Consumption of Fruit and Wine and the Decline in Cerebrovascular Disease Mortality in Spain (1975–1993)

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Background and Purpose—This study examines the changes in provincial distribution of cerebrovascular disease (CVD) mortality and its socioeconomic and lifestyle risk factors to identify those factors that have most greatly contributed to the decline in CVD mortality in Spain during the period 1975–1993.

Methods—We performed a study using data aggregated at a provincial level. Mortality data were taken from official vital statistics, while data on risk factors were obtained from surveys of representative large Spanish population samples. Correlation and multiple linear regression analyses were performed on percent changes in age-standardized CVD mortality from 1975–1979 to 1989–1993 and its potential determinants during the period 1964–1980.

Results—CVD mortality was higher in the southern and eastern (Mediterranean coast) provinces in 1975–1979 and again in 1989–1993. Between these periods there was a 55% decline in CVD mortality, which affected all provinces but was greater in those with a lower CVD mortality ($r = -0.31, P = 0.03$). The 1964–1980 period witnessed an increase in the intake of most foodstuffs and all types of fats. However, there was a decrease in the consumption of vegetables and legumes and in the proportion of illiteracy among the population older than 45 years. The greatest increase in fruit and fish consumption and the greatest decrease in illiteracy were registered by Spain’s northernmost provinces, the same provinces that recorded the greatest decline in CVD mortality. Changes in fruit, wine, and fish intake accounted for 22% of the variation in the decline in CVD mortality. The increase in fruit consumption and decrease in wine consumption showed a statistically significant relationship ($P = 0.04$) with the decline in CVD mortality.

Conclusions—The increase in fruit and decrease in wine consumption from 1964–1980 may have contributed to the decline in CVD mortality in Spain during 1975–1993. (Stroke. 1998;29:1556-1561.)

Key Words: geography ■ mortality ■ Spain ■ stroke ■ trends

Cerebrovascular disease (CVD) was the leading cause of death in Spain in 1993, registering a mortality rate of 107/100,000 population and thereby placing Spain in a middle-ranking position among developed countries. As is the case with many developed countries, CVD mortality in Spain has progressively declined from 1975 until the present. Identification of the factors responsible for this decline in CVD mortality could contribute to the establishment of intervention policies that would sustain or accelerate this decline. This study therefore examines the changes in provincial distribution of CVD mortality and its socioeconomic and lifestyle risk factors to identify those factors that have most greatly contributed to the decline in CVD mortality in Spain during 1975–1993.

Subjects and Methods

The following information was obtained for the 50 provinces of Spain: CVD mortality (International Classification of Diseases, Eighth Revision codes 430 to 438 for 1975–1979 and International Classification of Diseases, Ninth Revision codes 430 to 438 for 1989–1993) data were gathered from Spanish vital statistics. Age-standardized CVD mortality rates were calculated at the provincial level for 1975–1979 and 1989–1993. Rates were adjusted according to the direct method, with age-specific rates being computed in 5-year groups from ages 45 to 79 years, and the European population was taken as standard.

Information on consumption of foodstuffs, nutrients, and tobacco was drawn from the 196414 and 198015 Household Budget Surveys conducted by the National Statistics Office and National Nutrition Institute and based on representative Spanish population samples of 21,000 and 25,000 families, respectively. These surveys estimated food and tobacco intake on the basis of the amounts acquired by the families surveyed. Only food consumed at home was included. Food quantities were converted into nutrients by applying standard food composition tables. Information on tobacco was expressed as an expense in constant 1980 peseta values per person per annum because it was impossible to obtain the physical quantity of tobacco consumed on the basis of the expenditure recorded in the 1964 Household Budget Survey. Last, information on illiteracy among the
segment of the population older than 45 years was taken from the 1970 and 1981 population censuses.

Percent changes in CVD mortality and its potential determinants were computed with respect to the relevant values at the beginning of the period, according to the following formula:

$$\text{Percent Change in CVD Mortality} = \left(\frac{\text{Age-Adjusted Mortality Rate in 1989–1993} - \text{Age-Adjusted Mortality Rate in 1975–1979}}{\text{Age-Adjusted Mortality Rate in 1975–1979}}\right) \times 100.$$  

Similarly, the formula for risk factors was as follows:

$$\text{Percent Change} = \left(\frac{\text{Value of Risk Factor in 1980} - \text{Value of Risk Factor in 1964}}{\text{Value of Risk Factor in 1964}}\right) \times 100.$$  

For the variable "illiteracy among the segment older than 45 years," 1970 and 1980 values were used. In addition, Pearson correlation coefficients were calculated for these variables, and multiple linear regressions were performed on the percent change in the age-adjusted CVD mortality rate. Statistical analysis was performed with the aid of the SAS software package.

**Results**

CVD mortality was higher in the southern and eastern (Mediterranean coast) provinces in 1975–1979 and again in 1989–1993 (Figure 1). Between these periods there was a 55% decline in CVD mortality (Table 1), which affected all provinces but was greater in those with a lower CVD mortality ($r=-0.31$, $P=0.03$), thus serving to consolidate the north-south gradient in mortality due to this disease in Spain (Figure 1).

The 1964–1980 period witnessed an increase in the intake of most foodstuffs and all types of fats (Table 1). However, there was a decrease in the consumption of vegetables and legumes and in the proportion of illiteracy among the population older than 45 years. While the increases in the consumption of meat, chicken, fruit, total fats, and all types of fatty acids affected all provinces (with positive minimum values) (Table 1), for the remainder of the variables studied there were increases in some provinces and decreases in others. Wine, vegetable, oil, and milk consumption and illiteracy among the group older than 45 years yielded coefficients of variation in excess of 100% (Table 1). The greatest increase in fruit and fish consumption and the greatest decrease in illiteracy were registered by Spain’s northernmost provinces (Figures 1 and 2). In contrast, the changes in consumption of wine and vegetables failed to display any clear geographic pattern (Figure 2).

The changes in fruit, fish, oil, total fat, and polyunsaturated fatty acid intake showed a significant ($P<0.05$) negative correlation with changes in CVD mortality (Table 1). Changes in consumption of legumes, saturated and monounsaturated fatty acids, and tobacco correlated negatively, and changes in consumption of different types of meat, milk, and wine and illiteracy among the group older than 45 years correlated positively with changes in CVD mortality yet failed to attain statistical significance (Table 1).

To ascertain the independent contribution to changes in CVD mortality attributable to changes in the aforementioned factors, we constructed a multiple linear regression model with changes in age-standardized CVD mortality as the dependent variable. Oils, total fats, and polyunsaturated fats were not included in the model in view of the fact that no clear evidence of any link with CVD mortality was found in the literature. In contrast, changes in illiteracy and consumption of wine and tobacco were introduced because all
are risk factors for CVD,\textsuperscript{13-15} although none attained statistical significance in the crude analysis.

Taken together, the variables of the model accounted for 25\% of the variation in the decline in CVD mortality in Spain (model I, Table 2). Practically none of the model’s variables showed a statistically significant relationship with CVD mortality. The single exception was fruit and wine consumption, which registered a marginally statistically significant relationship, probably because of the high number of variables compared with the number of observations. On the basis of the six variables of the initial model, we then proceeded to construct a new model in which the definitive variables were selected by means of a forward stepwise procedure, with those having a regression coefficient of $P<0.20$ being retained (model II, Table 2). In this model, changes in fruit, fish, and wine consumption accounted for 22\% of the variation in the decline in CVD mortality. The increase in fruit consumption and decrease in wine consumption showed a statistically significant relationship ($P=0.04$) with the decline in CVD mortality nationwide.

**Discussion**

This study suggests that the increase in fruit and decrease in wine consumption during 1964–1980 may have contributed to the decline in CVD mortality in Spain during 1975–1993. There is a growing body of evidence to show that consumption of fruit and vegetables may protect against development of CVD. A recent review has reported that 3 of 5 ecological studies, 0 of 1 case-control study, and 6 of 8 cohort studies observed a statistically significant negative relationship between fruit and vegetable intake and occurrence of CVD.\textsuperscript{16} Our results provide new evidence of the protective role of fruit on CVD and moreover suggest that consumption of fruit may have been important at a community level in accounting for the decline in CVD mortality in Spain. However, one cannot totally exclude the possibility that this relationship might be due to confounding factors not controlled for in the analysis that are associated with high fruit intake: on the one hand, healthy lifestyles that may prevent CVD,\textsuperscript{17} and on the other, a lower consumption of salt and other foodstuffs that may increase the risk of CVD.\textsuperscript{16}

Evidence is likewise mounting with regard to the relationship between alcohol consumption and CVD.\textsuperscript{13,14,18} though ecological studies published to date have failed to report consistent results. Thus, while St Leger et al\textsuperscript{19} failed to find any linear association between alcohol consumption and CVD mortality in 18 mostly European countries, Ueshima et al\textsuperscript{20} found a fairly strong positive association using comparable data from 46 prefectures in Japan and adjusting for salt intake and several socioeconomic factors. Sasaki et al\textsuperscript{21} also reported a positive association between alcohol consumption and CVD mortality in a population correlation study covering 17 countries. Our results are consistent with a previous study in which we found that excess wine consumption was
associated with higher CVD mortality across regions in Spain during 1989–1993. The evidence presented both here and in the previous study supports the role played by wine consumption in the health of a typical Mediterranean country, thereby explaining in part the geographic distribution and temporal evolution of CVD, which is currently the leading cause of mortality in Spain.

In this study a negative relationship was observed between fish consumption and CVD mortality, yet it failed to attain statistical significance (Table 2). This relationship is not

**Figure 2.** Percent changes in the consumption of fruit, fish, wine, and vegetables during 1964–1980 in Spain. Quintiles of provincial distribution are shown. Upper parts of maps represent northern Spain.

**TABLE 2.** Multiple Linear Regression Analysis of Percent Changes in Age-Standardized Cerebrovascular Disease Mortality From 1975–1979 to 1989–1993 in Spain

<table>
<thead>
<tr>
<th>Variables</th>
<th>( \beta )</th>
<th>Standardized ( \beta^* )</th>
<th>Partial Correlation Coefficient</th>
<th>( P^\dagger )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model I</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruit</td>
<td>-0.01</td>
<td>-0.29</td>
<td>-0.27</td>
<td>0.07</td>
</tr>
<tr>
<td>Fish</td>
<td>-0.02</td>
<td>-0.16</td>
<td>-0.16</td>
<td>0.29</td>
</tr>
<tr>
<td>Wine</td>
<td>0.03</td>
<td>0.30</td>
<td>0.30</td>
<td>0.04</td>
</tr>
<tr>
<td>Vegetables</td>
<td>-0.02</td>
<td>-0.07</td>
<td>-0.07</td>
<td>0.63</td>
</tr>
<tr>
<td>Tobacco</td>
<td>-0.01</td>
<td>-0.05</td>
<td>-0.05</td>
<td>0.72</td>
</tr>
<tr>
<td>Illiteracy (&gt;45 years)</td>
<td>0.02</td>
<td>0.15</td>
<td>0.17</td>
<td>0.27</td>
</tr>
<tr>
<td>( R^2=0.25; P=0.05 )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Model II</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruit</td>
<td>-0.01</td>
<td>-0.31</td>
<td>-0.30</td>
<td>0.04</td>
</tr>
<tr>
<td>Fish</td>
<td>-0.02</td>
<td>-0.20</td>
<td>-0.20</td>
<td>0.16</td>
</tr>
<tr>
<td>Wine</td>
<td>0.03</td>
<td>0.30</td>
<td>0.31</td>
<td>0.03</td>
</tr>
<tr>
<td>( R^2=0.22; P=0.01 )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*\( \beta(S_x/S_y) \), where \( S \) is SD, \( x \) the independent variable, and \( y \) the changes in age-standardized cerebrovascular disease mortality.

†Statistical significance (two-sided test).
unequivocally clear in the literature. The Zutphen Study recorded an inverse relationship between fish consumption of more than 20 g/d and risk of CVD (relative risk, 0.49; 95% confidence interval, 0.24 to 0.99); and the NHANES I (National Health and Nutrition Examination Survey I) Epidemiologic Follow-Up Study observed a lower risk of CVD among white women and black persons of both sexes who consumed fish more than once a week.24 The results of a case-control study in Australia25 and data from Japan26 also support this relationship. However, no such protective effect afforded by fish against CVD was observed in the Physicians’ Health Study27 or in the Chicago Western Electric Study.28

Finally, a positive although not statistically significant association was seen between changes in the proportion of illiterates older than 45 years and changes in CVD mortality. It is known that CVD mortality registers a marked variation according to social class (the higher the class, the lower is the CVD mortality).35 Indeed, this association has been observed at an ecological level in the literature29–32 and in studies at an individual level in Spain.31 In a prior study we observed that socioeconomic status (as measured by illiteracy in the group older than 45 years) could account for the geographic distribution of CVD mortality in Spain during 1989–1993 and that part of this relationship was mediated by wine consumption.22

A certain degree of prudence is called for in evaluating the results of this study because neither the study design nor data were optimum. First, overall CVD mortality data were used because the technology capable of distinguishing a disease of ischemic origin from a disease of hemorrhagic origin (ie, CT) has only very recently become available. However, the respective risk factors may be partially different between the two,33,34 to the extent that some studies specifically suggest that the dose-response relationship between alcohol consumption and CVD mortality would be positive and continuous in the case of hemorrhagic origin yet J-shaped in the case of ischemic origin.18 It should be noted, however, that most CVD-induced deaths in Spain during the study period were ischemic in origin.3

Second, this is an ecological study. Our results suggest that changes in tobacco consumption, an important risk factor for cerebrovascular disease, fail to explain the changes in CVD mortality in Spain. Indeed, whereas tobacco consumption rose in Spain during 1964–1980,38 CVD mortality has declined from the 1960s to the present. Tobacco is likewise unable to account for a considerable part of the geographic distribution of CVD mortality both among the countries that participated in the Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Study36 and within the United States.37,38 although it would appear to have made a substantial contribution to the decline in CVD mortality in Finland.39 Our results do not imply that smoking is entirely devoid of influence on risk of CVD among the Spanish population. Such influence depends rather on the level of analysis40; there is ample evidence that smoking raises the risk of CVD at an individual level.3 However, this report in no way seeks to extend its inferences to levels of aggregation beyond that of the provincial geography of Spain during the study period. Similarly, our work does not pretend to extend its results to latency periods different from those actually considered: changes in risk factors during 1964–1980 in relation to changes in CVD mortality from 1975–1979 to 1989–1993.

Finally, no account was taken of changes in the prevalence and control of high blood pressure and in the availability of and accessibility to high-technology healthcare services in Spain. This was due to the dearth of data on these variables during the study period. Moreover, the contribution of antihypertensive treatment to the decline in CVD mortality is a controversial issue. There is abundant evidence to show that high blood pressure is a major risk factor for CVD,1,42 that effective medication for control exists,43 and that the degree of control has an influence on the risk of CVD.44 It is also true that prevalence of high blood pressure partially explains the geographic distribution of CVD in the MONICA Study36 and that control of blood pressure seems to have contributed to the decline in CVD mortality in Finland.39 Similarly, an ecological study conducted in districts of Catalonia (northeastern Spain) has emphasized the existence of a negative relationship between degree of control over blood pressure and CVD mortality.45 However, a remarkable inverse relationship has been observed between blood pressure level and CVD mortality during the study period. Moreover, the contribution of antihypertensive treatment to the decline in CVD mortality is a substantial part of the geographic distribution of CVD in the United States.37,38 Similarly, the contribution of antihypertensive treatment and control to the decline in CVD mortality in the United States47 and New Zealand48 seems to be only modest. Furthermore, advances in treatment and control of blood pressure are not consistent with the recent stabilization of CVD mortality in the United States.49–51 In Spain, the contribution of better control of high blood pressure to the decline of stroke mortality could not be substantial because the decline in stroke mortality antecedes the widespread use of antihypertensive medication and because high blood pressure control through medication had taken place in less than 5% of the hypertensive population in 1990.52 Finally, CVD treatments developed over the last few years are moderately effective at best, and their general use is a recent and as yet incomplete phenomenon in Spain; therefore, any contribution to the decline in CVD mortality must necessarily have been small.

Despite these limitations, we believe that our results may well be of practical importance. In concrete terms, they suggest that maintenance of traditionally Mediterranean lifestyle habits, involving a diet rich in fruit and vegetables and a moderate, preferably mealtime, consumption of wine, may contribute to sustaining the decline in CVD mortality in Spain.

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