Evaluation of Cardiovascular Risk in Seven Cities in Latin America: the Main Conclusions of the CARMELA Study and Substudies

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SUMMARY

Assessment of Cardiovascular Risk in Seven Latin American Cities. The Main Conclusions of the CARMELA Study and Substudies To assess the cardiovascular risk of the Latin American population, we conducted a homogeneous population-based sampling study in seven cities of the region following controlled and standardized methods, laboratory tests and physical examination and thus obtain reliable epidemiological data. The CARMELA study (Cardiovascular Risk Factor Multiple Evaluation in Latin America) evaluated 11550 subjects from the general population. The prevalence of hypertension mirrored the world average in 3 cities but was lower in the rest. Hypercholesterolemia was highly prevalent even in countries of different socioeconomic levels. The prevalence of diabetes ranged between 7% and 9% in Mexico City, Bogotá and Santiago de Chile.
Tobacco use was high in both sexes in Santiago and Buenos Aires. Abdominal obesity and the metabolic syndrome were more prevalent in women of low resources. Intima-media thickness and carotid plaque prevalence varied widely. The epidemiological data obtained in the CARMELA study complete the outlook of the cardiovascular risk in our region and indicate the need of rationale urban health policies.

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Abbreviations >

CCAIMT	Common Carotid Artery Intima-Media Thickness.	**TC**	Total Cholesterol
HDL C	Cholesterol in High-Density Lipoproteins	**HDI**	Human Development Index
LDL C	Cholesterol in Low-Density Lipoproteins	**BMI**	Body Mass Index
Non-HDL	CSingle photon emission computed tomography	**IMT**	Intima-Media Thickness

Latin America is undergoing by an epidemiological and nutritional transition, which is characterized by the acquisition of an urban-industrial lifestyle typically associated with an increase of incidence and prevalence of cardiovascular diseases, diabetes and smoking, which causes three quarters parts of the morbidity and mortality in the contemporary world. Many of epidemiological assessments undertook in Latin America have suffered from inconsistencies in the definition of risk factors, population sampling and evaluation methods. Disparities in health resources in the region lead to the need that epidemiological data are available representing each country in order to generate rational policies for surveillance, prevention and intervention.

The CARMELA study (Cardiovascular Risk Factor Multiple Evaluation in Latin America) evaluated 11,550 individuals of both sexes between 25 and 64 years probabilistically selected from the general population in seven big Latin America cities: Barquisimeto in Venezuela, Bogota in Colombia, Buenos Aires in Argentina, Lima in Peru, Mexico City in Mexico, Quito in Ecuador and Santiago de Chile in Chile. The objectives were to assess prevalence of cardiovascular risk factors and distribution of intima-media thickness of the distal wall of common carotid, CCAIMT (Common Carotid Artery Intima-Media Thickness) in individuals of those cities. CARMELA is an observational study, of cross-sectional, with the added value of having been mainly carried out by physicians in clinical practice, integrated into a continental network. The size of the study, method of multistage stratified sampling and its rigorous disign and implementation generated reliable and consistent assessments by the seven cities, thus avoiding the confounding factor in international comparisons of risk given by the heterogeneity between different studies with respect to the age groups included and

other criteria. From this database have been published to the present time, ten papers in international journals indexed in the US and Europe.

We will do a brief overview of methology and main outcomes of this study.

SAMPLING AND SURVEY
The CARMELA study was designed to enroll approximately 1,600 participants per city, with similar numbers of men and women in each one of the four age groups of 10 years. First, the cities were divided into geographical areas and then in primary sampling units (blocks from the city or other appropriate areas), which were randomly selected for a further sampling. The present households in selected primary sampling units were classified into four categories and then a systematic sample was obtained within each category. In category 1 were interviewed all eligible residents aged 25 to 64 years, in category 2 only to residents from 35 to 64 years, in category 3 only to residents from 45 to 64 years, and the category 4 only to residents aged 55 to 64 years. All individuals must give informed consent in writing. The sampling fraction in each category was determined in order to obtain equal probability sampling within each age and sex group. Each resident of the city between 25 and 64 years (and ultimately everyone in each defined age group) had a non-zero predefined probability of selection. Anyone who was within the age limits and lived on the selected addresses was eligible for his/her inclusion, the individuals were only included if they completed the survey and then were referred for clinical, laboratory and ultrasound evaluation to a single medical center previously selected and standardized. Exclusion criteria included people residing in addresses that were not home or were in marginal areas considered dangerous for interviewers, and people who were visiting the selected address. Interviewers, trained and certified by the CARMELA study researchers, used a questionnarie that was adapted from questionnaries validated cardiovascular epidemiology (WHO STEPwise approach to surveillance and US Behavioral Risk Factor Surveillance System) to collect information on demographic and cardiovascular risk factors.

CLINICAL DEFINITIONS
Hypertension: A systolic blood pressure ≥ 140mm Hg and a diastolic blood pressure ≥90mm Hg, or current antihypertensive treatment indication. We obtained two blood pressure readings at rest separated by 5 minutes with a mercury sphygmomanometer, with the individual sitting down. **Hypercholesterolemia:** A serum total cholesterol ≥240 mg/dl. **Diabetes:** A fasting glucose ≥126 mg/dl or diabetes reported by the individual. It was considered **impaired fasting glucose** at value of fasting glucose ≥110 mg/dl and <126 mg/dl. **Controlled value** in a diabetic patient: fasting glucose < 110 mg/dl. **Metabolic syndrome** was difened as the presence of three or more of the following parameters: waist >102cm in men, >88cm in women; triglycerides ≥150 mg/dl; cholesterol joint to high-density lipoprotein <40 mg/dl in men, <50 mg/dl in women; blood pressure ≥130/85mm Hg and fasting glucose ≥110 mg/dl or diabetes reported by the individual. **Obesity:** a body mass index (BMI) ≥30 (Kg/m2) and **abdominal obesity**, a waist circumference

>102cm in men and >88cm in women. **Smoking:** daily or occasional consumption of cigarettes, cigars, or pipe tobacco.

For **blood extraction** the individuals should avoid using laxatives with glycerin for 48 hours and products with glyceron for 24 hours prior to blood extraction. During the prior 12 hours to blood samplings, the individuals could only drink water, black coffee or tea without sugar and the fasting state was confirmed with them.

ULTRASONOGRAPHY
The intima-media thickness of the distal wall of the common carotid and the presence of plaque were assessed by the Mannheim consensus. The common carotid arteries were examined by B-mode ultrasound, with phased-array transducers of 7.5 MHz. The M'AthStd program was used (Intelligence in Medical Technologies, Paris, France) in order to automatically measure the intima-media thickness, the measurements were carried out over a lenght of 10mm and were averaged and quality of the acquisition was evaluated. The data were analyzed centrally on Intelligence in Medical Technologies, Paris, France, where they were sent electronically. The existence of plaque was determined, which was defined as a protrusion within the light that added ≥50% to the thickness of the intima-media surrounding or a maximum thickness >1.5mm in the carotid bifurcation or along the carotid arterial tree.

STANDARDIZATION OF ASSESSMENTS
The methods and devices for clinical and anthropometric measurements were standardized in all centers and the measurements were obtained by trained health personnel, certified and supervised by the CARMELA study researchers. For standardization among all laboratories and quality control, the procedures of Buenos Aires program of external quality assessment were followed, with fortnightly monitoring of performance. A group of medical specialists in vascular ultrasound carried out a centralized training and certification by the CARMELA study researchers and they sent ultrasound images of 3 randomly selected individuals and a standard phantom to the central laboratory (Intelligence in Medical Technologies, Paris, France) for their certification of quality before being allowed to obtain data for the study.

STATISTICAL ANALYSIS
The statistical processing took into account the structure of design and non- equiprobabilistic sample, to produce adjusted data for age and sex distribution of the population of each city. 95% confidence intervals for two-tailed were estimated by PROC SURVEYMEANS (SAS, Version 9.1, Cary, NC), considering the multistage stratified sampling design using CLUSTER and STRATA instructions. Cardiovascular risk was assessed with the algorithm of the Framingham score, which estimates the risk of cardiovascular events at 10 years starting from systolic blood pressure, smoking habit, total cholesterol and cholesterol joint to high-density lipoprotein, age and sex.

The study was carried out in accordance with the Helsinki Declaration, Good Clinical Practice Guidelines and local bioethical laws and regulations.

GENERAL FINDINGS OF THE STUDY

The mean age of the population ranged from 43.6 years for Lima and 45.1 years for Barquisimeto and Bogota and **overall findings of the study** were: the prevalence of hypertension was on average, 18% (9-29%); hypercholesterolemia, 14% (6-20%); diabetes, 7% (4-9%); metabolic syndrome, 20% (14-27%); obesity, 23% (18-27%); and smoking, 30% (22-45%). About 13% of the individuals reported that they had family members with cardiovascular disease and 2% declared that they had suffered a previous heart attack or stroke.

The presence of plaques in the carotid arteries was found in 8% (5-14%) and the CCIMT average was 0.65mm (0.60-0.74mm). All prevalences showed variations between the studied cities. According to the Framingham risk score, 1 in 7 people in the cities of the CARMELA study is at significant risk of suffering a cardiovascular event. Even though there is no evidence that the Framingham score is appropriate for populations outside the U.S., this tool was used as the initial mode to explore risk patterns until it is developed and validated a risk score system for Latin America. (1)

In the analysis of 6,119 **women** (52.97% of the population) showed an increased prevalence of hypertension as early as aged 35 years in Barquisimeto and Mexico City. But also metabolic syndrome and obesity are increasing at an early age in most cities. Smoking was prevalence in younger age group in all cities, but in Buenos Aires and Santiago de Chile this prevalence was compared to that of men hovering around 40%. Diabetes showed a high prevalence as early as aged 45 years in Bogota and Mexico City. Given the presence of risk factors at an early age, time in menopause adjusted for age did not show a significant impact on them, except for high blood pressure and LDL-C, which showed a different behaviour in some cities. HDL-C did not show impairment with time spent in menopause. (2)

The prevalence of **diabetes mellitus** and **impaired fasting blood glucose** was high in almost all the studied cities. Both prevalence of diabetes and impaired fasting blood glucose increased with age. In the age group 55-64 years, prevalence of diabetes was between 9% and 22%, and prevalence of impaired fasting glucose was between 3% and 6%. In individuals with a previous diagnosis of diabetes and specific treatment, glycemic control was only seen in 16.3% of them, although it should be noted that the definition used in our study was as fasting blood glucose and not by the most common method of glycosylated hemoglobin. Individuals with abdominal obesity showed twice higher prevalence of diabetes than those who did not. Those who had hypertension, high triglycerides and increased of CCAIMT mean had also more diabetes. This study confirmed the strong association between abdominal obesity, high triglycerides and increased CCAIMT with presence of diabetes.(3)

The prevalence of **metabolic syndrome** varied according to the considered cities between 14% and 27%. Prevalence was higher in Mexico City (27%) and in Barquisimeto (26%), followed by Santiago de Chile (21%), Bogota (20%), Lima (18%), Buenos Aire (17%) and Quito (14%). In non-diabetics individuals, prevalence was slightly lower. The pattern of association of the components of metabolic syndrome varied by sex, so in women was more often linked with high triglycerides, high blood pressure and glucose abnormalities, while in men was associated to a greater measure with abdominal obesity, high blood pressure and glucose abnormalities. Even though prevalence of the syndrome increased with age, this was more marked in women. The increase in the media thickness of CCAIMT and plaques was more prevalent as increasing numbers of present metabolic syndrome components in the individual. (4)

Dyslipidemia was highly prevalent, with variations, in the seven cities in both men and women. Respectively, for Barquisimeto: 75.5% and 48.7%; for Bogota: 70% and 47.7%; for Buenos Aires: 50.4% and 24.1%; for Lima: 73.1% and 62.8%; for Mexico City: 62.5% and 37.5%; for Quito: 52.2% and 38.1% and for Santiago de Chile: 50.8% and 32.8%. The TC/HDL-C relationship and non-HDL-C level beyond standard suggest high cardiovascular risk in some populations. Despite the high prevalence of hypercholesterolemia, pharmacological treatmen was dispar. Buenos Aires and Santiago de Chile with 45% and 42% respectively, they were the cities where greater use of drugs was reported, followed by Mexico City (22%), Lima (20%); Bogota (18%), Barquisimeto (8%) and Quito (8%). Individuals with elevated total cholesterol jointly presented a higher prevalence of other risk factors. (5)

With regard to **knowledge, diagnosis** and **treatment of risk factors**, as well as adherence to treatment and causes of non-adherence, the study showed that in addition to strengthening early diagnosis of the factors, there is a need to improve the patients' education. The frequency of previous diagnosis was acceptable for hypertension and diabetes (64% and 78% respectively, of affected individuals), but relatively low for hypercholesterolemia (41%). 88% of individuals affected by hypercholesterolemia, 67% of those had diabetes and 53% of hypertensive patients were without treatment. In those receiving drug, control values reached only 51% of hypertensive patients, 16% of diabetics and 52% of hypercholesterolemic. Adherence to treatment was observed in 69% in hypertensive, 63% in diabetics and 66% in the hypercholesterolemic patients. (6)

With respect to **hypertension**, according to age group in question between 13.4% and 44.2% of the population of these seven cities showed that they had this risk factor. Most hypertensive patients had other risk factors. Blood pressure increased with age in men and women and pulse pressure mainly increased in the group of 55 to 64 years. The prevalence range was between 9% for Quito and 29% for Buenos Aires. The range of uncontrolled hypertension oscillated from 12% for Lima and 41% for Mexico City. In addition to hypertension, most of them had other risk factors, only 9.19% of the affected population did not present other risk factors besides hypertension. Borderline values of blood pressure were observed in 5% to 15%

of the individuals of all participating cities.(7)

Smoking was highly prevalent in the seven cities, with variations in the pattern of use between them. Prevalence was very high for Santiago de Chile and Buenos Aires (45.4% and 38.6%, respectively), with similar values for men and women. In other cities, men smoked more than women, especially in Quito (49.4% vs 10.5%). In men, peak of prevalence was observed in the two younger groups (25-34 and 35-44 years). In Buenos Aires, men and women consumed a high average of cigarettes per day (15.7 and 12.4, respectively). Men were initiated on average earlier than women, ranging in age of onset between 13.7 and 20.0 years vs 14.2 and 21.1 years respectively. Passive smoking, defines as exposure to snuff smoke in the workplace at least 5 hours daily, was more prevalent in Barquisimeto (28.7%), followed by Buenos Aires (26.8%) and Santiago de Chile (21.5%). The higher prevalence of ex-smokers was observed in men of Buenos Aires, Santiago de Chile and Lima (30.0%, 26.8% and 26.0% respectively).(8)

There was a strong correlation between **CCAIMT** and **present risk factors**. In all the cities and in both sexes, CCAIMT increased with age and also with the number of present risk factors in individuals. A linear trend was observed, statistically significant, when the media CCAIMT was related to the number of present risk factors (p <0.001). After adjusting for gender and age, in every city presence of metabolic syndrome showed a strong association with CCAIMT increased (p <0.001). In some cities was also statistically significant the CCAIMT increased association with presence of hypercholesterolemia, obesity and diabetes (p <0.001). In multivariate analysis, hypertension showed an independent association with increased CCAIMT in all cities (p <0.001). CARMELA was the first large-scale population study which provided CCAIMT reference values according to sex and age in Latin American cities and showed the CCAIMT increased with presence of risk factors and in particular with metabolic syndrome. (9)

With regard to the relationship between **socioeconomic status** and **obesity** were found interesting results. It was analyzed by sex the relationship of educational level with BMI, waist circumference and metabolic syndrome. Participants in each city were divided according to the HDI (Human Development Index) of each country. An inverse gradient between socioeconomic status and BMI was present uniformly in women in places with high HDI (Buenos Aires, Santiago de Chile and Mexico City), but not in the medium HDI group (Barquisimeto, Bogota, Lima and Quito), in which two cities showed an inverse gradient and two others did not. In men did not show clear socioeconomic gradients. The results for waist circumference and metabolic syndrome were similar to those of BMI. In women (more than men), the found results give support to the hypothesis that obesity is associated with poverty and the concept extends to abdominal obesity and metabolic syndrome. This analysis confirms that obesity should be consideres as a disease socially generated and a disadvantage status indicator. (10)

CONCLUSIONS

We conclude that the epidemiological data collected in the CARMELA study complete the picture of cardiovarcular risk in our region and show that prevalence of these risk factors in major cities in Latin America indicates the need for rational health policy. These data will help shape America`s response to the changing situation of risk associated with epidemiological and nutritional transition.

RESUMEN

Evaluación del riesgo cardiovascular en siete ciudades de Latinoamérica: las principales conclusiones del estudio CARMELA y de los subestudios

Introducción

Para evaluar el nivel de riesgo cardiovascular de la población latinoamericana se diseñó un estudio en siete ciudades de la región a fin de realizar un muestreo poblacional homogéneo con metodología única, exámenes de laboratorio y físicos estandarizados y controlados para obtener así datos epidemiológicos confiables. El estudio CARMELA (Cardiovascular Risk Factor Multiple Evaluation in Latin America) evaluó 11.550 sujetos de la población general. Los resultados mostraron que la hipertensión tuvo una prevalencia equiparable a nivel mundial sólo en tres ciudades, en tanto que en el resto fue menor. La hipercolesterolemia fue muy prevalente aun en ciudades de diferente nivel socioeconómico. La diabetes se halló entre el 7% y el 9% en Ciudad de México, Bogotá y Santiago de Chile. El tabaquismo fue muy alto en ambos sexos en Santiago de Chile y en Buenos Aires. La obesidad abdominal y el síndrome metabólico predominaron en las mujeres de bajos recursos. El espesor íntima-media y la prevalencia de placa carotídea tuvieron una amplia variación entre ciudades.

Los datos epidemiológicos recabados en el estudio CARMELA completan el panorama del riesgo cardiovascular de nuestra región y muestran que su prevalencia indica la necesidad de contar con políticas de salud racionales.

Palabras clave >   Riesgo cardiovascular - Factores de riesgo Factores socioeconómicos - Espesor miointimal carotídeo – Placa carotídea - Estudio poblacional

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APPENDIX

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