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Association of Visceral Adipose Tissue and Subclinical Atherosclerosis in US-Born Mexican Americans but not First Generation Immigrants

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ORIGINAL RESEARCH

Association of Visceral Adipose Tissue and Subclinical Atherosclerosis in US-Born Mexican Americans but not First Generation Immigrants

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BACKGROUND: Excess visceral adipose tissue (VAT) is a primary driver for the cardiometabolic complications of obesity; VAT-associated cardiovascular disease risk varies by race, but most studies have been done on Non-Hispanics. This study aimed to evaluate the clinical and metabolic correlates of VAT, its association with subclinical atherosclerosis, and the factors affecting this association in Mexican Americans.

METHODS AND RESULTS: Participants (n=527) were drawn from the Cameron County Hispanic Cohort (CCHC), on whom a carotid ultrasound to assess carotid intima media thickness and a dual-energy X-ray absorptiometry scan to assess for VAT were obtained. Those in the highest quartiles of VAT were more likely to have hypertension, hypertriglyceridemia, low high-density lipoprotein, diabetes mellitus, and metabolic syndrome. Increased carotid intima media thickness was more prevalent in those in the highest quartile for VAT (57.4% versus 15.4% for the lowest quartile; $P<0.001$). There was a graded increase in mean carotid intima media thickness with increasing VAT, after adjusting for covariates; for every 10 cm^2 increase in VAT, there was an increase of 0.004 mm (SE=0.002; $P=0.0299$) in mean carotid intima media thickness. However, this association was only seen among second or higher generation US-born Mexican Americans but not among first generation immigrants ($P=0.024$).

CONCLUSIONS: Excess VAT is associated with indicators of metabolic disorders and subclinical atherosclerosis in Mexican Americans regardless of body mass index. However, acculturation appears to be an important modulator of this association. Longitudinal follow-up with targeted interventions among second or higher generation Hispanics to lower VAT and improve cardiometabolic risk may help prevent premature cardiovascular disease in this cohort.

Key Words: adipose tissue ■ subclinical atherosclerosis risk factor ■ cardiometabolic risk ■ health disparities ■ acculturation

Hispanics and Latinos face a disparately increased prevalence of coronary risk factors,[1] and in particular, obesity and metabolic syndrome have been shown to be higher in Hispanics than in non-Hispanics.[2] The Hispanic population is currently the third fastest growing population in the United States with the population size expected to increase by over 110% by the year 2060.[3] The role of the obesogenic US social culture on immigrants has been studied for other ethnicities,[4,5] and acculturation has similarly been linked to obesity, diabetes mellitus, and cardiometabolic risk among Mexican American immigrants.[6,7] Recent research, coupled with advances in imaging techniques, has demonstrated that central obesity and the accumulation of visceral adipose tissue (VAT) play important roles in the development of some of the components

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CLINICAL PERSPECTIVE

What Is New?

- Among Mexican Americans, increased visceral adipose tissue is an independent predictor of early atherosclerosis in US-born Mexican Americans, but not first generation immigrants.
- Acculturation appears to affect the association between excess visceral adipose tissue and atherosclerotic cardiovascular disease.

What Are the Clinical Implications?

- Targeted interventions among second or higher generation Hispanics to lower visceral adipose tissue and improve cardiometabolic risk may help prevent premature cardiovascular disease in these Americans.

Nonstandard Abbreviations and Acronyms

CCHC	Cameron County Hispanic Cohort
cIMT	carotid intima media thickness
DXA	dual-energy X-ray absorptiometry
VAT	visceral adipose tissue

of metabolic syndrome, specifically, hypertension, glucose intolerance, and dyslipidemia,[8–10] all of which are, in and of themselves, also important risk factors for the development of atherosclerotic cardiovascular and cerebrovascular diseases. Most studies, however, have been carried out in Non-Hispanic populations. Abdominal fat distribution varies significantly between racial and ethnic groups,[10,11] and research exploring these disparities is important.

Increased carotid intima media thickness (cIMT), as measured by ultrasonography, is a marker for early diffuse atherosclerosis and portends an increased risk for cardiovascular disease events.[12,13] Several investigations have shown a relationship between increased VAT and subclinical atherosclerosis independent of obesity and other metabolic risk factors.[14,15] Sparse research has been done to determine their associations in the adult Mexican American population. This study aimed to evaluate the clinical and metabolic correlates of VAT, its association with subclinical atherosclerosis, and the factors, including acculturation, that may account for this association in asymptomatic, community-dwelling adult Mexican Americans. Elucidation and early detection of predictors of cardiovascular risk in this health disparity minority population is imperative to design appropriate preventive strategies and optimal medical therapy.

METHODS

Study Population

Study subjects were drawn from the Cameron County Hispanic Cohort (CCHC, n=5000), recruited from randomly selected blocks according to the 2000 Census, as described previously.[16,17] The CCHC is an ongoing homogenous community-dwelling Mexican American cohort living in Brownsville, Texas, located on the lower Rio Grande River at the United States-Mexico border. Bilingual research and field workers obtained demographics of the participants including an extensive medical history, as described in previous studies.[16,17] Participants with a documented history of prior heart attack or stroke were excluded from the study. Participants for this study (n = 527) were a sequential subset of individuals drawn from the CCHC, on whom we had obtained both a carotid ultrasound to assess carotid intima media thickness (cIMT) and a dual-energy X-ray absorptiometry (DXA) scan to assess for VAT. The Institutional Review Board of the McGovern Medical School at the University of Texas Health Science Center at Houston approved this study with all participants giving written informed consent. The data that support the findings of this study are available upon reasonable request. Requests should be made to Susan P. Fisher-Hoch MD at Susan.P.Fisher-Hoch@uth.tmc.edu.

Measurements

Anthropometric measurements, including height, weight, and waist circumference, were obtained. Body mass index (BMI) was calculated as weight in kilograms divided by height squared in meters (kg/m^2). BMI was categorized according to the National Heart Lung and Blood Institute (NHLBI) with overweight defined as a BMI 25.0-29.9 kg/m^2 and obesity defined as a BMI ≥ 30.0 kg/m.[18] Hypertension was diagnosed using both questionnaires and obtained sphygmomanometer measurements. The subject was deemed to have hypertension if the participant self-reported a prior diagnosis of hypertension, was currently taking anti-hypertensive medications, or if his/her mean systolic blood pressure was ≥ 130 millimeters of mercury (mm Hg) and/or the mean diastolic blood pressure was ≥ 85 mm Hg. Participants were asked to fast for at least 10 hours overnight before a visit to the Clinical Research Unit. Routine laboratory studies performed included electrolytes, fasting lipid and metabolic panels, complete blood count, and glycated hemoglobin. Homeostasis model assessment insulin resistance (HOMA-IR) was calculated using the equation, HOMA-IR= (glucose x insulin)/405.[19] Metabolic syndrome was defined as the presence of at least 3 of the following risk factors:

(1) elevated waist circumference (≥102 cm in males and ≥ 88 cm in females); (2) elevated triglyceride (≥150 mg/dL) or treatment with triglyceride lowering medication, (3) low high-density lipoprotein cholesterol (<40 mg/dL in males and < 50 mg/dL in females) or treatment with high-density lipoprotein cholesterol raising medication; (4) elevated blood pressure (systolic ≥ 130 mm Hg and/or diastolic ≥ 85 mm Hg), previous diagnosis of hypertension, or treatment with an anti-hypertensive medication; and (5) elevated fasting glucose (≥100 mg/dL) or treatment with glucose lowering medication.[20] Total cholesterol was considered elevated if the measured value was ≥ 200 mg/dL, if the patient had previously been diagnosed with high total cholesterol, or if the patient was on cholesterol lowering medication. Low-density lipoprotein was considered elevated if the calculated value was ≥ 130 mg/dL or if the patient was on low-density lipoprotein lowering medication. Classification of diabetes mellitus was also determined from both self-reported diagnosis of diabetes mellitus and/or per the latest guidelines from the American Diabetes Association.[21] Fruit and vegetable consumption was assessed using the Two-item Food Frequency Questionnaire by asking participants how many portions of fruits and vegetables they consumed daily.[22] A portion size was determined based on a ½ cup of fresh, frozen, or canned fruit or vegetable or a medium-sized produce. If a participant reported consuming five or more portions of fruit and vegetable daily, that participant was considered as having met the US dietary guidelines.[23,24]

Acculturation represents the degree to which immigrant populations learn and adopt certain aspects of the dominant culture and/or retain aspects of their culture of origin.[25] Despite the absence of a gold standard to measure acculturation, surrogate measures include language preference and generational status. Because of the language homogeneity in this Mexican American border cohort, acculturation was evaluated in this study using country of birth rather than language.[26] Participants were categorized as first generation if the person was not born in the United States and at least one parent was also not born in the United States. Participants who were born in the United States, but has at least one parent not born in the United States were classified as second generation. Participants born in the United States with both parents born in the United States were classified as third generation.[26] Definition of these generational categories are similar to other studies in Mexican American populations.[25,27]

Carotid ultrasound to evaluate subclinical atherosclerosis was performed with the Siemens Acuson X300 ultrasound system (Malvern, PA) using a VF 13-5 linear array transducer as described in previous studies.[17] The protocol was designed following guidelines from the American Society of Echocardiography consensus statement on subclinical vascular disease.[25] Both left and right common carotid arteries were imaged from 3 different angles for a total of 6 images: anterior, lateral, and posterior images for both common carotid arteries. Carotid IMT (cIMT) was measured using the Carotid Analyzer software (Medical Imaging Applications, Coralville, IA), a semi-automated border detection program. Measurements were made at the R-wave of the electrocardiogram on a minimum of 2 clips from each side and the results were averaged as mean cIMT (mm). Increased cIMT (yes or no) was defined as mean cIMT ≥ 75th percentile for age and sex.[28] Carotid plaque was defined as an area of wall thickening that was >50% of the thickness of the surrounding wall. Carotid plaque presence was determined by examining the carotid bulb, its bifurcation, and the carotid branch arteries, in addition to the common carotid artery. Abnormal carotid ultrasound study was defined as increased cIMT and/or the presence of carotid plaque. A single blinded expert reader similarly performed all measurements. Replicate readings were performed on 5% of the cohort and the intra-class correlation coefficient for our laboratory was 0.96.

Total body composition was analyzed utilizing the Hologic APEX 3.1 software (Hologic) using standard procedures outlined in the user guide for the DXA machine (Discovery W, Hologic Inc., Marlborough, MA, USA).[29] DXA estimated VAT measurements were obtained in a 5-centimeter wide region across the entire abdomen slightly above the level of the iliac crest at a location that coincided with the 4th lumbar vertebrae. At this location, the software locates the outer and inner margins of the abdominal wall, utilizing the fat and lean mass profiles in this section to create the visceral region, which contains both subcutaneous fat and VAT. The software then measures the total fat mass within this visceral region. The amount of subcutaneous adipose tissue was then estimated by measuring the subcutaneous fat between the skin line and the outer abdominal wall. This estimated amount of subcutaneous adipose tissue was then subtracted from the total abdominal fat mass measured within the visceral region to give the measured DXA VAT area in centimeters squared (cm^2).[30]

Statistical Analysis

All descriptive results and the models reported were adjusted for the probability of sampling using age and sex adjusted sampling weights, and for the clustering effects arising from multiple participants

from the same household, as well as census tracks and blocks. Descriptive statistics of demographics and clinical characteristics were reported and compared. Data were summarized as mean and standard error for continuous variables and frequency and weighted column percentages for categorical variables. Continuous variables were compared using survey-weighted linear regression models from which Tukey-Kramer-adjusted p values were calculated. Survey-weighted logistic regression was used to compare categorical variables and to obtain the Rao-Scott F-adjusted chi-square p values. Survey-weighted multivariable linear regression models were constructed to evaluate the effect of increasing VAT, as a continuous variable and grouped into quartiles, on cIMT after adjusting for confounders. Multiplicative interaction effect between participants' immigration status and VAT area was tested in linear regression models, and the generation-specific effect of VAT on cIMT was reported. All analyses were performed using Statistical Analysis Software ver. 9.4 (SAS Institute Inc., Cary, NC). Statistical significance was set at $P<0.05$.

RESULTS

Demographic and biochemical characteristics are listed in Table 1. This study included 527 individuals (57.8% females) with an average age of 53.7±14.2 years. There was a high prevalence of cardiovascular disease risk factors in this cohort. More than a quarter of the subjects were diabetic (27.8%) and almost one-half were hypertensive (49.0%). An overwhelming majority of the individuals were classified as either overweight or obese (84.1%) with a mean BMI of 30.5±5.5 kg/m^2. Nearly half (44.9%) had a diagnosis of metabolic syndrome. Average household income was $29,100 and almost half (49.4%) have less than a high school education.

Participants who were in the highest quartile of VAT had larger anthropometric measurements, such as weight, waist circumference, hip circumference, waist-to hip ratio, and BMI ($p < 0.05$; Table 1). Subjects in the highest quartiles of VAT were also more likely to have hypertension, hypertriglyceridemia, low high-density lipoprotein, diabetes mellitus, and metabolic syndrome ($P<0.05$; Table 1). They also had higher insulin levels, higher HOMA-IR values, higher HbA1c values, and higher fasting blood glucose levels ($P<0.05$, Table 1). Transaminase levels did not differ significantly by VAT quartile. There was no difference in household income or education level between the VAT quartiles, however, a longer duration of residence in the United States was significantly associated with an increased amount of VAT ($P<0.05$, Table 1).

The mean cIMT for the cohort was 0.74±0.02 mm with a significant difference noted among individuals in the highest quartile of VAT ($P < 0.001$; Table 2). Nearly half (43.2%) of the subjects had an abnormal carotid ultrasound suggestive of a high prevalence of early atherosclerosis. Increased cIMT (i.e., mean cIMT≥75th percentile for age and sex) was found to be more prevalent in those individuals in the highest quartile for VAT compared to those in the lowest quartile (57.4% versus 15.4%; $P<0.001$).

Increasing VAT was significantly associated with increasing cIMT (β±SE = 0.005±0.002; $P=0.016$, Table 3), even after adjusting for age, sex, and BMI. In a multivariable weighted linear regression model, there was a graded increase in weighted mean cIMT with increasing VAT area, even after adjusting for age, sex, BMI, HbA1c, and systolic blood pressure; for every 10 cm^2 increase in VAT area there was an increase of 0.004 mm (SE=0.002; $P=0.0299$) in mean cIMT. However, this association between VAT area and cIMT varied by generational status ($P=0.043$), and there was an interaction effect between generational status (i.e., first generation immigrant versus later generations) and VAT area on cIMT. On the generational stratified analysis, the association between VAT area and cIMT was significant only among second or higher generation Mexican Americans, but not among first generation immigrants ($P=0.024$, Figure 1). Cohort demographics categorized by generational status (Table S1) showed no significant difference in mean age, BMI, blood pressure, lipid levels, prevalence of hypertension or diabetes mellitus, or statin use, although second or higher generation Mexican Americans were more likely to be male and had higher educational levels attained.

DISCUSSION

Our study showed that in asymptomatic community dwelling Mexican Americans, visceral adipose tissue was associated with early atherosclerosis, independent of age, sex, or BMI, and that there was a graded increase in carotid intimal media thickness with increasing VAT, regardless of BMI. Although this association has been shown in other racial groups,[31–33] our study is one of a few demonstrating this relationship in Hispanics.

The exact mechanisms by which VAT predisposes patients to atherosclerosis are still unclear, however, VAT is known to be metabolically active with endocrine, metabolic, and inflammatory activities.[34] This fat depot secretes numerous adipocytokines that can affect several metabolic, inflammatory, and vascular pathways, including plasminogen activator inhibitor type-1, tumor necrosis factor-alpha, interleukin 1and 6, and angiotensin II, all of which are linked to the atherosclerotic

Table 1. Cohort Demographics and Metabolic Characteristics (With Sampling Adjustment)

Continuous Variable	Total N=527	Visceral Adipose Tissue (VAT) Quartile				*P* Value
		1st	2nd	3rd	4th	
Age, y	53.6±1.3	47.0±2.4	50.6±1.8	55.2±1.4	62.0±2.4	<0.001
Weight, kg	78.1±1	68.2±2.2	75.1±1.4	82.2±1.2	87.8±1.6	<0.001
Body mass index, kg/m^2	30.3±0.3	26.7±0.7	28.7±0.5	31.7±0.5	34.1±0.5	<0.001
Waist circumference, cm	102.8±0.9	93.3±1.9	98.4±1.2	105.7±1.0	114.4±1.1	<0.001
Hip circumference, cm	108.3±0.7	101.9±1.4	105.6±1.1	109.8±0.8	116.2±1.1	<0.001
Waist-to-hip ratio	0.95±0.004	0.92±0.02	0.94±0.01	0.97±0.01	0.99±0.01	<0.001
VAT area, cm^2	176.0±6.9	80.9±5.0	152.2±1.6	198.5±2.5	277.5±8.1	<0.001
Systolic blood pressure, mm Hg	123.2±1.4	117.9±2.6	119.7±1.9	123.5±1.9	131.5±2.8	0.001
Diastolic blood pressure, mm Hg	73.2±0.6	69.9±1.4	73.2±0.8	75.4±1.1	74.6±0.9	0.0014
Fasting blood glucose, mg/dL	111.2±2.9	99.1±2.9	101.2±4.8	120.7±9.7	125.0±5.7	0.0003
Total cholesterol, mg/dL	184.7±2.4	180.8±4.4	187.2±4.1	189.2±5.0	182.9±6.4	0.5956
Triglycerides, mg/dL	153.8±7.5	124.4±7.2	146.9±11.7	153.6±12.0	190.5±20.1	0.0058
High-density lipoprotein, mg/dL	47.0±1.0	51.7±2.1	48.7±1.6	44.8±1.2	42.4±1.8	0.0013
Low-density lipoprotein, mg/dL	107.3±1.9	104.3±3.7	106.9±3.8	114.8±4.3	105.0±4.9	0.3508
Insulin level, mU/L	11.4±0.5	8.8±0.6	11.1±1.1	12.4±1.0	14.0±1.0	<0.0001
HOMA-IR	3.1±0.2	2.2±0.2	2.7±0.3	3.5±0.3	4.1±0.3	<0.0001
Hemoglobin A1c, %	6.3±0.1	5.9±0.1	6.0±0.2	6.5±0.2	6.8±0.2	0.0004
White blood cell count	6.6±0.1	6.4±0.2	6.8±0.2	6.6±0.2	6.9±0.2	0.4521
ALT	35.0±1.4	30.1±2.6	36.8±3.4	36.6±2.4	37.4±2.3	0.1318
AST	25.2±1.1	22.4±2.0	26.5±3.3	25.3±1.3	26.7±1.8	0.3636
Number of years lived in Brownsville	28.1±1.6	20.9±1.4	25.0±1.8	30.4±2.9	36.6±3.6	0.0002
Household income per year (1K$)	29.1±2.4	31.5±6.0	30.2±3.8	33.0±4.6	22.2±2.4	0.0737
Education level (y)	11.4±0.4	11.6±0.8	12.6±0.7	11.2±0.7	10.3±1.0	0.2218
Categorical variables weighted frequency (%, SE)	**Total**	**1st**	**2nd**	**3rd**	**4th**	***P* Value**
Male	42.2 (3.1)	33.6 (6.6)	50.5 (5.7)	43.1 (7.0)	42.9 (7.7)	0.397
Female	57.8 (3.1)	66.4 (6.6)	49.5 (5.7)	56.9 (7.0)	57.1 (7.7)	
Less than high school education	49.4 (3.6)	48.9 (7.0)	41.1 (5.5)	49.7 (6.7)	57.2 (7.0)	0.365
Immigration status						
1st generation	69.2 (3.5)	73.1 (6.5)	66.1 (6.2)	76.0 (5.2)	62.2 (8.0)	0.418
≥2nd generation	30.8 (3.5)	26.9 (6.5)	33.9 (6.2)	24.0 (5.2)	37.8 (8.0)	
Alcohol use	5.4 (1.6)	4.1 (3.1)	1.5 (0.8)	9.5 (4.0)	6.9 (3.5)	0.248
Meet daily fruit & vegetable intake	16.0 (3.4)	9.0 (3.0)	20.7 (5.4)	13.0 (5.3)	21.8 (9.7)	0.318
Central obesity	70.9 (3.0)	46.8 (6.8)	55.7 (5.7)	87.9 (3.6)	95.6 (1.8)	<0.0001
Hypertension	49.0 (3.7)	31.8 (6.9)	40.9 (5.6)	55.9 (6.6)	68.4 (5.8)	<0.0001
Total cholesterol ≥ 200 mg/dL	42.4 (3.1)	32.4 (5.7)	36.0 (5.5)	51.5 (6.9)	51.1 (7.3)	0.071
Triglycerides ≥ 150 mg/dL	45.1 (3.2)	30.3 (5.0)	38.3 (5.8)	44.5 (6.6)	67.0 (6.4)	<0.0001
High-density lipoprotein < 40 mg mg/dL in males and < 50 mg/dL in females[7]	52.1 (3.4)	42.1 (7.0)	41.3 (5.8)	53.4 (7.0)	71.0 (5.5)	0.002
Low-density lipoprotein ≥ 130 mg/dL	25.3 (3.2)	14.3 (4.2)	24.1 (4.5)	39.9 (7.5)	26.2 (8.6)	0.049
DM						0.001
Normal	31.4 (3.2)	45.2 (6.7)	39.4 (6.0)	27.9 (5.7)	12.7 (4.2)	
Impaired (or pre-DM)	40.8 (3.5)	33.0 (6.3)	45.8 (5.9)	41.0 (7.2)	43.9 (7.8)	
DM	27.8 (2.8)	21.7 (6.5)	14.8 (4.0)	31.0 (5.7)	43.4 (7.1)	
Metabolic syndrome	44.9 (3.3)	27.0 (6.6)	28.4 (5.3)	47.9 (6.7)	75.9 (5.6)	<0.001

*Student's t-test for continuous variables and Rao-Scott Chi-Square Test for categorical variables. ALT indicates alanine transaminase; AST, aspartate transaminase; DM, diabetes mellitus; HOMA-IR, homeostasis model assessment insulin resistance; and VAT, visceral adipose tissue.

Table 2. Carotid Ultrasound Findings

Variable	Total	VAT Quartile [Mean±SE or % (SE)]				*P* Value
		1st	2nd	3rd	4th	
Mean cIMT, mm	0.74±0.02	0.66±0.02	0.71±0.02	0.77±0.03	0.83±0.05	<0.001
Mean cIMT ≥ 75th percentile for age and sex (%)	35.49 (3.65)	15.38 (3.76)	28.54 (5.28)	42.51 (6.90)	57.36 (7.07)	<0.001
Presence of carotid plaque (%)	21.48 (3.14)	17.1 (5.15)	13.86 (3.88)	16.73 (5.19)	36.83 (7.96)	0.011
Abnormal carotid study (%)	43.18 (3.46)	25.9 (5.47)	31.99 (5.40)	49.77 (6.74)	65.76 (6.36)	<0.001

cIMT indicates carotid intima media thickness; and VAT, Visceral Adipose Tissue.
*Student's t-test for continuous variables and Rao-Scott Chi-Square Test for categorical variables.

process. Visceral adiposity increases with obesity and is a key component of insulin resistance. VAT can secrete large quantities of free fatty acids that affect the intrinsic methods for reducing blood glucose levels, including insulin-mediated glucose uptake, hepatic glycogen synthesis, and glucose oxidation, which then can result in insulin resistance and, in turn, metabolic syndrome, both of which are important risk factors for atherosclerotic cardiovascular disease.[34]

Another relevant finding in this study is the high prevalence of diabetes mellitus, hypertension, obesity, and metabolic syndrome in this population, which we have reported previously.[17,35,36] Given the rapidly growing Mexican American population in the United States, the very high prevalence of atherosclerotic cardiovascular disease risk factors in our cohort amplifies the pressing need for targeted preventive strategies in this disparity group. The presence of increased visceral adiposity should alert clinicians to screen for early atherosclerosis, with the goal of intensification of risk factor modification to reduce the risk of a first cardiovascular disease event.

A unique finding in this study was that the association between visceral adipose tissue and early atherosclerosis was significant only among second or higher generation Mexican Americans (i.e., US-born) and not among the first generation immigrants. This finding raises interesting insights into the role acculturation plays in the development of visceral adiposity and atherosclerotic cardiovascular disease. Data from MESA (Multi-Ethnic Study of Atherosclerosis) cohort showed that coronary artery calcium scores and the presence of carotid plaque increased as the years of residence in the United States increased,

Table 3. Multiple Linear Regression Results in Predicting Mean cIMT

	Model 1 (Unadjusted) †		Model 2†		Model 3†		Model 4†	
Mean cIMT (mm)*	β (SE)	95%CI	β (SE)	95%CI	β (SE)	95%CI	β (SE)	95%CI
VAT area (per 10 cm^2)	0.010 (0.003)‡	(0.004, 0.015)	0.004 (0.001)§	(0.001, 0.007)	0.005 (0.002)‖	(0.001, 0.009)	0.004 (0.002)‖	(0.0004, 0.008)
Age (per 1 years)	…		0.007 (0.001)‡	(0.006, 0.008)	0.007 (0.001)‡	(0.005, 0.008)	0.006 (0.001)‡	(0.005, 0.008)
Sex (male vs. female)	--		0.093 (0.019)‡	(0.056, 0.131)	0.090 (0.018)‡	(0.056, 0.126)	0.086 (0.018)‡	(0.052, 0.122)
BMI (per 1 kg/m^2)	…		…		-0.002 (0.002)	(–0.006, 0.002)	0.002 (0.002)	(–0.006, 0.002)
SBP (per 10 mm Hg)	…		…		…		0.010 (0.005)	(–0.001, 0.019)
HbA1c (per 1 %)	…		…		…		0.012 (0.007)	(–0.002, 0.025)
R^2 (%)	0.18		0.50		0.50		0.52	

95%CI indicates 95% Confidence Interval; BMI, body mass index; cIMT, carotid intima media thickness; HbA1c, hemoglobin A1c; R^2 = Adjusted multiple R^2; SBP, systolic blood pressure; VAT, Visceral Adipose Tissue; and β, regression coefficient.
Model 1: Multiple linear regression model including only VAT area in the model.
Model 2: Model 1+age, sex.
Model 3: Model 2+BMI.
Model 4: Model 3+SBP, HbA1c.
*Per 10 cm^2 of VAT area, beta coefficient (95% CI).
†Variables were included in models.
‡*P*<0.001.
§*P*<0.01.
‖*P*<0.05.

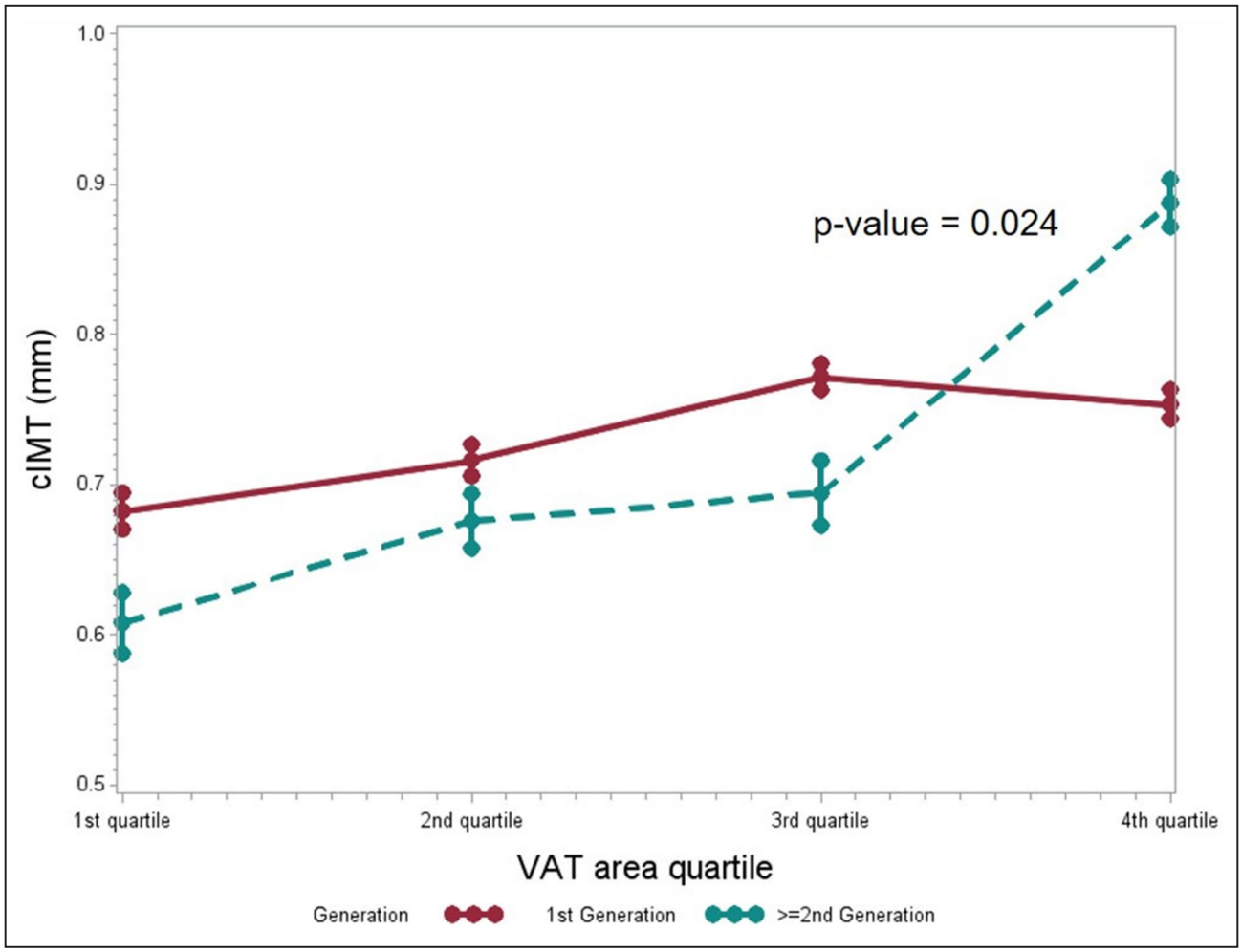

Figure. Weighted mean carotid intima media thickness (cIMT) across vascular adipose tissue (VAT) quartiles by generational status after adjusting for age, sex, body mass index, hemoglobin A1c, and systolic blood pressure, generated from an adjusted linear regression model (weighted mean cIMT±SE).
The *P* value pertains to the hypothesis that there is a significant overall interaction effect between generational status and VAT quartiles.

even after adjusting for conventional coronary artery disease risk factors.[37,38] One of the most well-recognized contributors to this increased risk is the role of the obesogenic US social culture on immigrants. Along with the increasing prevalence of a sedentary lifestyle, a change to a diet rich in saturated fats, excess trans-fats, and other energy dense nutrients likely plays a major role in the obesity epidemic plaguing Mexican American immigrants. As immigrants acculturate to the "US lifestyle" of overeating and lowered physical inactivity, their risk of developing abdominal obesity increases, with stimulation of neurohormonal pathways that result in insulin resistance and endothelial dysfunction, thus promoting the development of diabetes mellitus and other cardiovascular disease risk factors. Mexican Americans born in Mexico or first generation immigrants tend to stick with traditional native Mexican diets longer compared to Mexican Americans born in the United States, whose diets almost entirely represent that of a "US lifestyle."[39] They are more likely to eat beans, fruit, and vegetables, and less likely to eat fast food or desserts in comparison to their US-born Mexican American counterparts.[40] In the CCHC, we have shown that US-born Mexican Americans had lower dietary self-efficacy scores than Mexico born Mexican Americans,[26] and are more likely to not know how to cook or to rely on fast food restaurants and pre-made food items at the grocery store than their parents. This delayed acculturation of first generation Mexican Americans may be a factor in the so-called Hispanic health paradox, but these protective behaviors seem to be diminished with each succeeding generation of Mexican Americans. A longer percent of lifetime exposure to an adverse lifestyle, as well as learned behaviors that conform to the "US obesogenic lifestyle," appear to be modulators in the linkage between VAT and early atherosclerosis.

Limitations

A few limitations must be noted. This was a cross-sectional study, and as such, no causality of the results can be made; however, longitudinal follow-up studies are currently underway for this cohort. Although there are several surrogate measures to determine acculturation, including years of residence in the United States and preferred language, we chose to use country of birth as a measure of acculturation. We acknowledge that acculturation effects are complex, and these were not fully explored in this study. Only a small portion of our study cohort had inflammatory markers drawn and, hence, we did not have enough power to include this variable in our analysis. Although computed tomography and magnetic resonance imaging are considered gold standards for the measurement of visceral adipose tissue, the expense and limited availability of these imaging modality scanners make their use impractical in a disparity cohort. Used for a variety of purposes, such as bone densitometry and whole-body composition analysis, DXA scans are relatively inexpensive, have very minimal exposure to potentially harmful radiation, and are more readily obtainable in a community-based cohort such as ours. DXA estimated VAT has been validated with VAT obtained by computed tomography and magnetic resonance imaging.[41–43]

CONCLUSIONS

In Mexican Americans, increased VAT is an independent predictor of subclinical atherosclerosis among those born in the United States but not among first generation immigrants. With the growing rate of obesity in the Mexican American population, the metabolic manifestations of obesity, such as hypertension, impaired glucose tolerance, and dyslipidemia, have led to an alarming increase in the prevalence of the metabolic syndrome in this minority population. Although the precise mechanisms linking increased risk of both excess VAT and atherosclerotic cardiovascular disease are likely complex, acculturation appears to be an important modulator of this association. Longitudinal follow-up with targeted interventions among second or higher generation Hispanics to lower VAT and improve cardiometabolic risk may help prevent premature cardiovascular disease in this cohort. Insight from studies such as this could yield important preventive and therapeutic targets in the future public health planning of this rapidly growing population.

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Disclosures

None.

Supplementary Material

Table S1

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SUPPLEMENTAL MATERIAL

Table S1. Cohort Demographics and Metabolic Characteristics by generation status.

	1st generation (n =384)	≥ 2nd generation (n=142)	p-value
Continuous Variable			
Mean cIMT (mm)	0.73 ± 0.01	0.75 ± 0.05	0.631
Age (years)	55.6 ± 0.9	49.4 ± 3.7	0.100
Weight (kg)	76.4 ± 1.1	82.0 ± 1.9	**0.010**
Body Mass Index (kg/m^2)	30.1 ± 0.4	30.6 ± 0.7	0.594
Waist Circumference (cm)	102 ± 1	104.7 ± 1.8	0.181
Hip Circumference (cm)	107.6 ± 0.8	110.1 ± 1.3	0.092
Waist-to-hip ratio	0.9 ± 0	0.9 ± 0	0.975
VAT area (cm^2)	170.2 ± 6.3	189.5 ± 16.3	0.271
Systolic Blood Pressure (mm Hg)	122 ± 1.3	125.7 ± 3.1	0.275
Diastolic Blood Pressure (mm Hg)	72.3 ± 0.6	74.9 ± 1.4	0.091
Fasting Blood Glucose (mg/dL)	109.2 ± 2.6	115.9 ± 7	0.373
Total Cholesterol (mg/dL)	185.9 ± 2.4	181.8 ± 6	0.528
Triglycerides (mg/dL)	147 ± 6.2	169 ± 19.2	0.278
High Density Lipoprotein (mg/dL)	47.1 ± 0.9	46.7 ± 2.5	0.881
Low Density Lipoprotein (mg/dL)	108.9 ± 2.1	103.8 ± 4.3	0.298
Insulin Level (mU/L)	11 ± 0.5	12.4 ± 1.2	0.251
Homeostasis model assessment insulin resistance (HOMA-IR)	3 ± 0.1	3.4 ± 0.3	0.177
Hemoglobin A1c, %	6.3 ± 0.1	6.2 ± 0.2	0.847
White Blood Cell Count	6.7 ± 0.1	6.6 ± 0.2	0.818
Alanine Transaminase (ALT)	34.6 ± 1.7	35.5 ± 2.1	0.752
Aspartate Transaminase (AST)	25.3 ± 1.5	24.4 ± 1.1	0.612
Number of years lived in Brownsville	24.2 ± 1.3	37.1 ± 3.3	**<0.001**
Household Income per Year (1K$)	28.2 ± 2.9	31.3 ± 4.4	0.554
Education Level (years)	10.6 ± 0.5	13.3 ± 1.1	**0.024**
Categorical Variables Weighted frequency (%, SE)			
Mean cIMT ≥75% for age and sex	35.3 (3.6)	36.1 (7.8)	0.924
Male	36.2 (3.4)	55.3 (6.3)	**0.007**
Female	63.8 (3.4)	44.7 (6.3)	
Less than high school education	57.7 (3.9)	30.2 (7.7)	**<0.001**
Smoker (>100 cigarettes in lifetime)	41.4 (3.6)	36.2 (6.5)	0.506
Alcohol use	5.5 (1.8)	5.2 (3.0)	0.945
Meet daily fruit & vegetable intake (yes)	12.8 (2.3)	23.0 (8.3)	0.123
Central Obesity	69.7 (3.4)	73.9 (5.6)	0.518
Obesity[3]			0.291
Normal BMI	15.4 (2.7)	16.8 (4.6)	

Overweight	39.9 (3.6)	29.1 (5.9)	
Obese	44.6 (3.6)	54.1 (6.5)	
Hypertension	45.0 (3.9)	57.8 (7.1)	0.098
Total Cholesterol ≥200 mg/dL	46.2 (3.6)	37.1 (7.2)	0.291
Triglycerides ≥150 mg/dL	47.7 (3.4)	38.9 (7.8)	0.323
High Density Lipoprotein <40 mg mg/dL in Males and <50 mg/dL in Females[7]	52.1 (3.9)	52.5 (6.7)	0.959
Low Density Lipoprotein ≥130 mg/dL	26.5 (3.5)	22.6 (7.7)	0.666
Statin use	12.1 (2.2)	10.0 (3.8)	0.651
Diabetes Mellitus (DM)			0.480
Normal	28.8 (3.4)	36.8 (6.7)	
Impaired (or pre-DM)	41.3 (3.7)	39.6 (7.6)	
DM	29.9 (3.5)	23.7 (4.9)	
Metabolic syndrome	46.0 (3.8)	42.7 (7)	0.687