Available online at www.sciencedirect.com
ScienceDirect
Preventive Medicine 47 (2008) 61–65
Preventive Medicine
www.elsevier.com/locate/ypmed

Ten-year risk prediction in French men using the Framingham coronary score: Results from the national SU.VI.MAX cohort

A.-C. Vergnaud [a,*], S. Bertrais [a], P. Galan [a], S. Hercberg [a,b], S. Czernichow [a,b]

[a] INSERM, U557, Bobigny, France; INRA, U1125, Bobigny, France; CNAM, EA3200, Bobigny, France; Univ Paris13; CRNH-IdF, Bobigny, F-93017, France
[b] Departement de Santé Publique, Hôpital Avicenne (AP-HP), F-93017 Bobigny, France

Available online 10 March 2008

Abstract

Objective. To evaluate the ability of the Framingham risk function to predict the 10-year coronary heart disease (CHD) risk in French men.

Methods. 3440 men, aged 45 to 60years, free of CHD at baseline, were selected from the SU.VI.MAX cohort. The expected number of event, obtained from applying the Framingham risk score to the baseline SU.VI.MAX biological and clinical data of 1994/1996, were compared to the actual risks observed in the cohort. The accuracy of the Framingham risk function was assessed using the area under the receiver operating characteristic (ROC) curve.

Results. The overall Framingham risk function predicted twice as many CHD events than observed. The area under the ROC curve for Framingham risk score was 74%.

Conclusion. The Framingham risk function may discriminate between high risk from low risk subjects, but it is not valid for estimating absolute 10-year CHD risk in this French population.

Keywords: Framingham; Coronary; Risk equation; Score; Discrimination; Calibration

Introduction

Despite a decrease in incidence during the last decades (Immonen-Raiha et al., 1996; Lang et al., 1999; McGovern et al., 2001), coronary heart diseases (CHD) still account for a majority of deaths worldwide (Murray and Lopez, 1997; Sans et al., 1997) and are therefore an issue of primary concern in public health policies. Risk functions have been developed in order to estimate individual CHD risk depending on risk factors levels. These equations would be useful in clinical practice for determining which patients might need medical intervention or for educating patients about the necessity of risk factor reduction.

The most commonly used risk function is based on data from the Framingham cohort, which was initiated in the 1970's in an American population (Anderson et al., 1991). The Framingham equation estimates the probability of CHD within 4–12years according to age, sex, systolic blood pressure, total cholesterol/HDL-cholesterol ratio, diabetes, smoking status and electric left ventricular hypertrophy. High risk subjects have been defined as those with estimated 10-year CHD risk over 20%. However, several studies that assessed the applicability of Framingham risk model in various populations showed mixed results and its validity in low CHD rate countries is particularly questioned (Eichler et al., 2007). Few Several studies have investigated this issue in French populations (Bastuji-Garin et al., 2002; Empana et al., 2003; Laurier et al., 1994), but none with a follow-up of over 10years.

The aim of this study was to evaluate the predictive accuracy (discrimination, calibration) of the Framingham risk function in middle-aged men from a large French prospective study.

Methods

Study population

Subjects were participants in the SU.VI.MAX ("SUpplémentation en VItamines et Minéraux AntioXydants") Study, a randomized primary prevention

* Corresponding author. Centre de Recherche en Nutrition Humaine Ile-de-France, UMR (INSERM/INRA/CNAM/U.P13), UFR SMBH, 74 rue Marcel Cachin, 93017 Bobigny cedex, France. Fax: +33 01 48 38 89 31.
E-mail address: ac.vergnaud@uren.smbh.univ-paris13.fr (A.-C. Vergnaud).

0091-7435/$ - see front matter © 2008 Published by Elsevier Inc.
doi:10.1016/j.ypmed.2008.02.023

trial initially designed to test the effect of antioxidant vitamins and minerals, at nutritional doses, on the incidence of cardiovascular diseases and cancers (Hercberg et al., 1998; Hercberg et al., 2004). The 13017 subjects included were followed yearly since 1994/1995. They were invited to a medical visit each year, for either blood sampling (from 1994) or clinical examination (from 1995). The protocol was approved by a medical ethics committee and the national committee for the protection of privacy and civil liberties.

For the present analyses, the population was restricted to men due to the low incidence of CHD in women. Among the 5141 men randomized to participate in the intervention trial, 113 subjects were further excluded because they withdrew consent within 3days after inclusion or because they were found to be outside age range and declare ineligible. We included only subjects who attended the first medical visits (1994/1995 for the blood sampling and 1995/1996 for the clinical examination), with available data required to calculate the Framingham prediction score ($n=3492$). We excluded subjects with a past history of CHD ($n=42$), and those with incident CHD between the first biological and clinical examinations ($n=10$). In total, the present analyses were based on 3440 men aged 45 to 60years at baseline. Among these 3440 men, 50.5% received the antioxidant supplementation.

Baseline measurements

Blood samples were obtained after a 12-h fast. All biochemical measurements were centralized. Blood glucose, total cholesterol and triglycerides (TG) were measured using an enzymatic method (Advia 1650, Bayer Diagnostic). Apolipoprotein A and apolipoprotein B were also measured (nephelemetric assay, BNA Behring) which allowed us to calculate LDL-cholesterol using the Planella's equation (Planella et al., 1997) and then HDL-cholesterol using the Friedewald's formula (Friedewald et al., 1972). Systolic and diastolic blood pressures (SBP, DBP) were measured one time on each arm using a standard mercury sphygmomanometer in subjects who had been lying down for 10 min. The mean of the two measurements was used for analysis. If SBP was above 160 mmHg or DBP was above 90 mmHg, BP was measured after another 5 min rest, and the lowest value was kept. Smoking status and drug use were obtained from a questionnaire at enrollment (1994).

Coronary events

Information about coronary events was obtained from participant reports and from data collected at yearly visits. Participants were asked to report any hospitalizations or other health problems on a monthly basis via Minitel. The Minitel was a small terminal widely used in France as an adjunct to the telephone. Once a possible event was suspected, all relevant records, including results of diagnostic tests and procedures were obtained from hospitals, laboratories, or institutions or from the participants by the SU.VI.MAX medical staff and were examined at the study coordinating center. If any abnormality was detected at yearly visits, results were sent to the participant to be forwarded to his or her physician. Contact was maintained with the participant and the physician in order to verify the conclusions of follow-up visits. If the family or the SU.VI.MAX investigators reported that a patient had died, the underlying cause was verified with the official death certificate. In the case of long term lack of contact by a participant, his or her vital status was ascertained through the national register using birthday and district of birth. Staff members of the coordinating center regularly reviewed medical information and reports. All the individual health events were then coded using the Tenth International WHO Classification of Diseases (ICD), after consultation with the Technical Expert Committee for validation of individual clinical events. In the present study, coronary events were registered during 10years of follow-up for each subject in order to estimate the individual 10-year Framingham risk score.

Statistical analyses

Results are reported as percentages or mean (m)±standard deviation (SD). TG concentrations, fasting blood glucose and total cholesterol/HDL-cholesterol ratio were log-transformed due to skewed distributions, therefore geometric means and 95 % confidence intervals (95% CIs) are presented.

Analysis were performed in three steps. First, using baseline data, we calculated Framingham risk score which estimates the probability of developing CHD (i.e. coronary death, myocardial infraction, angina pectoris or coronary insufficiency) within 10years (Anderson et al., 1991). Since left ventricular hypertrophy was not assessed by central reading in the present study, this variable was entered as absent for all participants. This choice was also made in the Framingham cohort when left ventricular hypertrophy was not available (Anderson et al., 1991). Secondly, we performed a Cox model in the SU.VI.MAX. population using exclusively the same risk factors as in the Framingham risk function, named "the SU.VI.MAX. risk estimation". Thirdly, we assessed the quality of the Framingham risk score according to three methods: equality of regression coefficients, calibration and discrimination.

Equality of regression coefficients

To test the equality of regression coefficient, we performed another Cox model using the same categorical CHD risk factors as in the model developed by Wilson et al. in the Framingham study (Wilson et al., 1998). These covariables were age, blood pressure (4 categories: optimal+normal: SBP ≤ 129 mmHg; DBP ≤ 84 mmHg; high normal: 130 ≤ SBP ≤ 139 mmHg; 85 ≤ DBP ≤ 89 mmHg; Hypertension stage I: 140 ≤ SBP ≤ 159 mmHg; 90 ≤ DBP ≤ 99 mmHg; Hypertension stage II-IV: SBP ≥ 160 mmHg; DBP ≥ 100 mmHg), LDL-cholesterol (3 categories: LDL < 130 mg/dl; 130 ≤ LDL < 160 mg/dl; LDL ≥ 160 mg/dl), HDL-cholesterol (3 categories: HDL < 35 mg/dl; 35 ≤ HDL < 60; HDL ≥ 60 mg/dl), smoking (yes/no) and diabetes (defined as patients having a fasting blood glucose ≥ 140 mg/dl or treated with hypoglycemic agents such as oral antidiabetics or insulin). To evaluate the difference of prediction for each risk factor according to cohorts (Framingham or SU.VI.MAX), we compared HR for CHD risk recently published from the Framingham study with those corresponding in the SU.VI.MAX cohort, using z-tests.

Calibration

To test the calibration of the Framingham risk score (how closely the predicted probabilities reflect actual risk), we compared predicted versus observed number of CHD events by quintiles of Framingham risk scores.

Discrimination

Discrimination quality (ability to separate subjects with a high risk from those with a low risk) of Framingham function was assessed using the area under the receiver operating characteristic (ROC) curve. the area under the ROC curve

Table 1
Sample characteristics (France, 1994/95–2004/05, $n=3440$)

	Mean±SD
Age (years)	52.0±4.7
SBP (mmHg)	129.4±13.8
DBP (mmHg)	83.5±8.5
Total cholesterol (mmol/l)	6.2±1.0
HDL-c (mmol/l)	1.7±0.3
LDL-c (mmol/l)	3.9±0.7
Total cholesterol/HDL-c *	3.62 [3.60–3.64]
Apolipoprotein A1 (g/l)	1.5±0.2
Apolipoprotein B (g/l)	1.2±0.2
Triglycerides (mmol/l) *	1.15 [1.13–1.17]
Fasting blood glucose (mmol/l) *	5.90 [5.87–5.92]
Smoking status (%)	13.7
Diabetes (%) **	2.4
Antihypertensive treatment (%)	9.3
Median duration of follow-up (years)	10
Coronary events, *n* (%)	128 (3.7)
Angina pectoris	59
Non-fatal myocardial infarction	52
Sudden death	7
Coronary revascularisation	10

SBP, systolic blood pressure, DBP, diastolic blood pressure, HDL-c, high-density lipoprotein; LDL-c, low-density lipoprotein.
* Geometric means [95% CI].
** Fasting blood glucose ≥ 140 mg/dl or treatment (oral antidiabetic or insulin).