Adaptation of the Framingham-Wilson Coronary Risk Equation for the Population of Navarra (RICORNA)

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Introduction and objectives. The Framingham equations overestimate the risk of coronary disease in populations with a low disease incidence. It is more appropriate to take the local population's characteristics into account when estimating coronary risk. Accordingly, the Framingham-Wilson equation has been adapted for the population of Navarra, Spain. This article presents 10-year overall coronary risk charts.

Methods. The Framingham–Wilson equation was adapted using data on the prevalence of cardiovascular risk factors and the coronary event rate in the population of Navarra. The version of the Framingham-Wilson equation used included high-density lipoprotein cholesterol (HDL-C). The probability of an event at 10 years for different combinations of risk factors, with an HDL-C concentration of 35-59 mg/dL, are illustrated.

Results. Using the Framingham equation adapted for Navarra (ie, the RICORNA or Riesgo Coronario Navarra), the proportion with an estimated probability of a coronary event in the next 10 years greater than 9% is approximately half that in the original Framingham population, and the proportion with a high or very high probability (ie, 20%) is one-third. An HDL-C level <35 mg/dL increases the risk by 50% and a level ≥60 mg/dL reduces it by 50%, approximately. The average HDL-C level observed in the population was 63.9 mg/dL overall, and 70.1 mg/dL in women.

Conclusions. The RICORNA equation can provide a more precise estimate of overall coronary risk and could be useful in primary disease prevention in Navarra. The high HDL-C concentration observed in Navarra might contribute to the associated low coronary morbidity and mortality.

Key words: Cardiovascular risk equations. Coronary disease. Coronary disease risk. Primary prevention.

Adaptación de la función de riesgo coronary de Framingham-Wilson para la población de Navarra (RICORNA)

Introducción y objetivos. Las funciones de Framingham sobreestiman el riesgo de enfermedad coronaria en poblaciones con baja incidencia. Es más apropiado estimar el riesgo coronario considerando las características poblacionales locales. En este sentido, se ha adaptado la ecuación de Framingham-Wilson para la población de Navarra. Se presentan las tablas de riesgo coronario global a 10 años.

Métodos. Se ha adaptado la ecuación de Framingham-Wilson mediante los datos de prevalencia de los factores de riesgo cardiovascular y la tasa de acontecimientos coronarios de Navarra. Se ha utilizado la ecuación de Framingham-Wilson que incluye el colesterol unido a lipoproteínas de alta densidad (cHDL). Se muestran las probabilidades de acontecimientos a 10 años correspondientes a las distintas combinaciones de los factores de riesgo, para una concentración de cHDL de 35-59 mg/dl.

Resultados. En la función adaptada Framingham-Navarra (RICORNA), la proporción de estimaciones de probabilidad de acontecimiento coronario a 10 años superior al 9% es aproximadamente 2 veces menor, y la de riesgo alto o muy alto (≥20%) es 3 veces menor que en las originales de Framingham. Los valores de cHDL < 35 mg/dl incrementan el riesgo un 50% y los valores ≥ 60 mg/dl lo reducen un 50%, aproximadamente. El cHDL observado tuvo un valor medio poblacional de 63,9 mg/dl y de 70,1 mg/dl en las mujeres.

Conclusiones. La función RICORNA es una herramienta que puede ser utilizada para estimar con más precisión el riesgo coronario global en la prevención primaria de esta enfermedad en Navarra. La elevada concentración de cHDL observada en Navarra puede contribuir a su baja morbilidad coronaria.

INTRODUCTION

Coronary heart disease is one of the main public health problems in Navarra, Spain. Acute myocardial infarction (AMI) is the second leading cause of death in men and the third in women. One quarter of all deaths before patients reach hospital care occur during the first 28 days after onset of symptoms.

Some of these deaths could be avoided with effective primary prevention to improve the detection and appropriate management of risk factors for coronary heart disease. It is necessary to promote the primary prevention of cardiovascular disease, balancing activities dealing with prevention with those involving the care of persons who already have coronary heart disease.

Arteriosclerosis, the main etiopathological cause of ischemic heart disease, is a multiple factor entity. As far as is known, no particular factor is required for its development, but rather it depends on the coexistence and severity of different component factors and the synergistic or antagonistic effect of each factor. Its preventive approach should therefore be multi-factorial as well. Evaluation of the risk by means of multiple risk factor models predicts the overall individual risk more precisely and enables primary prevention priorities to be established, adjusting the intensity of the intervention aimed at avoiding the onset of a first cardiovascular episode in asymptomatic but vulnerable persons.

Cardiovascular risk equations are the best tool to establish priorities in primary prevention. These equations estimate the excess risk that a person has of experiencing an event over a certain period of time, usually 5 or 10 years, in relation to the average risk of the population to which that individual belongs. Several different equations or scales exist to calculate the coronary risk, all based on the findings of the North American Framingham cohort. Various epidemiological studies have identified that the use of these equations in Anglo-Saxon populations provides an adequate estimate of the future risk of an event, but their use in low-risk countries such as Spain systematically overestimates this risk.

The most used risk tables in Spain are REGICOR (REGistre Gironí del COR) and SCORE (Systematic Coronary Risk Evaluation). The REGICOR equation has proven to have a good prediction capacity for coronary events in Spanish persons aged 35-74 years. The SCORE equation, in its version adapted for use in low-risk countries, for the calculation of the risk of cardiovascular death in persons aged 40 to 65 years, has recently been adapted to Spain.

The estimation of the coronary risk should be based on the follow-up of large cross-sectional cohorts. Navarra currently has a population cohort, though the follow-up period is still not long enough to provide risk estimates according to age and sex that possess the required precision. This, therefore, demands that we use charts that have been generated in other populations or else adapt these charts. The aim of this study was to adapt the Framingham-Wilson equation by calibrating it using the rates of coronary events and the prevalence of cardiovascular risk factors found in Navarra.

METHODS

The estimation of the coronary risk was based on the original equation of the Framingham study in the version published by Wilson et al in 1998. This equation includes high-density lipoprotein cholesterol (HDLC), and estimates the 10-year risk of having a myocardial infarction, whether fatal or not, symptomatic or silent, and angina.

The method used to adapt the Framingham equation is known and has been evaluated in our setting. The calibration was done by substituting the comparison elements of the Framingham population with those of the Navarra population. Estimates are available of the prevalence of cardiovascular risk factors and the rates of major coronary events (fatal or non-fatal symptomatic AMI) of Navarra. Additionally, the original coefficients of the Framingham-Wilson equation were used. The calculation of the calibrated equation is described in the appendix.

Adaptation Process

The population data concerning cardiovascular risk factors were obtained from the Riesgo Vascular
en Navarra (Vascular risk in Navarra) (RIVANA) study, for the population aged 35 to 74 years in 2003.\textsuperscript{15,16} The sampling strategy recruited 5197 persons. The final rate of participation was 74.6%. The variables studied were sex, age, total cholesterol, HDL-C, systolic blood pressure (SBP), diastolic blood pressure (DBP), smoking, and a diagnosis of diabetes mellitus. The prevalence of the various risk factors was calculated for each group according to age and sex, using the definitions and cut-off points of the Framingham-Wilson cohort.\textsuperscript{14}

The blood pressure was measured 3 times, with an interval of at least 5 min between each measurement. At the first measurement the blood pressure was measured in both arms, and the value for the arm showing the highest SBP or DBP was used. The measurement was made with an automatic blood pressure monitor (OMRON\textsuperscript{8} M4-1).

**Laboratory Measurements**

All the analyses were centralized at the laboratory of the Hospital de Navarra (Pamplona). All the analytical procedures were calibrated and standardized in order to guarantee the quality of the biochemical determinations. Internal and external controls were made systematically. The internal quality control consisted of a daily control and weekly calibration. The internal controls were made with Precinorm U and Precipath U for the measurements of total cholesterol and glucose, and Precipath lipids for the HDL-C (Roche Diagnostics). Concurrent external quality controls were made with Unity (BioRad Laboratories). The total cholesterol was measured with the CHOD-PAP enzymatic-colorimetric method and the HDL-C with the second generation direct HDL plus method (without pretreatment). The glucose was measured by the hexokinase method.

The study used the data from the Navarra population registry of AMI, which records all patients with an AMI, both fatal and non-fatal. The registry covers the years 1997-1998 and 2003-2004.\textsuperscript{3,17} A simple weighting of the observed rate was made for each point in the series (1997, 1998, 2003, and 2004); each year had an equal contribution (weighting K = 2.5) to the estimated rate of coronary events at 10 years.

The calculation of the rates included all cases of myocardial infarction in Navarra, classified according to the algorithm of the MONICA project (MONItoring of trends and determinants in CArdiovascular diseases).\textsuperscript{3,18} Each case studied was classified as: definite AMI, fatal or not; possible AMI, or AMI with insufficient data. The 4 categories compose definition I of the MONICA study, which is that used to calculate the rate. Given that the Wilson equation, besides symptomatic AMI, also includes cases of angina and silent AMI, data that are not known in Navarra, the proportion was assumed to be similar to that of Framingham. The following ratio was used for the estimate:

\[
\frac{Ho(t)}{FramAll} \left\{ \frac{Ho(t)}{FramMajor} \right\}
\]

where \(t\) is the follow-up time, in our case 10 years; \(\frac{Ho(t)}{FramAll}\), the rate of coronary events including angina and silent myocardial infarction in Framingham, and \(\frac{Ho(t)}{FramMajor}\), the rate of fatal or non-fatal symptomatic infarction. The value of this quotient was 1.4 for men and 1.91 for women.\textsuperscript{7} Thus, as the rate of major events in Navarra in men according to the registry was 3.6%, this was multiplied by 1.4 to obtain the estimated rate of all coronary events (5.1%). This, in turn, enabled us to calculate the population rate free of coronary events at 10 years: 100% - 5.1% = 94.9%. For women, the rate of major events was 0.9%, which multiplied by 1.91 gives an estimated rate of all coronary events of 1.8%. The female population rate free of events was therefore 100% - 1.8% = 98.2%.

Charts were constructed to show the absolute risks, calculated with the adapted equation, rounded to the nearest whole figure, for each box of the combination of the risk factor categories. The absolute risks were calculated for an HDL-C concentration of 35-59 mg/dL. The risk was classified in 5 levels: low (<5%), mild (5%-9%), moderate (10%-19%), high (20%-39%), and very high (>39%). A color code was used for the intensity of the risk for the various risk factor combinations, for men and women, diabetic and non-diabetic, individually.

**RESULTS**

Table 1 shows the frequency distribution by sex of the risk factors of the population of Navarra, as well as the values for the Framingham population.

Comparison of the 2 distributions shows that they differ in several categories in a few factors, in both men and women. The most relevant finding here was the high concentration of HDL-C in the population of Navarra. The HDL-C had a mean population value of 63.9 mg/dL (95% confidence interval [CI], 63.4-64.4); 56.7 mg/dL (95% CI, 56.1-57.3) in men and 70.1 mg/dL (95% CI, 69.4-70.8) in women. Likewise, the prevalence of smoking was much lower in Navarra, in both men and women. The data for hypertension, however, showed a higher prevalence in the Navarra men but not the women.

Concerning the incidence rate of coronary events, the rate in both sexes was significantly lower in Navarra (Table 1).
La concentración de 60 mg/dL fue aproximadamente 50% mayor que la vista en las tablas, y para los valores menores de 35 mg/dL la correspondencia se mantuvo. Este ajuste se propone para simplificar el uso de las tablas.

La inclusión del efecto de HDL-C en la estimación del riesgo en nuestro contexto es definitivamente importante, ya que 73% de las mujeres y 36% de los hombres de 35 a 74 años de edad en Navarra tenían un nivel de HDL-C ≥60 mg/dL.

**DISCUSSION**

Presentamos las tablas propuestas para el riesgo general de 10 años en la población de Navarra, basado en la ecuación de Framingham-Wilson, calibrada según la prevalencia de factores de riesgo y la tasa de eventos registrados para Navarra.

Generalmente hablando, el riesgo calculado con el modelo RICORNA (Framingham-Navarra) para diferentes combinaciones de factores de riesgo es significativamente más bajo que los calculados con las tablas originales de Framingham. La reducción fue notable en el grupo de mujeres no-diabéticas.
Several different epidemiological studies have shown that mathematical functions based on the original data of the Framingham cohort overestimate the absolute coronary risk in populations with a lower than in the original Framingham study. The proportion of coronary risk estimations that were moderate to very high was 1.82 times lower in the adapted tables than in the original tables.

### Figure 1.
Risk of myocardial infarction, fatal or non-fatal, with or without symptoms, or angina in non-diabetic men with high-density lipoprotein cholesterol (HDL-C) concentrations of 35-59 mg/dL.

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<th>HDL-C (mg/dL)</th>
<th>Risk to 10 Years</th>
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<td>Very High</td>
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low incidence of coronary disease and associated mortality rate. Navarra is among the regions of the developed world with the lowest mortality rates, both for overall mortality due to cardiovascular disease and for mortality due to coronary heart disease, as well as for cerebrovascular disease. The results of our study are in accordance with these data and corroborate the starting hypothesis.
that the coronary risk is overestimated in our population.

The guidelines of the national and international scientific societies are aimed at promoting the adaptation of the recommendations concerning cardiovascular prevention to the particular characteristics and circumstances of the end-user population. In accordance with these

Figure 3. Risk of myocardial infarction, fatal or non-fatal, with or without symptoms, or angina in non-diabetic women with HDL-C of 35-59 mg/dL.

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recommendations, various Spanish research groups over recent years have undertaken notable efforts to obtain precise, reliable prediction models, adapted to the characteristics of the Spanish population. For instance, the 1998 version of the Framingham equation has been calibrated according to the data for the population of Gerona, and the REGICOR equation obtained. With the same method as that
has a population cohort of 4168 persons aged between 35 and 84 years, though the follow-up period is still short (4 years). This therefore explains the need for the time being to use equations generated in other populations or else to adapt these equations. Spain is a country with a wide geographic variability in the pattern of the incidence and mortality from coronary heart disease,24-26 as well as marked geographic differences in the burden and distribution of risk factors that could contribute to the explanation of these differences.27,28 In this study we characterized a representative sample of the population of Navarra with an HDL-C concentration of 63.9 mg/dL (56.7 mg/dL in men and 70.1 mg/dL in women). These figures are higher than those of other regions in our setting, especially those found for women.27,28 Numerous studies have shown that HDL is one of the most important independent protectors against the arteriosclerosis that underlies coronary heart disease.29-31 The high concentration of HDL-C found in the population of Navarra may well contribute to the low coronary morbidity and mortality.

Comparison of the risk tables adapted for Navarra with those of REGICOR7 shows that the risk of a coronary event is slightly higher in the population of Navarra, reflecting the different pattern of prevalence of risk factors included in the model, in spite of the fact that the 2 populations have similar rates of heart disease. In this context, it seems justified to have risk tables adjusted to the particular characteristics of our population. The present study

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HDL-C indicates high-density lipoprotein cholesterol.
was designed to respond to this need using a well-established method. 

The study reported here has certain limitations that should be taken into account. One limitation is that the tables shown have not been validated in a prospective, population-based study. Nevertheless, the method used to adapt the tables has been used before and has a reasonable guarantee of validity.

Population data are not available that would enable us to confirm that the proportion of silent AMI and angina with respect to the total number of coronary events in Navarra is similar to that found in the Framingham study. This option, chosen as a measure of safety, endows the tables with a conservative character, as is it very unlikely that the true values in Navarra are greater than those of the American city.

Finally, the cardiovascular risk equations, despite their limitations, are the best screening tool that we currently have for the selection of patients in whom to apply the various different primary prevention strategies, as well as to determine their intensity. Any equation nowadays is far from being an ideal tool, and it should simply be considered as useful in primary prevention and is no substitute for the correct clinical judgment, and any specific conditions must be taken into account when the tool is applied.

**CONCLUSIONS**

We believe that the tables proposed here may be useful instruments for the more precise estimation of the overall coronary risk of the population of Navarra. The RICORNA equation answers the need for tables to calculate the coronary risk adapted to the characteristics of the population of Navarra.

Use of the original Framingham equation should be avoided as it overestimates excessively the true risk of coronary heart disease in the population of Navarra.

The population-based cohort in the RIVANA Study could provide information that will soon enable the RICORNA equation to be validated.

**REFERENCES**


**APPENDIX**

The predictive equation is based on the calculation of the likelihood of an event using the Cox proportional hazards model:

\[ P_{m} = 1 - \exp(-\exp(\sum_{i} b_{i}x_{i} \log(1+e))) \]

where \( P_{m} \) is the probability of a coronary event in a time \( t \) (10 years) in a person with a group of risk factors \( x \), \( \sum_{i} (b_{i}x_{i}) \) is a linear equation of the average risk of the group of values \( x_{i} \), of each category for each factor in the population, and \( \sum_{i} (b_{i}x_{i}) \) is the linear equation calculated for the group of values \( x \), that represents the value of each factor in a specific person. In both linear equations, \( b_{i} \) is the coefficient of the Cox proportional hazards equation for each category of each factor considered. \( S_{m} \) is the probability that no coronary event will occur in time \( t \) in the study population and \( e \) is the base of the natural logarithms. \( \sum_{i} (b_{i}x_{i}) \) is obtained by multiplying the coefficients \( b_{i} \) of the model that appears in Table 1 by the value \( x_{i} \) of each one of that person’s risk factors, using (1) when the factor degree is present and (0) for the remaining factor degrees. In the case of age, \( x_{1} \) is replaced by the age in years and, additionally, in women by the age squared, and diabetes and smoking by (0) or (1), depending on whether they are or are not present. \( \sum_{i} (b_{i}x_{i}) \) is obtained by multiplying the same coefficients \( b_{i} \) by the prevalence of the risk factors in the study population. For a 54 year-old woman, with a total cholesterol of 246 mg/dL, HDL-C of 54 mg/dL, SBP of 143 mm Hg and DBP of 89 mm Hg, with diabetes and a non-smoker, the value would be calculated as follows:

\[ \sum_{i} (b_{i}x_{i}) = 0.3377(54) + (-0.0027(54) - 0.018(1) + 0.2439(1) + 0(1) + 0.2629(1) + 0.5963(1) + 1) = 11.4 \]

\[ S_{m} = 1 - 0.018 = 0.981 \]

\[ P_{m} = 1 - 0.981 = 0.019 \]

The probability of a woman with the characteristics described above having a coronary event in our setting in the next 10 years is 8.9%, a very similar figure to that seen in the box corresponding to the risk tables presented (9%).