Chapter 13. Atherosclerosis in relation to tuberculosis and chronic lung disease

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The relation between atherosclerosis and tuberculosis and other chronic lung diseases was studied in extensive autopsy material. Aortic atherosclerosis in subjects with such conditions was generally similar in extent to that in the standardized atherosclerosis group and more extensive than that in the low atherosclerosis group, while coronary atherosclerosis was less extensive than in the standardized average group and, especially in women, approximated to that in the low atherosclerosis group. The prevalence of coronary stenosis and myocardial lesions was very low in subjects with tuberculosis and other chronic lung diseases. The presence of such diseases seemed to increase the development of atherosclerosis in the thoracic part of the aorta in relation to the abdominal part.

Tuberculosis is one of the diseases that has been thought to be associated with a low degree of atherosclerosis or retarded development of the condition (1, 2, 5). However, this opinion, based mainly on old studies, was not supported by data from the International Atherosclerosis Project study (4) and because of these discrepancies another study of this problem seemed justifiable. It was also thought worth while to study the question of whether tuberculosis and other chronic lung diseases, by, for instance, impairing blood and lymphatic circulation in the mediastinum, have a selective influence on the development of atherosclerosis in the thoracic aorta as compared with the abdominal aorta. Deaths from coronary thrombosis (but not from other forms of coronary heart disease) have been said to decrease with increasing respiratory disability (3). The availability of extensive autopsy material collected from five European towns made it possible to study all these problems with better controls.

MATERIAL AND METHODS

The thoracic and abdominal aorta and the three main coronary arteries were collected from about 17 500 subjects in five European towns according to the methods described in Chapter 1. The number of cases of tuberculosis of any kind was high in both men and women in the age range 30–89 and these subjects were used for a study of the prevalence of atherosclerotic lesions. The number of subjects in whom tuberculosis was considered as the principal disease was, however, much lower, especially outside the age range 40–79. A separate analysis was performed on subjects within this age range; their age, sex, and geographical distribution is shown in Table 40.

For the study of other chronic lung diseases two groups were used, one in which chronic lung disease was recorded as the principal disease and another in which it was not (subjects with cor pulmonale were assigned to this group). Table 41 shows the age and sex distribution of these two groups, but not their geographical distribution, because of the small numbers involved.

Subjects with tuberculosis or other chronic lung diseases were compared for prevalence of atherosclerosis with the low atherosclerosis group (exclusive of subjects with tuberculosis) and for extent of atherosclerosis also with the standardized average and high atherosclerosis groups.

RESULTS

Tuberculosis

Tuberculosis, whether or not the principal disease, was recorded much more frequently in older than in younger age groups. Less than 5% of all males above age 10 in whom tuberculosis was revealed were below 40 years of age; the corresponding figure for women was 3%. In Malmö and Prague, where a more detailed record form was used (see Chapter 1), in only about 10% of all cases of tuberculosis was it considered to be the principal disease.
Table 41. Number of subjects with pneumosclerosis as the principal disease and with cor pulmonale, by age and sex

<table>
<thead>
<tr>
<th>Age group</th>
<th>Pneumosclerosis, principal</th>
<th>Pneumosclerosis + cor pulmonale</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>40–49</td>
<td>12</td>
<td>1.9</td>
</tr>
<tr>
<td>50–59</td>
<td>20</td>
<td>1.2</td>
</tr>
<tr>
<td>60–69</td>
<td>25</td>
<td>0.9</td>
</tr>
<tr>
<td>70–79</td>
<td>21</td>
<td>1.1</td>
</tr>
<tr>
<td>40–79</td>
<td>78</td>
<td>1.2</td>
</tr>
</tbody>
</table>

The percentage denotes frequency in relation to number of non-violent deaths.

Tuberculosis as the principal disease also tended to be more frequent in the higher age groups. In the combined material from all five towns about 15% of both men and women who died of tuberculosis were below 40. The frequency varied considerably among towns, however. In Malmö, Prague, and Tallin less than 10% of the men who died of tuberculosis were below age 40, and the same frequency was found for women in Tallin, while in Malmö and Prague no woman below 40 died of tuberculosis. In contrast, the proportion of people who died of tuberculosis below age 40, especially women, was much higher in both Ryazan and Yalta (which is a resort for tuberculosis patients).

Other chronic lung diseases were most often reported from Prague and Yalta in both men and women, with or without cor pulmonale.

Prevalence

Compared with the low atherosclerosis group (excluding tuberculosis) the tuberculosis subjects, both men and women, had a higher prevalence of complicated and calcified aortic lesions, while the difference in the prevalence of raised lesions was small. Correspondingly, subjects with mild atherosclerosis (fatty streak only or fatty streak with fibrous plaque only) were more prevalent in the low atherosclerosis group. The same pattern was found for the coronary arteries, where the prevalence of stenosis was also considerably higher in subjects, especially men, with tuberculosis than in the low atherosclerosis group. The differences were statistically significant for aortic complicated and calcified
lesions in men and sometimes, but less frequently, for such lesions in the coronary arteries also.

The results of analyses using only subjects in whom tuberculosis was the principal disease were similar but the differences were mostly reduced and less frequently significant.

**Extent**

For studies of the extent of atherosclerosis both the age-grouped (by decade) material and the pooled material (age range 40–79) were used. Subjects with tuberculosis in all decades had more extensive aortic and coronary lesions of all kinds (except fatty streak) than the low atherosclerosis group. These differences were always highly significant in men; in women, however, they were significant only in the case of fibrous plaque and raised aortic lesions. When only subjects with tuberculosis as the principal disease were studied, the differences remained in men and were also mostly significant, while in women they were not significant in any single decade.

In the pooled age group the extent of raised aortic lesions in men was intermediate between that for the standardized average and high atherosclerosis groups (and significantly different from both); in women it was the same as in the standardized average group. Aortic calcified lesions were extensive in both men and women and did not differ significantly from those in either the standardized average or low atherosclerosis groups. When only subjects with tuberculosis as the principal disease were studied, the extent of aortic raised lesions was the same as in the standardized average group in men and somewhat lower, but not significantly so, in women. Aortic calcified lesions remained relatively extensive in both sexes.

The pattern of coronary atherosclerosis was similar to that in the aorta for all tuberculosis subjects in the decade-grouped material; in the pooled group (age range 40–79), however, men with tuberculosis had significantly less extensive raised lesions than the standardized average atherosclerosis group, while women had lesions of similar extent to those in that group. No differences were found for the extent of coronary calcified lesions. When only subjects with tuberculosis as the principal disease were studied, almost all differences disappeared and the extent of coronary lesions was similar to that in the low atherosclerosis group except for calcified lesions in men, which were significantly more extensive among those with tuberculosis.

Coronary stenosis and myocardial lesions did not differ in frequency in the pooled subjects with tuberculosis from those in men and women in the standardized average atherosclerosis group but occurred more frequently than in the low atherosclerosis group. In subjects with tuberculosis as the principal disease, the prevalence of these lesions was similar to the prevalence in the low atherosclerosis group but was significantly lower than in the standardized average atherosclerosis group. In both men and women, the prevalence of fresh and old myocardial infarction was significantly lower than in the standardized average group, irrespective of whether tuberculosis was the principal cause of death. No subject with tuberculosis as the principal cause of death had a fresh myocardial infarction.

**Differences between aortic segments**

The development of atherosclerosis in the thoracic and the abdominal part of the aorta was studied separately in subjects with tuberculosis, irrespective of whether it was recorded as the primary disease or not. They were compared with the low atherosclerosis group (exclusive of subjects with tuberculosis). Comparison of the different types of lesion in the thoracic and abdominal aorta showed that they were always more extensive in the thoracic aorta, the only exceptions being calcified lesions in men and complicated lesions in women. Thus there was a relative increase in thoracic as compared with abdominal aortic atherosclerosis. A similar comparison of the three coronary arteries revealed no constant pattern. When only subjects with tuberculosis as the principal disease were studied, a similar trend was found, but calcified lesions in both men and women seemed to be more extensive in the abdominal than in the thoracic aorta.

**Chronic lung disease and cor pulmonale**

**Prevalence**

The relation between atherosclerosis and chronic lung disease other than tuberculosis was studied in the same way as described above for tuberculosis. Men between 40 and 69 and women between 50 and 69 in the chronic lung disease group had a higher prevalence of abdominal aortic complicated and calcified lesions than men in the low atherosclerosis group (in women this was partly true of raised lesions also in some age groups), while in the eighth decade prevalence was higher in the low atherosclerosis group. This finding indicates that milder forms of atherosclerosis were more common in the low
atherosclerosis group in the earlier ages. No differences were found in the prevalence of coronary lesions. Men in the chronic lung disease group had a lower prevalence of coronary stenosis than the corresponding low atherosclerosis group; in women the rates were the same in both groups. Thus, subjects with chronic lung disease generally showed a prevalence of coronary atherosclerosis that was as low as or lower than that for the corresponding low atherosclerosis group.

Extent

The extent of atherosclerosis was studied both in age-grouped material by decade and in the pooled 40–79-year age group and was compared with the extent in the three atherosclerosis reference groups. Subjects with chronic lung disease as the principal disease were found to have more extensive atherosclerosis, especially raised lesions, in the average aorta than the low atherosclerosis group. The differences in the age decades were often significant. The differences in women, however, were slight and showed no constant pattern. The findings for coronary atherosclerosis corroborated the prevalence analysis: subjects with chronic lung disease tended to have less extensive lesions than the corresponding low atherosclerosis group, the differences being mostly insignificant. In women, however, atherosclerosis was often far less extensive than in the low atherosclerosis group.

In the pooled 40–79-year age group two subgroups were studied, one with chronic lung disease as the principal disease and one with cor pulmonale, whether or not the lung disease was indicated. The extent of raised and calcified lesions in the average aorta and average coronary artery, and also the prevalence of coronary stenosis and myocardial lesions, were similar in these two groups. Aortic atherosclerosis in men did not differ significantly in extent from that in the standardized average atherosclerosis group, and in women it was lower. The extent of coronary raised lesions in both men and women with only chronic lung disease was similar to that in the standardized average group; in the cor pulmonale group, however, the extent was significantly lower than that in the standardized average group. Calcified lesions in the aorta and the coronary arteries did not show any definite pattern. The prevalence of coronary stenosis and myocardial lesions was in both groups lower in both men and women than in the standardized average group and the differences were often significant. No men in either of the disease groups had a fresh myocardial infarction.

The possible influence of chronic lung disease on the development of atherosclerosis in the thoracic and abdominal aorta was studied in subjects where chronic lung disease was the principal disease. The total amount of atherosclerosis, fatty streak, fibrous plaque, and raised lesions was generally higher in the thoracic than in the abdominal aorta, while complicated and calcified lesions showed no definite trend. The results are, however, uncertain and difficult to interpret since the number of cases was rather small.

DISCUSSION

The frequency of tuberculosis as the principal disease in relation to the number of deaths from natural causes varied considerably among the towns. Malmö had the lowest frequency for both men and women, the towns of USSR had the highest for men, and Prague the highest for women. Since the figures are based on a high proportion of all deaths in the towns (except for ages above 70 in USSR), they probably reflect the true pattern. Comparisons for the subjects with chronic lung disease are less reliable, but Yalta had the highest frequency for both men and women, followed by Prague, and Malmö had the lowest. For all towns combined, the frequency of chronic lung disease as the principal disease was the same in men and women, whereas cor pulmonale was more frequent in men than in women.

Atherosclerosis in subjects with tuberculosis as the principal disease was of similar extent in the case of aortic but less extensive in the case of coronary atherosclerosis than in the standardized average atherosclerosis group, in both men and women. The extent of calcified lesions was rather high in the aorta and coronary arteries in both sexes. The frequency of coronary stenosis occupied an intermediate position between the frequencies in the low and standardized average atherosclerosis groups in men but was the same as in the low atherosclerosis group in women. This finding corresponded well to the very low frequency of myocardial lesions in both sexes; fresh infarction was not found in a single case and large scars were found only rarely, especially in women.

Most previous studies on the relation between tuberculosis and atherosclerosis have shown less atherosclerosis in tuberculosis subjects. The International Atherosclerosis Project study did not, how-
ever, show any such negative association; results varied among the different places but there was no consistent trend. The relation between tuberculosis and atherosclerosis in this study was similar to that found between malignant diseases and atherosclerosis. Wasting in subjects with tuberculosis may thus be one explanation of the generally low extent of coronary atherosclerosis. The data do not support the view that the presence of tuberculosis means a general decrease in the amount of atherosclerosis. The data do not support the view that the presence of tuberculosis means a general decrease in the amount of atherosclerosis.

Subjects with chronic lung disease showed a similar pattern to those with tuberculosis, i.e., aortic atherosclerosis was similar in extent to that in the standardized average atherosclerosis group while coronary atherosclerosis was generally less extensive than in this group. No comparable studies were

found in the literature. There have, however, been discussions about the possible negative relation between chronic pulmonary diseases and myocardial lesions. This study, in which there was a very low prevalence of coronary stenosis and fresh and old myocardial lesions in people dying from chronic lung disease supports the view that ischaemic heart disease is a rare finding in this condition.

A separate analysis of the development of atherosclerosis in the thoracic and abdominal aorta in subjects with various kinds of chronic lung disease showed that the development in the thoracic aorta is somewhat increased in comparison with the abdominal aorta. This feature may be the result of impairment of the blood or lymphatic circulation in the vicinity of the thoracic aorta in such subjects.

RÉSUMÉ

CHAPITRE 13. RAPPORTS DE L'ATHÉROSCLÉOSE AVEC LA TUBERCULOSE ET LES PNEUMOPATHIES CHRONIQUES

Les rapports entre l'athérosclérose d'une part, la tuberculose et diverses pneumopathies chroniques de l'autre, ont été étudiés sur un vaste matériel d'autopsie. L'athérosclérose aortique chez de tels malades est en général analogue en importance à celle que l'on rencontre dans le groupe normalisé d'athérosclérose et beaucoup plus étendue que dans le groupe à degré d'athérosclérose faible, tandis que l'athérosclérose coronarienne est moins étendue que dans le groupe normalisé moyen et, notamment chez les femmes, elle est voisine de celle du groupe à degré d'athérosclérose faible. La prévalence des sténoses coronariennes et des lésions myocardiques est très basse chez les sujets atteints de tuberculose ou d'autres pneumopathies chroniques. La présence de ces maladies semble augmenter le développement de l'athérosclérose dans la portion thoracique de l'aorte par rapport à la portion abdominale.

REFERENCES