Multivariate Prediction of the First Major Cerebrovascular Event in an Italian Population Sample of Middle-Aged Men Followed Up for 25 Years

Alessandro Menotti, MD, PhD; Mariapia Lanti, MD, PhD; Fulvia Seccareccia, DSc; Simona Giampaoli, MD; and Francesco Dima, BA

Background and Purpose: The present investigation was aimed at evaluating the incidence and prediction of a first major cerebrovascular (fatal or nonfatal) event.

Methods: The study population included the two Italian rural samples of the Seven Countries Study (namely, Montegiorgio and Crevalcore), accounting for a total of 1,712 men aged 40–59 years at entry and followed up for mortality and morbidity for 25 years. A number of individual variables measured at baseline, at the fifth year, and at the tenth year of follow-up and possibly related to cerebrovascular events were considered. Of the 1,709 subjects free from major cerebrovascular events at entry 171 developed a first major cerebrovascular event, but for the multivariate Cox model analysis only 1,572 subjects and 152 events were employed due to some exclusions for missing data.

Results: Systolic blood pressure, indexes of respiratory function (protective), and physical activity at work (protective) demonstrated significant predictive roles for all ages and all lengths of follow-up considered. Other factors (presence of arrhythmias, presence of arcus senilis, and skinfold thickness [protective]), significantly contributed to the prediction, but in only some models. Time-related changes in systolic blood pressure significantly improved the prediction of cerebrovascular events.

Conclusions: The multivariate prediction performed in this report allowed the validation of three risk factors (systolic blood pressure, respiratory function indexes, and physical activity at work) whose predictive powers remain stable with aging. The need for further studies specifically aimed at discriminating hemorrhagic from thrombotic events is suggested. (Stroke 1993;24:42–48)

KEY WORDS • epidemiology • incidence • Italy • risk factors

In the prediction of cerebrovascular events, a major role is played by systolic blood pressure, as confirmed in many published papers. However, the significance of other factors possibly related to these events is not always uniformly underlined and pointed out in the available literature.

In addition, when the follow-up becomes particularly long, some more specific questions can be asked, i.e., 1) whether single measurements of risk factors are predictive of events for different lengths of follow-up, 2) whether subsequent measurements of risk factors in aging cohorts are equally predictive, and 3) whether changes in risk factors over given periods of time contribute to the prediction of events in subsequent time periods.

In Italy, within the Seven Countries Study on Cardiovascular Diseases three cohorts of men aged 40–59 years were enrolled in 1960–1962, but only two cohorts (i.e., the rural ones) were monitored for both fatal and nonfatal cerebrovascular events during up to 25 years of follow-up (only mortality, after the tenth year, for the third cohort).

Little data on cerebrovascular incidence and mortality and on their prediction have been published elsewhere, but the three questions mentioned above were never tackled in a systematic way.

Subjects and Methods

The study population includes the pool of two rural samples enrolled and first examined in 1960. They were made of men aged 40–59 years and resident in defined geographical-administrative areas corresponding to the rural municipalities of Crevalcore in northern Italy and of Montegiorgio in central Italy. Within the enrolled samples 993 men were examined in Crevalcore and 719 in Montegiorgio, with participation rates of 98.5% and 99.0%, respectively (average, 98.8%). There were slight differences in the general characteristics of the two samples, but the possibility of pooling them has been shown several times in the past. Therefore, from now...
on we will deal with the lumped samples and a total of 1,712 men.

The entry examination was conducted by an international team of doctors, nurses, and technicians and included a number of questionnaires, tests, diagnostic procedures, and physical and chemical measurements following standard procedures described elsewhere. For the purpose of this analysis, men who had already suffered a cerebrovascular event at the time of examination at year 0, 5, or 10 were excluded from the analyses starting at each of those times, as were men with missing information about even one of the risk factors mentioned below.

A number of individual characteristics possibly related to the end point were employed in this analysis. The following techniques were used for measurement of the chosen variables. Age was expressed in years and rounded off at the nearest birthday. Cigarettes were expressed as the average number smoked per day derived from a questionnaire. Physical activity at work was scored by combining the result of a simple questionnaire with the declared work (1, sedentary work; 2, moderate work; and 3, heavy work). Body mass index was computed as weight in kilograms divided by squared height in meters. Laterality-linearity index was computed as the sum of the biacromial and bicipital diameters in centimeters divided by the height in centimeters multiplied by 100. Skinfold thickness was the sum of measurements in millimeters of two subcutaneous skinfold thicknesses (at the right triceps and subcapital sites) obtained using a Harpenden caliper. Arm circumference in centimeters was measured on the right arm at the measured midpoint between the tip of the acromion and the tip of the olecranon and deputed from triceps skinfold thickness. Presence of arcus senilis was as recognized during physical examination (yes, 1; no, 0). Presence of xanthelasms was as recognized during physical examination (yes, 1; no, 0). Diabetes was as derived from medical history (yes, 1; no, 0). Blood pressure, both systolic and diastolic, was expressed in millimeters of mercury and measured following a standard procedure in the supine position; for diastolic blood pressure the fifth phase of the Korotkoff sounds was considered, and both systolic and diastolic blood pressures were the mean of two measurements taken 1 minute apart (only systolic blood pressure was used for the analysis). Serum cholesterol was expressed in milligrams per deciliter as measured on casual blood samples following the technique of Abell Kendall as modified by Anderson and Keys. Arrhythmias were expressed as prevalence (percent) as described by any item 8 of the Minnesota Code. Vital capacity was expressed as deciliters of air per meter of height, obtained from a simple spirometric test. Forced expiratory volume in 1/4 second was expressed as deciliters of air per meter of height and derived from a spirometric test.

The same measurements obtained following the same techniques were made beyond year 0 and at years 5 and 10 of follow-up, when the participation rates among the survivors were 96.4% and 87.4%, respectively. Similar field examinations were also held at years 20 and 25 of follow-up, with participation rates among the survivors of 79.2% and 75.6%, respectively. However, the risk factor measurements taken at years 20 and 25 were not employed for this analysis and the examinations contributed only to the identification of part of the events.

Two different indicators were employed for defining risk factor changes, that is, the level at year 10 minus the level at year 0 and the time-factor integral of levels at years 0, 5, and 10 (DELT). The latter indicator of change corresponds to the mean level of the risk factor above or below the entry level to which men were exposed multiplied by the 10 years of exposure. Details of such a procedure were presented and have been employed elsewhere.

The end point of the analysis was the first fatal or nonfatal cerebrovascular event that occurred during defined periods in men originally free from such events. The events were identified by a complex monitoring system including 1) periodic field examinations carried out at years 5, 10, 20, and 25 of follow-up; 2) periodic information on deaths and their causes, obtained from the local register office; 3) periodic visits to local doctors and hospitals, with interviews and review of clinical records; and 4) interviews with patients and their relatives and with the relatives of dead persons. Such a complex and expensive system gave reasonable guarantees of completeness for coronary heart disease as well as for cerebrovascular disease. The same criteria were employed for defining the first major cerebrovascular event as well as for identifying those subjects who at the start of each follow-up period had to be excluded from the analysis. Following the above procedure there were no losses to follow-up.

The first major cerebrovascular event, either fatal (≤30 days after the onset of symptoms) or nonfatal, was defined as 1) history and objective evidence of clinical signs of local disturbance of cerebral function, either acute or chronic and lasting at least 24 hours, with no apparent cause other than a vascular origin, with paralysis, paresis, or aphasia or 2) history and evidence of global cerebral vascular insufficiency, lasting at least 24 hours. It was impossible to segregate atherothrombotic strokes from hemorrhagic ones due to limitations of the available clinical information, and therefore the two types of event were pooled under the definition of cerebrovascular events. In this analysis a few cases (15 of 171; only 11 in multivariate models) of a first major cerebrovascular event could be defined as being of a chronic type because no major symptoms or signs could be elicited except for a global and gradual decay of cerebral function ending with cerebral coma and death (see “Discussion”).

To identify factors related to the end point, the stepwise proportional hazards Cox model was used with a tolerance to enter of \( p=0.15 \), which was deliberately chosen to allow marginally predictive factors to be identified. Censored cases were made only by fatal noncerebrovascular events because there were no losses to follow up.

Results

During the 25 years of observation 171 men developed a first major cerebrovascular event from among the 1,709 who were free from this condition at the entry examination, giving an overall incidence rate of 10%, corresponding to an average of four per 1,000 per year. However, due to some missing values only 1,572 men with 152 events were used in the multivariate analyses.
Table 1 reports the mean levels of the covariates considered for the analysis as measured at years 0 (including and excluding men with events occurring during the first 10 years of follow-up), 5, and 10, showing their time trends. As expected, the mean levels of some characteristics (skinfold thickness, blood pressure, serum cholesterol, and arrhythmias) increased with age while the levels of some others (physical activity score, vital capacity, and forced expiratory volume) decreased.

Almost always the same set of risk factors was offered to the multivariate model, but different entry examinations and different periods of follow-up were considered and several solutions were generated. The different solutions yielded different denominators (men exposed to the risk of a first major cerebrovascular event) and numerators (events).

Solutions reported in Table 2 refer to factors measured at year 0 and to follow-ups of 25 (between years 0 and 25) and 15 (between years 10 and 25) years. Of the 15 covariates offered to the model, only nine were present in the final solution for the 25-year follow-up. Age, arcus senilis, diabetes, systolic blood pressure, serum cholesterol, and arrhythmias showed positive coefficients and odds ratios greater than 1, thus indicating a direct association with the event over the 25 years of follow-up. On the contrary, physical activity score, skinfold thickness, and vital capacity showed negative coefficients with odds ratios less than 1 and 95% confidence intervals not comprising 1.

The final solution obtained for a 15-year follow-up (from year 10 to year 25) still using measurements taken at year 0 (Table 2) demonstrates that almost all the

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**Table 1. Mean±SD Levels of Risk Factors Measured in Men Free From Cerebrovascular Events at Years 0, 5, and 10 and at Year 0 After Exclusion of Events Occurring During First 10 Years of Follow-Up**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Year</th>
<th>0 (n=1,572)</th>
<th>5 (n=1,317)</th>
<th>10 (n=986)</th>
<th>0 (n=1,378)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td>49.7±5.1</td>
<td>54.5±5.0</td>
<td>59.0±4.7</td>
<td>49.3±4.9</td>
</tr>
<tr>
<td>Cigarettes (no./day)</td>
<td></td>
<td>8.8±9.9</td>
<td>8.7±10.1</td>
<td>6.8±8.6</td>
<td>8.5±9.7</td>
</tr>
<tr>
<td>Physical activity score</td>
<td></td>
<td>2.6±0.6</td>
<td>2.5±0.7</td>
<td>2.2±0.8</td>
<td>2.6±0.6</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td></td>
<td>25.2±3.7</td>
<td>25.8±3.8</td>
<td>26.2±3.9</td>
<td>25.2±3.6</td>
</tr>
<tr>
<td>Laterality-linearity index</td>
<td></td>
<td>40.9±1.8</td>
<td>40.5±1.6</td>
<td>41.3±1.7</td>
<td>40.9±1.8</td>
</tr>
<tr>
<td>Skinfold thickness (mm)</td>
<td></td>
<td>21.1±10.3</td>
<td>22.0±10.0</td>
<td>25.7±11.4</td>
<td>21.1±10.2</td>
</tr>
<tr>
<td>Arm circumference (cm)</td>
<td></td>
<td>26.9±2.3</td>
<td>27.8±2.4</td>
<td>26.8±2.4</td>
<td>27.1±2.3</td>
</tr>
<tr>
<td>Arcus senilis prevalence (%)</td>
<td></td>
<td>13.9</td>
<td>18.6</td>
<td>17.0</td>
<td>12.4</td>
</tr>
<tr>
<td>Xanthelasma prevalence (%)</td>
<td></td>
<td>1.5</td>
<td>1.5</td>
<td>1.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Diabetes prevalence (%)</td>
<td></td>
<td>0.7</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic</td>
<td></td>
<td>85.3±11.2</td>
<td>89.7±12.5</td>
<td>94.1±12.2</td>
<td>84.6±10.5</td>
</tr>
<tr>
<td>Systolic</td>
<td></td>
<td>143.2±20.9</td>
<td>148.6±22.4</td>
<td>152.6±22.5</td>
<td>141.2±18.8</td>
</tr>
<tr>
<td>Serum cholesterol (mg/dl)</td>
<td></td>
<td>201.9±41.1</td>
<td>217.3±41.2</td>
<td>222.5±46.9</td>
<td>201.2±40.5</td>
</tr>
<tr>
<td>Arrhythmias prevalence (%)</td>
<td></td>
<td>2.2</td>
<td>3.3</td>
<td>4.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Vital capacity (dl/m)</td>
<td></td>
<td>28.1±3.9</td>
<td>27.8±4.1</td>
<td>25.1±4.5</td>
<td>28.4±3.7</td>
</tr>
<tr>
<td>Forced expiratory volume (dl/m)</td>
<td></td>
<td>18.6±2.4</td>
<td>16.1±2.8</td>
<td>15.8±4.2</td>
<td>18.8±2.3</td>
</tr>
</tbody>
</table>

Diabetes was considered only at year 0 and for 25-year follow-up because on other occasions it created problems of convergence.

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**Table 2. Final Solutions for Two Stepwise Cox Models Predicting Cerebrovascular Events Using Factors Measured at Year 0 in Men Aged 40–59 Years**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Follow-up from years 0 to 25</th>
<th>Follow-up from years 10 to 25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Order</td>
<td>Coeff OR 95% CI</td>
<td>Order</td>
</tr>
<tr>
<td>Age</td>
<td>2 0.0778 1.08* 1.04–1.11</td>
<td>1 0.0784 1.08* 1.04–1.13</td>
</tr>
<tr>
<td>Physical activity score</td>
<td>5 –0.3253 0.72† 0.57–0.91</td>
<td>7 –0.2800 0.76‡ 0.57–0.999</td>
</tr>
<tr>
<td>Laterality-linearity index</td>
<td>– – – –</td>
<td>8 0.0909 1.10 0.99–1.22</td>
</tr>
<tr>
<td>Skinfold thickness</td>
<td>6 –0.0263 0.97† 0.96–0.99</td>
<td>6 –0.0273 0.97‡ 0.95–0.99</td>
</tr>
<tr>
<td>Arcus senilis</td>
<td>4 0.4345 1.54‡ 1.04–2.29</td>
<td>2 0.7567 2.13* 1.37–3.30</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9 1.2231 3.40‡ 1.03–11.22</td>
<td>12222...</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>1 0.0218 1.02‡ 1.01–1.02</td>
<td>3 0.0138 1.01‡ 1.00–1.023</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>8 0.0042 1.004‡ 1.0003–1.01</td>
<td>4 0.0051 1.005‡ 1.0004–1.01</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>7 0.8319 2.30§ 1.15–4.57</td>
<td>– – – –</td>
</tr>
<tr>
<td>Vital capacity</td>
<td>3 –0.0832 0.93† 0.89–0.98</td>
<td>5 –0.0564 0.95§ 0.896–0.997</td>
</tr>
</tbody>
</table>

Years 0 to 25, 152 events in 1,572 men aged 40–59 years; years 10 to 25, 115 events in 1,378 men aged 40–49 years; order of entrance into model; Coeff, coefficient; OR, odds ratio; CI, confidence interval. Diabetes not considered for years 10 to 25 because problems of convergence arose.

* p<0.001, †p<0.01, §p<0.05, $p<0.02$ different from 1.
same factors involved in the long-term prediction of cerebrovascular events are associated with the event when a shorter and delayed follow-up is considered. Arrhythmias failed to maintain a significant association, probably as a consequence of the low prevalence of such disturbances. Skinfold thickness entered the solution with a negative coefficient, while the laterality–linearity index showed a borderline significant ($t=1.71$) positive coefficient. Diabetes was excluded from the initial pool of covariates because problems of convergence arose for this covariate when considering shorter follow-ups and smaller numerators and denominators.

Table 3 summarizes three solutions for the same follow-up period (15 years) but different ages at entry (40–59, 45–64, and 50–69 years). Systolic blood pressure was the first covariate to be included in all three models, with a positive coefficient and the same odds ratio for all three age groups. Physical activity score, even if entering in different orders and with decreasing levels of significance, maintained a role in the prediction of stroke events, with an inverse relation for all age groups. The protective role of physical activity at work decreased with age, as demonstrated by the odds ratio decreasing from 0.70 in the “young” men to 0.77 in the “old” men. This phenomenon could be linked to the relative decrease in physical activity at work while age increases (Table 1). However, the two above-mentioned factors are the only covariates present in all three models. Respiratory indexes, represented by forced expiratory volume and vital capacity, entered the three solutions with negative coefficients, but while vital capacity was a powerful predictor in the solution related to older men and a less powerful predictor in the solution related to middle-aged men, forced expiratory volume appeared as a significant predictor only for the youngest group. Age was not included in the model in the solution referring to older men, while for the first time serum cholesterol was added with a borderline significant ($t=1.78$) positive coefficient and the negative coefficient of skinfold thickness was significant.

Two attempts were made to assess the role of changes in systolic blood pressure and serum cholesterol in the prediction of cerebrovascular events for a follow-up from year 10 to year 25 (Table 4). The first attempt used covariates representing the net change in levels of the factor between years 10 and 0; changes in systolic blood pressure entered the model with a positive significant ($t=2.05$) coefficient, while serum cholesterol did not enter the model. When a similar attempt included the changes expressed by the time–factor integral of risk factor levels (where the 5-year measurements are also considered) the picture was almost the same, with the positive coefficient of changes in systolic blood pressure showing a slightly greater $t$ value ($t=2.40$). Again, the coefficient of changes in serum cholesterol did not reach a significant level. All this implies that increasing levels of systolic blood pressure in 10 years are associated with an increased risk, whereas decreasing levels are associated with a decreased risk. This is true above and beyond the role of the entry level, which retains its predictive power. This was not the case for serum cholesterol. The odds ratio obtained for DELTA of systolic blood pressure is small because it concerns the risk due to each unit increase of pressure in 10 years.

When the coefficients of the first solution reported in Table 4 were applied to arbitrary systolic blood pressure changes, some interesting information could be gathered (Table 5). Starting from a baseline corresponding to the population mean systolic blood pressure, arbitrary DELTA's above or below the “natural trend” were associated with changes of cerebrovascular risk. The risk decreases if systolic blood pressure remains stable or changes in the direction opposite to the natural trend.

Other analyses, not reported here in detail, were conducted to answer specific questions arising during the interpretation of these data. In particular, a Cox model was solved separately for the few (11) cases of chronic cerebrovascular disease in 25 years; the small numbers involved prevented some factors from yielding stable coefficients, but age and forced expiratory volume were significantly predictive with the same algebraic sign of the basic solution; another Cox model was solved testing the predictive power of the systolic blood pressure × physical activity score interaction term, which produced a small and nonsignificant coefficient; and the prevalence of coronary heart disease (old myocardial infarction, angina pectoris, and heart failure) were fed
into Cox models of 25 (years 0 to 25) and 15 (years 10 to 25) years of follow-up; in no case did the coefficient reach a significant level.

**Discussion**

The main results of the present investigation confirm that in the prediction of cerebrovascular events a major role is played by blood pressure, as already found in this study population and in many others, although other factors also have some predictive relevance. The time-related changes of blood pressure as estimated by two different indicators seem to significantly improve the prediction, confirming the role of this variable, already tested in a previously published paper, but dealing only with fatal cases. A natural experiment confirming these estimates is represented by the recent decreasing trends in stroke mortality observed in many countries, with the exception of those of eastern Europe, which are likely explained by the improved and widespread treatment of high blood pressure in some advanced societies.

The role of serum cholesterol in the prediction of cerebrovascular events has been variously reported in the literature. The association between cholesterol and cerebrovascular events was previously investigated in this study population, using shorter follow-up periods or only fatal events as an end point, thus dealing with smaller numerators. This is the first time that in this population a positive and significant predictive role of serum cholesterol is shown in regard to stroke events. From a simply statistical point of view, the greater numbers employed in this analysis could explain why some factors previously found not to be significantly related to the event became so on this occasion. However, inspection of the models in Table 3, all dealing with 15 years of follow-up with almost equal numerators but different ages at entry, shows that serum cholesterol entered the solution only when referring to older men (age at entry 50–69 years) and including the 25th year of follow-up. In general, it is known that thrombotic events are more common in older persons than in relatively young people, and this could explain the lack of predictive power of serum cholesterol during early follow-up. The present data also show a decrease in the predictive power of systolic blood pressure when moving from the younger to the older age groups, possibly bound to a relative decrease of hemorrhagic events compared with thrombotic ones. Moreover, a long period of latency may be needed before the effect of cholesterol can be seen. Finally, it is known that in Italy during the period corresponding to the follow-up of this population, a similar trend has occurred, with a decreasing ratio of deaths attributed to hemorrhagic versus thrombotic stroke.

In this population no relation was found between cigarette smoking and cerebrovascular events, in contrast with other studies. The possible confounding effect of respiratory function indexes was supposed, but even excluding them from the pool of covariates offered to the model, the lack of association between smoking and stroke persisted. One possible explanation for this finding could be the widespread use of Turkish tobacco cigarettes (with their supposedly lesser hazards to...
health), which were popular in Italy during the years of exposure of this population (follow-up started in 1960).

Among the other factors, an important role was played by the indexes of respiratory function and by physical activity. The protective role of respiratory function indexes on cerebrovascular events has already been shown in previous analyses conducted on the fatal component of this material and is largely confirmed in this analysis. However, it remains a relatively rare finding in the literature.2,7,9,10,30–32 In one of the above-mentioned papers30 this association was confirmed, but only in fatal cases. The mechanisms underlying this association can be only indirectly supposed because these indexes could reflect physical fitness or they could be influenced by physiopathologic abnormalities such as polycythemia or sleep apnea, which are, on the other hand, likely to be rare conditions.

The protective role of physical activity against cardiovascular events has already been observed and confirmed in different population studies.33,34 However, a major stable role of this factor in the prediction of cerebrovascular events is stressed here, although a decrease in the t value of the coefficients is observed with increasing age, which resembles the relation observed for systolic blood pressure. At the same time there is a decrease in the protective effect of this variable as suggested by the progressive increase in the odds ratio (from 0.70 to 0.77) not observed for systolic blood pressure. However, the interaction between systolic blood pressure and physical activity score was not significant in predicting cerebrovascular events. It should be recalled that this analysis deals only with work-related physical activity, which in rural communities in the 1960s was practically the only one performed by the majority of men.

Diabetes35–37 and arrhythmias,1,38,39 mainly atrial fibrillation, are commonly mentioned in the literature as risk factors for stroke. In the present investigation all arrhythmias reported in item 8 of the Minnesota Code were considered, and their predictive role was confirmed. On the other hand, as reported before the predictive power of coronary heart disease itself was nil. Diabetes could not be included in all solutions because problems of convergence arose. However, for the 25-year prediction the inclusion of this covariate among those significantly associated with stroke events confirmed the usual literature findings.1,35–37

In this analysis skinfold thickness showed a negative coefficient, in contrast with other findings that indicate a direct relation of this obesity indicator with cerebrovascular events.40 This difference could partly be explained supposing a curvilinear relation between skinfold thickness and stroke, as frequently observed for all-cause mortality. However, when the quadratic term of skinfold thickness was added to the model, both the linear and the quadratic coefficients failed to reach the statistically critical level.

The instability of the coefficients of arrhythmias, diabetesth, arcos senilis, and skinfold thickness could be related to the small sample size (namely, for arrhythmias), to a true change in their predictive power when the durations of follow-up were different, or to unknown mechanisms related to the aging process. In fact, almost all these factors were contemporarily present and significant only when the models covered a follow-up of 25 years. On the other hand, when a uniform 15-year follow-up was considered, starting from different ages at entry, some factors failed to show a predictive association, with variously represented combinations.

The special analysis of the 15 cases (only 11 for the multivariate analyses because of missing data) of chronic cerebrovascular events was hampered by the small number involved. However, in a previous paper covering many cohorts and more cases, we separately considered the acute and chronic types of cerebrovascular diseases, which have been kept together in this analysis in contrast with some studies in which only acute strokes were considered. On that occasion, no substantial differences were found between the two groups in terms of association with the major risk factors.6

In conclusion, it seems that in spite of the increasing knowledge about risk factors for stroke and the declining trends in mortality and likely morbidity, more investigation is needed on their determinants, trying by means of modern technology to keep separate hemorrhagic and thrombotic cases.

References


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