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Herman Schargrodsky[1], Jorge Rozlosnik[1], Mario Ciruzzi[1], Rosa Ruffa[1], Carlos Paterno[1], Manuel Ardariz[1], Alberto Caccavo[1], Barbara D'Avanzo[2], Eva Negri[2], Carlo La Vecchia[2,3], Gianni Tognoni[2]

[1] *Consejo de Epidemiologia de la Sociedad Argentina de Cardiologia, Buenos Aires, Argentina*
[2] *Instituto di Recerche Farmacologiche «Mario Negri», Milano, Italy*
[3] *Institute of Social and Preventive Medicine, University of Lausanne, Lausanne, Switzerland*

Body weight and nonfatal myocardial infarction in a case-control study from Argentina

Summary

The relationship between overweight and obesity and the risk of acute nonfatal myocardial infarction was analyzed, using data from a case-control study from Buenos Aires, Argentina. The study included 1000 patients with acute myocardial infarction and 1000 controls, who had been admitted to the same hospitals in which the cases had been identified, for acute conditions unrelated to known or potential risk factors for coronary heart disease. Only 32% of the cases and 41% of the controls had a Quetelet's index (body mass index, BMI, kg m^{-2}) under 25% of the cases and 51% of the controls were overweight (BMI 25 to 30), and 15% of the cases and 8% of the controls severely obese (BMI > 30). After allowance for age and sex, the relative risks (RR) were 1.4 (95% confidence interval, CI, 1.1 to 1.7) for subjects with a body mass index of 25 to 30 and 2.2 (95% CI 1.7 to 3.1) for those with a body mass index more than 30. When additional adjustment was made for hypertension, diabetes, smoking and a family history of coronary heart diesease, the RR was 1.2 (95% CI 1.0 to 1.6) among subjects with a body mass index of 25 to 30 and 1.7 (95% CI 1.3 to 2.4) for those with a body mass index more than 30. The trend in risk was significant. In the stratified analysis, the RR in younger people (30–44 years) with a body mass index more than 30 was 4.7 (95% CI 2.0 to 10.8), and the association was less strong in middle and older age. No significant interaction was observed with any of the other identified risk factors. Thus, overweight is a major independent risk factor for myocardial infarction, and in this Southern American population is responsible for over 40% of nonfatal infarctions under age 45 and 25% above age 45.

The epidemiology of acute myocardial infarction has been developed almost exclusively from data related to the populations of the Northern hemisphere. Cardiovascular diseases, however, have also begun to play an increasing role in determining the burden of moribidity and mortality in many countries of the South of the world, where the distribution and the prevalence of risk factors may have a different pattern. To explore this neglected area of investigation, a pilot case-control study scheme has been developed in Buenos Aires, Argentina, with the perspective of expanding it to other settings in Latin America. We report here the first results of this study with respect to the factors overweight and obesity. This could appear to be a provocative choice, but it is one which allows a direct exploration of the similarities which may exist across economic and social frontiers.

Several studies have examined the relationship between measures of body mass and ischaemic heart disease[1–19]. It is clear that sevverely overweight and obese subjects have an elevated risk of ischaemic heart disease, but there is still discussion on the role of obesity independently of diabetes, hypertension or serum lipid abnormalities, since some of these conditions are strongly correlated with overweight. Further, the slope of the exposure-risk relationship has not been clearly established, since some studies found a directly linear exposure-risk relationship[1–5] while in others the elevated risk was restricted to severely obese individual, and the curves were J- or U-shaped[6–12].

It is possible that some of these apparent inconsistencies are due to

imprecise classification of the disease, to inadequate allowance for smoking (which is inversely related to body weight) to other major risk factors for coronary heart diseases, or to preexisting diseases[16].

In cohort studies, moreover, there is a delay between data collection and outcome, and subsequent changes in body weight may modify the true relationship. Further, the association between overweight and coronary heart disease may vary at different ages, between males and females and in different populations.

To provide further information on this issue, we considered data from a large case-control study of acute myocardial infarction conducted in Argentina, where allowance was possible for smoking, hypertension, diabetes and other major correlates of overweight and ischaemic heart disease.

Subjects and methods

The data were derived from a hospital-based case-control study conducted between 1984 and 1989 in a network including major coronary care units in the metropolitan area of Buenos Aires. Trained interviewers identified and questioned cases of acute myocardial infarction (AMI) and controls admitted for a wide spectrum of acute conditions, unrelated to nutrition or diet or to known or suspected risk factors for coronary heart disease.

Cases were patients aged 30 to 65 who had been admitted for a first episode of acute myocardial infarction to coronary care units of 11 hospitals of metropolitan Buenos Aires (capital and suburbs). They were eligible if they had pathological Q waves with evolution or any of the following conditions: typical history of chest pain for at least 30 minutes, plus other electrocardiographic changes with evolution, and elevated cardiac enzymes. Only nonfatal cases were included. A total of 1000 subjets (873 males, 127 females) were interviewed. The median age of the cases was 55 years.

Controls were subjects aged 30 to 65 who had been admitted to the same network of hospitals where cases had been identified for a wide spectrum of acute conditions unrelated to known or potential risk factors for myocardial infarction and to cigarette smoking. Patients with a history of AMI or other ischaemic heart diseases, including angina pectoris or cardiac surgery, were excluded. Also excluded were subjects admitted for neoplastic, cardio- and cerebrovascular disorders, or any chronic condition. This, however, applied only to the admission diagnoses. The main diagnostic categories were traumatic conditions (43%), surgical diseases (35%), and other miscellaneous illnesses, such as skin, ear, nose and throat or dental disorders (23%). Controls were not individually matched with cases, but cases and controls were comparable with reference to sex, age and hospital. The median age for the control group was 54 years.

Variable	Males		Females	
	Myocardial infarction	Controls	Myocardial infarction	Controls
Age group				
30–44	130	130	5	4
45–54	257	256	22	26
55–65	486	487	100	97
Smoking status				
Never smokers	134	261	82	90
Ex-smokers	172	198	9	11
Current smokers, cigarettes per day				
<15	102	121	15	11
15–24	200	202	14	9
≥25	265	91	7	6
Diabetes				
No	716	789	96	108
Yes	157	84	31	19
Hypertension				
No	484	620	47	95
Yes	389	253	80	32
Family history of coronary heart disease				
No	689	746	96	101
Yes	184	127	31	26

Table 1. *Distribution of 1000 cases of acute myocardial infarction and 1000 controls according to sex, age, cirgarette smoking and selected medical conditions. Buenos Aires, Argentina 1984–1989.*

A structured questionnaire was used to obtain information about socio-demographic habits including occupation, personal characteristics and habits, cigarette smoking, physical activity, history of diabetes and (diagnosed) hypertension and personal and family history of coronary heart disease. Information on self-reported weight and height before the onset of symptoms of myocardial infarction (for cases) or of the disease which led to hospital admission (for controls) was also obtained, and used to compute Quetelet's index (kg m^{-2}), as a measure of body mass index (BMI)[20].

Data analysis and control of confounding. Odds ratios of acute myocardial infarction, as estimators of relative risk (RR), according to different levels of BMI, were computed using unconditional multiple logistic regression models[21,22]. Included in the regression equations were terms for age (in decades), sex, education (<7 years; 7–11 years; ≥12 years), cigarette smoking (never smokers/ex-smokers, current smokers of <15/15–24/≥25 cigarettes per day), diabetes (yes/no), hypertension (yes/no) and family history of coronary heart disease (yes/no). The significance of the linear trends in risk was based on the difference in the deviance of the models with and without the variable of interest[21].

Results

The distribution of cases and controls according to sex, age and other major covariates (smoking habits, diabetes, hypertension and family history of coronary heart disease) is shown in Table 1. More than 55% of male cases and about 40% of controls were current smokers, whereas in females 28% of the cases and 20% of the controls were current smokers. Thus, current smokers had an elevated risk of myocardial infarction (RR = 2.5, 95% CI 2.0 to 3.1). Both in males and in females controls were slightly more frequently ex-smokers. Likewise, associations were observed with diabetes, with a RR of 2.0 (95% CI 1.5 to 2.6), hypertension, with a RR of 2.3 (95% CI 1.8 to 2.8) and with family history of coronary heart disease, with a RR of 1.5 (95% CI 1.2 to 1.9).

Table 2 reports the distribution of cases and controls, and the corresponding RRs according to measures of body mass index. Only 32% of the cases and 41% of the controls had a Quetelet's inddex under 25; 54% of the cases and 51% of the controls were overweight (Quetelet's index 25 to 30) and 15% of the cases and 8% of the controls were severely obese (Quetelet's index >30). Compared to subjects whose BMI was <25, the RRs adjusted for sex and age were 1.4 (95% CI 1.1 to 1.7) for subjects whose BMI was 25 to 30, and 2.2 (95% CI 1.7 to 3.1) for severely obese subjects. Relativve risks adjusted also for hypertension, diabetes and family history of coronary heart disease were 1.2 (95% CI 1.0 to 1.6) for overweight subjects, and 1.7 (95% CI 1.3 to 2.4) for severely obese ones. The test for linear trend was highly significant ($\chi^2_1 = 28.81$, $p < 0.001$).

The relative risks were also computed within strata of selected covariates (Table 3). The association with overweight and obesity was stronger in younger subjects: under age 45 the RR was 2.1 (95% CI 1.2 to 3.7) for subjects with a Quetelet's index between 25 and 30 kg m^{-2} and 4.7 (95% CI 2.0 to 10.8) for á Quetelet's index of more than 30 kg m^{-2}. Another apparent interaction was with hypertension: among subjects with the highest BMI, the RR in hypertensive subjects was 1.4 (95% CI 0.9 to 2.3) versus 2.7 (95% CI 1.7 to 4.7) in normotensive subjects. With reference to smoking, the RR among severely obese subjects were 2.5 among never-smokers, 1.9 among ex-smokers, 3.0 among moderate,

	Myocardial infarction	Controls	Relative risk estimates (95% CI)	
			RR[1]	RR[2]
Body mass index (kg m^{-2})				
<25	315	407	1+	1+
25–30	540	509	1.4 (1.1–1.7)	1.2 (1.0–1.6)
>30	145	84	2.2 (1.7–3.1)	1.7 (1.3–2.4)
χ^2_1 trend			33.0 p<0.001	28.8 p<0.001

[1] Estimates from multiple logistic regression models including terms for age and sex.
[2] Estimates from multiple logistic regression models including terms for age, sex, cigarette smoking, diabetes, hypertension, and family history of coronary heart disease.
+ Reference category.

Table 2. *Distribution of 1000 cases of acute myocardial infarction and 1000 controls according to body mass index. Buenos Aires, Argentina 1984–1989.*

Covariates	Body mass index (Kg m^{-2})			
	< 25	25–30	> 30	χ^2_1 (trend)
Sex				
Males	1* (258:339)	1.4 (488:457)	2.2 (127:77)	24.9[a]
Fernales	1* (57:68)	1.3 (52:52)	3.3 (18:7)	5.4[b]
Age group (years)				
30–44	1* (246:307)	2.1 (412:382)	4.7 (107:66)	16.4[a]
45–54	1* (52:68)	1.2 (96:105)	1.7 (26:13)	3.0
55–65	1* (17:32)	1.4 (32:22)	2.1 (12:5)	16.9[a]
Hypertension				
No	1* (292:333)	1.7 (511:461)	2.7 (140:75)	25.0[a]
Yes	1* (23:74)	0.9 (29:48)	1.4 (5:9)	1.0
Diabetes				
No	1* (243:320)	1.4 (408:400)	1.9 (98:68)	16.1[a]
Yes	1* (72:87)	1.6 (132:109)	4.6 (47:16)	25.3[a]
Smoking status				
Never smokers	1* (84:162)	1.3 (102:164)	2.5 (30:25)	8.5[a]
Ex smokers	1* (48:74)	1.5 (103:108)	1.9 (30:527)	4.2[b]
Current smokers, cigarettes/day				
< 15	1* (38:60)	1.6 (65:63)	3.0 (14:9)	5.8[b]
15–24	1* (74:81)	1.1 (114:117)	2.5 (26:13)	4.0[b]
≥ 25	1* (71:30)	1.2 (156:57)	1.8 (45:10)	2.0
Family history of coronary heart disease				
No	1* (252:340)	1.3 (413:434)	2.3 (120:73)	23.0[a]
Yes	1* (63:67)	1.7 (127:75)	2.4 (25:11)	6.3[b]

+ Estimates from multiple logistic regression equations including terms for age and sex.
* Reference category.
** (No. of Cases: No. of Controls)
a = $p < 0.01$; b = $p < 0.05$.

Table 3. *Relative risks+ of acute myocardial infarction according to body mass index and separate strata of selected covariates. Buenos Aires, Argentina, 1984–1989.*

2.5 among intermediate and 1.8 among heavy smokers. Likewise, no apparent interaction was observed with family history of coronary heart disease.

Discussion

The present study confirms that there is a strong direct relationship between body weight and ischaemic heart disease. The relative risk was increased by 40% in overweight subjects, and over twofold higher in severely obese ones. This finding is of particular interest, since it comes from an area of South America with relatively low myocardial infarction rates[23], but with an extremely high prevalence of overweight and obesity. The association was only partly explained through the modifying effect of other major known risk factors for ischaemic heart disease and recognised correlates of overweight, such as diabetes and hypertension. The multivariate relative risk, moreover, may imply some overadjustment, since diabetes and hypertension may well represent a step in the pathogenic linke between overweight and coronary heart disease. The association was consistent across strata of major covariates, although apparently stronger at younger age.

The study design was limited by the resouces available for epidemiological research in this area of the world, and consequently by the small number of variables collected and by the fact that information was based only on self-report, in the absence of any objective validation. A systematic tendency towards overestimating height and underestimating weight is known[24,25]. However, self-reported measures of height and weight show very high correlation with actual ones and, more important, there is little reason to assume a differential reporting of weight and height among cases and controls

and therefore a major distorting effect in the relative risk estimates. If there is an aspecific reduction in the precision of the measures of height and weight for cases and controls, moreover, this should lead to an underestimation of the true association. Some studies suggested that the pattern of body fat distribution (i.e., the deposition of fat predominantly in the abdomen and upper body) may predispose to higher cardiovascular disease risk[26–27]. Since we were unable to distinguish various types of obesity, if this is true we may well have underestimated the true riskk for such a pattern.

Another potential limitation of this study is its hospital-based design. However, since cases and controls were recruited in the main hospitals of the area, the scope for major selection bias was limited. Specific exclusion from the comparison group was made of all diagnoses known or potentially related to risk factors for coronary heart disease, to nutritional status or implying long-term modification of diet. Still, the choice of hospital controls for body weight may lead to an underestimate of the true association, since overweight is related to several diseases[12]. In relation to confounding, the association between acute myocardial infarction and overweight was still significant (although less strongly) after allowance for a number of potentially important distorting factors. We had no information on hypercholesterolaemia, and it is possible that this variable further explains pat of the association, although hypercholesterolaemia (like hypertension or diabetes) may be linked with both overweight and infarction, and hence cause potential overadjustment.

Among the strenghts of this study, on the other hand, are the standardised diagnostic criteria for acute myocardial infarction, the almost complete participation, and the comparability of catchment areas of cases and controls.

The linear direct relationship between body weight and myocardial infarction confirms the observation from several studies, including the Framingham Heart study cohort[1], the American Nurses Health Study[2], two American Cancer Society cohort investigations[3,4], a prospective study of Hawaiian Japanese men[5], and an Italian case-control study[28].

Other studies, however, found non-linear relationship, including the Seven Countries Study[6], two Finnish cohorts[7,8] a smaller Swedish study[9], the Whiteball Study of British civil servants[10], the Pooling Project Research Group[11] and a large Italian National Health Survey[12]. Some of the studies, however, included relatively few events, used imprecise diagnostic criteria or inappropriate adjustment for smoking and other covariates, or had inadequate control for changes or modifications of weight during the follow-up period of cohort studies, and this may well have flattened or distorted the slope of the relationship, particularly if recent weight is of major relevance.

This study further confirms that the importance of overweight and obesity as a risk factor for cardiovascular disease is higher at younger ages. Similar observations were made by the Pooling Project Research Group[11] and from a large case-control study from Italy[28]. These findings, if true, would imply that the public health and social relevance of obesity in relation to cardiovascular disease are even greater than is indicated by the overall age-adjusted relative risk, at least in relative terms. The same pattern of higher relative risks at younger age has been observed for other major cardiovascular risk factors such as smoking[29].

If the observed association is real, in terms of population attributable risk[30] over 40% of acute myocardial infarctions under age 45 and about 25% over age 45 in the Buenos Aires area could be avoided by preventing overweight and obesity. Undoubtly, therefore, intervention aimed at this risk factor is a priority on a public health level in this population. The representativeness of these findings for other urban areas of Latin America, which can be expected to have a different history of alimentation, and in addition a far greater proportion of undernourished people in the population, will be checked in forthcoming investigations. These will be conducted with internationally comparable schemes of sampling and data collection.

Résumé

Poids corporel et risque d'infarctus non mortel du myocarde: Résultats d'une étude cas-témoin conduite en Argentine

La relation entre l'excès pondéral et l'obésité, d'une part, et le risque d'infarctus aigu et non mortel du myocarde, d'autre part, a été analysée à partir des données d'une étude cas-témoin conduite à Buenos Aires, Argentine. Cette étude englobait 1000 patients ayant présenté un infarctus aigu du myocarde et 1000 témoins admis dans les mêmes hôpitaux que les cas pour des affections aiguës non liées aux facteurs connus ou suspectés pour les maladies coronariennes. Seulement 32% des cas et 41% des témoins avaient un index de Quetelet (index de masse corporelle, IMC, Kg m^{-2}) inférieur à 25% des cas et 51% des témoins avaient un excès pondéral (IMC entre 25 et 30) et 15% des cas et 8% des témoins étaient sévèrement obèses (IMC > 30). Après ajustement pour l'âge et le sexe, les risques relatifs (RR) étaient de 1,4 (intervalle de confiance à 95%, IC: 1,1–1,7) pour les sujets dont l'IMC était compris entre 25 et 30 et de 2,2 (95% IC: 1,7–3,1) pour un index supérieur à 30. Après un ultérieur ajustement pour le diagnostic d'hypertension, le diabète, la fumée de tabac et l'histoire familiale de maladies coronariennes, le RR était de 1,2 (95% IC: 1,0–1,6) parmi les sujets avec un index de masse compris entre 25 et 30 et de 1,7 (95% IC: 1,3–2,4) pour ceux avec un index supérieur à 30. La tendance du risque en fonction de la classe d'IMC étaiut statistiquement significative. Dans l'analyse stratifiée, le RR parmi les sujets plus jeunes (30–44 ans) présentant un index supérieur à 30 était de 4,7 (95% CI: 2,0–10,8), alors que l'association était moins prononcée dans les catégories d'âge moyen ou plus avancé. L'étude n'a pas montré d'intéraction avec aucun des autres facteurs de risque identifiés. Ainsi, l'excès pondéral représente un risque majeur et indépendant pour l'infarctus du myocarde, dans cette population d'Amérique du Sud, il est responsable de plus de 40% des cas non mortels d'infarctus du myocarde avant 45 ans et de 25% après 45 ans.

Zusammenfassung

Körpergewicht und nicht tödlicher Herzinfarkt: Resultate einer Fall-Kontroll-Studie aus Argentinien

Die Beziehung zwischen Übergewicht und Fettsucht einerseits und dem Risiko einen akuten, nicht tödlichen Herzinfarkt zu erleiden andererseits, wurde anhand von Daten einer Fall-Kontroll-Studie aus Buenos-Aires, Argentinien, analysiert. Diese Studie verglich 1000 Infarkt-Patienten mit 1000 Kontrollpatienten. Diese waren in dieselben Krankenhäusern wie die Fälle eingeliefert worden wegen akuten Erkrankungen, die nicht mit bekannten oder potentiellen Risikofaktoren für Koronarkrankheiten in Verbindung gebracht werden. Nur 32% der Fälle und 41% der Kontrollen wiesen einen Körpermassenindex (BMI = kg m^{-2}) unter 25 auf, 54% der Fälle und 51% der Kontrollen waren übergewichtig (BMI zwischen 25 und 30) und 15% der Fälle und 8% der Kontrollen litten an Fettsucht (BMI > 30). Nach Standardisierung für Alter und Geschlecht betrugen die relativen Risiken (RR) 1,4 (95% Vertrauensintervall (VI): 1,1–1,7) für das Übergewicht und 2,2 (VI: 1,7–3,1) für die Fettsucht. Nach zusätzlicher Korrektur für diagnostizierten Bluthochdruck, Diabetes, Rauchen und die Familienanamnese einer Koronarkrankheit, belief sich das RR auf 1,2 (VI: 1,0–1,6) für das Übergewicht und auf 1,7 (VI: 1,3–2,4) für die Fettsucht. Der Risikotrend war statistisch signifikant. In der Analyse nach Altersklassen lag das RR einer Fettsucht bei jüngeren Patienten (30–44 Jahre) bei 4,7 (VI: 2,0–10,8), im mittleren und vorgeschrittenen Alter war es geringer. Es wurden keine signifikanten Interaktionen mit den anderen Risikofaktoren festgestellt. Deshalb kann Übergewicht als ein hauptsächlicher und unabhängiger Risikofaktor für Herzinfarkt betrachtet werden, welcher in dieser südamerikanischen Bevölkerung für über 40% der nicht tödlichen Herzinfarkte unter 45 Jahren und für 25% der Fälle über 45 Jahre verantwortlich ist.

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Address for correspondence

Carlo La Vecchia
Instituto di Ricerche Farmacologiche «Mario Negri»
via Eritrea 62
I-20157 Milano/Italy