Cardiovascular Risk in People Older Than 55 Years and Cognitive Performance at 5 Years: an Estimation Model Based on Spanish Population. NEDICES-2-RISK study.

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Dementia is unique in terms of prevalence, cost and impact. Any small advance in the prevention of dementia would benefit millions of people. Current data indicate that cardiovascular risk factors increase the risk of cognitive decline. The cardiovascular risk estimation by means of cardiovascular risk functions seems to be useful in the prediction of risk of cognitive deterioration. However, in the Spanish population, the incidence of coronary heart disease and stroke are lower than expected taking into account the cardiovascular risk factors.

The purpose of this study is to study the association between the cardiovascular risk of the study population, using the Framingham REGICOR and FRESCO cardiovascular risk functions, and the cognitive performance after 5 years of follow-up. The identification of individuals who have a high risk of cognitive decline in later years using predictive models of vascular risk would be a good approach to the prevention of cognitive impairment.

OBJECTIVES

Primary

The main objective is to evaluate the association between cardiovascular risk, calculated with the Framingham REGICOR and FRESCO risk functions, and the cognitive decline after 5 years of follow-up in the NEDICES-2-RISK cohort.

Secondary

(a) To describe the profile of patients according to their cardiovascular risk

(b) To study the association between each cardiovascular risk factor in isolation and the cognitive decline after a 5-year follow-up

(c) To study the association between calculated cardiovascular risk with the risk functions Framingham REGICOR and FRESCO and other non-neurological diseases

(d) To analyze possible mediating effects between cardiovascular risk, cognitive decline and lifestyle

(e) To investigate the effect of mediation of cognitive reserve indicators (verbal intelligence, education, occupation and lifestyle) on cognitive deterioration in different tests of the neuropsychological evaluation.

METHODS / DESIGN

Design. Prospective longitudinal analytical observational study of cohort with 5 years of follow-up.

Scope of study. The scope of study is the Primary Care setting of the Spanish national health system.

Study population. The population of the NEDICES-2-RISK study are patients aged 55 to 74 who were included in the NEDICES-2 cohort (2014-2017), in which the presence of dementia in the initial neuropsychological evaluation was ruled out. The population of the NEDICES-2 study comes from the list of users with health cards of the participating doctors of the health centers

included and the sample selection was carried out by random sampling stratified by sex and age in groups of 5-year increase of people of 55 years and over.

Patient selection criteria.

1. Inclusion criteria:
    a. Age 55 to 74 years
    b. Agreeing to participate and provide written informed consent
    c. Having completed the neuropsychological assessment of the NEDICES-2 study
2. Exclusion criteria:
    a. To have dementia at the beginning of the study

Sample size

The sample size is 965 patients.

Procedure

Patients who agree to participate and sign the informed consent will undergo a neuropsychological assessment (after 5 years of follow-up) with the same test battery as in the first evaluation (performed between 2014-2017) by trained interviewers and The clinical variables (morbidity and cardiovascular risk factors) and treatment variables will be collected through a clinical interview.

Anthropometric variables, as well as chronic diseases and medication will be collected by the patient's doctor. The rest of the information will be collected by interviewers. See Table 1.

Table 1. Variables and measurements collected during the study

	Variables collected at baseline	Variables collected after 5 years of follow-up
Social and demographic variables collected by interviewers:		
- Age	X	
- Gender	X	
- Marital status	X	X
- Education	X	
- Profession	X	X
Health related variables collected by primary care physicians:		
- Blood pressure	X	X
- Cholesterol levels	X	X
- Weight and height	X	X
- Morbidity	X	X
- Pharmacotherapeutic treatment	X	X
Variables on lifestyle and health status collected by interviewers:		
- Alcohol consumption	X	X
- Caffeine consumption	X	X
- Tobacco use	X	X
- Physical activity	X	X
- Mediterranean diet		X
- EuroQoL 5D-3L	X	X
- Quality of life measurement scales	X	X
Neuropsychological assessment carried out by interviewers:		
- CES-D scale		
- Word accentuation test	X	X
- MMSE 37	X	X
- Instrumental activities of daily living, Pfeffer scale	X	X

- Semantic Verbal Fluency test	X	X
- Six-Object Memory Recall Test	X	X
- Trail Making test	X	X
- Clock-drawing test	X	X
Exposure variables calculated by the research team:		
- Framingham REGICOR function	X	X
- FRESCO function	X	X

CES-D scale: Center for Epidemiologic Studies Depression Scale; MMSE-37: Mini Mental State Examination 37 item-version; FRESCO: Función de Riesgo Española de acontecimientos Coronarios y Otros; REGICOR: Registre Gironí del Cor

STATISTICAL ANALYSIS

Initially, a review of the quality of the study data will be carried out: detection of errors in the coding, missing data and possible biases related to representativeness of the sample (for example, selection of subjects and loss in follow-up, among others).

Different descriptive statistics will be used to analyze the baseline characteristics (qualitative and quantitative variables) of the patients included in the study. For the categorical variables, such as the sociodemographic and clinical variables of the patients, they will be analyzed and represented by frequency tables (globally and by strata). For numerical variables, means and standard deviations will be calculated. Patients who leave the study will be described, including the characteristics of the patients and the reasons for the loss of follow-up.

The bivariate analysis will try to find the presence of a significant association between baseline cardiovascular risk and the score obtained in the cognitive and functional tests (MMSE 37, Trail Making Test, Semantic Verbal Fluency test, Six-Object Memory Recall Test, Clock drawing test, Pfeffer functional assessment scale). For this, the Pearson´s Chi-square and Spearman statistical coefficients will be used, as appropriate.

Finally, multivariate analyses (multiple regression, analysis of covariance) will study the association between baseline cardiovascular risk (4 categories) and the psychometric and functional tests adjusted for relevant sociodemographic and clinical variables as potential confounding factors. Linear regression models of mixed effects (which take into account intrasubject variability when considering repeated measures) will be used, considering as a dependent variable the score obtained in each of the tests studied (one model for each scale) and as an independent, the cardiovascular risk basal (4 categories).

In addition, the reliable change in each of the tests will be analyzed to verify which clinically significant changes occur in subjects with high cardiovascular risk. The reliable change will be analyzed following the Hsu method, while the McSweeny and Duff method will be used to calculate simple and complex standards based in regression to estimate the cutoff points of change adjusted for age, sex and educational level. The data analysis will try to adhere to the standards for the diagnostic accuracy report. A statistically significant association will be considered when the contrast statistic has $p < 0.05$.