ORIGINAL ARTICLE

Association between insulin resistance and arterial stiffness in Mexican patients without type 2 diabetes

Roopa Mehta,[1,2]* *Neftali E. Antonio-Villa,*[1,3] *Omar Y. Bello-Chavolla,*[4] *Alexandro J. Martagón,*[1,5] *Daniel Elias-López,*[1,2] *Arsenio Vargas-Vázquez,*[1,3] *Donaji V. Gómez-Velasco,*[1] *Paloma Almeda-Valdés,*[1,2] *Liliana Muñoz-Hernandez,*[1,2] *Ivette Cruz-Bautista*[1,2] *and Carlos A. Aguilar-Salinas*[1,2,5]

[1]*Metabolic Diseases Research Unit, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán;* [2]*Endocrinology and Metabolism Department, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán;* [3]*Faculty of Medicine, Universidad Nacional Autónoma de México;* [4]*Research Division, Instituto Nacional de Geriatría;* [5]*School of Medicine and Health Sciences Tec Salud, Instituto Tecnológico y de Estudios Superiores de Monterrey. Mexico City, Mexico*

Abstract

Background: *Central aortic arterial stiffness (CAAS) is an independent cardiovascular risk factor. Insulin resistance (IR) contributes to CAAS-associated risk.* **Objective:** *To evaluate the association between IR and CAAS in a Mexican population without diabetes.* **Methods:** *IR was estimated with Homeostatic Model Assessment 2-Insulin Resistance (HOMA2-IR) and other surrogate markers (Metabolic score for IR [METS-IR], Quantitative Insulin Sensitivity Check Index [QUICKI], triglycerides/glucose index [TyG], TyG*body mass index [TyG*BMI] and triglycerides/high-density lipoprotein cholesterol ratio [TG/HDL-C]). CAAS was evaluated using carotid-femoral pulse wave velocity analysis (PWV_{cf}) and the standardized augmentation index (AI-75). Bivariate correlations were made between surrogate markers and PWV_{cf}. Increased CAAS was defined as PWV_{cf} above the 90th percentile. Thresholds and area under the curve (AUC) were obtained for each surrogate marker in order to evaluate their performance in estimating increased CAAS.* **Results:** *Three hundred and fifty-eight patients were included. A correlation was found between HOMA2-IR and PWV_{cf}; this correlation was replicated with other surrogate markers. METS-IR and TyG*BMI had the highest degree of correlation with PWV_{cf}. When adjustments were made for covariates, the correlations with TyG*BMI, METS-IR, HOMA2-IR and QUICKI maintained significance. HOMA2-IR showed the strongest correlation with AI-75. METS-IR and TyG showed the best AUC. Patients with prediabetes had the highest PWV_{cf}.* **Conclusions:** *The relationship between IR and CAAS is present before the onset of diabetes; this association may entail higher cardiovascular risk.*

KEY WORDS: *Insulin resistance Arterial stiffness. Prediabetes. Cardiometabolic profile.*

La asociación entre la resistencia a la insulina y la rigidez arterial en pacientes mexicanos sin diabetes mellitus tipo 2

Resumen

Antecedentes: *La rigidez arterial central aórtica (RACA) es un factor de riesgo cardiovascular independiente. La resistencia a la insulina (RI) contribuye al riesgo asociado a RACA.* **Objetivo:** *Evaluar la asociación entre RI y RACA en una población mexicana sin diabetes.* **Métodos:** *La RI se estimó con HOMA2-IR y (Homeostatic Model Assessment 2-Insulin Resistance) otros subrogados (METS-IR [Metabolic score for IR], QUICKI [Quantitative Insulin Sensitivity Check Index], TyG [ratio triglicéridos/glucosa], TyG*IMC [TyG*índice de masa corporal] y TG/HDL [ratio TG/lipoproteínas de alta densidad]). Se evaluó la RACA mediante el análisis de velocidad de onda del pulso carotídeo-femoral (VOP_{cf}) y el índice de aumentación estandarizado (AI-75).*

Correspondence:
*Roopa Mehta
E-mail: roopamehta@yahoo.com

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Se realizaron correlaciones bivariante entre los subrogados y la VOP_{cf}. RACA aumentada se definió como VOP_{cf} arriba del percentil 90. Se obtuvieron puntos de corte y área bajo la curva (ABC) para cada subrogado para estimar RACA aumentada. **Resultados:** *Se incluyó 358 pacientes. Se encontró una correlación entre HOMA2-IR y VOP_{cf}; esta correlación se replicó con los subrogados. METS-IR y TyG*IMC tuvieron el mayor grado de correlación con VOP_{cf}. Al ajustar, las correlaciones con TyG*IMC, METS-IR, HOMA2-IR y QUICKI mantuvieron significancia. La correlación con AI-75 fue mayor para HOMA2-IR. METS-IR y TyG mostraron la mejor ABC. Los pacientes con prediabetes tuvieron mayor VOP_{cf}.* **Conclusiones:** *La relación entre la RI y la RACA está presente desde etapas no diabéticas; esta asociación puede conllevar mayor riesgo cardiovascular.*

PALABRAS CLAVE: *Resistencia a la insulina. Rigidez arterial. Prediabetes. Perfil cardiometabólico.*

Introduction

Insulin resistance (IR) is characterized by a decrease in tissue sensitivity to insulin. It is associated with type 2 diabetes (T2D), obesity and metabolic syndrome; this parameter contributes to the cardiovascular (CV) risk associated with these conditions.[1-3] The pathophysiological mechanisms involved in the relationship between IR and CV morbidity and mortality are not well known.[4] Some researchers have explored the association between IR and central aortic arterial stiffness (CAAS).[5]

The arterial system maintains adequate blood flow and has a "cushioning or dampening" function.[6] This depends on arterial elasticity. Arteries can lose their vascular compliance with age and with hypertension, chronic kidney disease, T2D and atherosclerosis.[7] CAAS is an independent CV risk factor.[8,9] When an artery is rigid, forward pulse wave is faster and is reflected from the periphery more rapidly and reaches the heart during early systole, thus producing an increase in systolic blood pressure; at the same time, diastolic pressure is reduced and there is a decrease in coronary diastolic perfusion,[10] in addition to the transmission of more pulsatile energy to the small arteries, which causes microvascular damage.

The gold standard for measuring insulin sensitivity is euglycemic-hyperinsulinemic clamp.[11] This method is not useful in clinical practice because it is laborious, invasive and high-priced.[12] A widely used surrogate index for estimating IR is the Homeostatic Model Assessment for Insulin Resistance (HOMA2-IR). Other indices such as the Quantitative Insulin Check Index (QUICKI), and surrogate markers that use metabolic and anthropometric parameters in their formulas (e.g., Metabolic score for IR [METS-IR], triglycerides/glucose ratio [TyG], TyG*body mass index [TyG*BMI] and triglycerides/high-density lipoprotein cholesterol ratio [TG/HDL-C])[13-15] also have a good correlation with the clamp method.

Carotid-femoral pulse wave velocity (PWV_{cf}) is the gold standard for CAAS non-invasive evaluation.[16,17] The role played by IR in promoting CAAS increase has not been clarified. In addition, this relationship may be biased by the sum of metabolic alterations seen in patients with T2D. The purpose of this study is to evaluate the association between IR and CAAS (PWV_{cf}) in a Mexican population without diabetes.

Methodology

Design and study population

A cross-sectional study was conducted with subjects being recruited between January 2017 and December 2020 at the Metabolic Diseases Research Unit of Salvador Zubirán National Institute of Medical Sciences and Nutrition. Participants were aged between 18 and 70 years and had no T2D previous diagnosis. Patients with previous prediabetes diagnoses (fasting glucose levels of 100-125 mg/dL or glycated hemoglobin [HbA1c] of 5.7-6.4%), hypertension (blood pressure ≥ 140/80 mmHg and/or on treatment with antihypertensive drugs), obesity (BMI ≥ 30 kg/m^2), and subjects with high CV risk (e.g., atherogenic primary dyslipidemia) were included. Individuals with CV disease, chronic kidney disease and life expectancy of less than one year were excluded. The study was carried out in accordance with the statutes of the Declaration of Helsinki. All participants signed an informed consent document prior to participating in the study. Salvador Zubirán National Institute of Medical Sciences Ethics Committee approved the study.

Biochemical, anthropometric evaluation

Venous blood samples were obtained after an 8 to 12 hour fasting period. Plasma glucose analysis was carried out using an automated analyzer (Yellow Springs Instruments, Yellow Springs, OH, USA),

insulin concentrations were measured by chemiluminescence immunoassay (Beckman Coulter Access 2), HbA1C levels were measured by chromatography (Variant II Turbo, BIORAD) and lipid profile concentrations were measured by colorimetry assays (Unicel DxC 600 Synchron Clinical System Beckman Coulter). Low-density lipoprotein cholesterol (LDL-C) was calculated according to Martín's formula.[18] All subjects were weighted using SECA mBCA 514 calibrated scales and measured with SECA stadiometers. Waist circumference was measured using a non-elastic tape between the intersecting midpoint of the ribcase margin and the upper edge of the rib. BMI was calculated by dividing weight in kilograms by height in squared meters. The HOMA2-IR index was used as the standard to evaluate IR. Subsequently, the association was replicated using the QUICKI, TG/HDL-C, TyG, TyG*BMI and METS-IR surrogate markers. Table 1 shows the formulas for IR surrogate markers estimation.

Table 1. Formulas of surrogated indices for estimating insulin resistance. Glucose, TG and HDL-C units are expressed in mg/dL. Insulin units expressed in IU/mL

Index	Formula
HOMA2-IR	https://www.dtu.ox.ac.uk/homacalculator/
METS-IR	$\frac{\left(Ln\left[(2*glucose)+triglycerides\right]\right)*BMI}{Ln(HDL\ cholesterol)}$
QUICKI	$\frac{1}{(log(insulin)+log(glucose))}$
TyG	$\mathrm{Ln}\left(triglycerides*\frac{[glucose]}{2}\right)$
TyG*BMI	$(TyG)*(BMI)$
TG/HDL-C	(*Triglycerides*) / (*HDL cholesterol*)

HOMA2-IR: Homeostatic Model Assessment 2-Insulin Resistance; METS-IR: Metabolic score for IR; QUICKI: Quantitative Insulin Sensitivity Check Index; TyG: triglycerides/glucose ratio; TyG*BMI: TyG*body mass index; TG/HDL-C: TG/high-density lipoprotein cholesterol ratio.

Carotid wave analysis evaluation

Subjects were asked not to consume caffeine and to refrain from smoking for the previous 48 hours. Carotid wave analysis was carried out using a semiautomatic device (SphygmoCore XCEL, AtCor Medical Pty Ltd, USA). At the time of evaluation of the participants, they were placed in the supine position for 10 minutes. A sphygmomanometer was placed between the proximal third of the patient's right leg to record the femoral wave. PWV_{cf} and the standardized augmentation index at 75 beats per minute (AI-75) (to reduce the effect attributable to heart rate) were measured by flattening tonometry using the carotid-to-femoral arterial wave corrected time of delay.[19] The augmentation index estimates the reflection of the peripheral wave; earlier return occurs with increased pulse velocity. Arterial stiffness was defined as those subjects with PWV_{cf} above the 90th percentile ($p \geq 90$) (> 7.77 mm/s).

Statistical analysis

Qualitative variables were expressed as absolute count and percentage; quantitative variables, as the mean (standard deviation) or median (interquartile range [IQR]) according to their normal distribution. Log transformations were applied. Subjects with arterial stiffness were compared with those without arterial stiffness using Student's t or Mann-Whitney's U statistical tests.

Correlation between insulin resistance surrogate markers

The correlation of HOMA2-IR and the other surrogate markers with PWV_{cf} and AI-75 was evaluated. Correlations were adjusted for age, gender, hypertension, smoking, HbA1c, waist circumference and dyslipidemia. To evaluate the differences between subjects with IR with our surrogate markers, the cutoff points previously published by Almeda-Valdez et al.[20] were used. PWV_{cf} parameters were compared between subjects with IR using Student's t-test.

Evaluation of cutoff points for identifying arterial stiffness

Cutoff points for identifying arterial stiffness were calculated. Sensitivity, specificity, positive and negative predictive value of each IR surrogate marker were estimated. The area under the curve (AUC) of each surrogate marker was obtained. Statistical analysis was carried out with the R programming language (Version 3.6.1).

Results

Three hundred and fifty-eight subjects were included, out of whom 260 (72.6%) were women, with median

Table 2. General characteristics of the study population

Parameter	Total population (n = 358)	No arterial stiffness (n = 323)	Arterial stiffness (n = 35)	p-value
Female gender, n (%)	260 (72.6%)	238 (75.1)	18 (51.4)	0.001
Age, years (range)	50 (39-57)	46.6 (12.7)	53 (7.65)	< 0.001
Prediabetes, n (%)	254 (70.9)	223 (70.3)	26 (74.3)	0.627
Weight, kg (SD)	76.2 (± 14.9)	75.7 (± 14.9)	81.7 (± 15.8)	0.005
Waist, cm (SD)	95.5 (± 12.1)	93.6 (± 11.7)	98.8 (± 11.3)	0.003
BMI, kg/m^2 (range)	28.9 (26.4-32.2)	28 (26-32)	29.2 (26.6-35)	0.065
Glucose, mg/dL (SD)	96.3 (± 12.8)	95.6 (± 11.1)	102.2 (± 22.6)	0.004
Triglycerides, mg/dL (range)	137 (95-187)	133 (92-182)	159 (108-197)	0.093
Total cholesterol, mg/dL (SD)	197 (± 43.1)	194 (± 42)	188 (± 45.8)	0.239
HDL cholesterol, mg/dL (SD)	46.3 (± 12.2)	46.7 (± 12)	41.9 (± 12)	0.027
LDL cholesterol, mg/dL (SD)	123 (± 35.5)	121 (± 35)	116 (± 35.7)	0.320
Insulin, IU/dL (range)	8.9 (6-12.9)	8.7 (5.7-11.9)	9.9 (6.8-14.9)	0.313
HbA1c, % (SD)	5.8 (± 0.75)	5.8 (± 0.60)	6.3 (± 1.18)	< 0.001
Uric acid, mg/dL (SD)	5.4 (± 1.3)	5.3 (± 1.29)	5.6 (± 1.36)	0.343
Creatinine, mg/dL (SD)	0.87 (± 1.9)	0.86 (± 2.45)	0.81 (± 0.21)	0.712
AST, mg/dL (SD)	28.2 (± 16.2)	28.3 (± 17)	27.8 (± 8.2)	0.879
ALT, mg/dL (SD)	28.3 (± 19.9)	28.3 (± 17)	30.1 (± 15.9)	0.534
GGT, mg/dL (SD)	26.4 (± 26.2)	25.9 (± 26.8)	28.9 (± 21.7)	0.550
APO B, mg/dL (SD)	112.25 (± 28.4)	109 (± 27.7)	102 (± 29.5)	0.321
PWV_{cf}, mm/s (SD)	6.52 (± 1.34)	5.92 (± 0.84)	8.58 (± 0.65)	< 0.001
AI-75, % (SD)	34.97 (± 13.22)	34.3 (± 13.9)	33.7 (± 9.71)	0.604
HOMA2-IR (range)	1.2 (0.8-1.7)	1.2 (0.8-1.6)	1.3 (0.9-2.0)	0.144
METS-IR (SD)	45.6 (± 9.47)	45.1 (± 9.25)	48.8 (± 10.5)	0.026
QUICKI (SD)	0.344 (± 0.033)	0.346 (± 0.033)	0.335 (± 0.033)	0.079
TyG (SD)	8.78 (± 0.58)	8.73 (± 0.58)	8.99 (± 0.57)	0.075
TyG*BMI (SD)	259.8 (± 49.4)	257.4 (± 47.63)	273.9 (± 54.4)	0.057
TG/HDL-C (range)	2.99 (1.8-4.6)	2.8 (1.7-4.5)	3.8 (2.4-5.8)	0.017

BMI: body mass index; HDL: high-density lipoprotein; LDL: low-density lipoprotein; HbA1c: glycated hemoglobin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma-glutamyl transferase; APO B: apolipoprotein B; PWVcf: carotid-femoral pulse wave velocity; AI-75: standardized augmentation index; HOMA2-IR: Homeostatic Model Assessment 2-Insulin Resistance; METS-IR: Metabolic score for IR; QUICKI: Quantitative Insulin Sensitivity Check Index; TyG: triglycerides/glucose ratio; TyG*BMI: TyG*body mass index; TG/HDL-C: TG/high-density lipoprotein cholesterol ratio.

age being 50 years (IQR: 39-57). Population characteristics are shown in table 2. The subjects with greater arterial stiffness were older men, with higher weight, waist circumference and with a higher concentration of fasting glucose, TG and HbA1c, and lower concentrations of HDL-C. PWV_{cf} and AI-75 mean values in this population were 6.52 (± 1.34) mm/s and 34.9 (± 13.22)%, respectively. Regarding the surrogate indices (Table 1), mean/median values were: HOMA2-IR, 1.2 (IQR: 0.8-1.7); METS-IR, 45.6 (± 9.47); QUICKI, 0.344 (± 0.03); TyG, 8.78 (± 0.58); TyG*BMI, 259.8 (± 49.4); and TG/HDL-C, 2.99 (IQR: 1.8-4.6). Only the METS-IR and TG/HDL-C indices were significantly related to greater arterial stiffness.

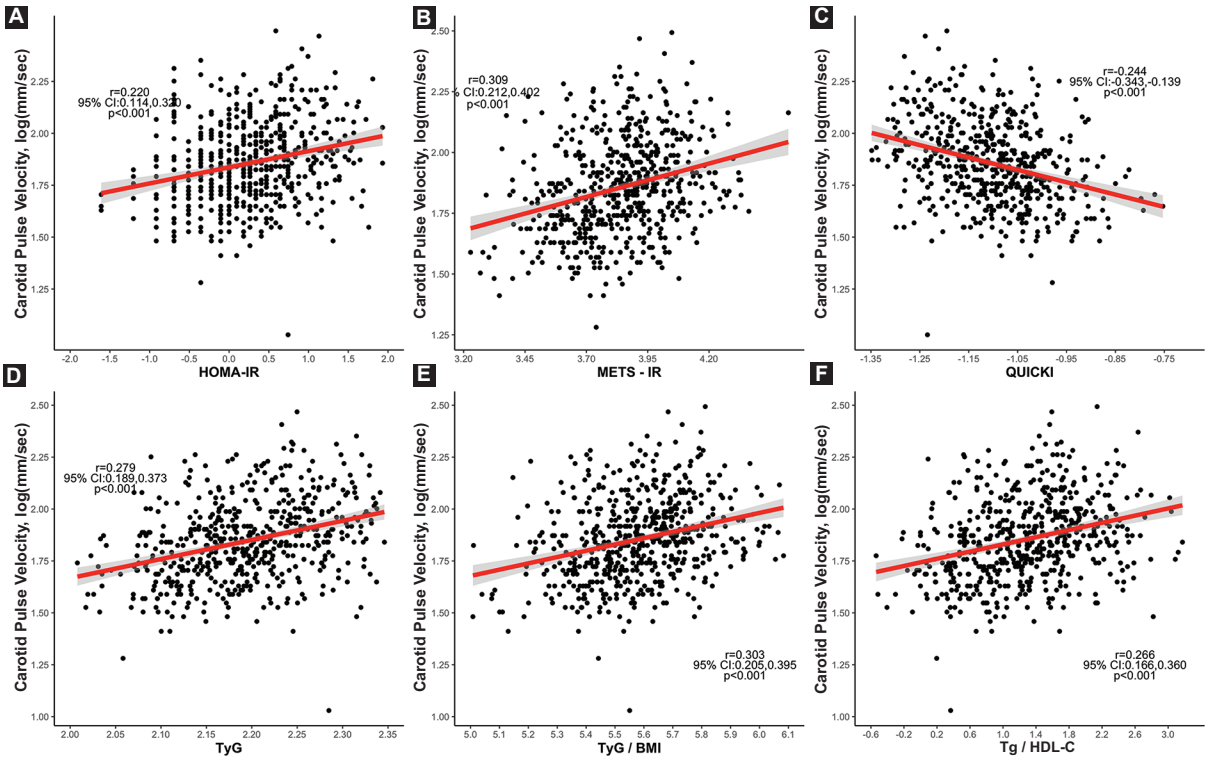

Figure 1. *Insulin resistance surrogate markers correlation with carotid pulse velocity. The variables were transformed to their log values to reach parametric distribution. CI: confidence interval; HOMA2-IR: Homeostatic Model Assessment 2-Insulin Resistance; METS-IR: Metabolic score for IR; QUICKI: Quantitative Insulin Sensitivity Check Index; TyG: triglycerides/glucose ratio; TyG*BMI: TyG*body mass index; Tg/HDL-C: Tg/high-density lipoprotein cholesterol ratio.*

Carotid pulse velocity correlation with insulin resistance surrogate markers

In the bivariate correlation analysis, a correlation was observed with HOMA2-IR and PWV_{cf} (r: 0.220; 95% confidence interval [CI]: 0.114-0.320), which was maintained when adjustments were made for covariates (r: 0.128; 95 % CI: 0.018-0.234). The association was replicated with the rest of the surrogate indices. The highest correlation was observed for METS-IR index (r: 0.309; 95% CI: 0.212-0.402) and TyG*BMI index (r: 0.279; 95% CI: 0.189-0.373) (Fig. 1). For AI-75, the TyG*BMI index had the highest degree of correlation (r: 0.131; 95% CI: 0.027-0.231). However, when adjustments were made for covariates, the HOMA2-IR index maintained the strongest association with AI-75 (r: 0.168; 95% CI: 0.060-0.272) (Table 3). Finally, patients with IR had an increase in PWV_{cf} values evaluated by all surrogate markers (Fig. 2). When PWV_{cf} values were explored in subjects with prediabetes, we confirmed that this population had greater arterial stiffness in comparison with those without prediabetes (Fig. 3).

Cutoff points for identifying arterial stiffness

The best cutoff point for detecting arterial stiffness was determined for each surrogate marker. The HOMA2-IR index showed adequate predictive performance. This association was replicated for the rest of IR surrogate markers. The indices with the best area under the curve (AUC) were the METS-IR index (AUC: 0.61; 95% CI: 0.51-0.71) and TyG index (AUC: 0.61; 95% CI: 0.51-0.69). The surrogate index with the highest sensitivity, with a significant AUC, was the TyG index (S: 0.94; 95% CI: 0.81-0.99), while the TyG*BMI index had the best specificity (Sp: 0.84; 95% CI: 079-0.88) with a significant AUC (Table 4).

Discussion

The association between IR and pulse wave velocity was evaluated in a Mexican population without T2D. Patients with IR, evaluated by surrogate markers, had an increase in PWV_{cf} values that was independent of

Table 3. Pearson's correlation between insulin resistance surrogate markers and arterial stiffness estimate. Adjustment variables are: age, gender, active smoking, hypertension, glycated hemoglobin and waist circumference

Surrogate markers	PWV_{cf}		AI-75	
	Bivariate	Adjusted	Bivariate	Adjusted
HOMA2–IR	0.220 (0.114, 0.320)	0.128 (0.018, 0.234)	0.033 (–0.074, 0.141)	0.168 (0.060, 0.272)
METS–IR	0.309 (0.212, 0.402)	0.171 (0.063, 0.275)	0.099 (0.018, 0.178)	0.164 (0.082–0.241)
QUICKI	–0.244 (–0.343, –0.139)	–0.119 (–0.226, –0.01)	–0.063 (–0.145, 0.019)	–0.144 (–0.225, –0.062)
TyG	0.279 (0.189, 0.373)	0.081 (–0.027, 0.189)	0.021 (–0.083, 0.124)	0.126 (0.018, 0.232)
TyG*BMI	0.303 (0.205, 0.395)	0.183 (0.053, 0.286)	0.131 (0.027, 0.231)	0.164 (0.059, 0.269)
TG/HDL-C	0.266 (0.166, 0.360)	0.085 (–0.024, 0.193)	–0.042 (–0.145,0.062)	0.118 (0.009, 0.223)

PWV_{cf}: carotid-femoral pulse wave velocity; AI-75: standardized augmentation index; HOMA2-IR: Homeostatic Model Assessment 2-Insulin Resistance; METS-IR: Metabolic score for IR; QUICKI: Quantitative Insulin Sensitivity Check Index; TyG: triglycerides/glucose ratio; TyG*BMI: TyG*body mass index; TG/HDL-C: TG/high-density lipoprotein cholesterol ratio.

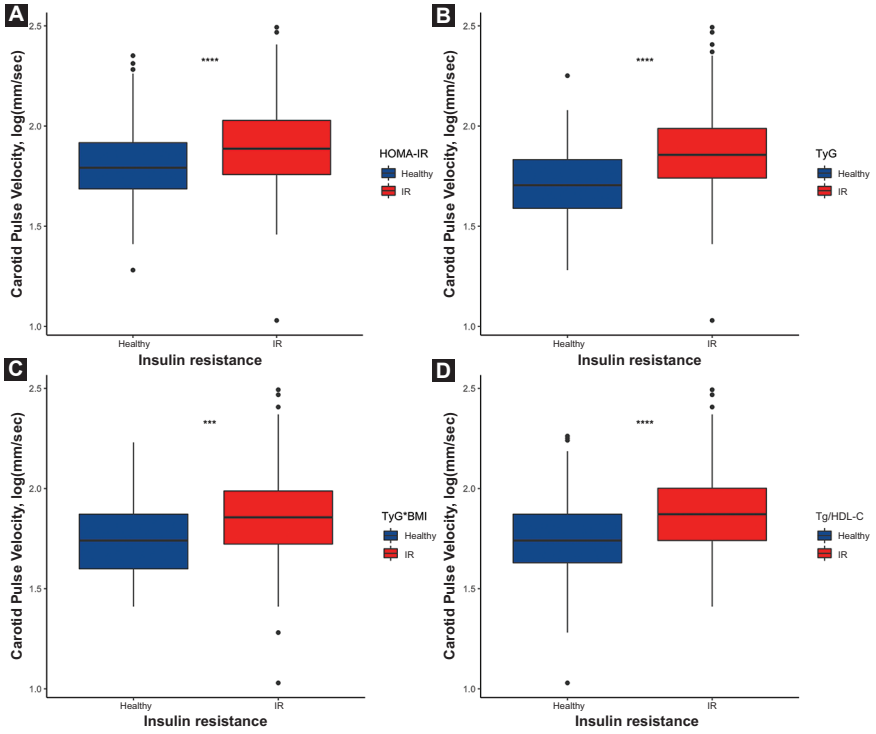

Figure 2. Carotid pulse velocity differences between subjects with insulin resistance evaluated by surrogate marker.
**p < 0.05.*
†p < 0.001.
‡p < 0.0001.
*IR: insulin resistance; HOMA2-IR: Homeostatic Model Assessment 2-Insulin Resistance; TyG: triglycerides/glucose ratio; TyG*BMI: TyG*body mass index; Tg/HDL-C: TG/high-density lipoprotein cholesterol ratio.*

risk factors. The indices with the highest degree of association were METS-IR and TyG*BMI, and those with the best AUC for detecting arterial stiffness were METS-IR and TyG. Subjects with prediabetes had greater arterial stiffness in comparison with those without prediabetes.

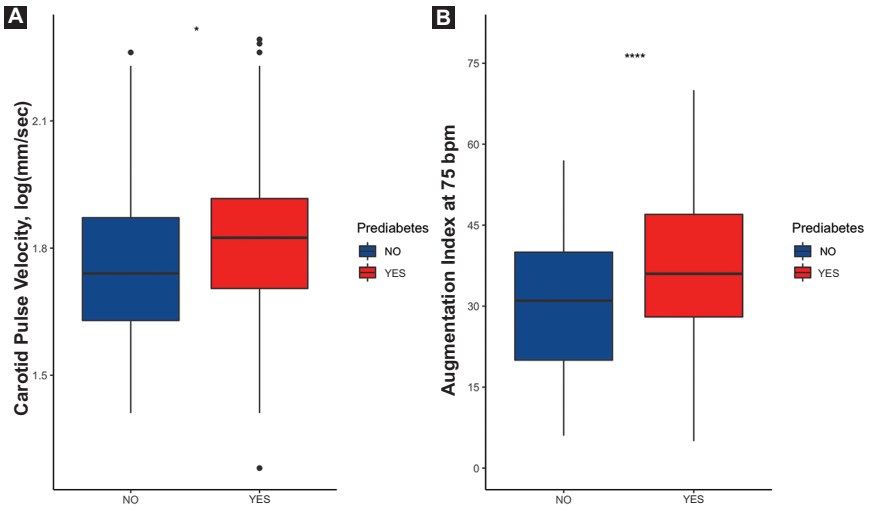

Figure 3. *Differences in carotid pulse velocity* **(A)** *and augmentation index at 75 bpm* **(B)** *between subjects with and without prediabetes.*
**p < 0.05.*
†p < 0.001.
‡p < 0.0001.

Table 4. Cutoff points for identifying arterial stiffness (PWV_{cf} p ≥ 90) in healthy subjects. Arterial stiffness was defined as those subjects with PWVcf above the 90th percentile (p > 90) with a value of 7.77

Variables	Cutoff point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC
HOMA2-IR	1.7	0.43 (0.26-0.62)	0.76 (0.71-0.81)	0.17 (0.14-0.30)	0.92 (0.85-0.94)	0.59 (0.48-0.69)
METS-IR	41.6	0.82 (0.66-0.93)	0.39 (0.33-0.48)	0.13 (0.11-0.31)	0.95 (0.89-0.96)	0.61 (0.51-0.71)
QUICKI	0.39	0.13 (0.04-0.29)	0.91 (0.88-0.94)	0.14 (0.10-0.32)	0.91 (0.71-0.94)	0.40 (0.29-0.51)
TyG	8.4	0.94 (0.81-0.99)	0.27 (0.22-0.32)	0.27 (0.10-0.55)	0.98 (0.92-0.98)	0.61 (0.51-0.70)
TyG*BMI	301.9	0.34 (0.19-0.52)	0.84 (0.79-0.88)	0.19 (0.15-0.33)	0.92 (0.84-0.94)	0.59 (0.48-0.69)
TG/HDL-C	3.05	0.69 (0.51-0.83)	0.52 (0.47-0.58)	0.14 (0.11-0.27)	0.94 (0.88-0.95)	0.60 (0.51-0.70)

PWV_{cf}: carotid-femoral pulse wave velocity; PPV: positive predictive value; NPV: negative predictive value; AUC: area under the curve; HOMA2-IR: Homeostatic Model Assessment 2-Insulin Resistance; METS-IR: Metabolic score for IR; QUICKI: Quantitative Insulin Sensitivity Check Index; TyG: triglycerides/glucose ratio; TyG*BMI: TyG*body mass index; TG/HDL-C: TG/high-density lipoprotein cholesterol ratio.

A direct relationship between PWV_{cf} and atherosclerosis has been shown and, in longitudinal studies, this parameter is an independent CV risk marker.[21] An increase in arterial stiffness may be one of the mechanisms that explains the association between CV risk and IR. Epidemiological studies have shown that IR is an independent factor for the development of arterial stiffness. In the ARIC trial, individuals with T2D or carbohydrate intolerance had stiffer arteries than subjects with normoglycemia.[22] It was speculated that the effect of glucose, insulin and TG together play a role in the development of arterial stiffness. Significant differences have been shown in PWV_{cf} between subjects with and without metabolic syndrome.[23] The specific mechanisms involved are not clear, but we do know that IR has direct and indirect effects on vasculature. Hyperinsulinemia can increase sympathetic tone, activate the renin-angiotensin system, stimulate vascular inflammation and reduce flow-mediated endothelium-dependent vasodilation. The end result is endothelial dysfunction and an inadequate vasomotor response to a

pro-inflammatory and pro-coagulant endothelium, which increases the risk for arterial stiffness.[24]

Several authors have evaluated the association between IR surrogate markers and arterial stiffness. In subjects without CV disease, a significant association between TyG and PWV_{cf} has been confirmed.[25] HOMA2-IR was independently associated with PWV_{cf} in individuals without diabetes or with prediabetes.[26,27] Webb et al. evaluated PWV_{cf} in subjects with normoglycemia, abnormal glucose regulation (abnormal fasting glucose and/or carbohydrate intolerance) and TD2.[28] In the latter two groups, there was a significant association with arterial stiffness. Glucose intolerance and HOMA2-IR were the most important independent predictors of arterial stiffness.

This study has some limitations. Surrogate markers were used for RI in replacement of the gold standard. The population was heterogeneous and may not be representative of the general population. The majority were women, which represents a potential selection bias. Data on exercise and medications that could influence the atherosclerosis process and IR were not obtained.

Conclusions

This is the first study in a Mexican population that confirms the relationship between IR and arterial stiffness in people without diabetes. The fact that the relationship between IR and arterial stiffness is present before the onset of diabetes is corroborated; this association may entail higher CV risk in the future. The HOMA2-IR index showed an association that was replicated with the different IR surrogate markers. The best performance for detecting arterial stiffness was with METS-IR and TyG indices. These are easy-to-calculate parameters and can be included in CV risk assessment.

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Conflict of interests

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

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