Cerebral Atherosclerosis in European Populations: A Preliminary Report

BY A. B. BAKER, M.D., J. A. RESCH, M.D., AND RUTH B. LOEWENSON, Ph.D.

Abstract: Cerebral Atherosclerosis in European Populations: A Preliminary Report

Atherosclerosis in the arteries of the circle of Willis was studied in European populations using a coding technique developed by Baker and his associates. Results from six countries (Finland, Germany, Greece, Norway, Italy, and Poland) were compared with results from Minnesota. The material from the first four countries was coded by the Minnesota team, whereas the material from Italy and Poland was coded by their respective investigators. The frequency of cerebral atherosclerosis was highest in the German and Finnish populations and was lowest in the Polish population. The Norwegian, Greek and Italian populations showed frequencies of cerebral atherosclerosis quite similar to those in the Minnesota material. The average amount of cerebral atherosclerosis was established by determining the median vessel scores by ten-year age groups for the material coded by the Minnesota team. The Finnish population had the highest average involvement; the Finnish, German, and Greek populations all showed higher average vessel scores for cerebral atherosclerosis than the Minnesota population.

Degenerative arterial disease is one of the most important health problems in our country today. Surveys based mainly on clinical diagnosis and vital statistics have indicated that in its various manifestations it now ranks first among the causes of death in the United States. It may have a vastly lower incidence among certain other peoples of the world, particularly the Africans1-3 and in some of the population groups of Italy, Spain, and Greenland.4, 5

Many of the current concepts regarding human atherosclerosis stem from epidemiological studies and from consideration of geographic differences in mortality from coronary disease. These studies have suggested that factors such as climate, geographic location, economic status and social stratum, as well as genetic factors, may exert an influence on the unknown agents active in the atherosclerotic process.

When clinical data are used for such studies, the question of the accuracy of death certificates and hospital diagnoses must be kept in mind. When one considers the many possibilities for error in a comparative study based on the foregoing, it would appear that statistics on the prevalence of atherosclerosis might better be based on autopsy material. Evaluation of the prevalence of atherosclerosis in a population studied by the use of autopsy material is less fraught with variables of judgment than is a purely clinical appraisal. It is significant that many of the reports based upon pathological findings of atherosclerosis indicate that the differences among race and population groups are somewhat less pronounced than those suggested by clinical surveys alone. Undoubtedly some of the sources of error in clinical studies also influence necropsy statistics so that reviews and comparisons of autopsy data from different countries are not necessarily comparable. Pathologists in many lands differ almost as much as do the clinicians in the evaluations of their material; this is particularly true of the quantitative estimates of the severity of the disease. The many systems of grading atherosclerosis which have been used and subsequently reported in the literature make objective comparison difficult. Errors can be minimized only when one observer examines the pathological specimens without reference to their country of origin, race, age, sex, or other clinical data. Despite the acknowledged selectivity of autopsy populations6-8 the authors believe that much significant information can be obtained from autopsy material.

The circle of Willis was considered to be an appropriate area for the study of cerebral atherosclerosis. This structure is easily approached, can be

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readily removed and preserved, and is the primary focus of atherosclerosis of the brain.

A system of coding, to be truly useful for a comparative study, should meet a number of criteria as follows:

1. It should be simple enough so that the coding can be completed within minutes and without delaying the general autopsy. This enables a large series of cases to be studied in a relatively short period of time.

2. The different grades of involvement must be well defined so that the coding can readily be duplicated by different investigators.

3. Enough areas should be coded to give an adequate indication of both the degree and extent of the atherosclerotic involvement of the entire circle of Willis.

4. Areas of the circle of Willis to be coded must be clearly defined so that identical areas can be coded in each case.

5. Finally, the coding system must indicate involvement not only of the vessel wall, but also of the vessel lumen.

The coding technique developed and reported by Baker et al.9 meets these criteria and was used in the present study. An investigator using this coding system carefully inspects the circle of Willis. If necessary, a hand lens is used for closer observation. The involved area of the vessel is sectioned to determine the extent of the lumen narrowing. An existing atherosclerotic process is then graded from 1 to 4 as follows:

Grade 1: Opacity involving only a small part of the vessel wall. No lumen narrowing.

Grade 2: (A) A diffuse, thin plaque that does not involve the entire vessel circumference with minimal lumen narrowing. (B) A small, thick plaque that produces less than 25% lumen narrowing.

Grade 3: (A) A diffuse, thin plaque involving the entire vessel circumference with mild lumen narrowing. (B) A localized, thick plaque producing 25% to 50% lumen narrowing.

Grade 4: (A) A thick plaque involving the entire vessel circumference with moderate or marked lumen narrowing. (B) A localized plaque resulting in more than 50% lumen narrowing.

In order to determine the extent of the atherosclerotic process, the entire circle of Willis was divided into 22 clearly defined areas9 and each of these areas was graded from 0 to 4 according to the system outlined above. The total numerical value for the degree of the atherosclerotic process can be obtained by adding the scores of all the graded areas. Thus, since there are 22 areas coded and the most severe change is 4, the greatest degree of atherosclerosis possible using this coding system is 88 points.

Reliability studies on the scoring method were conducted earlier and led to the conclusion that coding should be carried out by a single team of investigators at the University of Minnesota.10 All specimens from the European countries were fixed in formalin and shipped to the University of Minnesota where they were coded without knowledge of the source, age, and sex of the autopsy case.

The material in the Minnesota series came from routine autopsies performed at the University of Minnesota Hospitals and at the Hennepin County General Hospital (Minneapolis, Minnesota). The autopsy rates for these two hospitals were 84% and 70%, respectively, for the year in which the material was obtained. To date, 3,942 cases more than 19 years of age have been coded. Using the Minnesota data as basis for comparison, we have been engaged during the past decade in a geographic study of cerebral atherosclerosis in an attempt to determine differences among population groups. Enough cases have been obtained and coded from a number of European countries to justify a preliminary report. In three of the European countries (Finland, Germany, and Greece) the coding was carried out by the Minnesota team. The Polish and Italian investigators used the Minnesota coding technique but carried out their own studies. The Norwegian study was actually the first one instituted. However, it was carried out by the Minnesota team before the present technique was slightly modified. For the above reasons, the observations on the Polish, Italian, and Norwegian populations have been analyzed separately.

Median vessel scores for each ten-year age group were used as a measure of the average amount of cerebral atherosclerosis. Furthermore, the percent of cases with cerebral atherosclerosis, regardless of amount, was used to indicate the prevalence of the process. Median vessel scores were not determined for any age group in which sample size was less than 20.

<table>
<thead>
<tr>
<th>Age</th>
<th>Germany</th>
<th>Finland</th>
<th>Greece</th>
<th>Minnesota</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–29</td>
<td>10</td>
<td>11</td>
<td>23</td>
<td>260</td>
</tr>
<tr>
<td>30–39</td>
<td>17</td>
<td>17</td>
<td>19</td>
<td>323</td>
</tr>
<tr>
<td>40–49</td>
<td>35</td>
<td>38</td>
<td>35</td>
<td>596</td>
</tr>
<tr>
<td>50–59</td>
<td>67</td>
<td>80</td>
<td>59</td>
<td>846</td>
</tr>
<tr>
<td>60–69</td>
<td>150</td>
<td>134</td>
<td>83</td>
<td>872</td>
</tr>
<tr>
<td>70–79</td>
<td>139</td>
<td>143</td>
<td>35</td>
<td>753</td>
</tr>
<tr>
<td>80+</td>
<td>76</td>
<td>77</td>
<td>11</td>
<td>292</td>
</tr>
<tr>
<td>Total</td>
<td>494</td>
<td>500</td>
<td>265</td>
<td>3,942</td>
</tr>
</tbody>
</table>

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Pezold studied the extent of coronary atherosclerosis in 3,462 autopsies carried out in Berlin. By the fourth decade, 47% of the cases showed sclerotic changes, and at ages 60 to 69, 75% had changes. No similar studies are available on cerebral atherosclerosis. In our studies, 494 cases (table 1) were available for coding. In the age group 20 to 29, 30% showed atherosclerotic changes in the cerebral arteries (fig. 1). The frequency of cerebral atherosclerosis increased very rapidly so that by age 65, 97% of the population had some degree of cerebral atherosclerosis (fig. 1). The average severity of cerebral atherosclerosis was considerably greater, decade by decade, than that observed in the Minnesota population (fig. 2). At age 65 years the German group had, on the average, 22 points of atherosclerosis as compared to 11 for the Minnesota population (fig. 2).
FINLAND

In age-adjusted death rates for both arteriosclerotic heart disease and for vascular lesions affecting the nervous system (table 2), Finland has ranked the highest of any country in Europe from which data could be obtained. This also appeared to be the case in our studies on cerebral atherosclerosis. We had available to us 500 cases (table 1). Cerebral atherosclerosis first appeared in the age group 30 to 39 and increased rapidly so that at age 65 years, 96% of the population was involved (fig. 1). The frequency of cerebral atherosclerosis was very similar in the German and Finnish populations (fig. 1). Likewise, there was little difference in the severity of cerebral atherosclerosis between the Finnish and the German populations (fig. 3). When compared to the Minnesota population, the increased severity of cerebral atherosclerosis in the Finnish and German populations was quite marked. At age 65 years the average severity score for the Minnesota population was only 11 as compared to 23.5 for the Finnish population (fig. 4).

GREECE

When one considers the age-adjusted death rates from vascular disease affecting the central nervous system, Greece ranks very low when compared to other European countries (table 2). Only 265 cases were available for coding (table 1). The frequency of cerebral atherosclerosis was almost identical to that found in the Minnesota population and considerably less than in the Finnish and German material (fig. 1). In severity, cerebral atherosclerosis in Greece is greater than in the Minnesota population (fig. 5), but considerably less than in the Finnish and German groups (fig. 3).

NORWAY

The frequency and severity of atherosclerosis in the aorta, coronary, and cerebral arteries were studied by Baker and his associates in 579 cases. Cerebral atherosclerosis in the Norwegian population increased from 36% in the fourth decade (fig. 6) to 93% in the seventh decade. When compared to the Minnesota population, there was very little difference in the frequency of cerebral atherosclerosis after the sixth decade of life.

TABLE 2

<table>
<thead>
<tr>
<th>Country</th>
<th>Age-adjusted death rates* per 100,000 population† (both sexes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finland</td>
<td>169</td>
</tr>
<tr>
<td>Italy</td>
<td>138</td>
</tr>
<tr>
<td>West Berlin</td>
<td>132</td>
</tr>
<tr>
<td>Norway</td>
<td>130</td>
</tr>
<tr>
<td>Greece</td>
<td>108</td>
</tr>
<tr>
<td>Poland</td>
<td>43</td>
</tr>
<tr>
<td>United States</td>
<td>110</td>
</tr>
</tbody>
</table>

*Age-adjusted by the direct method using U.S. 1970 population as standard.

FIGURE 3

Median vessel scores, Germany, Finland, Greece, and Minnesota.

FIGURE 4

Median vessel scores, Finland versus Minnesota.
Poland

Poland has the lowest age-adjusted death rate from vascular lesions affecting the central nervous system (table 2). The Polish investigators \(^{15,16}\) studied the degree of cerebral atherosclerosis in 600 consecutive cases using the coding technique described by Baker et al. At age 65 years, 80% of the population showed atherosclerosis. This compares to a frequency of 88% for Minnesota, 93% for Norway, and 96% and 97% for Finland and Germany, respectively (figs. 1 and 6). This frequency of cerebral atherosclerosis was, together with that of Greece (82%), the lowest of any European country reported to date.

Italy

The atherosclerotic changes within the cerebral vessels were studied by Stramignoni \(^{17}\) using the coding system of Baker et al. He studied the changes within cerebral arteries in 186 cases in northern Italy. The data in his article furnish information only from ages 0 to 30 years and 41 to 60 years. A comparison of his results with those of other investigators is somewhat uncertain because of the limitation in age groups and small number of cases used. It would appear from the material available that the frequency of cerebral atherosclerosis in Italy is quite similar to that observed in the Minnesota population (fig. 6).

Summary and Conclusions

1. A simple macroscopic coding technique for the arteries of the circle of Willis is presented. To date, 3,942 cases more than 19 years of age in a Minnesota population have been coded by a single coding team and median vessel scores for ten-year age groups were established. This Minnesota curve allows a graphical comparison with similar median vessel scores obtained from different population groups in Europe.

2. It is believed that an evaluation of the prevalence of cerebral atherosclerosis in a population by a study of autopsy material is less fraught with extraneous variables than is a purely clinical appraisal and has the advantage that nonsymptomatic cases can be considered in the final conclusion.

3. Six European countries were included in this report, namely, Finland, Germany, Greece, Norway, Italy, and Poland. The material from the first four were coded by the Minnesota team whereas the material from Italy and Poland was coded by their respective investigators using the coding technique of Baker et al. In each country the results obtained were compared to those observed in the Minnesota population.

4. The greatest frequency of cerebral atherosclerosis occurred within the German and Finnish populations. Both these countries had considerably more involvement than that observed in the Minnesota material.

5. The Norwegian, Greek, and Italian populations showed about the same frequency of cerebral atherosclerosis as the Minnesota population, but considerably less than the German and Finnish cases.

6. The least involvement occurred in the Polish cases.
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7. The average amount of cerebral atherosclerosis was established by determining the median vessel scores by ten-year age groups. By this analysis, it appeared that the Finnish population had the highest average amount of cerebral atherosclerosis.

8. Finland, Germany, and Greece had higher average cerebral atherosclerosis scores than did the Minnesota population.

Acknowledgments
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