten tumors had diameters of ≤10 mm. In 27 patients, superposing structures were present: in 11 cases, the ribs sometimes with the clavicle or sternum; in 7 cases, the hilar structures; the vessels 5 times; advanced silicosis 2 times; and the heart and the diaphragm each one time. In two patients, a resolving infiltrate and a hematoma after trauma were the reasons. In 9 of the remaining 10 patients, the tumor had a diameter between 11 and 14 mm. In the 10th case, the diameter was 21 mm with no obvious reason for the missed diagnosis.

The delay in diagnosis in the 49 patients with missed NSCLC had a wide range. The number of patients with a delay <6 months, between 6 and 12 months, between 12 and 24 months, and >24 months was, respectively, 12 (24.5%), 9 (18%), 16 (33%), and 12 (24.5%).

**Table 2—Comparison of the Characteristics of the Missed and the Detected Malignant Nodular Lesions**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Missed Lesions</th>
<th>Detected Lesions</th>
<th>p Value (2-Tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No.</td>
<td>49</td>
<td>210</td>
<td></td>
</tr>
<tr>
<td>No. of men (%)</td>
<td>40 (82)</td>
<td>157 (75)</td>
<td>0.3‡</td>
</tr>
<tr>
<td>Age, yr, median (range)</td>
<td>71 (48–88)</td>
<td>68 (37–87)</td>
<td>0.02§</td>
</tr>
<tr>
<td>Location of nodular lesions†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hilar, No. (%)</td>
<td>7 (14)</td>
<td>25 (12)</td>
<td>0.6‡</td>
</tr>
<tr>
<td>Parahilar, No. (%)</td>
<td>15 (31)</td>
<td>71 (34)</td>
<td>0.7‡</td>
</tr>
<tr>
<td>Peripheral, No. (%)</td>
<td>27 (55)</td>
<td>118 (56)</td>
<td>0.91</td>
</tr>
<tr>
<td>RUL, No. (%)</td>
<td>21 (43)</td>
<td>70 (33)</td>
<td>0.2‡</td>
</tr>
<tr>
<td>LUL, No. (%)</td>
<td>10 (20)</td>
<td>71 (34)</td>
<td>0.07†</td>
</tr>
<tr>
<td>RLL, No. (%)</td>
<td>10 (20)</td>
<td>36 (17)</td>
<td>0.6‡</td>
</tr>
<tr>
<td>LLL, No. (%)</td>
<td>8 (16)</td>
<td>28 (13)</td>
<td>0.6‡</td>
</tr>
<tr>
<td>RML, No. (%)</td>
<td>0</td>
<td>12 (6)</td>
<td>0.13‖</td>
</tr>
<tr>
<td>LING, No. (%)</td>
<td>0</td>
<td>9 (4)</td>
<td>0.2‖</td>
</tr>
<tr>
<td>Superposing structures, No. (%)</td>
<td>35 (71)</td>
<td>4 (2)</td>
<td>&lt;0.0001‖</td>
</tr>
<tr>
<td>Diameter, mm, median (range)</td>
<td>16 (6–38)</td>
<td>40 (5–159)</td>
<td>&lt;0.0001‡</td>
</tr>
<tr>
<td>Delay in days, median (range)</td>
<td>472 (7–3,233)</td>
<td>29 (0–4,148)</td>
<td>&lt;0.0001‡</td>
</tr>
</tbody>
</table>

*RUL = right upper lobe; LUL = left upper lobe; RLL = right lower lobe; LLL = left lower lobe; RML = right middle lobe; LING = lingula.†Numbers do not add up to 210; 11 patients had more than one lesion.‡x² test. §Mann-Whitney test. ‖Fisher’s Exact Test.

**Table 3—Miss Rate and Comparison Between the Diameter of the Missed and Detected Lesions Stratified for Location**

<table>
<thead>
<tr>
<th>Location</th>
<th>Hilar</th>
<th>Parahilar</th>
<th>Peripheral</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detected lesions</td>
<td>23</td>
<td>71</td>
<td>116</td>
</tr>
<tr>
<td>Missed lesions</td>
<td>7</td>
<td>15</td>
<td>27</td>
</tr>
<tr>
<td>Miss rate, %</td>
<td>21</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>Median diameter (range), mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detected lesions</td>
<td>35 (15–90)</td>
<td>40 (12–130)</td>
<td>40 (5–160)</td>
</tr>
<tr>
<td>Missed lesions</td>
<td>27 (11–32)</td>
<td>17 (9–37)</td>
<td>13 (6–38)</td>
</tr>
<tr>
<td>Test† for difference</td>
<td>p = 0.025</td>
<td>p &lt; 0.0001</td>
<td>p &lt; 0.0001</td>
</tr>
</tbody>
</table>

*If more than one lesion was present, the location and diameter of the largest lesion were taken. †Mann-Whitney test.

**Figure 1.** Graph showing the change in tumor stage of the missed cancers.
Figure 1 shows a scatterplot with the diameter when first missed on the X-axis and the diameter first detected on the Y-axis of the 49 missed tumors. In 28 (57%), the tumor stage did not change despite the delay; 22 patients (45%) remained in the T1 stage, and 6 (12%) remained in the T2 stage. In 21 of the 49 patients (43%), the tumor stage changed from T1 into T2.

**Discussion**

To our knowledge, no studies have been reported that addressed the miss rate of the chest radiography in detecting lung cancer in clinical practice. In the literature, the miss rate of such lesions varied between 25% and 90%, but as indicated in the introduction, these figures originate from studies that differ largely in objective and design. In our study, a miss rate of 19% was found.

In 99 of the 495 cases, a chest radiograph was not available for analysis. However, there was no indication that this was a selected group and we assume that our study population is representative. Furthermore, our population of 396 cases did not differ demographically from the cancer registration of the particular region: the percentage of men in the study population of our study was 76% vs 80% in the registry, and the median age in both populations was 68 years.

We found that in 65% of the studied cases, the tumors were visible as a nodular lesion on the chest radiograph; their diameter varied from 6 to 160 mm and was mostly in the range of 10 to 50 mm (Fig 2). The median diameter of the lesions was 30 mm, which is comparable to those reported by other authors.

In the study of Theros, 52% of the malignant nodular lesions were located peripherally and about 60% were in the upper lobes. Several authors also reported a preference of missed lesions for the upper lobes. In this regard, we found a preference of the upper lobes for the detected lesions as well as the missed lesions (Table 2). Some authors suggest that overlying anatomic structures, such as vessels, ribs, the heart, etc, are far more important for missing a lesion, particularly small ones, than the location. In general, it is assumed that detection of hilar cancers is hampered by the wide variability of the hilar anatomy. In a screening program, Muhm et al found that 65% of the lung cancers arising in the hilum were missed. In this study, 7 of 32 hilar lesions (22%) were missed and, surprisingly, no substantial differences in miss rates among the peripheral, parahilar, and hilar regions (Table 3) were found.

The diameters of the missed lesions located peripherally or in the parahilar region are significantly smaller than those of the detected lesions (Table 3). Centrally located lesions that are missed are larger than peripherally located lesions.

In our study, the median diameter of a missed lesion was 16 mm (range, 6 to 38 mm). Heelan et al, in a screening program, and Austin et al, in a series of 27 patients, found mean diameters of missed lesions of, respectively, 13 and 16 mm. However, some authors state that on a good-quality chest radiograph, a nodule of 3 to 4 mm is the smallest lesion that can be detected. In two studies with lesions of 8 to 10 mm in size, detection rates of 40% and 87% were found. In the present study, a detection rate of 29% in lesions ≤10 mm in diameter was found. In lesions > 10 mm, the miss rate drops promptly and lesions > 40 mm were not missed (Fig 2).

The detection probability is strongly related to the blur or unsharpness of the edges of pulmonary nodules. Kundel et al have shown that detection probability can fall from almost 90% in sharply bordered to 30% in unsharply bordered lesions. Austin et al found that 95% of the missed lesions were unsharply bordered. In our series, 73% of the missed lesions were partly or totally unsharply bordered.

In our study, in six patients, the lesion was missed more than two times in the same patient. In two of these patients, the lesion showed hardly any growth in several years. The radiologist did not describe the lesion, probably presuming that it concerned a non-malignant scar lesion. This would also explain the long delay. The other four cases were slowly growing tumors and were missed a few times in succession.

Different opinions exist about the necessity of performing posterior-anterior and lateral chest radiographs at all times. Tala stated that a lateral radiograph is decisive in 20% of the patients for diagnosing lung cancer. Other authors found 3 to 4% of the
lung cancers only on the lateral chest radiographs. Forrest and Sagel found all NSCLC visible on posterior-anterior chest radiographs, suggesting that lateral chest radiographs are superfluous for detection. In our study, one lesion was visible only on the lateral radiograph and this lesion was missed. We think that both the posterior-anterior and lateral chest radiographs are necessary for determining the exact location of the tumor but not for detecting it.

The reasons for missing the lesions were the small size (< 15 mm) and superposing structures. In one lesion with a diameter of 21 mm, there was no apparent explanation for not detecting. Therefore, we think a miss rate of 19% as found in our study is realistic and difficult to improve. This is also suggested by the generally accepted miss rate of 20 to 50% as reported in the literature.

Prognosis is influenced by the growth of the tumor and thus is dependent on the length of the delay time. There is a wide variability of the interval between the actual detection of lung cancer on the chest radiographs and its retrospective presence. In the study of Forrest and Friedman, in 15 of 27 patients with radiologically missed lung cancers, the time from the first radiologic appearance to the first diagnosis was > 6 months and in two instances it was > 3 years. In our study, 75% of the patients with missed lung cancers had a delay of > 6 months and eight patients had even > 3 years.

In 28 patients (57%), the tumor stage did not change and in 21 patients (43%), the tumor stage changed from T1 to T2 (Fig 1). According to Mountain, the 5-year survival rate of a patient with T1 N0 M0 stage is 61% and a patient with T2 N0 M0 stage is 38%. Assuming that the status of the node and the metastases remain unchanged, in 43% of the patients with undetected early lung cancer the 5-year survival drops by 23%.

It seems that a miss rate of 19% can hardly be improved, but missing a tumor has a major impact on the prognosis in most cases. Therefore, we think that patients at risk with a normal chest radiograph should be referred for further evaluation.

A study was performed by Kaneko et al. to investigate if low-dose spiral CT is a better tool to detect early lung cancer with promising results. They suggest using low-dose spiral CT as a screening modality for lung cancer. Considering the potential of spiral CT to lower the miss rate in the detection of early lung cancer, we think this modality should play a major role in the case finding of patients at risk in the near future.

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