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ATTRIBUTABLE RISKS FOR ACUTE MYOCARDIAL INFARCTION IN FOUR COUNTRIES OF LATIN AMERICA

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Abstract This multicenter case control study investigated, in four countries of America, the proportions of acute myocardial infarction (AMI) attributable to cholesterol, smoking, hypertension, body mass index, diabetes and family history of coronary heart disease (attributable risks, AR). AR were estimated using information from 1060 cases of AMI and 1071 controls from Argentina, 323 cases of AMI and 314 controls from Cuba, 200 cases of AMI and 200 controls from Mexico and 266 cases of AMI and 264 controls from Venezuela. AR were obtained from the prevalence of coronary risk factors in the cases and the corresponding Odds Ratio (OR) derived through appropriate multivariate models. The AR for AMI observed for hypercholesterolaemia were the following: Venezuela 27%, Mexico 3%, Cuba 30% and Argentina 36%; for diabetes: Venezuela 10%, Mexico 15%, Cuba 5% and Argentina 7% and for body mass index: Venezuela 12%, Mexico 3%, Cuba 19% and Argentina 17%. The same risk factor may have a different attributable risk in different populations. Together, hypercholesterolaemia, hypertension, smoking, diabetes, body mass index and family history of coronary heart disease accounted for 76% of all cases of AMI in Venezuela, 70% in Mexico, 81% in Cuba and 79% in Argentina. The knowledge of attributable risks could have important implications for public health strategies, especially in those countries with limited health care resources.

Key words: smoking, cholesterol, coronary risk factors, diabetes, hypertension

Resumen ***Riesgos atribuibles para el infarto agudo de miocardio en cuatro paìses de AmÈrica Latina.*** Este estudio caso-control y multicéntrico, investigó en cuatro países de América, la proporción de casos de infarto agudo de miocardio (IAM) atribuidos al colesterol, tabaquismo, hipertensión, índice de masa corporal e historia familiar de enfermedad coronaria (riesgo atribuible, RA). Los RA fueron estimados a partir de la información de 1060 casos de IAM y 1071 controles de Argentina, 323 casos de IAM y 314 controles de Cuba, 200 casos de IAM y 200 controles de México y 266 casos de IAM y 264 controles de Venezuela. Los RA fueron obtenidos a partir de la prevalencia de los factores de riesgo coronario en los casos y sus correspondientes Odds Ratios (OR) obtenidos luego de un análisis multivariado. Los RA para IAM observados para hipercolesterolemia fueron los siguientes: Venezuela 27%, México 3%, Cuba 30% y Argentina 36%; para diabetes: Venezuela 10%, México 15%, Cuba 5% y Argentina 7% y para índice de masa corporal: Venezuela 12%, México 3%, Cuba 19% y Argentina 17%. El mismo factor de riesgo tendría diferentes RA en diferentes poblaciones. Juntos el colesterol sérico, el tabaquismo, la hipertensión, el índice de masa corporal y la historia familiar de enfermedad coronaria fueron responsables del 76% de todos los casos de IAM en Venezuela, 70% en México, 81% en Cuba y 79% en Argentina. El conocimiento del RA tendría importantes implicancias en las estrategias de salud pública, especialmente en aquellos países con limitados recursos sanitarios.

Palabras clave: tabaquismo, colesterol, factores de riesgo coronario, diabetes, hipertensión

Cardiovascular disease (CVD) accounts for approximately 30% of all mortality worldwide and leads to almost fifteen million deaths annually[1]. Its rates have declined over the last two decades in the United States, Canada, Western Europe, Australia and New Zealand, but these gains have been offset by an increased incidence in developing countries. In some of these last countries non-communicable diseases, especially cardiovascular diseases, because of the considerable increase in ischaemic heart disease, have overtaken communicable disease as the leading cause of death[2]. It has been estimated that the increment in the incidence of heart disease will continue until 2020, mainly due to the large increase in developing countries and in economies in transition[2].

There are several factors that may explain the increase in ischaemic heart disease in developing countries[3]. These

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include a) increasing average lifespan, b) decreasing infant mortality, c) reduced caloric intake during the early years of life, d) increase in gross national product and per capita income in some countries, leading to the adoption of the unhealthy eating habits and behavior of western countries, e) genetic factors and f) increase in smoking.

The relative risk of coronary risk factors vary between different populations, e.g., cholesterol levels may not be a strong predictor of coronary heart disease (CHD) among South Asians[4] while in other countries total cholesterol and low density lipoprotein (LDL) cholesterol are important risk factors for ischaemic heart disease[5, 6].

The relative risk is important as a measure of the strength of the association between risk factor and the disease. Whereas it is important in establishing etiologic relationships, the attributable risk (AR) is more important in public health because it estimates how much of the risk of disease can we prevented if we eliminate exposure to the agent in question.

In cohort studies the AR can be calculated on the basis of the incidence of the disease and in case control studies can be obtained from the prevalence of the risk factors in cases and the corresponding multivariate OR, provided that cases are representative of the population of disease.

If a relative risk of a risk factor for CHD is similar between two populations, the AR (quantification of the proportion of diseased individuals due to a certain risk factor), could differ according the prevalence of the coronary risk factor (e.g. mean cholesterol levels in China[7] and in some African[8] countries are lower than in the West). Therefore even if cholesterol levels are similarly related to CHD, the attributable risk would be different.

A large case-control study conducted in four countries of Latin America (Argentina, Cuba, Mexico and Venezuela), was a suitable basis to provide an estimate of the AR of AMI in each country.

Material and Methods

This investigation was a multicenter case-control study of acute myocardial infarction (AMI) that took place between 1992 and 1998, in four countries of Latin America. It included 1060 cases and 1071 controls from Argentina, 323 cases and 314 controls from Cuba, 200 cases and 200 controls from Mexico and 266 cases and 264 controls from Venezuela.

The investigation began in 1992 and it had been originally foreseen the participation of all South American countries. To include enough number of patients from each country, we choose a multicenter study. The Argentine-branch finished the recruitment of patients in August 1994. Except Venezuela, the other countries, for different reasons, had inconveniences to be incorporated in the study. Then, the steering committee decided to invite other countries of Latin America such as Cuba and Mexico. Both countries accepted to participate in 1996 and finished the inclusion of patients in 1998.

All cases and controls were interviewed by trained interviewers using a structured questionnaire designed to obtain information on education, social class, personal characteristics and addictions such as smoking, self-reported weight and height, physical activity (days of physical exercise per week) and history of diabetes and hypertension. The stress was not measured, because it was not included in the objectives of the study. Case patient and control subject were interviewed by the same interviewer.

Social class was classified in three strata according to the ownership of a house or car: low stratum: subjects owning neither house nor car, medium stratum: subjects owning either a house or car, and high stratum: subjects owning both a house and a car. As a measure of body mass index (BMI) we used Quetelet's index [kg/m^2][9].

Those subjects who smoked one or more cigarettes per day during the last year were considered as smokers. For this paper we stratified the smoking status in two strata: smoker and no smoker. Hypertensives or diabetics were defined as subjects who had been prescribed specific treatment (diet and/or drugs) at any time. Information on family history of subjects included occurrence of AMI in their first-degree relatives (parents and siblings).

A non-fasting blood sample was taken within 24 hours of onset of symptoms in cases. Therefore glucemia was not measured because not all the included subjects with AMI were in fast. Serum cholesterol levels were measured at admission in both cases and controls. The requirement requested to each center was that the cholesterol should be measured by the same laboratory and method for cases and controls.

The reliability of this information was confirmed in most cases and controls by checking the clinical records and by asking further details about hospital or physician diagnosis in order to confirm, whenever possible, the subject's replies to the questions.

Cases were patients consecutively admitted to the hospital for a first episode of AMI. Those who had a history of ischemic heart disease, rheumatic valvular disease, cardiomyopathy or cardiac surgery were excluded. They were eligible if they met the standard World Health Organization criteria for AMI, including pathologic Q waves with evolution, or any two of the following: a typical history of chest pain for at least 30 min, electrocardiographic (ECG) changes with evolution or elevated cardiac enzyme levels[10].

Controls comprised a sample of subjects without clinical evidence of coronary heart disease, who were recruited from the hospital where the patient who had an AMI had been diagnosed. They were matched to the cases by age, sex and medical center. Subjects with conditions judged to be related to risk factors for myocardial infarction or with other ischaemic heart diseases, including angina pectoris or cardiac surgery, were excluded from the comparison group. Also excluded were subjects admitted for neoplastic and cerebrovascular disorders, or with any chronic condition. This however, applied only to the admission diagnosis. Fifty per cent of controls were admitted for traumatic conditions, 25% for acute surgical diseases and 25% for other miscellaneous illnesses, such as skin, ear, nose and throat, or dental disorders. Overall, less than 5% of cases and controls refused to be interviewed.

Data analysis

The sample size for the study was chosen so that by assuming an a level of 0.05 (two sided) and a power of 80%, we would be able to detect associations with an odds ratio of 2.0 or more for risk factors with a prevalence between 0.1 and 0.8.

Four percents forms had incomplete data, so they were excluded of the analysis.

Odds ratios (OR), used as a close approximation to relative risk, and the corresponding 95 percent confidence intervals were computed from data stratified by sex and age decade (<45, 45-54, 55-64 and ≥65 years) using the Mantel-Haenszel procedure[11]. Multivariate analysis by means of multiple logistic regression was used including terms for sex, age, years of education, social status, smoking, physical exercise, BMI,

history of diabetes and hypertension, cholesterolaemia and family history of myocardial infarction[12].

AR were computed by means of the method described by Bruzzi et al[13], which allows their estimation by using data from case control studies. The method requires knowledge of the prevalence of the risk factor among cases, provided that they are repre-sentative of the whole diseased population, and of the OR associated to the exposure. It was calculated by the following for-mula: AR = 1- (∑Pj /Rrj) in which Pj = prevalence of risk factor in each level of coronary risk factor and Rrj = relative risk in each level.

Data analyses were performed with Statistica software[14]

Results

The median age for cases was: Argentina 60 years, Cuba 57 years, Mexico 61 years and Venezuela 58.5 years, and for controls: Argentina 60 years, Cuba 57 years, Mexico 60.5 years and Venezuela 57 years.

Table 1 shows the distribution of cases and controls according to major covariates of interest in each country. Cases and controls in Argentina and Mexico were older than cases and controls in Cuba and Venezuela. There was no significant difference for sex. Controls were more educated than cases in Mexico. In Cuba 34% of cases and 12% of controls reported university education. In all countries, cases more frequently reported hypertension, diabetes, and family history of coronary heart disease, were more frequently current smokers and had higher serum cholesterol levels than controls. In Argentina cases were more obese than controls.

Table 2 shows the OR for AMI according to coronary risk factors. The OR for AMI, adjusted for age and sex, for the highest versus the lowest tertile of cholesterol level varies from 1.45 in Mexico to 8.92 in Cuba. The OR of

TABLE 1.– *Distribution of selected variables in cases of acute myocardial infarction (AMI) and controls.*

	Venezuela				Mexico				Cuba				Argentina			
	Cases (266)		Controls (264)		Cases (200)		Controls (200)		Cases (323)		Controls (314)		Cases (1060)		Controls (1071)	
	n	%	n	%	N	%	n	%	n	%	n	%	n	%	n	%
Age (years)																
<60	141	53.0	149	56.4	91	45.5	97	48.5	188	58.2	180	57.3	511	48.2	519	48.5
≥60	125	47.0	115	43.6	109	54.5	103	51.5	135	41.8	134	42.7	549	51.8	552	51.5
Sex																
Females	79	29.7	77	29.2	46	23.0	46	23.0	75	23.2	76	24.2	266	25.1	284	26.5
Males	187	70.3	187	70.8	154	77.0	154	77.0	248	76.8	238	75.8	794	74.9	787	73.5
Education (years)																
<7	176	66.2	195	73.9	115	57.5	46	23.0	61	18.9	139	44.3	543	51.2	549	51.3
7-12	69	25.9	51	19.3	46	23.0	68	34.0	153	47.4	137	43.6	335	31.6	307	28.7
>12	21	7.9	18	6.8	39	19.5	86	43.0	109	33.7	38	12.1	182	17.2	215	20.1
Cholesterol (mg/dl)																
<200	135	50.8	177	67.0	99	49.5	95	47.5	197	61.0	268	85.4	305	28.8	514	48.0
200-239	68	25.6	53	20.1	43	21.5	65	32.5	81	25.1	39	12.4	391	36.9	377	35.2
≥240	63	23.7	34	12.9	58	29.0	40	20.0	45	13.9	7	2.2	364	34.3	180	16.8
Hypertension																
No	137	51.5	208	78.8	101	50.5	154	77.0	145	44.9	210	66.9	511	48.2	750	70.0
Yes	129	48.5	56	21.2	99	49.5	46	23.0	178	55.1	104	33.1	549	51.8	321	30.0
Smoking																
No	163	61.3	206	78.0	117	58.5	146	73.0	142	44.0	191	60.8	596	56.2	778	72.6
Yes	103	38.7	58	22.0	83	41.5	54	27.0	181	56.0	123	39.2	464	43.8	293	27.4
Diabetes																
No	223	83.8	247	93.6	135	67.5	182	91.0	279	86.4	275	87.6	896	84.5	980	91.5
Yes	43	16.2	17	6.4	65	32.5	18	9.0	44	13.6	39	12.4	164	15.5	91	8.5
Body mass index (kg/m²)																
<25	115	43.2	129	48.9	42	21.0	53	26.5	162	50.2	196	62.4	320	30.2	427	39.9
25-30	107	40.2	103	39.0	115	57.5	100	50.0	130	40.2	93	29.6	520	49.1	469	43.8
>30	44	16.5	32	12.1	43	21.5	47	23.5	31	9.6	25	8.0	220	20.8	175	16.3
Family history of coronary heart disease																
No	175	65.8	203	76.9	154	77.0	158	79.0	129	39.9	165	52.5	727	68.6	907	84.7
Yes	91	34.2	61	23.1	46	23.0	42	21.0	194	60.1	149	47.5	333	31.4	164	15.3

AMI for hypertensives in relation to normotensives was more than two-fold in Cuba and Argentina and more than three-fold in Venezuela and Mexico. For all countries studied the OR was more than two-fold for smokers in relation to non-smokers. In comparison with non-diabetics, in diabetics the OR of AMI was 1.12 in Cuba, 2.00 in Argentina, 2.75 in Venezuela and 4.85 in Mexico. The OR of AMI for obesity was 1.18 in Mexico, 1.50 in Cuba, 1.56 in Venezuela and 1.69 in Argentina. The OR for those with a family history of coronary heart disease compared to those without such history varies between countries from 1.13 to 2.57.

The multivariate OR for AMI, according to coronary risk factors is depicted in Table 3. The risk of AMI, for the highest in relation to the lowest tertile of cholesterol level, was statistically non-significant in Mexico and nine times greater in Cuba. The odds ratios for hypertension, smoking, diabetes, overweight, obesity and family history of coronary heart disease, showed non-substantial differences between those adjusted for age and sex and those with the multivariate adjustment.

Table 4 gives the AR percentage for the six coronary risk factors considered. Cholesterolaemia had the highest AR in Argentina (36%), Venezuela (27%) and Cuba (30%) and the lowest in Mexico (3%). Hypertension accounted for one third of AMI in all countries studied. Smoking was responsible for nearly a quarter of AMI in Venezuela, Mexico and Argentina and for one third in Cuba. The AR of diabetes was extremely high in Mexico (25%) where the AR of BMI was very low (3%). The AR for AMI of the family history of coronary heart disease varied markedly: 7% in Mexico, 15% in Venezuela, 18% in Argentina and 22% in Cuba. Together these factors accounted for 76% of all cases of AMI in Venezuela, 70% in Mexico, 81% in Cuba and 79% in Argentina.

Discussion

In our study we estimated the proportion of AMI that is explained by a set of known risk factors in four countries of America. In Venezuela, Cuba and Argentina the most important AR for AMI were smoking, cholesterolaemia and hypertension. In Mexico, diabetes accounted for 25% of all AMI and hypercholesterolaemia is not important as an attributable risk. In Cuba, family history of coronary heart disease accounted for nearly a quarter of AMI while in Mexico it is not important.

The concept of AR is essential for understanding causation and the potential for prevention. The results of

TABLE 2.– *Odds Ratios† for AMI according to the Coronary Risk Factors adjusted for age and sex*

	Venezuela		Mexico		Cuba		Argentina	
	Odds ratio†	95% CI	Odds ratio†	95% CI	Odds ratio†	95% CI	Odds ratio†	95% CI
Cholesterol (mg/dl)								
<200	1*		1*		1*		1*	
200-239	1.72	1.12-2.64	0.64	0.39-1.03	2.82	1.84-4.31	1.77	1.45-2.16
³240	2.45	1.52-3.94	1.45	0.87-2.39	8.92	3.93-20.24	3.46	2.75-4.36
Hypertension								
No	1*		1*		1*		1*	
Yes	3.65	2.45-5.42	3.36	2.17-5.21	2.53	1.83-3.51	2.51	2.10-3.00
Smoking								
No	1*		1*		1*		1*	
Yes	2.50	1.68-3.73	2.12	1.36-3.32	2.04	1.47-2.81	2.40	1.96-2.93
Diabetes								
No	1*		1*		1*		1*	
Yes	2.75	1.52-4.97	4.85	2.75-8.57	1.12	0.70-1.78	2.00	1.53-2.64
Body mass index (kg/m²)								
<25	1*		1*		1*		1*	
25-30	1.19	0.82-1.73	1.44	0.89-2.35	1.69	1.21-2.37	1.49	1.23-1.81
>30	1.56	0.92-2.63	1.18	0.66-2.11	1.50	0.85-2.64	1.69	1.32-2.17
Family history of coronary heart disease.								
No	1*		1*		1*		1*	
Yes	1.71	1.17-2.51	1.13	0.70-1.81	1.68	1.22-2.30	2.57	2.07-3.17

**Reference*

† Mantel-Haenzel estimate adjusted for age and sex.

TABLE 3.– *Odds Ratios† for AMI according to the coronary risk factors. Multivariate analysis*

	Venezuela		Mexico		Cuba		Argentina	
	Odds ratio†	95% CI	Odds ratio†	95% CI	Odds ratio†	95% CI	Odds ratio†	95% CI
Cholesterol (mg/dl)								
<200	1*		1*		1*		1*	
200-239	1.82	1.14-2.91	0.92	0.60-1.45	3.48	2.14-5.65	1.60	1.29-1.98
≥240	2.84	1.69-4.78	1.22	0.67-2.22	9.81	4.06-23.68	2.86	2.24-3.66
Hypertension								
No	1*		1*		1*		1*	
Yes	3.72	2.43-5.70	3.67	2.19-6.15	2.46	1.69-3.58	2.44	2.01-2.96
Smoking								
No	1*		1*		1*		1*	
Yes	2.87	1.86-4.42	3.11	1.81-5.31	2.25	1.53-3.29	2.44	1.96-3.03
Diabetes								
No	1*		1*		1*		1*	
Yes	2.63	1.38-4.39	4.39	2.30-8.36	1.62	0.93-2.81	1.76	1.30-2.37
Body mass index (kg/m²)								
<25	1*		1*		1*		1*	
25-30	1.23	0.81-1.87	1.08	0.61-1.93	1.51	1.01-2.24	1.32	1.06-1.65
>30	1.33	0.75-2.37	0.94	0.47-1.90	2.08	1.07-4.06	1.35	1.03-1.77
Family history of coronary heart disease								
No	1*		1*		1*		1*	
Yes	1.77	1.16-2.71	1.46	0.82-2.60	1.57	1.08-2.28	2.27	1.81-2.85

**Reference*
† Estimates are from multiple logistic regression equations including terms for age (in years), sex, cholesterolaemia, smoking, hypertension, body mass index, years of education, social status, physical exercise and family history of myocardial infarction.

TABLE 4.– *Attributable Risk for AMI according to the country. Percentages*

	Venezuela	Mexico	Cuba	Argentina
Cholesterolaemia	27.0	3.0	30.0	36.0
Hypertension	35.0	36.0	33.0	31.0
Smoking	25.0	28.0	31.0	26.0
Diabetes	10.0	25.0	5.0	7.0
Body mass index	12.0	3.0	19.0	17.0
Family history of coronary heart disease.	15.0	7.0	22.0	18.0

our study are a warning for physicians and health promotion personnel, who should have to consider ancestry and culture when implementing CVD prevention efforts in a population. A small reduction in levels of risk factors with a highest AR would likely reduce morbidity and mortality from future CVD and related conditions. In our study, a higher AR, such as cholesterolaemia in Argentina (36% of AMI), will have important implications for public health strategies. In this country, priority for prevention should be reserved for those with hypercholesterolaemia. Thus, AR provides the rationale for the population approach to CVD prevention, especially in developing countries in which the economic resources for public health polices are not sufficient.

During the past decades, there has been major progress in understanding risk factors for cardiovascular disease; however, many epidemiological and clinical investigations have been limited to populations of industrialized countries. The paucity of research on cardiovascular disease in American populations is probably related to the lack of national funding priorities. This is the first investigation that compares AR for AMI

between countries of America. Another study, conducted in a single country (Italy) between 1988 and 1989, estimated the proportions of AMI attributable to six coronary risk factors[15]. The AR for cigarette smoking was 49%, and for cholesterol, body mass, family history of coronary heart disease, hypertension and diabetes 49%, 16%, 14%, 13% and 6% respectively.

In our study the selection bias must be considered, but the rates of participation among cases and controls were high. The choice of hospital controls could be criticized too, for not being representative of the general population and hence potentially introducing a selection bias. However, we considered only patients admitted to the same hospitals as the cases. They were admitted for various acute diseases not related to known or potential risk factors for AMI, so that they were drawn from the same population as the cases. Moreover, the distribution of subjects in each hospital with reference to age, sex and geographic area was similar for cases and controls. A further advantage of using hospital controls is that the information collected is more directly comparable to that of cases, because both groups had been ill when admitted to hospital, and hence sensitized to medical history.

A possible source of bias in our study is the recall bias. The assessment of information about the history of hypertension, diabetes, and family history of coronary heart disease was based on self-reporting, and both underestimation and overestimation can occur here. It is unknown whether the experience of the myocardial infarction as such, influenced the participants' answers to the questions. It is possible that during an AMI a patient may misinterpret his/her memories about the coronary risk factors before the infarct. Nevertheless, this recall bias between cases and controls, if present, is difficult to assess.

The influence of social class and education on the AMI risk of coronary heart disease as another source of bias, was minimized by means of a carefully and detailed allowance for these potential confounding factors. It is therefore conceivable that even a more detailed allowance could not totally explain the association observed.

Another possible limitation of this study is the exclusion of fatal cases of acute myocardial infarction. We only analyzed data from the patients with AMI who had lived long enough to be interviewed. Nonetheless, the association between coronary risk factors and AMI was observed in studies both on fatal and non-fatal AMI.[16-18]

In Argentina cases were recruited in hospitals throughout several cities of the country and therefore the AR, at least at first approximation, can refer to the whole Argentine population. The small number of participating centers included in Mexico, Venezuela and Cuba, implies a substantial random variation in the estimation of both the OR and the AR. Then, the extrapolation to other centers of these countries should be done cautiously.

Among the strengths of the study, we can mention the almost complete participation, the comparable catchment area of cases and controls, the accuracy of the diagnosis of AMI and the exclusion of subjects with a history of CVD from the analysis, which could have led to modifications in lifestyle habits.

It is accepted that coronary heart disease is multifactorial and polygenic, with many genetic and environmental factors contributing to the development of the clinical features[19]. Thus for any individual risk, variations at different gene loci will interact with different environmental factors to determine the overall risk of coronary artery disease. These interactions might explain the differences in AR found among the countries studied.

In our study, the coronary risk factors analyzed accounted for three-quarters of AMI in Argentina, Mexico, Cuba and Venezuela. Other risk factors, not analyzed in this investigation, such as physical activity, hyperhomocysteinemia, hyperinsulinemia and dietary factors may explain a further proportion of AMI. Importantly, our findings regarding the etiology of AMI may enable us to conduct a specific public health practice in each country.

Further information is needed about Latin-American populations' major risk factors for heart disease such as degree of acculturation, socio-economic status, traditional diet and other lifestyle factors. Only after acquiring this information, will each country be able to improve its own preventive health strategies.

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Appendix

STEERING COMMITTEE
Schargrodsky H, Ciruzzi M, Pramparo P, Rozlosnik J
COORDINATING COMMITTEE
Abecasis B, Brenner C, César J, Delmonte H, Esteban O, Labonia B, Montagna H, Paterno C, Rudich V, Soifer S, Tartaglione J

ARGENTINA
Buenos Aires (Capital)
- *Alemán Hospital*: Siskos D
- *Argerich Hospital*: Centeno S
- *Churruca Hospital*: Galván D, Cherkerdemian S
- *Fernández Hospital:* Nejamsky C, Rigou D
- *Israelita Hospital:* Kiezelstein A, D'agostino S, Bronstein A
- *Italiano Hospital:* Rudich V, Oliveri R
- *Pirovano Hospital:* Luluaga I, Zylberstejn H, Fortunato M, Soria P, Lázzari J
- *Zubizarreta Hospital:* Brenner C, Plotquin Y
- *Anchorena Medical Center:* Mele E, Quintana L
- *Güemes Medical Center:* Ahuad R
- *Hacienda Medical Center:* Haquim M
- *Mater Dei Medical Center:* Calvino R, Iavicoli O
- *Méndez Medical Center:* Monetti A, Eda L, Kogan B
- *Trinidad Medical Center:* Festa M, Fromen B
- *Clínica Del Sol Medical Center:* Esparza Iraola E, Taquini C

Buenos Aires Province
- *La Matanza Hospital:* Rodrigo C
- *San Isidro Hospital:* Romero Matos D
- *Posadas Hospital:* Abecasis B
- *San Juan de Dios Hospital:* Abecasis B

Bahía Blanca (City): Camou O, Solís D
Coronel Suárez (City): Caccavo A
La Plata (City): De Marco R, Pardo P
Tres Lomas (City): Alfonso A
Corrientes: Vaccaro J
Entre Ríos (Concordia): De la Cruz Ojeda J
Jujuy (San Salvador de Jujuy): Peleteiro R, Bustamante Labarta G
Misiones (Posadas): Castillo S
Neuquén (San Martín De Los Andes): Pichel G
Rio Negro (Viedma): Coniglio R
Santa Fe (Rosario): Piskorz D, Grisolía R, Girino C, Mancini M
Tucumán (San Miguel de Tucumán): De Rosa J, Waisman J

CUBA
Principal Investigator: Rivas Estany E
La Habana
- *La Habana Institute of Cardiology:* de la Noval R, Rodriguez Nande L, Hernández R, Díaz M, Alvarez Gómez J, Hernández Cañero A

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México DF.
- *1 de Octubre Hospital, ISSSTE.* Meaney E, Meaney A, Luna D, Mendoza E

Tepic Nayanit
- *Aquiles Calles Ramírez Hospital, ISSSTE.* Castillón M

Mazatlán, Sinaloa
- *Dr. Héctor González Guevara Hospital, IMSS,* Pacheco A

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- *de Zona Hospital, IMSS, Ciudad Mante*

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- *Valentín Gómez Farías Hospital, ISSSTE, Guadalajara, Jalisco, México*

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Associated Investigators: Finizola B, Morales E
Barquisimeto
- *Cardiovascular Regional Ascardio Center:* Alvarez M
- *Antonio María Pineda Hospital:* Castillo L. M
- *Pastor Oropeza Hospital:* Martínez B

San Cristóbal
- *San Cristóbal Hospital:* Zapata JR

Bolívar
- *Ruiz Páez Hospital:* Rodney H

Maturin
- *Orient Cardiovascular Center:* Alvarez MA

Barinas
- *Luis Razetti Hospital:* Marín J

Maracaibo
- *University Hospital:* Vergara S