Impact of age and radiographic presentation on the presumptive diagnosis of pulmonary tuberculosis

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Abstract We compared delay in presumptive diagnosing pulmonary tuberculosis (PTB) in elderly and younger patients, yield of diagnosis and whether the yield is influenced by the radiographic presentation, even when PTB was suspected.

Time from first complaints to first consideration of PTB was determined as suspicion interval (SI) and from first consideration to diagnosis as recognition interval (RI). Presumptive diagnosis was defined as positive staining for acid-fast bacilli or presence of granulomatous lesions in pulmonary specimens.

In the elderly and in the younger patients, the mean SI was 111.1 and 87.8 days respectively (P=NS), and the mean RI was 5.9 and 8.3 days, respectively (P=NS). The mean RI was longer in uncharacteristic than in characteristic radiographic findings in both elderly (8.2 and 4.6 days; P=0.007) and younger patients (10.6 and 3.9 days; P=0.0001). A diagnosis was obtained in 89/113 elderly (79%) and in 109/138 younger (79%) patients (P=NS) and also in 59/80 (73%) patients with uncharacteristic findings and in 139/170 (82%) patients with characteristic findings (P=NS). In the latter, sputum contributed for 66% of diagnosis, whereas it was only 31% in patients with uncharacteristic findings (P<0.005). In elderly patients with uncharacteristic radiographic findings, diagnosis was obtained from sputum in 41% and from other specimens in 35% (P=NS); in the younger group diagnosis was obtained from sputum in 23% and from other specimens in 48% (P<0.05).

In conclusion, there was no difference in SI and RI in elderly patients in comparison with younger patients. Uncharacteristic radiographic findings increased RI in both age groups. Age or radiographic presentation did not influence diagnosing PTB. In patients with characteristic radiographic findings, diagnosis was especially made from examination of sputum, whereas in those with uncharacteristic findings, diagnosis was more often obtained from the complementary investigation of other specimens. © 2002 Elsevier Science Ltd. All rights reserved.

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Keywords pulmonary tuberculosis; diagnosis; delay; suspicion interval; recognition interval; elderly.

INTRODUCTION

Tuberculosis (TB) represents again an emerging problem for world health care and if case detection and cure rates are maintained at the present level, the annual incidence of TB is expected to increase with 41% between 1998 and 2020, especially in developing (or low-income) countries (1). In Western countries, a decline of the TB incidence is observed in recent years and TB seems to be confined to some groups in the community: immigrants, patients infected with the Human Immunodeficiency Virus, persons detained in jail, asylum seekers, homeless people, drug abusers, people living in poverty and indigenous elderly persons (2,3).

Elderly patients represent a particular problem since mortality of TB and especially of pulmonary TB (PTB) is higher in this age group and diagnosis may often be made only at autopsy (4). One possible reason for the increased mortality could be the progression of the disease because of postponement of adequate therapy, the latter due to delay in obtaining an early and appropriate diagnosis (5).

An early or presumptive diagnosis of PTB can be obtained by staining for acid-fast bacilli (AFB) of different specimens of pulmonary content such as sputum, gastric
lavage, bronchial washing or biopsy specimens, of which sputum is the easiest to obtain. Although staining for AFB can be considered the gold standard for a rapid and cheap identification of TB, it lacks sensitivity (6). Recent techniques, such as nucleic acid amplification can be used to determine whether sputum contains Mycobacterium tuberculosis (M. tuberculosis) complex, but this technique is not sensitive enough to detect M. tuberculosis in specimens with low bacterial load (7).

Postponement of diagnosing TB can be due to the long delay between the onset of complaints and the first moment of suspicion of TB, which we defined as the 'suspicion interval' (SI). However, even when PTB is highly suspected, diagnosis can also be delayed because of the lack of early recognition of M. tuberculosis in the investigated specimens and this delay we defined as the 'recognition interval' (RI).

Elderly patients are often not able to expectorate adequate sputum samples for examination and this could be especially true in the presence of uncharacteristic radiographic features for this age group, which includes findings other than infiltrates with or without cavitation in the upper lobes (8,9). It could be expected that the recognition interval therefore will be longer in elderly patients, even when PTB is highly suspected.

We compared in elderly and younger patients with suspected PTB but in whom diagnosis of TB had to be confirmed later on by positive cultures for M. tuberculosis (a) whether the suspicion and recognition interval differs in both age groups, (b) whether a presumptive diagnosis is obtained less often in the elderly age group and (c) whether the yield of diagnosing PTB is influenced by the presence of uncharacteristic radiographic findings.

**MATERIALS AND METHODS**

In a retrospective study from 1985 to 1995, 251 patients with finally proven TB by positive culture of M. tuberculosis, were included: 113 were 70 years of age or older (mean age: 82 years, range 70–94) and were labelled ‘the elderly group’; 138 were younger than 60 years of age (mean age: 35 years, range 18–59) and were labelled ‘the younger group’. Patients were admitted at the pulmonary division of a University Hospital, located in an area with a TB incidence of 11.8 per 100 000 population in 1998. Twenty-four patients (±9.5%) were referred from a general hospital: in those patients the presumptive diagnosis of TB was already explicit since investigation was yet performed to exclude other pathologies including malignancy, systemic disease and other infectious disease.

The SI was determined as the time elapsed from the onset of the complaints (as derived from patients comments) to the first moment of suspicion of PTB (by either the referring physician or at our institution). The RI was defined as the period between the presumptive diagnosis of PTB and the moment of diagnosing PTB or the initiation of antituberculous medication. The time between the first symptoms and the final diagnosis, i.e., the combination of SI and RI can be defined as the diagnosing interval.

Presumptive diagnosis of TB was considered as positive staining for AFB in sputum and/or (if negative after three samples) in bronchial washing, pulmonary biopsy specimens, pleural fluid or gastric lavage. Presumptive diagnosis was also based on the presence of granulomatous lesions with caseous necrosis in histological preparations. Final diagnosis had to be confirmed later on by positive culture for M. tuberculosis.

Chest X-rays were divided into two groups, as described earlier (9,10). Characteristic findings consisted of infiltrates with or without cavitation in the apicoposterior segments of one or both upper lobes or in the apical segment of the lower lobes, whether or not those findings were found in combination with uncharacteristic findings. The latter consisted of absence of characteristic findings and the presence of pleural effusion, hilar and/or mediastinal lymphadenopathies, atelectasis, ventrobasal infiltrations, clear chest X-ray, rounded nodules, miliary pattern or diffuse infiltrates.

Data are reported as mean (±sem) and were compared with each other using the Student’s t-test for independent variables. Statistical analysis consisted of the chi-square method (or Fischer’s exact test in the case the expected cell value is less than 5) to compare frequencies between groups. Effects were judged to be statistically significant if the associated P value was < 0.05.

**RESULTS**

**Suspicion interval SI recognition interval (RI)**

The diagnosis interval was 1170 days in the elderly and 96.1 days in the younger group (P = NS). The division of the diagnosis interval into SI and RI is shown in Table I. There was no statistically significant difference between the two intervals in the elderly group and the younger group; yet, the SI tended to be longer in the elderly age group (III.I vs. 878 days in the younger group) whereas the RI tended to be longer in the younger age group (8.3 vs. 5.9 days in the elderly group). There was also no difference between elderly and younger age group when the RI was compared between characteristic and uncharacteristic findings. However, within each age group the RI was longer in cases of uncharacteristic findings than in cases of characteristic findings: 8.2 vs. 4.6 days in the elderly age group (P = 0.007) and 10.6 vs. 3.9 days in the younger age group (P = 0.0001).
Effect of age on presumptive diagnosis of pulmonary tuberculosis

Presumptive diagnosis of TB could be obtained in 198 of the 251 patients (79%). There was no effect of age, since diagnosis was found in 89 of the 113 elderly patients (79%) and in 109 out of the 138 younger patients (79%) (P=NS). Sputum was the most important source since the diagnosis was obtained from staining for AFB on sputum in 137 of the 198 patients (69%). In the 61 cases with initially three negative sputum smears, diagnosis was further obtained from bronchial washing in 12/198 (6%), from gastric aspiration in 14/198 (7%) and from histological examination in 35/198 (18%); the latter in 18 cases (9%) from pleural biopsy and in 17 cases (9%) from pulmonary biopsy.

A presumptive diagnosis could not be obtained in 53 of the 251 patients (21%): in 25 of the 113 elderly (22%) and in 28 of the 138 younger (20%) patients (P=NS). In three of these 25 elderly patients diagnosis was made by autopsy (all had uncharacteristic findings on chest X-ray) and in another four at the moment of a diagnostic thoracotomy. In three of the 28 younger patients diagnosis was obtained at the moment of a thoracotomy. In those 10 patients diagnosis was confirmed later-on by growth of M. tuberculosis from sputum or other specimens. In those cases, antituberculous therapy was initially not started. In the remaining 43 patients (18 elderly and 25 younger patients) with initial negative investigations, antituberculous treatment was initiated empirically: subsequently, cultures grew for M. tuberculosis.

Initial diagnosis from sputum examination could be obtained in 137 of the 251 patients (55%), equally divided between the elderly (60/113=53%) and the younger (77/138=56%) age group (P=NS).

Effect of radiographic presentation on early diagnosis of pulmonary tuberculosis

The yield of diagnosing PTB in relation to the presentation on chest X-ray is shown in Table 2. Of the total group of 251 patients, the diagnosis of TB was obtained in 59 of the 81 (=73%) patients with uncharacteristic findings on chest X-ray and in 139 of the 170 (=82%) patients with characteristic findings; this difference was not statistically significant (P=0.1). Sputum as first contributing factor in obtaining a diagnosis was found in 112 of the 170 patients with characteristic findings (=66%) but in only 25 of the 81 of the patients with uncharacteristic findings on chest X-ray (=31%) (P<0.005).

In patients with uncharacteristic findings, a diagnosis could be obtained in the same proportion in both age groups: in 28/37 (=76%) of the elderly and in 31/44 (=70%) of the younger patients (P=NS). However, in the elderly age group diagnosis was made in the same proportion from examination of sputum as from other specimens, i.e., in 41 and 35%, respectively (P=NS), whereas in the younger age group, diagnosis was obtained more often from specimens other than sputum, i.e., 48 and 23%, respectively (P<0.05). The yield of diagnosing PTB could be increased by examining other specimens and this was more pronounced in the younger age group (+47%) than in the elderly age group (+35%).

In patients with characteristic findings, a diagnosis was obtained in 61/76 (=80%) of the elderly and in 78/94 (=83%) of the younger patients, respectively (P=NS). The diagnosis was obtained especially from sputum: in

<p>| Table 1. Suspicion interval (SI) and recognition interval (RI), expressed in days ± SEM in the elderly and younger age groups |
|------------------------------|------------------|-----------------|--------|</p>
<table>
<thead>
<tr>
<th>Suspicion interval (SI)</th>
<th>Elderly patients</th>
<th>Younger patients</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncharacteristic findings</td>
<td>11.1 ± 1.5</td>
<td>8.7 ± 1.0</td>
<td>0.21</td>
</tr>
<tr>
<td>Characteristic findings</td>
<td>5.9 ± 0.6</td>
<td>8.3 ± 1.6</td>
<td>0.17</td>
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<tr>
<td>Recognition interval (RI)</td>
<td>8.2 ± 1.4*</td>
<td>10.6 ± 1.2**</td>
<td>0.22</td>
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<td>------------------------------</td>
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</tr>
<tr>
<td>K Uncharacteristic findings</td>
<td>4.6 ± 0.5</td>
<td>3.9 ± 0.3</td>
<td>0.23</td>
</tr>
</tbody>
</table>

P=0.007* and 0.0001** between uncharacteristic and characteristic findings in the elderly and younger patients, respectively.

| Table 2. Yield of early diagnosis in pulmonary tuberculosis by age groups and by roentgenographic presentation |
|--------------------------|------------------|------------------|--------|
| Uncharacteristic findings| Elderly patients | Younger patients |       |
| Sputum                   | 15/37 (41)       | 10/44 (23)       |       |
| Other specimen           | 13/37 (35)       | 2/44 (48)        |       |
| Total                    | 28/37 (76)       | 3/44 (70)        |       |
| Characteristic findings  |                   |                  |       |
| Sputum                   | 45/76 (59)       | 67/94 (71)       |       |
| Other specimen           | 16/76 (21)       | 11/94 (12)       |       |
| Total                    | 61/76 (80)       | 78/94 (83)       |       |

Numbers between brackets represent percentage.
59% of the elderly and in 71% of the younger age group; yet this difference was not statistically significant. The yield of diagnosing PTB by sputum examination could be increased by examining other specimens and this additional yield was more pronounced in the elderly patients (+21%) than in the younger patients (+12%).

**DISCUSSION**

In this study we evaluated the impact of age and radiographic presentation on possible delay in diagnosing PTB. We defined the SI as the period between the first complaints (as mentioned by the patient) and the first moment of suspecting TB by the attending physician. We defined the RI as the time elapsed from the moment of considering TB and the presumptive diagnosis of TB. The sum of SI and RI can be considered as the diagnosing interval. For both age groups, there was no difference between SI and RI and RI was significantly longer in patients with uncharacteristic radiographic findings. The yield of obtaining an early diagnosis of PTB is high and this yield is neither influenced by age, nor by the initial radiographic presentation. Finally, in patients presenting with characteristic radiographic findings, a diagnosis was mainly obtained from examination of the sputum, whereas in patients with uncharacteristic findings, specimens other than sputum contributed also substantially to the diagnosis.

We did not find any difference in SI and RI between our elderly and younger population, although the SI tended to be longer in the elderly and the RI to be longer in the younger group. In the literature, data on this issue are scarce and especially, there is no uniformity in the used terminology. The intervals described in the studies by Asch et al. (10) and by Rocha et al. (11) are comparable with our SI and are otherwise the same in terms of duration. We assume that differences in intervals between studies (5,12–14) can be attributed in part to non-uniformity in terminology and differences in setting: in a university hospital, more invasive confirmatory investigations are probably instituted relatively faster than they would in a district general hospital, especially in the elderly population. Therefore we think that the distinction we made between SI and RI is a plausible and operational one, since two different problems are covered. The SI is mainly determined by the patient and it fits the notion ‘patients delay’, whereas the RI is mainly determined by the accuracy of demonstrating *M. tuberculosis*. The RI is likely to be different from the notion ‘doctors delay’ which includes both the consideration of TB and the consequent search for *M. tuberculosis*. Considering TB is often postponed because of an uncharacteristic clinico-radiological presentation; demonstration of *M. tuberculosis* is influenced by practical problems in obtaining adequate material for investigation. We observed a positive staining for AFB of sputum in half of the younger and elderly patients and those findings are in-between the results of other investigators (13–17). The yield of sputum positivity depends partially on the radiological appearance and is found to be higher in cavitary disease (7,16). We detected positive sputum smears in 66% of our patients with characteristic findings (mostly upper lobe disease) but in only 31% of the patients with uncharacteristic findings, similar to other studies (17,18). In our patients with characteristic findings, cavitary disease was found in 71% of the elderly and in 81% of the younger patients (P=NS). It is not surprising that the yield of positive sputum is higher in cavitary disease if we consider that approximately 10⁴ bacilli/ml are needed for positive staining and that in cavitary disease almost 10⁹ bacilli can be present whereas only half of this number is found in non-cavitary lesions.

The rather low yield of sputum examination (69%) could be increased to 79% after investigation of other specimens. We therefore advocate the use of investigation of additional pulmonary or other samples in patients suspected of PTB, especially in those with uncharacteristic radiographic findings.

Although it has been shown that the delay between the onset of symptoms and the diagnosis and/or initiation of adequate therapy is longer in elderly than in younger adults (5,11,14,18), we could not confirm this finding. Prolongation of the SI can be due to the patient who delays seeking help or to the doctor who did not include TB in the initial differential diagnosis. Especially in elderly patients, uncharacteristic clinico-radiographic findings can lead to a search for other diseases such as pulmonary cancer, other infectious or systemic diseases (9,19). In a patient suspected of having TB, prolongation of the RI should be avoided by prompt initiation of diagnostic procedures, even in the presence of negative sputum examination.

The yield of early diagnosing TB from sputum was higher in younger patients with characteristic radiological findings and this probably reflects the fact that failing to obtain adequate sputum is more pronounced in elderly patients. This could be attributed to their inability to produce sputum (due to weakness or to lack of cooperation) or to the ‘lower’ quality of the delivered sputum, ie, more saliva secretion than pulmonary secretion.

In conclusion, there is no difference in SI and RI between elderly and younger patients, yet the RI is longer in both age groups when presenting with uncharacteristic findings. A presumptive diagnosis can be obtained in a large number of both age groups by sputum examination, which is still the preferred method especially in patients with characteristic radiological findings. In patients with uncharacteristic findings, the diagnosis was made more substantially by the additional investigation of specimens other than sputum. In order to obtain a diagnosis and subsequently to avoid the postponement of adequate delay.
therapy, more invasive exploration is warranted, even in the elderly.

REFERENCES