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Risk Factors for Acute Myocardial Infarction in Latin America

The INTERHEART Latin American Study

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Background—Current knowledge of the impact of cardiovascular risk factors in Latin America is limited.

Methods and Results—As part of the INTERHEART study, 1237 cases of first acute myocardial infarction and 1888 age-, sex-, and center-matched controls were enrolled from Argentina, Brazil, Colombia, Chile, Guatemala, and Mexico. History of smoking, hypertension, diabetes mellitus, diet, physical activity, alcohol consumption, psychosocial factors, anthropometry, and blood pressure were recorded. Nonfasting blood samples were analyzed for apolipoproteins A-1 and B-100. Logistic regression was used to estimate multivariate adjusted odds ratios (ORs) and their 95% confidence intervals (CIs). Persistent psychosocial stress (OR, 2.81; 95% CI, 2.07 to 3.82), history of hypertension (OR, 2.81; 95% CI, 2.39 to 3.31), diabetes mellitus (OR, 2.59; 95% CI, 2.09 to 3.22), current smoking (OR, 2.31; 95% CI, 1.97 to 2.71), increased waist-to-hip ratio (OR for first versus third tertile, 2.49; 95% CI, 1.97 to 3.14), and increased ratio of apolipoprotein B to A-1 (OR for first versus third tertile, 2.31; 95% CI, 1.83 to 2.94) were associated with higher risk of acute myocardial infarction. Daily consumption of fruits or vegetables (OR, 0.63; 95% CI, 0.51 to 0.78) and regular exercise (OR, 0.67; 95% CI, 0.55 to 0.82) reduced the risk of acute myocardial infarction. Abdominal obesity, abnormal lipids, and smoking were associated with high population-attributable risks of 48.5%, 40.8%, and 38.4%, respectively. Collectively, these risk factors accounted for 88% of the population-attributable risk.

Conclusions—Interventions aimed at decreasing behavioral risk factors, lowering blood pressure, and modifying lipids could have a large impact on the risk of acute myocardial infarction among Latin Americans. (*Circulation*. 2007;115:1067-1074.)

Key Words: cardiovascular diseases ■ epidemiology ■ Latin America ■ lipoproteins ■ myocardial infarction ■ obesity ■ risk factors

Ishemic heart disease is the leading cause of death worldwide.¹ Additionally, in 1990, 26% of all deaths in Latin America (LA) were caused by cardiovascular disease (CVD),² which is expected to remain the main cause of death in the region for several decades.³ LA has experienced a major demographic, epidemiological, and nutritional transition during the last 3 decades, marked by economic growth, urbanization, a decrease in mortality from infant and infectious diseases, and an increase in life expectancy.⁴ This transition has led to large increases in morbidity and mortality attributable to CVD.⁵ Although previous studies have described the prevalence of risk factors,⁶⁻⁸ knowledge of the impact on coronary heart disease in LA is limited.

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INTERHEART is an international case-control study designed to ascertain the impact of conventional and emerging cardiovascular risk factors on acute myocardial infarction (AMI) in all major regions of the world.⁹ A secondary objective was to estimate the population-attributable risk (PAR) for all risk factors and their combination in different regions. About 15 000 cases of first AMI and a similar number of controls were enrolled from 52 countries; 6 countries from LA participated in INTERHEART, which is the largest study of risk factors for AMI conducted in this region. The present report addresses in detail the strength of

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The online-only Data Supplement, consisting of a list of national coordinators and investigators in Latin America, is available with this article at <http://circ.ahajournals.org/cgi/content/full/115/9/1067/DC1>.

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TABLE 1. Overall LA Cases and Controls by Ethnicity and Country

	Cases	Controls	Total
Countries, n			
Argentina	234	178	412
Brazil	313	364	677
Colombia	275	550	825
Chile	322	672	994
Guatemala	85	107	192
Mexico	8	17	25
Ethnic groups, n (%)			
Latino/Aboriginal	1105 (89.3)	1793 (95.0)	2898 (92.7)
European	112 (9.1)	74 (3.9)	186 (5.9)
Other	20 (1.6)	21 (1.1)	41 (1.3)
All participants, n	1237	1888	3125

the associations and the absolute impact of traditional cardiovascular risk factors in the development of AMI in LA.

Methods

The methods used in the overall INTERHEART study have been previously reported.^{9,10}

Study Design and Participants

This case-control study included incident cases of first AMI and controls from each center matched by sex and age (± 5 years) recruited from Argentina, Brazil, Colombia, Chile, Guatemala, and Mexico (Table 1).

Cases

Included in the present study were patients with first AMI presenting within 24 hours of the onset of symptoms with characteristic ECG changes. Subsequent confirmation included significant enzyme elevation or evolution of ECG changes. Potential subjects were excluded if they had cardiogenic shock, previous history of CVD, or a chronic medical illness that may affect risk factors for CVD.

Controls

One or 2 age- and sex-matched controls were recruited for every case at each center. Controls met the same exclusion criteria as cases and had no history of CVD or exertional chest pain. Hospital-based controls should have been admitted to the same hospital for a disease not related to risk factors for AMI. "Community"-based controls were attendants or relatives of a patient from noncardiac ward or an unrelated attendant of another cardiac patient.

Procedures

Information on demographic factors, socioeconomic status (education, income), lifestyle (smoking, physical activity, dietary patterns), psychosocial factors (depression, locus of control, perceived stress, and life events), personal and family history of CVD, and risk factors (hypertension, diabetes mellitus) was obtained through the use of a structured questionnaire. Height, weight, and waist and hip circumferences were measured using a standardized protocol.

We defined current smokers as individuals who had smoked any tobacco in the previous 12 months. Former smokers were defined as those who had stopped smoking >1 year earlier. For waist-to-hip ratio (WHR), tertile cutoff values derived from the whole INTERHEART sample were used: 0.90 and 0.95 in men and 0.83 and 0.90 in women. Individuals were considered physically active if they were regularly involved in moderate or strenuous exercise for ≥ 4 hours a week. Regular alcohol use was defined as consumption ≥ 3 times a week. Blood samples were shipped to Hamilton, Canada, for central analysis.

Statistical Analysis

Univariate associations were assessed with frequency tables and Pearson's χ^2 tests for 2 independent proportions. Means were compared through the use of *t* tests. When data were categorized, the cut points were calculated from the observed distribution in all INTERHEART controls; categories used in logistic regression are defined in Table 2. For protective factors (exercise, diet, and alcohol), PAR was calculated for the group without the exposure. The odds ratios (ORs) for smoking status are adjusted for age and sex. All other ORs are adjusted for age, sex, and smoking status. Perfect matching was not possible in all cases and controls. Therefore, to increase study power, unconditional logistic regression with adjustment for matching factors was used to estimate the independent effect of each factor on the risk of AMI. This approach allows the inclusion of unmatched cases in the analysis, and the results were

TABLE 2. Comparison of the LA INTERHEART Study Risk Factor Profiles With the Overall INTERHEART Study, Excluding LA

Risk Factor	Controls, %		OR (95% CI)		PAR (95% CI)	
	LA	IH-ROW	LA	IH-ROW	LA	IH-ROW
ApoB/ApoA-1*	42.0	32.0	2.31 (1.83–2.94)	3.0 (2.8–3.3)	40.8 (30.3–52.2)	44.2 (41.3–47.1)
Smoking†	48.1	48.1	2.31 (1.97–2.71)	2.26 (2.1–2.4)	38.4 (32.8–44.4)	35.3 (33.3–37.4)
Diabetes mellitus	9.5	7.2	2.59 (2.09–3.22)	3.16 (2.9–3.49)	12.9 (10.3–16.1)	12.2 (11.3–13.1)
Hypertension	29.1	20.8	2.81 (2.39–3.31)	2.41 (2.3–2.6)	32.9 (28.7–37.5)	22.0 (20.7–23.4)
WHR*	48.6	31.2	2.49 (1.97–3.14)	2.22 (2.1–2.4)	48.5 (35.8–56.2)	30.2 (27.4–33.2)
Depression	28.9	15.8	1.17 (0.98–1.38)	1.60 (1.5–1.7)	4.7 (1.4–13.9)	8.4 (7.3–9.7)
Permanent stress‡	6.8	3.9	2.81 (2.07–3.82)	2.10 (1.8–2.4)	28.1 (18.5–40.3)	7.8 (4.6–13.1)
Regular exercise	22.0	18.9	0.67 (0.55–0.82)	0.70 (0.65–0.76)	28.0 (17.7–41.3)	24.8 (20.6–29.6)
Alcohol	19.4	11.9	1.05 (0.86–1.27)	0.78 (0.74–0.84)	–3.2 (–18–11.7)	16.3 (12.7–20.6)
Daily consumption of fruits and/or vegetables	84.3	83.7	0.63 (0.51–0.78)	0.78 (0.73–0.84)	6.9 (3.35–10.5)	4.1 (2.9–5.3)
All of the above risk factors combined using logistic regression			63 (23.7–168)	71.8 (51.5–100)	88.1 (82.3–93.8)	85.1 (82.9–87.2)

IH-ROW indicates subjects in INTERHEART overall sample from the rest of the world, excluding LA.

*First vs third tertile.

†Never vs current and former.

‡Never vs permanent. For protective factors (diet, exercise, and alcohol), PARs are provided for the group without these factors.

TABLE 3. Odds Ratios of Acute Myocardial Infarction and Corresponding Population-Attributable Risks by Gender

Risk Factor	Controls, %		OR (95% CI)		PAR (95% CI)	
	Women	Men	Women	Men	Women	Men
ApoB/ApoA-1*	31.6	45.2	3.40 (2.20–5.25)	2.0 (1.51–2.66)	46.5 (30.6–63.3)	36.0 (23.8–52.3)
Smoking†	25.4	56.6	2.33 (1.71–3.18)	2.31 (1.92–2.78)	25.7 (18.2–35.1)	42.5 (35.4–50.0)
Diabetes mellitus	11.8	8.8	3.52 (2.41–5.15)	2.23 (1.71–2.9)	22.6 (16.8–29.6)	9.8 (7.1–13.4)
Hypertension	35.8	27.0	3.68 (2.69–5.05)	2.55 (2.11–3.08)	48.2 (39.3–57.1)	28.3 (23.5–33.5)
WHR*	40.1	50.8	4.10 (2.59–6.48)	2.02 (1.54–2.65)	63.1 (48.5–75.7)	35.8 (22.9–51.1)
Depression	36.7	26.4	1.07 (0.77–1.47)	1.21 (0.99–1.47)	1.4 (0.0–99.3)	5.3 (1.7–15.0)
Permanent stress‡	8.2	3.9	1.97 (1.12–3.45)	3.22 (2.24–4.63)	15.5 (2.6–56.1)	32.0 (21.3–45.1)
Regular exercise	15.7	24.4	0.68 (0.43–1.07)	0.67 (0.54–0.84)	27.9 (8.0–63.3)	28.1 (17.1–42.5)
Alcohol	6.3	25.3	0.58 (0.29–1.13)	1.11 (0.91–1.35)	44.6 (15.6–77.8)	–7.2 (–22.0–7.8)
Daily consumption of fruit and/or vegetables	88.7	83.7	0.64 (0.40–1.02)	0.63 (0.49–0.8)	5.5 (0–11.5)	7.5 (3.2–11.74)

Data are adjusted for age and smoking.

*First vs third tertile.

†Prevalence based on current and former smoking; ORs are based on never vs current and former.

‡Never vs permanent. For protective factors (diet, exercise, and alcohol), PARs are provided for the group without these factors.

comparable to those from conditional logistic regression. Estimated ORs and confidence intervals (CIs) calculated with both methods were within 5% of each other.⁹

Estimates of ORs and accompanying 95% CIs are presented for each risk factor and their combinations. Statistical analyses used SAS version 8.2 and S-Plus version 6. All statistical tests of hypotheses are 2 sided. For countries with <200 subjects, no ORs by country are provided; however, they are included in the overall data for the region. PAR was calculated using the usual formula for simple dichotomous exposure and disease that has been described previously.¹¹

The authors had full access to and take responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Between February 1999 and March 2003, 1237 AMI cases and 1888 controls were enrolled. Of the cases, 74.9% were male, with mean age of 59±12 years. Women were older than men by 5.4 years. Within LA, the age of first AMI was lower

in those with Latino or aboriginal ethnicity (59.8±12.1 years) compared with those of other ethnic groups (mainly Europeans; 64.6±12.9 years; *P*<0.001). The prevalence of risk factors in controls and the ORs and PARs for LA and the other countries participating in the INTERHEART study are listed in Table 2. The same parameters for women and men are listed in Table 3 and for specific LA countries in Table 4. The most common risk factors in the control group were abdominal obesity (48.6%; 50.8% in men) and smoking (48.1%; 56.6% in men). Perceived global permanent stress and history of hypertension had the strongest association with AMI, but the highest PARs were abdominal obesity, abnormal ratio of apolipoprotein (Apo) B to ApoA-1, and smoking. Abdominal obesity was more important in the LA region than in the rest of the world. Marked differences in PAR between the countries in the region were observed for abdominal obesity, permanent stress, and abnormal ratio of ApoB to ApoA-1.

TABLE 4. Odds Ratios of Acute Myocardial Infarction and Population-Attributable Risks by Country

Risk Factor	Argentina		Brazil		Chile		Colombia	
	OR	PAR	OR	PAR	OR	PAR	OR	PAR
ApoB/ApoA-1*	5.52 (2.8–10.7)	67.6 (51–80.7)	3.3 (1.9–5.8)	57.0 (38.6–73.4)	2.05 (1.4–3.0)	35.2 (19.0–55.8)	2.49 (1.4–4.3)	37.4 (14.2–68.4)
Smoking†	2.33 (1.5–3.7)	42.9 (27.9–93.0)	2.4 (1.7–3.4)	40.3 (28.9–52.8)	3.10 (2.3–4.2)	42.0 (33.2–51.4)	1.44 (1.0–2.0)	19.8 (7.2–43.7)
Diabetes mellitus	2.73 (1.5–5.1)	13.1 (7.5–21.9)	4.2 (2.5–7.1)	17.0 (12.2–23.1)	2.0 (1.4–2.9)	10.8 (6.1–18.3)	1.74 (1.1–2.7)	7.4 (3.3–15.8)
Hypertension	2.62 (1.7–4.1)	33.4 (22.7–62.0)	4.4 (3.0–6.3)	43.2 (35.4–51.4)	2.86 (2.1–3.9)	32.0 (24.5–40.8)	2.27 (1.6–3.2)	25.5 (17.3–36.0)
WHR*	4.22 (2.3–7.8)	58.1 (37–66.0)	2.5 (1.4–4.6)	51.0 (27.2–74.4)	1.26 (0.8–1.9)	16.6 (2.4–61.2)	4.16 (2.7–6.5)	53.5 (38.9–67.5)
Depression	1.12 (0.7–1.7)	4.0 (0.1–66.9)	1.48 (1–2.2)	10.1 (3.7–24.7)	0.95 (0.7–1.3)	–2.2 (–13.0–8.7)	1.21 (0.9–1.7)	6.2 (0.9–32.5)
Stress‡	4.17 (1.5–11.3)	41.7 (19.1–68.4)	8.0 (3.7–17.3)	43.8 (25–64.7)	2.19 (1.3–2.8)	12.0 (2.3–44.1)	1.87 (1.1–3.3)	15.4 (2.0–62.3)
Regular exercise	0.46 (0.3–0.8)	47.5 (26.3–69.7)	0.8 (0.5–1.3)	18.3 (2.3–68.1)	0.82 (0.6–1.2)	14.7 (2.6–52.3)	0.75 (0.5–1.1)	20.4 (4.8–56.5)
Alcohol	0.85 (0.6–1.3)	7.8 (0.4–62.9)	0.7 (0.4–1)	27.6 (12–51.8)	1.20 (0.8–1.7)	–16.0 (–50–18.4)	0.92 (0.6–1.5)	6.5 (0.0–97.1)
Daily consumption of fruits and/or vegetables	1.10 (0.7–1.9)	–6.7 (–34.0–20.2)	0.7 (0.4–1)	4.95 (2.2–12.2)	0.54 (0.4–0.8)	12.1 (6.1–18.1)	0.84 (0.6–1.3)	4.8 (–2.8–12.45)

For protective factors (diet, exercise, and alcohol), PARs are provided for the group without these factors.

*First vs third tertile.

†Never vs current and former.

‡Never vs persistent.

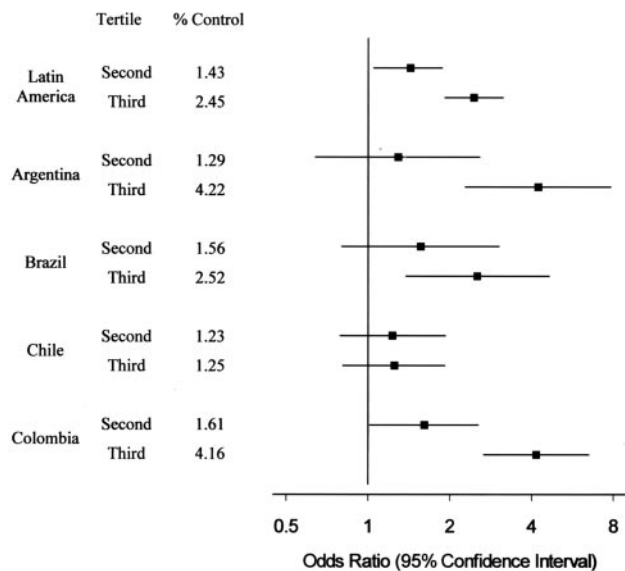


Figure 1. Odds ratio of acute myocardial infarction by tertiles of waist-to-hip ratio. The first tertile is the reference.

Prevalence of Risk Factors in Controls

The most prevalent risk factor was abdominal obesity (Table 2). Overall, 48.6% of the controls were in the highest tertile compared with 31.2% in the other countries participating in INTERHEART. Prevalence of current and former smoking was 48.1% in the control group, which is similar to that in other countries. The third most prevalent risk factor was dyslipidemia: 42% of the controls were in the upper tertile compared with 32% in the other INTERHEART countries. Hypertension was reported by 29.1% in LA, higher than the 20.8% in the other participating countries. Daily consumption of fruits and vegetables was reported by 43.8%; daily consumption of either fruits or vegetables was reported by 40.5%; and exercise was performed regularly by only 22%. These frequencies were similar to overall INTERHEART data.

Relationship of Risk Factors to AMI

Permanent stress and history of hypertension had the strongest association with AMI (Table 2), followed by a history of

diabetes mellitus and abdominal obesity (Figure 1). With “never experience” as the stress comparator, the OR of those who reported permanent stress was 2.81 (95% CI, 2.07 to 3.82); in those with several periods of stress, the OR was 2.03 (95% CI, 1.59 to 2.58); and in the group with some periods of stress, the OR was 1.2 (95% CI, 0.99 to 1.48). High or severe financial stress also was associated with AMI (OR, 1.38; 95% CI, 1.12 to 1.71), as well as having ≥ 2 stressful events the previous year (OR, 1.22; 95% CI, 1.01 to 1.48). Depression had an OR of 1.17 (95% CI, 0.98 to 1.38), which was weaker than that observed in the other regions (OR, 1.60; 95% CI, 1.5 to 1.7). Education level was not associated with AMI; with ≤ 8 years of education as the reference, the OR for those with 9 to 12 years of education was 1.03 (95% CI, 0.85 to 1.26) and those with >12 years of education was 0.98 (95% CI, 0.81 to 1.2). In addition, income levels were not associated with AMI (OR, 0.94; 95% CI, 0.73 to 1.22 for the fourth and fifth quintiles compared with the first and second quintiles).

Increasing levels of smoking increased the risk of AMI. Compared with nonsmokers, former smokers had an OR of 1.53 (95% CI, 1.28 to 1.84), current smokers who smoked 1 to 19 cigarettes a day had an OR of 2.46 (95% CI, 1.96 to 3.1), and those smoking ≥ 20 cigarettes a day had an OR of 9.07 (95% CI, 6.75 to 12.19) (Figure 2). Similarly, there was a graded relationship with increasing quintiles of the ratio of ApoB to ApoA; with the lower quintile for comparison, OR was 1.28 (95% CI, 0.89 to 1.85) for the second, 1.44 (95% CI, 1.02 to 2.04) for the third, 2.29 (95% CI, 1.65 to 3.20) for the fourth, and 2.76 (95% CI, 2.0 to 3.79) for the fifth quintile (Figure 3). Daily consumption of fruits or vegetables and regular exercise were associated with a risk reduction of 37% and 33%, respectively. However, alcohol consumption (OR, 1.05; 95% CI, 0.86 to 1.27) was not associated with AMI. A healthy lifestyle—avoidance of smoking, regular exercise, and regular fruit and vegetable consumption—was associated with an OR of 0.25 (95% CI, 0.13 to 0.48), indicating that the majority of risk of AMI in the region can be avoided by lifestyle modification.

Sex Differences

After adjustment for differences in age, ORs were higher in women compared with men (Table 3) for the following:

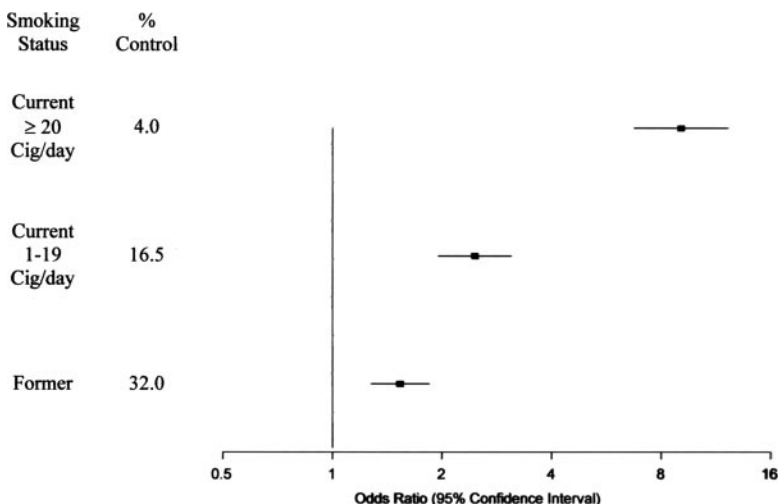


Figure 2. Odds ratios of acute myocardial infarction in smokers compared with never-smokers. Never smoking is the reference. Cig indicates cigarettes.

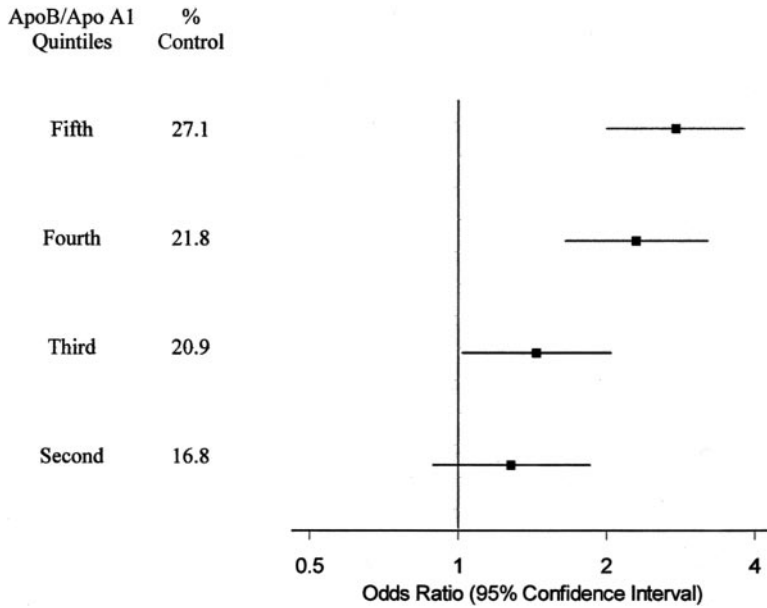


Figure 3. Odds ratio of acute myocardial infarction by quintiles of ApoB/ApoA-1 ratio. The first quintile is the reference.

abnormal WHR: women, 4.10 (95% CI, 2.59 to 6.48); men, 2.02 (95% CI, 1.54 to 2.65); ratio of ApoB to ApoA-1: women, 3.40 (95% CI, 2.20 to 5.25); men, 2.0 (95% CI, 1.51 to 2.66); diabetes mellitus: women, 3.52 (95% CI, 2.41 to 5.15); men, 2.23 (95% CI, 1.71 to 2.9); and hypertension: women, 3.68 (95% CI, 2.69 to 5.05), men 2.55 (95% CI, 2.11 to 3.08). The association was stronger in men for permanent stress (OR for women, 1.97; 95% CI, 1.12 to 3.45; OR for men, 3.22 (95% CI, 2.24 to 4.63). The association of smoking, depression, exercise, and fruit and vegetable consumption with AMI was similar in both sexes. Lower prevalence of risk factors in the control group was observed in women for current smoking (men, 37.1%; women, 7.9%), alcohol consumption (men, 25.3%; women, 6.3%), ratio of ApoB to ApoA-1 in the upper tertile (men, 45.2%; women, 31.6%), and WHR in the upper tertile (men, 50.8%; women, 40.1%).

Population-Attributable Risk

Abdominal obesity was the most important risk factor in LA, with an average PAR for the region of 48.5%, followed by abnormal ratio of ApoB to ApoA-1 (40.8%) and smoking (38.4%); the collective impact of these 3 risk factors is 77.6% (95% CI, 70.9 to 84.3). Hypertension (32.9%), stress (28.1%), and lack of exercise (28%) were of intermediate importance (Tables 2 and 4). The influence of diabetes mellitus was less important because of its lower prevalence.

The PARs for the major risk factors were similar between countries. Differences in the magnitude of PARs were observed mainly in risk factors with a small effect: depression, alcohol consumption, and fruit and vegetable consumption, which likely represent the play of chance. Important differences between countries were observed in the PAR of the WHR, with 16.6% in Chile and values >50% in the other countries, and permanent stress, with 12% in Chile and 15.4% in Colombia compared with 41.7% in Argentina and 43.8% in Brazil. The PAR for the ratio of ApoB to ApoA-1 was larger

in Argentina (67.6%) and Brazil (57.0%) than in Colombia (37.4%) and Chile (35.2%).

When we compare PARs in LA with those from the other countries participating in the INTERHEART study, with a similar mean age (57.2±12.2 years) and sex distribution (25% women), the greatest differences were observed in permanent stress (28.1% in LA versus 7.8% in other countries), abnormal WHR (48.5% versus 30.2%, respectively), and hypertension (32.9% versus 22%). The protective effect of alcohol observed in other countries was not present in LA. The importance of diabetes mellitus, depression, exercise, and fruit and vegetable consumption was similar.

Discussion

The most important risk factors in LA are abdominal obesity, dyslipidemia, smoking, and hypertension as estimated by PAR. Two previous case-control studies have related factors to AMI risk in LA. A study involving 1060 cases and 1071 controls conducted in Argentina, Cuba, Mexico, and Venezuela reported an independent association with AMI for total cholesterol, hypertension, smoking, and diabetes mellitus.¹² Recently, the Acute Myocardial Infarction Risk Factor Assessment in Brazil (AFIRMAR) reported results similar to those of INTERHEART: smoking, diabetes mellitus, WHR, family history of coronary artery disease, low-density lipoprotein (LDL) cholesterol, and reported hypertension were the main risk factors. Unlike INTERHEART, alcohol consumption had a significant protective effect in that study.¹³ These results are generally consistent with our findings from INTERHEART, which indicate that these 4 risk factors account for most of the PAR for AMI in this region.

The importance of abdominal obesity as a risk factor in LA may be related to the recent rapid transition experienced in the region. Improvement in socioeconomic status was associated with increased life expectancy, urbanization, and obesity.^{14,15} These changes are evidenced in the high prevalence observed in our control group of abdominal obesity, history of high blood pressure and diabetes mellitus, seden-

tarism, and abnormal lipids. Although the prevalence of risk factors among controls in INTERHEART is not necessarily representative of the population prevalence, they provide a rough approximation because the rates of most risk factors are similar to those found in some previous prevalence studies. WHRs in the upper tertile were observed in one third of the controls in the total INTERHEART sample and in 46.8% of the LA controls, with a high rate of 61.2% in Brazil. These results are consistent with the International Clinical Epidemiology Network study, which reported that obesity was more prevalent in LA than in Asian countries.¹⁶ Other studies in the region have indicated a high prevalence of obesity: 38% of the Mexican urban adult population are overweight and 21% are obese,⁸ and prevalences of 30% and 50% for overweight and obesity have been reported for several LA countries.¹⁷

During recent decades, considerable evidence has accumulated on the association of psychosocial factors with CVD. Psychosocial variables such as stress or depression are difficult to define objectively; they may act alone or together and may exert their effects throughout life,¹⁸ making measurement difficult. Furthermore, all study designs evaluating stress have important limitations. For example, case-control studies could eventually be influenced by reporting biases, whereas cohort studies may fail to detect recent episodes of stress just before AMI. Despite these drawbacks, reports from the literature appear to be consistent in indicating a relationship between anxiety and depression and coronary heart disease.^{19–21} Our study indicates that individuals suffering permanent stress or several periods of stress in their lives, identified by simple questions, have an increased risk of AMI. Although intriguing, these results should be interpreted cautiously because patients who have recently experienced an AMI may be more likely to report stress. For depression, we observed a modest association with AMI (OR, 1.17; 95% CI, 0.98 to 1.38) in the LA region, which is consistent with the results in the overall INTERHEART study.²² In LA, we observed no relationship between socioeconomic status and AMI; these results differ from those observed in the rest of the world. It is possible that when modest differences in OR are examined in subgroups (ie, by region), the results may vary as a result of chance. It is also possible that LA is at an earlier stage of the epidemiological transition compared with Western countries, which may explain the lack of an inverse association between education and AMI risk. Similar factors may influence the relationship between psychosocial variables and AMI in this region.

About 9.0% of the controls reported a history of diabetes mellitus, consistent with previous data indicating a high prevalence in this region. It is estimated that 13 million individuals in LA and the Caribbean had diabetes mellitus in the year 2000 and that the number will increase to 33 million by 2030.²³ This increase is explained by the rise in life expectancy, obesity, and sedentarism. A high level of LDL cholesterol is one of the strongest risk factors for coronary artery disease; however, the levels may be influenced in the acute phase of AMI by the nonfasting state and the impact of AMI itself on LDL cholesterol levels. ApoB levels are not affected by the fasting status and are a reflection of the

number of potentially atherogenic lipoprotein particles, whereas ApoA-1 reflects antiatherogenic high-density lipoprotein.²⁴ Substantial evidence exists that apolipoproteins are even better predictors of future coronary artery disease events than lipoproteins.^{25–27} For example, in the Apolipoprotein-related Mortality Risk (AMORIS) study, the ratio of ApoB to ApoA was more predictive of AMI than the ratio of LDL to high-density lipoprotein.²⁸ In the INTERHEART results, the ratio of ApoB/ApoA-1 had the highest PAR for AMI in the overall sample and had a consistent and important impact in each region, including LA.⁹ It was clearly more predictive of AMI than the ratio of LDL to high-density lipoprotein (unpublished results). In the present study, the apolipoprotein ratio showed a linear relationship with the OR of AMI, reaching an OR of 2.75 in the highest quintile.

Although the prevalence of smoking has decreased in developed countries, it is increasing in many low- and middle-income countries, especially among young people and women. Surveys in 14 LA countries in individuals >15 years of age demonstrated that smoking prevalence among men varied from 24.1% (Paraguay) to 66.3% (Dominican Republic) and the prevalence among women from 5.5% (Paraguay) to 26.6% (Uruguay). In countries participating in this study, the prevalence of smoking was 35.1% to 40.0% in men and 19.1% to 25.4% in women.²⁹ Projections from the World Health Organization suggest that by the year 2020 tobacco will become the largest single cause of death, accounting for 12.3% of deaths worldwide.³⁰

Daily consumption of fruits and/or vegetables and regular physical exercise were protective, with each being associated with a 30% to 40% relative risk reduction. Fruits or vegetables were consumed daily by 85% of the control group, representing a frequent practice in the LA population. This is a major protective factor in this study. However, given its high prevalence, the number who did not consume daily fruits and vegetables was low, which accounts for the low PAR associated with the consumption of fruits and vegetables in LA. The proportion of physically active persons is low; only one fifth of the control group exercised regularly. The low proportion of physically active subjects in this study is consistent with previous studies from the region on physical activity.^{31,32} The lack of a protective effect of alcohol in LA may simply be due to the play of chance or to variations in the patterns or type of alcohol consumption. The global INTERHEART study⁹ and the AFIRMAR study¹³ reported a protective effect of moderate alcohol consumption against AMI.

In this region, PAR associated with various risk factors can be categorized into 3 groups. Those with a large impact, PAR >38%, include abdominal obesity, abnormal lipids, and smoking; those with a moderate impact, PAR of 12.9% to 33%, include history of hypertension and diabetes mellitus, stress, and lack of regular exercise; and those with a small impact were alcohol, depression, and fruit and vegetable consumption. The collective impact of all these risk factors is high at a PAR of 88% (95% CI, 82.3 to 93.8). Even after exclusion of the effect of self-reported stress (which has the potential to be influenced by recall bias), the overall PAR is

86% (95% CI, 80.9 to 92.7). This suggests that intervention strategies based on current knowledge have the potential to prevent most of the AMI in this region.

Study Limitations

Case-control studies are potentially open to biases. In our study, selection biases were reduced in cases by including patients who suffered their first AMI because those with a previous history of CVD could have modified their lifestyle. Hospital controls had diseases not known to be related to cardiovascular risk factors, and our results were similar for hospital- and community-based controls. Measurement biases were reduced by using standardized methods for data collection; anthropometry and apolipoprotein levels are objective measurements. Accuracy of smoking report was confirmed by measuring cotinine in 1000 individuals with total concordance with history (data not published). Because of changes in blood pressure and glucose observed in AMI, diagnosis for diabetes mellitus and hypertension was based on history. Therefore, the strength of association between these risk factors and AMI may have been underestimated. However, our overall result indicating that the majority of PAR is predicted by known risk factors is consistent with the estimates from other studies that used different designs. Of the psychosocial variables, the risk factor that is most susceptible to measurement bias is stress. However, objective measurements (such as life events) or questions that are not generally considered to be associated with AMI by the lay public (like locus of control or depression) provided similar results in the overall study. The combined effect of all 10 risk factors in PAR is 88%. This estimate is model dependent, given that few individuals had no or all risk factors. However, the collective PAR of abdominal obesity, abnormal ratio of ApoB to ApoA-1, and smoking is 77.6%. In the overall INTERHEART study, the PAR of these 3 factors plus hypertension and diabetes mellitus was 80%,⁹ similar to the results of Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico study, in which adding family history of AMI gave a PAR of 85%.³³ The similarity of results with other studies supports the validity of our estimates. Finally, our estimates of the prevalence of risk factors are based on controls hospitalized for non-CVD conditions or visitors of noncardiac patients. Although the prevalences in the our controls are unlikely to represent the population prevalence of risk factors in an entire country, they are approximately similar to those reported in previous prevalence studies from this region, suggesting no major biases.

Conclusions

The majority of risk of AMI in LA can be explained by tobacco use, abnormal lipids, abdominal obesity, and hypertension. Given that all of these factors are modifiable, the INTERHEART Latin America Study provides a scientific basis to develop preventive strategies that are practical and generally similar in all countries in the entire region.

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Disclosures

None.

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