Body Weight, Cerebral Atherosclerosis and Cerebral Vascular Disease: An Autopsy Study

BY A. C. KLASSEN, M.D., R. B. LOEWENSON, Ph.D., AND J. A. RESCH, M.D.

Abstract:

The severity of atherosclerotic involvement of intracranial cerebral arteries was assessed at autopsy in 3,315 adult subjects. Ponderal index values were calculated for each sex and ten-year age group. In most age groups, subjects with cerebral vascular disease, or one or more of several conditions known to be associated with increased cerebral atherosclerosis, had higher relative body weight than did subjects without those conditions. Subjects in the lower quartile of ponderal index distribution ("overweight" group) had more severe cerebral atherosclerosis than did subjects in the upper quartile ("underweight" group). However, when subjects with disease conditions known to be associated with increased cerebral atherosclerosis were excluded from the analysis, no relationship between relative body weight and severity of cerebral atherosclerosis could be demonstrated. Clinical and/or pathological evidence of cerebral vascular disease was apparently present more often in "overweight" than in "underweight" subjects, at least in certain age groups.

Additional Key Words

overweight stroke underweight ponderal index

Introduction

Numerous studies, especially those based on life insurance data, have demonstrated an association between excessive body weight or obesity and increased mortality rates. Excessive adiposity or relative obesity also has been demonstrated to be associated with hypertension, impaired glucose tolerance, and elevated serum lipid values. Therefore, it might be expected that relative obesity would be associated, in turn, with increased mortality and morbidity due to ischemic cardiac disease and cerebral vascular disease. Such associations, especially between obesity and cerebral vascular disease, as yet have not been clearly established. The present study examines the relationship between terminal body weight and the degree or severity of cerebral atherosclerosis in an autopsy population. The possibility of a relationship between body weight and the prevalence of cerebral vascular disease in the same population also is explored. The study is based on the assumption that atherosclerosis of cerebral arteries is probably etiologically related to the subsequent development of clinical and/or pathological evidence of cerebral vascular disease.

Methods

The intracranial cerebral arteries utilized in this study were obtained from subjects undergoing consecutive routine autopsies at the University of Minnesota Hospitals and Hennepin County General Hospital (Minneapolis, Minnesota) during the years 1961 to 1965. The clinical and pathological data were obtained by retrospective review of the hospital records and pathological reports. Of a total of 3,942 subjects over 19 years of age, information regarding body weight and height was available in 3,315 and, hence, only the latter were included in this study. Body weight and height measurements were obtained from the hospital clinical record using the last recorded height and weight during the terminal illness. When no "live" terminal measurements were available, the autopsy measurements were used. Table 1 lists the numbers of subjects by sex and ten-year age groups.

The ponderal index, or the ratio of height in inches to the cube root of the weight in pounds, was used as a measure of body weight relative to body height. A low ponderal index value thus corresponds to high relative body weight and a high ponderal index to a low body weight. For each sex and ten-year age group, the distributions of the ponderal index values were determined. The subjects in the lowest and highest quartiles of the ponderal index distributions were then designated as "overweight" and "underweight," respectively.

The semiquantitative scoring method for assessing the severity of atherosclerotic involvement of cerebral arteries has been previously described and validated. In brief, the method assigns a numerical grade of 0 to 4 related to the degree of luminal encroachment by atherosclerosis to each of 22 sites in the circle of Willis and its major branches. The sum of the grades for all 22 sites is utilized as the numerical...
BODY WEIGHT, CEREBRAL ATHEROSCLEROSIS AND CVD

TABLE 1
Numbers of Subjects by Age and Sex

<table>
<thead>
<tr>
<th>Age group</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–29</td>
<td>137</td>
<td>70</td>
</tr>
<tr>
<td>30–39</td>
<td>155</td>
<td>130</td>
</tr>
<tr>
<td>40–49</td>
<td>275</td>
<td>245</td>
</tr>
<tr>
<td>50–59</td>
<td>454</td>
<td>274</td>
</tr>
<tr>
<td>60–69</td>
<td>439</td>
<td>282</td>
</tr>
<tr>
<td>70–79</td>
<td>410</td>
<td>213</td>
</tr>
<tr>
<td>80+</td>
<td>155</td>
<td>76</td>
</tr>
<tr>
<td>Total</td>
<td>2,025</td>
<td>1,290</td>
</tr>
</tbody>
</table>

cerebral atherosclerosis vessel score for each subject. Vessel score distributions were obtained for each sex and in each ten-year age group.

Percentiles of ponderal index and vessel score distributions were utilized for purposes of this presentation. The 25th and 75th percentiles of the ponderal index distributions determined the lower and upper quartiles, that is, the "overweight" and "underweight" groups, respectively. For these two groups the median vessel scores were plotted at the appropriate midpoints of the ten-year age intervals to provide a graphical comparison of cerebral atherosclerotic involvement between "overweight" and "underweight" subjects.

Previous studies using this same autopsy population have demonstrated that certain clinical and pathological disease conditions are associated with increased severity of cerebral atherosclerosis. These conditions or disease states include cerebral vascular disease, atherosclerotic heart disease, diabetes mellitus, and hypertension. Because these disease states also may be associated with obesity, further data analysis regarding possible relationships between relative body weight and cerebral atherosclerosis was performed after exclusion of subjects with one or more of the above-mentioned conditions. Table 2 lists the sample sizes in each of the disease subgroups for subjects for whom clinical and pathological information as well as ponderal index values were available. Because of the high prevalence of these diseases, especially in the older age groups, the sample sizes for the remaining cases are quite small; age groups with sample sizes of less than ten subjects were omitted from the analysis.

Median values of ponderal index also were obtained for subjects with and without clinical or pathological evidence of cerebral vascular disease. Similarly, median values of ponderal index for subjects with one or more of cerebral vascular disease, atherosclerotic heart disease, diabetes mellitus, and hypertension were compared with those of subjects without these conditions.

Finally, the frequency of occurrence of cerebral vascular disease was determined in subjects in the "overweight" and "underweight" groups using the clinical records and brain autopsy reports.

Results
Ponderal index distributions, including the 25th, 50th (median), and 75th percentiles, for ten-year age groups are plotted in figure 1. In males, ponderal index remained relatively constant in all age groups. In females, a gradual tendency toward lower ponderal index, that is, increased relative weight, with increasing age was noted which continued until the eighth decade; in the oldest age group the relative weight was decreased.

Subjects in whom there was clinical or pathological evidence of cerebral vascular disease tended, in general, to have lower median ponderal index values than did subjects without cerebral vascular disease (fig. 2). In other words, relative body weight tended to be higher in subjects with cerebral vascular disease. These differences in median ponderal index values were most prominent in males 40 to 49 years of age and females 50 to 59 and 60 to 69 years of age. Groups below age 40 years were too small to be included in this comparison.

A similar comparison of median ponderal index values for groups of subjects with and without one or more of cerebral vascular disease, atherosclerotic heart disease, diabetes mellitus, and hypertension revealed an even more striking relationship between decreased ponderal index and the presence of one or more of these disease states (fig. 3). Thus, groups of

TABLE 2
Disease Subgroups Associated With Increased Cerebral Atherosclerosis

<table>
<thead>
<tr>
<th>Disease Subgroup</th>
<th>Males (n = 1,038)</th>
<th>Females (n = 1,290)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral vascular disease</td>
<td>334</td>
<td>179</td>
</tr>
<tr>
<td>Atherosclerotic heart disease</td>
<td>1,031</td>
<td>446</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>114</td>
<td>115</td>
</tr>
<tr>
<td>Hypertension</td>
<td>322</td>
<td>248</td>
</tr>
<tr>
<td>One or more of the above</td>
<td>1,227</td>
<td>612</td>
</tr>
</tbody>
</table>

Stroke, Vol. 5, May-June 1974
subjects with one or more of those conditions known to be associated with increased cerebral atherosclerosis demonstrated the presence of increased relative body weight in all age groups over 40.

Groups of subjects with ponderal index values in the lower and upper quartiles, respectively, were then compared by plotting median values of the cerebral atherosclerosis vessel scores obtained from these subjects (fig. 4). Males with low ponderal index, that is, the relatively "overweight" group, had more severe cerebral atherosclerosis in all age groups from the fourth through the eighth decades with median vessel scores being approximately equal in subjects 80 years of age and older. In females, a similar relationship between "overweight" subjects and higher vessel scores could not be as readily identified, but the severity of cerebral atherosclerosis in this group was apparently greater in the sixth and eighth decades.

Because of the previously demonstrated relationship between increased cerebral atherosclerosis and the presence of cerebral vascular disease, atherosclerotic heart disease, diabetes mellitus and hypertension, a similar comparison of vessel scores between subjects in the lower and upper quartiles of ponderal index distribution was made after exclusion of all subjects with these disease conditions (fig. 5). When these exclusions were made, no clear relationship between ponderal index and the severity of cerebral atherosclerosis could be demonstrated. In other words, it appeared that relative body weight by itself was not related to the degree or severity of atherosclerosis of cerebral arteries in this autopsy population. Irregularity of the curves resulting from joining mid-decade median vessel scores as seen in figure 5 is probably related to small sample sizes, especially in the oldest age groups.

A comparison of the prevalence of cerebral vascular disease in groups of subjects in the lower and upper ponderal index quartiles is made in table 3. These data suggest that cerebral vascular disease may have been present more frequently in "overweight" males in the 40-year to 79-year age groups and in "overweight" females aged 50 to 69 and over age 80. The removal of subjects with hypertension, atherosclerotic heart disease and diabetes mellitus from these groups left too few subjects to perform a similar comparison.

Discussion
The ponderal index is admittedly imperfect in its ability to accurately quantify degrees of "overweight"
and "underweight" for either individuals or groups. In the present study, however, the use of this index permitted identification of groups of subjects at both extremes of relative weights at varying ages. The use of quartiles also obviated the need to establish other criteria for normal, "underweight" and "overweight." The use of terminal body weights in such a study also presents problems in interpretation inasmuch as some patients may well have lost considerable weight during their final illness. The most likely effect of such weight loss would be that subjects who were "overweight" before their terminal illness were not considered "overweight" in this analysis. This would, in turn, tend to obscure some of the differences in severity of cerebral atherosclerosis between groups of subjects in the "overweight" and "underweight" categories.

Prior to the present study, there have been little pathological data available relating relative body weight with the degree of cerebral atherosclerosis or pathological and clinical evidence of cerebral vascular disease. Life insurance studies and prospective studies such as the Framingham study have demonstrated increased frequency of hypertension and coronary artery disease in "overweight" subjects. Other studies have suggested that the apparent relationship between obesity and cardiovascular disease was due to an increased incidence of hypertension and diabetes in the obese population. On the other hand, a relationship between obesity and coronary artery disease may be present independent of the presence of hypertension. Prospective clinical studies of ischemic and hemorrhagic cerebral vascular disease have been inconclusive as to the role of obesity as a "risk factor" in the subsequent development of stroke.

In the present study, groups of subjects with diseases or disorders associated with increased cerebral atherosclerosis tended to have lower median ponderal index values than did subjects without these conditions. This would tend to support the hypothesis that excessive body weight or obesity may, indeed, be a "risk factor" for the subsequent development of such conditions. This contention also is supported by the finding that the median cerebral atherosclerosis vessel scores tended to be higher in "overweight" subjects, especially in males. Furthermore, in many age groups, especially in males, clinical and/or pathological evidence of cerebral vascular disease appeared to be present more frequently in the relatively "overweight" subjects. On the other hand, when subjects with those conditions known to be associated with increased

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**Median vessel scores (50th percentiles) for subjects in the lower ("overweight") and upper ("underweight") quartiles of ponderal index distribution.**

**Median vessel scores (50th percentiles) for subjects in the lower and upper quartiles of ponderal index distribution excluding all subjects with one or more of cerebral vascular disease, atherosclerotic heart disease, diabetes mellitus and hypertension.**

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cerebral atherosclerosis were removed from the group comparisons of median vessel scores, no consistent relationships between body weight and severity of cerebral atherosclerosis could be demonstrated.

It is suggested, therefore, that excessive body weight or relative obesity as measured by the ponderal index is not, by itself, related to the severity of cerebral atherosclerosis. The data do not preclude the possibility that excessive body weight may be related to increased atherogenesis in which, however, the cerebral arteries do not participate to a degree detectable by the methods used in this study. It also is apparent that excessive body weight appears to be only one of a complex group of factors which may be related causally or casually to the development of atherosclerosis and vascular lesions of the nervous system. Those additional factors which, in the presence of hypertension and diabetes mellitus, appear to predispose some individuals to the development of atherosclerosis and its complications still require further elucidation.

References
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