Brief report

Carotid Intima-Media Thickness in Diabetics and Hypertensive Patients

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A B S T R A C T

The aims of this study are to describe the mean values of carotid intima-media thickness and how it increases with age, and to compare carotid injury in diabetics and hypertensive patients with that of controls. We included 562 subjects (121 diabetics, 352 hypertensive patients, 89 controls). The mean intima-media thickness was 0.781 mm in diabetics, 0.738 mm in hypertensive patients and 0.686 mm in controls. The difference in intima-media thickness between diabetics and controls and between hypertensive patients and controls, adjusted for age, was 0.040 and 0.026 mm, respectively. We observed an increase in intima-media thickness of 0.005 mm in diabetics and of 0.005 mm in controls with every additional year of age. We found carotid damage in 23% of the diabetics, 12% of the hypertensive patients and 3.4% of the controls. In conclusion, the intima-media thickness is greater in diabetics, but the annual increase in the thickness is greater in hypertensive patients.

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Grosor íntima-media carotídeo en diabéticos e hipertensos

R E S U M E N

El objetivo del estudio es describir los valores medios del grosor íntima-media carotídeo (GIMc), la evolución con la edad y la presencia de lesión carotídea en diabéticos e hipertensos comparados con controles. Estudiamos a 562 sujetos (121 diabéticos, 352 hipertensos y 89 controles). El valor medio del GIMc fue 0,781 ± 0,119 mm en diabéticos, 0,738 ± 0,108 mm en hipertensos y 0,686 ± 0,093 mm en controles. La diferencia del GIMc entre diabéticos y controles e hipertensos y controles ajustado por edad fue 0,040 y 0,026 mm respectivamente. Por cada año que aumenta la edad, cabe esperar un incremento del GIMc de 0,005 mm en diabéticos, 0,006 mm en hipertensos y 0,005 mm en controles. Presentaron lesión carotídea el 23% de los diabéticos, el 12% de los hipertensos y el 3,4% de los controles. En conclusión, el GIMc es mayor en diabéticos, pero el incremento anual del grosor es superior en hipertensos.

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INTRODUCTION

Carotid intima-media thickness (IMT) is related to cardiovascular risk factors and diseases, and its measurement by means of ultrasound makes it possible to detect thickening in the initial phases of atherosclerosis.[1,2] For every 0.1-mm increase in carotid IMT, the relative risk of ischemic heart disease increases by 15% and that of cerebrovascular disease by 18%.[3] In type 2 diabetes mellitus (DM2) patients, the carotid IMT is 0.13 mm greater than in the controls. This implies an increase in age of 10 years, a circumstance that is related to a 40% higher cardiovascular risk.[4] Hypertensive patients, even those in a state of prehypertension, have a greater carotid IMT than controls.[5] In Spain, carotid IMT values in patients with no cardiovascular risk factors are available,[6,7] but we have no data on the carotid IMT in DM2 and hypertensive patients. The objective of this study is to compare the mean carotid IMT values and incidence of carotid injury in DM2 and hypertensive patients versus controls and to analyze the increase in carotid IMT with age.

METHODS

We performed a descriptive, cross-sectional study from December 2006 to June 2009. We included consecutively all patients between the ages of 25 and 80 years without previous cardiovascular disease referred to the research unit. The sample was comprised of 352 hypertensive patients, 121 diabetics and 89 individuals who had neither of these diseases. The protocol was approved by the Clinical Research Ethics Committee of the

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Table 1

Clinical Characteristics, Traditional Risk Factors, Emerging Risk Factors and Carotid Intima-Media Values of the Groups of Subjects Included in the Study.

	Diabetics	Hypertensive patients	Controls	Diabetics versus controls, P
Subjects, n (%)	121 (21.5)	352 (62.6)	89 (15.8)	<.001
Age, mean (SD), years	60.23 (10.085)	55.051 (1.333)	50.531 (2.261)	<.001
Sex				.168
Men, n (%)	79 (65.3)	218 (61.9)	47 (52.8)	
Women, n (%)	32 (34.7)	134 (38.1)	42 (47.2)	
Traditional risk factors				
Smokers, n (%)	30 (24.8)	79 (22.4)	27 (30.3)	.295
Office SBP, mean (SD), mmHg	136.22 (16.99)	142.65 (16.92)	125.20 (9.66)	<.001
Office DBP, mean (SD), mmHg	83.58 (9.77)	90.91 (10.43)	80.41 (6.44)	<.001
Pulse pressure, mean (SD), mmHg	53.09 (13.86)	51.96 (13.39)	44.95 (9.87)	<.001
Heart rate, mean (SD), bpm	73.46 (12.75)	73.01 (12.33)	73.19 (14.75)	.967
BMI, mean (SD)	29.77 (5)	28.25 (3.64)	26.79 (3.51)	<.001
LDL-C, mean (SD), mg/dL	112.96 (27.43)	134.48 (33.69)	131.70 (31.69)	<.001
HDL-C, mean (SD), mg/dL	50.60 (12.66)	53.05 (13.03)	55.39 (14.27)	.033
Triglycerides, mean (SD), mg/dL	135.90 (75.28)	132.87 (80.23)	114.57 (61.09)	.092
Altered baseline blood glucose, mean (SD), mg/dL	0.25 (0.43)	0.14 (0.35)	0.05 (0.23)	<.001
Emerging risk factors				
Waist circumference, mean (SD), cm	101.33 (12.68)	97.58 (10.7)	92.84 (11.26)	<.001
Insulin resistance, mean (SD), μU/mL (HOMA index)	4.07 (4.07)	2.43 (1.94)	2.01 (1.56)	<.001
C-reactive protein, mean (SD), mg/dL	0.27 (0.41)	0.27 (0.4)	0.18 (0.18)	.199
Plasma fibrinogen, mean (SD), mg/dL	325.62 (60.12)	316.10 (63.33)	307.63 (71.1)	.156
Common carotid artery ultrasound				
Maximum mean carotid IMT, mean (SD), mm	0.985 (0.27)	0.940 (0.17)	0.816 (0.12)	<.001
Minimum mean carotid IMT, mean (SD), mm	0.628 (0.09)	0.590 (80.08)	0.568 (0.08)	<.001
Average maximum carotid IMT, mean (SD), mm	0.964 (0.14)	0.910 (0.12)	0.850 (0.1)	<.001
Highest maximum carotid IMT, mean (SD), mm	1.237 (0.3)	1.161 (0.2)	1.065 (0.15)	<.001
Lowest maximum carotid IMT, mean (SD), mm	0.749 (0.11)	0.713 (0.1)	0.670 (0.1)	<.001
Average mean carotid IMT, mean (SD), mm	0.781 (0.11)	0.737 (0.1)	0.686 (0.09)	<.001
Carotid injury,[*] n (%)	28 (23.1)	43 (12.2)	3 (3.4)	<.001

BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HOMA, Homeostasis Model Assessment; IMT, intima-media thickness; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; SD, standard deviation.

[*] Carotid injury: if the mean carotid IMT was > 0.9 mm and/or there were arteriosclerotic plaques (carotid IMT ≥ 1.5 mm).

University of Salamanca and all the participants signed an informed consent form.

The clinical, anthropometric and analytical data collected are shown in Table 1. The measurement procedure has been described previously.[8]

Two trained researchers measured the carotid IMT, and reliability was evaluated prior to beginning the study by means of the intraclass correlation coefficient, with values of 0.974 for intraobserver agreement with regard to repeated measurements in 20 subjects, and 0.897 for interobserver agreement. To optimize reproducibility, we employed a SonoSite Micromaxx ultrasound system (SonoSite Inc, Bothell, Washington, United States) using a 5-10 MHz multifrequency high-resolution linear transducer with the Sonocal software package to perform automated measurements of the mean and maximum carotid IMT, with a discrimination limit expressed in microns. The measurements were carried out in common carotid artery, with the subject lying down, neck extended and head slightly turned in the direction opposite to the carotid artery being examined. A 10-mm longitudinal section located at a distance of 1 cm from the bifurcation was studied and measurements were performed in the proximal and distal walls in lateral, anterior and posterior projections, along an axis perpendicular to the artery, to establish two lines: the intima-media interface and the media-adventitia interface. A total of six measurements were obtained in each carotid artery, and the average mean and maximum values were recorded. We considered vascular injury to be present when the mean carotid IMT was greater than 0.9 mm or arteriosclerotic plaques (carotid IMT greater than or equal to 1.5 mm) were detected.[9] The researchers who performed the ultrasound had no data on the patient.

Statistical Analysis

The quantitative variables are expressed as measures of central tendency and dispersion and the categorical variables as percentages. We assessed the association between qualitative variables with the chi-square test and between-group differences in means using analysis of variance (ANOVA) and, as a *post hoc* test, that of Scheffe, with an alpha value of .05. We controlled for the effect of age in the comparison of the means by analysis of covariance (ANCOVA).

We determined the influence of age on carotid IMT using multivariate linear regression analysis, establishing four models: model 1, adjusting for age; model 2, adjusting for age and sex; model 3, adding the traditional risk factors (smoking habit, systolic blood pressure, diastolic blood pressure, pulse pressure, heart rate, body mass index, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides and baseline blood glucose), and model 4, adding the emerging risk factors (waist circumference, C-reactive protein, plasma fibrinogen and insulin resistance evaluated using the HOMA [Homeostasis Model Assessment] index). We identified the variables associated with the presence of carotid injury by means of logistic regression analysis. In the equation, we included as independent variables those used in the multiple linear regression model. We employed the SPSS/PC+ 17.0 statistical software package.

RESULTS

The traditional and emerging risk factors and the ultrasound variables are shown according to groups in Table 1. The difference in carotid IMT between diabetics and controls was 0.095 mm

Table 2

Multiple Regression Analysis of the Carotid Intima-Media Thickness in Diabetics, Hypertensive Patients and Controls According to Different Models.

	β (95% CI)	P
Diabetics		
Model 1: age	0.005 (0.003-0.007)	<.001
Model 2: age and sex	0.005 (0.004-0.007)	<.001
Model 3: age, sex and traditional risk factors	0.005 (0.002-0.008)	<.001
Model 4: age, sex, traditional risk factors and emerging risk factors	0.004 (0.001-0.008)	.014
Hypertensive patients		
Model 1: age	0.006 (0.005-0.007)	<.001
Model 2: age and sex	0.006 (0.005-0.007)	<.001
Model 3: age, sex and traditional risk factors	0.006 (0.005-0.007)	<.001
Model 4: age, sex, traditional risk factors and emerging risk factors	0.006 (0.005-0.007)	<.001
Controls		
Model 1: age	0.005 (0.004-0.007)	<.001
Model 2: age and sex	0.006 (0.004-0.007)	<.001
Model 3: age, sex and traditional risk factors	0.005 (0.002-0.008)	<.001
Model 4: age, sex, traditional risk factors and emerging risk factors	0.004 (0.003-0.008)	<.001

CI: confidence interval.
Dependent variable: average mean carotid intima-media thickness. Reference variable: age. Model 1: adjusted for age. Model 2: adjusted for age and sex. Model 3: adjusted for age, sex and traditional risk factors (smoking habit, office systolic blood pressure, office diastolic blood pressure, pulse pressure, heart rate, body mass index, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides and altered baseline blood glucose). Model 4: adjusted for age, sex, traditional risk factors and emerging risk factors (waist circumference, C-reactive protein, plasma fibrinogen and HOMA [Homeostasis Model Assessment] index).

(95% confidence interval [CI], 0.058-0.132); between hypertensive patients and controls, 0.052 mm (95% CI, 0.020-0.084), and between diabetics and hypertensive patients, 0.043 mm (95% CI, 0.012-0.071). Adjusting these differences for age by means of ANCOVA, we observed differences in the carotid IMT of 0.040 mm between diabetics and controls and 0.026 mm between hypertensive patients and controls (*P* < .05). However, between diabetic and hypertensive patients, the difference was 0.013 mm (*P* > .05).

Multiple linear regression analysis showed that, in diabetics, for every one-year increase in age we can expect an increment in carotid IMT of 0.005 mm in the first three models and of 0.004 mm upon adding the emerging risk factors in model 4. In hypertensive patients, the increment in carotid IMT for every one-year increase in age remains constant in the four models (0.006 mm). In the controls, the beta coefficient ranged from 0.004 mm to 0.006 mm, and the greatest increment in carotid IMT was produced when adjustment was made for sex (0.006 mm); upon adjustment for the traditional and emerging

risk factors, the increase in carotid IMT was 0.005 mm and 0.004 mm, respectively (Table 2).

According to the linear regression line (Fig. 1), the carotid IMT increased by 0.005 mm for every year of age in diabetics and in controls, and by 0.006 mm per year in hypertensive patients, but diabetic and hypertensive patients had higher carotid IMT values at the start of the study.

In the logistic regression analysis, using the presence of carotid injury as a dependent variable and age as a reference variable, in diabetics, for each one-year increase in age, the odds ratio (OR) for presence of carotid injury was 1.05 (95% CI, 1-1.11; ß = 0.052; *P* = .041) in model 1 and 1.06 (95% CI, 1-1.11; ß = 0.057; *P* = .032) in model 2, with no significant changes in models 3 and 4. In hypertensive patients, in model 1, the OR was 1.12 (95% CI, 1.07-1.16; ß = 0.112; *P* < .001); in model 2, OR = 1.12 (95% CI, 1.08-1.17; ß = 0.115; *P* < .001); in model 3, OR = 1.22 (95% CI, 1.06-1.61; ß = 0.276; *P* = .002); and in model 4, OR = 1.39 (95% CI, 1.06-1.61; ß = 0.276; *P* = .007); the controls were not included because only three subjects had carotid injury.

y = 0.458 mm + (0.005 mm * Age)   y = 0.415 mm + (0.006 mm * Age)   y = 0.414 mm + (0.005 mm * Age)
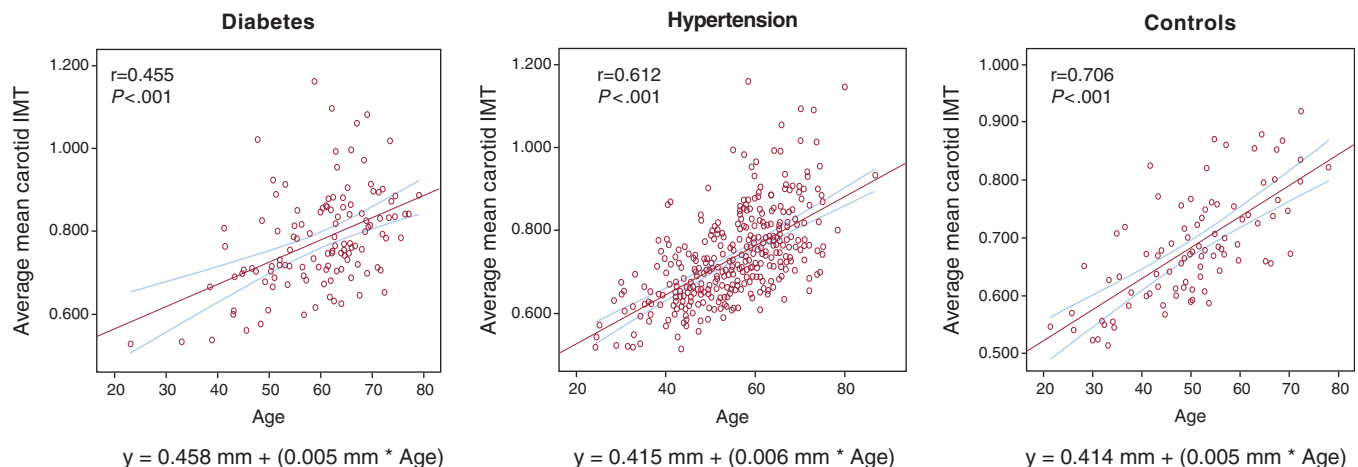
Figure 1. Simple linear regression lines, regression equations and r and *P* values showing the correlations between mean intima-media thickness and age in diabetics, hypertensive patients and controls.

DISCUSSION

Our study shows that the carotid IMT and the incidence of carotid injury are greater in diabetics; hypertensive patients have intermediate values and the controls, lower; the differences in carotid IMT are maintained after adjustment for age.

Patients with DM2 have an average mean age-adjusted carotid IMT 0.04 mm greater than the controls, a value lower than that reported by Brohall et al,[4] who measured the carotid IMT in predefined segments (0.09 mm). The difference between hypertensive patients and controls in terms of carotid IMT is 0.026 mm, with an annual increment of 0.006 mm. These findings are similar to those of Puato et al[5] with respect to the difference in carotid IMT, but lower than the annual mean increment of 0.11 mm over 5 years of follow-up.

The data in Spain in individuals without risk factors[6,7] reflect an increase in the annual mean carotid IMT of 0.005 mm and 0.006 mm per year, similar to the controls in this report. In the United States,[3] based on annual carotid IMT measurements, a yearly progression of 0.010 mm has been estimated and, in Japan,[10] this value is 0.006 mm. The differences can be explained, in addition to the origin of the population, by the method utilized and the segment of carotid examined. One noteworthy observation is the loss of influence of age on carotid IMT upon adjustment for the traditional and emerging risk factors among diabetic subjects and controls, there being no clear explanation for this circumstance, although it is probably due to the fact that, from the time they receive the diagnosis of their disease, the majority of diabetic individuals are being treated with statins, drugs that reduce the carotid IMT; nevertheless, it is a finding that needs to be confirmed in prospective studies.

In conclusion, the carotid IMT is greater in diabetics, but the annual increase in thickness is higher in hypertensive patients.

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CONFLICTS OF INTEREST

None declared.

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