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Original Article

Ten years cardiovascular risk estimation according to Framingham score and non HDL-cholesterol in blood donors

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ABSTRACT

Cardiovascular disease (CVD) is currently the primary cause of morbidity and mortality.
Aims: (1) Assess the 10 years risk for CVD in Argentinean blood donors, according to Framingham score (updated by ATP III), (2) evaluate the prevalence of the MS, (3) evaluate non HDL-cholesterol level in this population as other risk for CVD.
Materials and methods: A prospective, epidemiological, transversal study was performed to evaluate 585 volunteer blood donors for two years. Non HDL-C was calculated as total cholesterol minus HDL-C and we evaluated the 10 years risk for CVD according to Framingham score (updated by ATP III).
Results: Metabolic syndrome prevalence was estimated according to ATP III and IDF criteria. Non HDL-C was (media ± SD) 178.3 ± 48.0 mg/dl in participants with MS and 143.7 ± 39.3 mg/dl without MS (ATPIII) and 160.1 ± 43.6 mg/dl in participants with MS and 139.8 ± 43.1 mg/dl without MS (IDF). Participants with MS presented an OR of 3.1; IC 95% (2–5) of CVD according to de Framingham score.
Conclusion: Individuals with MS and elevated non HDL-C are at a higher estimated risk for cardiovascular events in the next 10 years according to the Framingham risk score.

1. Introduction

Cardiovascular disease (CVD) is rapidly increasing all over the world, mainly as a consequence of physical inactivity and over nutrition [1]. CVD is the lead cause of death in western countries [2] and that is the reason for the importance of knowing the prevalence of its associated risk factors (RF). They include dysglycemia, high blood pressure, elevated triglyceride levels, low high-density lipoprotein cholesterol levels, and obesity (particularly central adiposity). Metabolic syndrome (MS) is defined by both, the Adult Treatment Panel III of the National Cholesterol Education Program, Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III) [3] and the International Diabetes Federation (IDF) [4] as the presence of at least 3 of these conditions. However, IDF has the strictest cut off for abdominal obesity.

Risk factor scoring in ATP III derives from an update of the Framingham database and methodology reported by Wilson et al. [5]. In the Framingham calculation of 10-year risk the risk factors there are included: age, total cholesterol, HDL cholesterol, systolic blood pressure and cigarette smoking. Regarding the lipid profile, ATP III identified non HDL-cholesterol (non HDL-C) as a secondary target after LDL-C because its accurate measurement is more readily available in clinical practice. Non HDL-C is calculated as total cholesterol minus HDL-C [6]. The addition of non HDL-C to the Lipid Panel reflects the recognition of this calculated value as a predictive factor in cardiovascular disease based on the ATP III [3]. As several of the risk factors for CVD mentioned above could be targeted it is useful to know their prevalence in order to design and implement primary prevention programs accordingly.

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The goal of this study was: (1) to assess the 10 years risk for CVD in blood donors, according to Framingham score (updated by ATP III), (2) to evaluate the prevalence of the MS, (3) to evaluate non HDL-cholesterol level in this population as other risk for CVD.

2. Subjects and methods

2.1. Study design

A prospective, epidemiological, transversal study was performed in order to evaluate volunteer blood donors for two years. We enrolled 605 consecutive subjects (165 women, 37 ± 12 years; 420 men, 36 ± 11 years), who attended the Hemotherapy Department from public hospitals of Buenos Aires City. Twenty-two individuals refused to participate in this project an 8 were not included as they did not have 12 h of fasting. All the samples were analyzed at central and endocrine laboratories of the Durand Hospital. Blood samples were taken after 12 h of fasting. Subjects with diabetes, hypertension and/or dyslipidaemia previously diagnosed were excluded. Diabetes was diagnosed according to ADA criteria, hypertension according to The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure and dyslipidaemia according to ATP III criteria

The study had the approval of the ethic committees of each participating hospital according to the Helsinki Declaration and informed written consent was obtained of each subject

2.2. Background and biomedical

These included age, body mass index (BMI), waist circumference (WC) and blood pressure. In order to calculate the BMI, weight and height were obtained from each patient. WC was measured at the middle level between the lateral lower rib margin and the superior anterior iliac crest, in a standing position and always by the same investigator. Blood pressure was measured in a sitting position. A thorough medical examination was performed in order to record general health conditions, medical disorders, lifestyle, smoking, personal and familiar history of cardiovascular risk and physical activity (modified scale from 1 to 4 according to The Da Qing IGT and Diabetes Study) [7].

2.3. Biological tests

After 12 h fasting, blood samples were obtained from peripheral vein puncture following a 15-min rest. Serum samples were separated by centrifugation at 1500 × *g* for 5 min; glucose was measured within the same day. For lipid and lipoprotein determinations, serum was kept at 4 °C until processing, within 48 h. Triglycerides (TG), total cholesterol (TC), high density lipoprotein (HDL-C) and glucose were measured in a Hitachi 917 autoanalyzer by enzymatic colorimetric methods (Roche Diagnostics GmbH, Mannheim, Germany). Intra-assay coefficients of variation and inter- assay coefficients of variation were 1.3% and 2.4% (TG), 1.1% and 2.2% (TC), 1.5% and 2.6% (HDL-C), and 1.1% and 2.2% (glucose), respectively. LDL-C was estimated according to Friedewald and non-HDL-C was calculated as TC minus HDL-C. Insulin was measured by a chemoluminiscent method (Immulite/Immulite 1000 Siemens, USA). CVi and CVe were 8%.

In order to estimate insulin resistance, the homeostasis model assessment for insulin resistance (HOMA) index was calculated as fasting insulin (mU/L) × fasting glucose (mmol/l)/22.5 [8], considering a cut-off value of 2.17, according to previous results [9].

The MS was diagnosed according to the National Cholesterol Education Program (NCEP), Adult Treatment Panel-III (ATP III) (2001) and the International Diabetes Federation (IDF) criteria [4].

Table 1
Metabolic and clinical characteristics of the population.

Risk factors	Females (*n*: 165) Age (years): 37 ± 12 % (CI 95%)	Males (*n*: 420) Age (years): 36 ± 11 % (CI 95%)	*p*
Overweight	37.2 (29.8–44.6)	49.5 (44.4–54.0)	0.012
Obesity	18.3 (12.4–24.2)	21.6 (17.7–25.5)	NS
Central obesity	37.0 (29.8–44.6)	24.3 (20.2–28.4)	0.003
Glycemia ≥ 110 mg/dL	7.0 (2.0–12.0)	8.1 (4.9–11.3)	NS
Total cholesterol ≥ 200 mg/dL	27.2 (18.2–34.6)	41.4 (35.8–45.0)	0.008
Triglycerides ≥ 150 mg/dL	10.0 (4.3–15.5)	26.0 (21.0–30.0)	<0.001
HOMA > 2.17	34.0 (27.9–40.1)	25.0 (14.9–35.1)	NS

NS: non significative.

Patients were classified as having MS, according to ATP-III, if they met three or more of the following criteria: WC > 102 cm in men and >88 cm in women, TG ≥ 150 mg/dL, HDL-C < 40 mg/dL in men and <50 mg/dL in women, systolic and/or diastolic blood pressure ≥130/85 mmHg, and impaired fasting glucose ≥110 mg/dL. Using the IDF definition, patients were classified as having MS if they presented WC ≥94 cm in men and ≥80 in women plus two of the following criteria: TG ≥150 mg/dL, HDL-C < 40 mg/dL in men and < 50 mg/dL in women, systolic and/or diastolic blood pressure ≥130/85 mmHg, and impaired fasting glucose ≥100 mg/dL. Therefore, the studied population was divided into two groups, with and without MS, using both criteria.

We evaluated the 10 years risk for CVD according to Framingham score (updated by ATP III) [3].

2.4. Statistical analysis

Continuous variables data are expressed as mean ± SD and compared by the *t* test. Differences between groups were tested using the independent Student's *t* test for normally distributed data. Pearson or Spearman analyses, for parametric or non-parametric variables, were used to determine correlations between parameters. Categorical variables were compared by χ^2 test. The SPSS 20.0 software package (Chicago, IL) was used for statistical analysis. A $p < 0.05$ was considered significant.

3. Results

The characteristics of the study population according to sex are shown in Table 1. Men presented higher overweight ($p = 0.012$), total cholesterol ($p = 0.008$) and triglycerides ($p < 0.0001$) than women. Women presented waist circumference over the cut off value in a higher percentage than men ($p = 0.003$).

In reference to MS, men presented higher prevalence than women by IDF criteria (tendency, p 0.06) (Table 2).

No differences were observed in Non HDL-C in MS according to ATP-III and IDF. Non HDL-C was higher in subjects with MS than without MS by both criteria: (mean ± SD) 181 ± 48 mg/dL vs.

Table 2
Prevalence of metabolic syndrome.

MS *n* = 385	Study population Frecuency (%)	Males (*n* = 283) Frecuency (%)	Females (*n* = 102) Frecuency (%)	*p*
MS (ATPIII)	86 (22.3)	69 (24.4)	17 (16.7)	0.146
MS (IDF)	126 (32.7)	101 (35.7)	25 (24.5)	0.060

MS: metabolic syndrome (ATPIII) vs. MS (IDF) $p = 0.0017$.

Table 3
Non HDL-Cholesterol according to ATP III and IDF.

MS (n = 385)		Non HDL-cholesterol (mg/dL)	
		(Mean ± SD)	p
IDF	MS	176 ± 46	<0.001
	Without MS	141 ± 38	
ATP III	MS	181 ± 48	<0.001
	Without MS	144 ± 39	

MS: Metabolic syndrome.
p = 0.001 MS vs. Without MS.

Table 4
Risk of CVD according to Framingham score with and without MS.

MS (n = 385)		Framingham risk score (10-year risk)		MS/Without MS odds ratio (CI 95%)
		≥10%	<10%	
		Frecuency (%)	Frecuency (%)	
ATP III	MS	36 (41.4)	50 (16.8)	3.5 (2.1–5.9)
	Without MS	51 (58.6)	248 (83.2)	
IDF	MS	47 (54.0)	79 (26.5)	3.3 (2.0–5.3)
	Without MS	40 (46.0)	219 (73.5)	

MS: Metabolic syndrome. χ^2 test.

144 ± 39 mg/dL (p = 0.001; ATPIII) and 176 ± 46 mg/dL vs. 141 ± 38 mg/dL (p = 0.001, IDF) (Table 3).

As it is shown in Table 4, subjects with MS according to ATP III and IDF presented higher risk for CVD than those without MS.

Participants with MS, by both criteria, presented an OR of 3.1; IC 95% (2–5) of CVD according to de Framingham score.

4. Discussion

In this study in a general population of blood donors we found a high prevalence of metabolic syndrome (MS), taking into account that these people believe to be healthy.

As it was shown above, men presented higher prevalence of MS than women. Similar result was found in a study which took place in blood donors in Mexico [10].

MS includes various risk factors that are found in the same individual placing him at a higher risk for type 2 diabetes mellitus and CVD [11]. We also showed that people with MS and high levels of non-HDL-C have increased risk of cardiovascular events when compared with those without MS.

Atherosclerosis begins in childhood and dislipidemia is one of its major risk factors. Serum concentrations of low density lipoprotein (LDL-C) and high-density lipoprotein (HDL-C) cholesterol are usually used to determine atherogenic risk. However, non-HDL-C is the sum of the masses of cholesterol in the atherogenic ApoB lipoprotein particles and it is considered by the ATPIII as the second target of therapy for people with elevated triglycerides. The treatment goal for non HDL-C is 30 mg/dL above the LDL-C treatment target.

Non HDL-C has been shown to be a better marker of risk in both primary and secondary prevention studies.

A meta-analysis which evaluated 68 long- term prospective studies, mostly in Europe and North America, involving a total of 302430 participants without history of coronary heart disease or stroke at the initial examination found that hazard ratios for CVD with non HDL-C and HDL-C were nearly identical to those seen with ApoB and ApoA1 [12].

The superiority of non HDL-C as a marker of vascular risk is due to the fact that non HDL-C is a better marker of LDL particle number (LDL-P) than LDL-C. In addition, non HDL-C can be used as a surrogate marker of LDL levels when the Friedewald formula cannot be applied [13].

Nevertheless, a recent meta-analysis showed that Apo B is superior to non HDL-C and that non HDL-C is superior to LDL-C as a predictor of cardiovascular risk [14].

There are other reasons for the usefulness of non HDL-C. It is easily calculated from a lipid profile and so it is less expensive than other measures. As opposed to LDL-C, it can be determined from a sample in a non-fasting patient [6].

The increase in the incidence of MS probably decreases the accuracy of risk prediction for coronary artery disease events when LDL-C is used, whereas non HDL-C, Apo B and LDL particle concentration are better predictors in this population [15].

Coronary heart disease continues to be a leading cause of morbidity and mortality among adults all over the world. In this study we used a risk factor scoring for prediction of coronary heart disease using risk factors update of the Framingham score by ATPIII [5] for determining 10-year risk.

Accordingly to Framingham risk score subjects with MS showed an OR of 3.1; CI 95% [2–5] of CVD in the next 10-years.

5. Conclusions

Measurement of non HDL-cholesterol is a simple and economic determination of every cholesterol particles because any additional test is required.

Individuals with MS (diagnosed by ATPIII and IDF) and elevated non HDL-C are at higher risk for cardiovascular events in the next 10 years, data that correlate with Framingham risk score. The present findings are consistent with and reinforce the robust data available.

Conflict of interest

The authors declare no conflict of interest.

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