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A Body Shape Index and Pulse Wave Velocity: strong markers of coronary artery calcification in dyslipidemic patients

A Body Shape Index e Velocidade de Onda de Pulso: fortes marcadores de calcificação da artéria coronária em pacientes dislipidêmicos

A Body Shape Index y la Velocidad de la Onda de Pulso: fuertes marcadores de calcificación de la arteria coronaria en pacientes dislipidémicos

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Abstract
Objective: To identify, among different Cardiovascular Risk Predictors (CVRP), which have the best associations with Coronary Artery Calcification (CAC). Methodology: Cross-sectional study, with dyslipidemic (age >18), to investigate the association between CVRP [anthropometrics, biochemicals, clinicals, Ankle-Brachial Index (ABI), arterial stiffness] and Coronary Calcium Score (CCS), which was classified according to (1) CCS=0, CCS=1-100, CCS>100, (2) CCS=0, CCS=1-99, CCS=100-299, CCS>300 and (3) dichotomous (CCS=0 or CCS>P75/CCS>100). Bivariate descriptive and inferential statistics were performed. ROC curves estimated the CAC risk of the independent variable. The univariate logistic regression model identified the probability of CAC and established the sensitivity and the specificity of each predictor and the multivariate identified higher risk variables and their respective Odds Ratio (OR). Results: 180 patients evaluated, 65.5% were women, mean age 59.8. CAC was associated with Waist Circumference (p=0.03), A Body Shape Index Risk-ABSIR (p<0.001), Conicity Index (p<0.001), Waist-to-Height Ratio (p<0.001) (T Student test); Pulse Wave Velocity-PWV was associated with CAC for both (1) and (2) CCS classification (p<0.001) (Anova test with Duncan post-hoc test) and it also showed greater sensitivity on ROC curve (3) (AUC 0.61, with a sensitivity of 72.2). In multi-adjusted regression, ABSIR increased the risk of CAC by 3.5 times (CI 95%=1.38-1.64, p=0.001) and PWV by 36% (CI 95%=1.13-1.64, p<0.01). Conclusions: ABSIR and arterial stiffness (PWV) made it possible to obtain a better value for CAC prognosis, being the ABSIR an easy and cheap method, very useful in Public Health.
Keywords: Coronary artery calcification; Cardiovascular risk predictors; Central obesity; Arterial stiffness.

Resumo
Objetivo: Identificar, entre diferentes Preditores de Risco Cardiovascular (PRCV), quais têm as melhores associações com Calcificação de Artéria Coronária (CAC). Metodologia: Estudo transversal, com dislipidêmicos (idade > 18 anos), investigou a associação entre CVRP [antropométricos, bioquímicos, clínicos, índice tornozelo-braquial (ITB) e rigidez arterial]com o Escore de Cálcio Coronariano (ECC), que foi classificado de acordo com (1) ECC=0, ECC=1-

100, ECC>100, (2) ECC=0, ECC=1-99, ECC=100-299, ECC>300 e (3) dicotômico (ECC=0 ou ECC>P75/ECC>100). Foram realizadas estatísticas descritivas e inferenciais bivariadas. As curvas ROC estimaram o risco CAC da variável independente. O modelo de regressão logística univariado identificou a probabilidade de CAC e estabeleceu a sensibilidade e a especificidade de cada preditor e o multivariado identificou variáveis de maior risco e suas respectivas Odds Ratio (OR). Resultados: 180 pacientes avaliados, 65,5% mulheres, idade média de 59,8. CAC foi associada com Circunferência da Cintura (p=0,03), *A Body Shape Index Risk*-ABSIR (p<0,001), Índice de Conicidade (p<0,001), Relação Cintura-Altura (p<0,001) (teste T Student); Velocidade de Onda de Pulso -VOP foi associado com CAC para ambas classificações do ECC (1) e (2) (p<0,001)(teste Anova com teste post-hoc de Duncan) e também mostrou maior sensibilidade na curva ROC (3) (AUC 0,61, com sensibilidade de 72,2). Na regressão multi-ajustada, ABSIR aumentou o risco de CAC em 3,5 vezes (IC 95%=1,38-1,64; p=0,001) e VOP em 36% (IC 95%=1,13-1,64; p<0,01). Conclusões: O ABSIR e a rigidez arterial (VOP) possibilitaram obter um melhor valor prognóstico da CAC, sendo o ABSIR um método fácil e barato, muito útil em Saúde Pública.
Palavras-chave: Calcificação da artéria coronária; Preditores de risco cardiovascular; Obesidade central; Rigidez arterial.

Resumen
Objetivo: Identificar, entre diferentes Predictores de Riesgo Cardiovascular (PRCV), cuáles tienen las mejores asociaciones con la Calcificación de la Arteria Coronaria (CAC). Metodología: Estudio transversal, con dislipidémicos (edad >18), para investigar la asociación entre PRCV [antropométricos, bioquímicos, clínicos, índice tobillo-brazo (ITB), rigidez arterial] y el puntaje de calcio en las arterias coronárias (PCC), que se clasificó según (1) PCC=0, PCC=1-100, PCC>100, (2) PCC=0, PCC=1-99, PCC=100-299, PCC>300 y (3) dicotómico (PCC=0 o PCC>P75/PCC>100). Se realizó estadística descriptiva e inferencial bivariada. Las curvas ROC estimaron el riesgo CAC de la variable independiente. El modelo de regresión logística univariante identificó la probabilidad de CAC y estableció la sensibilidad y la especificidad de cada predictor y el multivariante identificó las variables de mayor riesgo y sus respectivas Odds Ratio (OR). Resultados: 180 pacientes evaluados, 65,5% mujeres, edad promedia 59,8. El CAC se asoció con la Circunferencia de la Cintura (p=0,03), *A Body Shape Index Risk*-ABSIR (p<0,001), Índice de Conicidad (p<0,001), Relación Cintura-Altura (p<0,001) (test T de Student); Velocidad de Onda de Pulso-VOP se asoció con CAC tanto para (1) como para (2) la clasificación PCC (p<0,001) (Anova test con post-hoc test de Duncan) y también mostró una mayor sensibilidad en la curva ROC (3) (AUC 0,61, con una sensibilidad de 72,2). En la regresión multiajustada, ABSIR aumentó el riesgo de CAC en 3,5 veces (IC 95%=1,38-1,64; p=0,001) y VOP en 36 % (IC 95 %=1,13-1,64; p<0,01). Conclusiones: ABSIR y la rigidez arterial (VOP) permitieron obtener un mejor valor para el pronóstico de CAC, siendo el ABSIR un método fácil y barato, de gran utilidad en Salud Pública.
Palabras clave: Calcificación de la arteria coronaria; Predictores de riesgo cardiovascular; Obesidad central; Rigidez arterial.

1. Introduction

Coronary Artery Calcification (CAC) has already been considered an independent predictor of cardiovascular events in men and women (Ferencik *et al*., 2017), but requires expensive equipment and specialized professional to be accomplished, so the use of cardiovascular risk predictors (CVRP) with broad access, low cost, easy applicability, promoting an earlier implementation of a drug intervention, and lifestyle change, characterizes an extremely useful clinical measure to reduce cardiac events and, positively, impact on healthcare cost around the world.

Data show that life expectancy increased from age 42.7 to 76 between 1940 and 2018 (Borges *et al*., 2019), rates of morbidity and mortality caused by chronic non-communicable diseases, including cardiovascular diseases (CVD), have been growing significantly, generating high social and economic expenditures. According to the World Health Organization, 17.7 million people died of CVD in 2015, representing 31% of all global deaths. From those deaths, 7.4 million died of heart disease and 6.7 million from strokes, as estimated (OPAS Brasil, 2017).

The objective of this study was to identify among the different cardiovascular risk predictors (CVRP) which one is best associated with CAC and therefore add value in predicting cardiovascular events risk (CVER).

2. Methodology

A cross-sectional study was carried out in Paraná/Brazil, from February 2018 to February 2020, with individuals of both sexes. Inclusion criteria: age >18 years old; evidence of dyslipidemia. Exclusion criteria: conditions that would prevent

from obtaining reliable clinical and anthropometric data (amputation, oedema, ascites); goitre; pregnancy or lactation; diagnosis of coronary artery disease (CAD) or cardiovascular event (present in medical records); failure to undergo the CCS.

Coronary Calcium Score

The determination of CAC was assessed by CCS and performed utilizing multi-detector computed tomography, with a non-contrasted acquisition of 3-mm axial slices during diastole. The area and density of all calcified zones were measured, and CCS calculated using the Agatston method.

CCS was grouped according to:

a) Numeric variable - used in the correlation analysis with other CVRP.

b) Dichotomous form - presence or absence of CAC (0=without calcification and 1=presence of calcification, considering a >P75 or CAC>100 when it was not possible to calculate percentile (Xavier *et al*., 2013), to compose Receiver Operating Characteristic (ROC) curve.

c) Stratified form- there were two classifications to arrange patients into groups:

1.By Bhaha: category 0 for CCS = 0; category 1 for CCS = 1 - 100; category 2 for CCS > 100 (Blaha *et al*., 2011).

2.By Hecht: category 0 for CCS = 0, category 1 for CCS = 1-99, category 2 for CCS = 100 - 299 and category 3 for CCS > 300 (Hecht *et al*., 2017).

Cardiovascular Risk Predictors (CVRP)

The predictors were obtained and classified by the literature: Body Mass Index (BMI) (Coutinho, 2019; OPAS, 2001); Neck Circumference (NC) (Ben-Noun *et al*., 2001); Waist Circumference (WC) (WHO, 2008); Waist to Height Ratio (WtHR) (Li *et al*., 2013); A Body Shape Index (ABSI) and A Body Shape Index Risk (ABSIR) were calculated from http://www-e.ccny.cuny.edu/nir/sw/absi-calculator.html) and then classified (Krakauer & Krakauer, 2012); Conicity Index (C Index) (Neta *et al*., 2017; Pitanga & Lessa, 2004); Castelli I Index (CI I) and Castelli II Index (CII I) (Castelli *et al*., 1983), being that Low Density Protein Cholesterol, calculated by Martin (Martin *et al*., 2013), if the Triglycerides (TG) > 400 mg/dL, and by Friedwald (Friedwald *et al.*, 1972) if TG < 400 mg/dL; Triglycerides to High Density Lipoprotein Cholesterol Ratio (TG/HDL-c)(Hanak *et al*., 2004); Framingham Score (FS) proposed by American Heart Association and American College of Cardiology according to Framingham Heart Study; Score Score (SS) calculated from https://www.escardio.org/static_file/Escardio/Subspeciality/EACPR/Documents/score-charts.pdf and Global Risk Score/Lifetime Score (GRS/LTS) from http://departamentos.cardiol.br/sbc-da/2015/CALCULADORAER2017/index.html; Ankle Brachial Index (ABI) obtained using a mini Doppler (MEDPEJ® DV-2001), classified by literature (Azizi, 2015) and Arterial Stiffening acquired by Mobil-O-Graph®-PWA [Pulse Wave Velocity (PWV); Central Pressure (CtP); Augmentation Index (AI); Augmentation Pressure (AP); Vascular Resistance (VR) and Reflection Coefficient (RC). Reference values of PWV, CtP and AI used to classify those predictors (Brandão *et al*., 2017).

Statistical analysis

After performing the tests of normality, the parametric variables were represented as average and standard deviation and non-parametric variables as median and interquartile range. The statistical significance was 5% in all the comparisons, categorical variables were described as absolute and relative in their frequencies, also descriptive statistics and bivariate inferential were executed.

The following analyses were applied:

a) To compare the quantitative variables between the groups: T Student's test and Anova one-way with Duncan *post-hoc* test, if symmetric, and Mann-Whitney and Anova of Kruskal-Wallis tests, if asymmetric.

b) To specify the qualitative variables: Pearson's Chi-square and Pearson's Chi-square test with the Yates correction.

c) To identify the highest risk variables and their respective Odds Ratio (OR): multivariate logistic regression model.

d) To detect the probability of CAC according to different scores and to establish the sensitivity, specificity, and cut-off point: the univariate logistic regression model.

e) To measure the degree of association between the categorical predictive variables and verify their discriminating power: multiple correspondence analyses.

ROC curves constructed to estimate the discriminating power of independent variables to identify CAC risk, classified as extremely poor (AUC of 0.50 - 0.60), poor (0.60 - 0.70), reasonable (0.70 - 0.80), good (0.80 - 0.90) and excellent (0.90 - 1.00).

Pearson's and Spearman's correlation analyses carried out to evaluate the association between continuous variables of symmetric and asymmetric distribution, respectively, and considering them as perfect correlation (1.00), extraordinarily strong (0.90 - 0.99), strong (0.70 - 0.89), moderate (0.40 - 0.69), weak (0.20 - 0.39) and very weak (0.00 - 0.19).

The back wise multivariate logistic regression model was executed considering all variables studied, adjusting the model for the progressive exclusion of non-significant variables for the outcome.

The significance level was 5% having the assistance of the software Statistica v. 10 (Statsoft®), Medcalc® v. 7.4 and Minitab® 18.

This study complies with the Declaration of Helsinki, that the locally appointed ethics committee has approved the research protocol under number 78653817.2.0000.0096 and that informed consent has been obtained from the patients (or their legally authorized representative).

3. Results

The survey was developed with the participation of 196 individuals. There were 16 withdrawals, therefore leaving 180 patients participating, being 62 males (34.4%) and 118 females (65.5%), with a median age of 59.8 ± 11.3, consequently there was no age difference between sexes (p = 0.48). Table 1 displays the sample characteristics.

From the variables in Table 1, only age was selected as predictive of CAC with a 40% increase in risk (OR=1.04, 95% CI=1.01-1.07, p=0.02) using the multivariate logistic regression model.

Table 1 - Baseline Characteristics.

CHARACTERISTICS	n (%)/median + SD/median (IQR)
Male	62 (34.4 %)
Female	118 (65.5 %)
Age (years)	59.8 ± 11.3
Referred History of Familiar Coronary Artery Disease[a]	70 (40.2 %)
Diabetes	63 (35.0 %)
Hypertension	138 (76.7 %)
Metabolic syndrome	84 (46.7 %)
Fibrate intake	29 (16.1 %)
Statin intake	148 (82.2 %)
Other lipid-lowering therapy	36 (20.0 %)
hypoglycemic agents or insulin intake	72 (40.0 %)
Antihypertensive intake	139 (77.2 %)
Smoking current	12 (6.7 %)
Smoking previous	60 (33.3 %)
Alcohol intake	65 (36.1 %)
Systolic Blood Pressure (mmHg)	138.1 ± 20.9
Diastolic Blood Pressure (mmHg)	86.2 ± 12.8
Total cholesterol (mg/dL)	180.2 ± 54.0
Tryglicerides (mg/dL)	133.0 (90 - 203)
LDL-c (mg/dL)	96.0 (74 - 127.6)
HDL-c (mg/dL)	45.1 ± 13.7
Fasting glucose (g/dL)	99.0 (89 - 117)
Glycated haemoglobin (%)[b]	6.1± 1.3
Urea (mg/dL)	36.0 (28.6 - 44.0)
Creatinine (mg/dL)[c]	0.87 (0.80 - 1.09)
CPK – EPI* (ml/min/1,73m²)	76.6 ± 20.3

Note: **Chronic Kidney Disease Epidemiology Collaboration*, LDL-c = *Low Density Lipoprotein Cholesterol*, HDL-c = *High Density Lipoprotein Cholesterol*. [a] n = 174 [b] n = 177 [c] n = 175. Source: Authors.

Cardiovascular Risk Predictors

When considering the classifications for cardiovascular risk, a higher frequency for men was observed only for NC (93.5 for men vs 74.6 for women, $p < 0.01$). Men showed higher NC ($p < 0.001$), WC ($p < 0.01$), ABSI ($p < 0.01$); and lower C Index ($p = 0.02$).

TG-HDL-c demonstrated higher frequency of inadequacy classification for men (51.6%) than for women (33.0%), ($p = 0.02$).

There was not a significant difference for the values above normal, between sexes, in the frequency of ABI (8.5 women vs 8.2 men), PWV (27.1 women vs 27.4 male) and CtP (75.4 women vs 83.9 male) ($p > 0.05$ for all), although men presented higher ABI (0.01) and lower AI ($p < 0.01$), AP ($p < 0.001$).

FS and SS presented more elevated scores, most frequently for men than women (19.3% vs 4.2%, $p<0.01$ and 24.2% vs 9.3% for high score and 8.1% vs 0.8% for very high score, $p<0.001$, respectively) and cardiovascular risk was significantly higher among men.

Table 2 presents the Anthropometric, Biochemical, ABI and arterial stiffness CVRP.

Table 2 – Cardiovascular risk predictors by sex.

	Women (n = 118)	Men (n = 62)	p
Body Mass Index	30.8 ± 5.9	29.9 ± 3.9	0.28[1]
Neck Circumference	36.0 ± 3.4	41.1 ± 2.7	< 0.001[1]
Waist Circumference	100.2 ± 12.9	105.3 ± 10.1	< 0.01[1]
Waist Height Ratio	0.64 ± 0.08	0.62 ± 0.05	0.08[1]
A Body Shape Index	0.082 ± 0.005	0.084 ± 0.003	< 0.01[1]
A Body Shape Index Risk	1.09 ± 0.36	1.05 ± 0.31	0.54[1]
Conicity Index	1.33 ± 0.08	1.35 ± 0.06	0.02[1]
Castelli I Index	3.8 (3.2 - 4.6)	4.2 (3.4 - 5.7)	0.08[2]
Castelli II Index	2.1 (1.5 - 2.9)	2.4 (1.8 - 3.1)	0.18[2]
Triglyceride to High Density Lipoprotein Ratio	2.9 (1.9 - 4.3)	3.9 (1.9 - 7.7)	0.02[2]
Ankle Brachial Index	1.0 5 ± 0.10	1.1 ± 0.17	0.01 [1]
Central Pressure	126.5 ± 19.0	127.1 ± 16.8	0.83 [1]
Augmentation Index	26.0 (14 - 35)	16.0 (4 - 33)	< 0.01 [2]
Augmentation Pressure	10.0 (5 - 18)	4.5 (3 - 14)	< 0.001 [2]
Vascular Resistance	1.34 ± 0.24	1.33 ± 0.24	0.97 [1]
Reflection Coefficient	65.9 ± 10.6	62.9 ± 10.9	0.07 [1]
Pulse Wave Velocity	9.1 ± 1.9	8.9 ± 1.7	0.50 [1]

Note: 1: T Student test; 2: Mann-Whitney test. Source: Authors.

Coronary Calcium Score

Men presented higher CCS than women [8.0 (0 - 137) vs 44.2 (0 - 171), p = 0.09] while for the CCS percentile and Hecht classification there was not a significant difference between male and female sex. To Blaha classification a tendency of higher risk ratings among men (p = 0.13) was observed when Chi-square of Pearson/Yates test was completed.

CVRP associated with CCS.

There was no apparent correlation among CCS and the continuous variables of characteristic, laboratory tests, anthropometric, biochemical, ABI and arterial stiffness measures, when Pearson/Spearman Correlation were applied: age (years): 0.21; Systolic Blood Pressure (mmHg): 0.13; Diastolic Blood Pressure (mmHg): 0.06; Total cholesterol (mg/dL): -0.12; Triglycerides (mg/dL): -0.05; LDL-c (mg/dL): -0.12; HDL-c (mg/dL): -0.04; Fasting glucose (g/dL): 0.03; Glycated hemoglobin (%): 0.04; Urea (mg/dL): 0.13; Creatinine (mg/dL): 0.08; CPK – EPI* (ml/min/1,73m²): -0.13; Body Mass Index: 0.03; Neck Circumference: 0.03; Waist Circumference: 0.07; Waist Height Ratio: 0.10; A Body Shape Index: 0.12; A Body Shape Index Risk: 0.03; Conicity Index: 0.13; Castelli Index: -0.07; Castelli Index II: -0.08; Triglycerides to High-Density Lipoprotein Ratio: -0.04; Ankle Brachial Index: 0.08; Pulse Wave Velocity: 0.23; Central Pressure: 0.15; Vascular Resistance: 0.12; Augmentation Pressure: 0.09; Reflection Coefficient: - 0.01; Augmentation Index: 0.05.

Anthropometric Predictors

There was no association observed between BMI (p = 0.17) and NC (p = 0.48) with an increased in CAC. However, with a WC of 60 cm, an estimated 20% probability for CAC, increasing to 50% with roughly 120 cm and to 70% with 150 cm was observed, and approximately 15% of CAC chances with 0.4 WHtR, rising to 50% with 0.7 and to 80% with 1, was also detected. Likewise, the possibility of CAC has significantly increased according to C Index (30% with 0.6, 50% with 1.5 and 70% with 2.4) and ABSIR (10% with 1.0, 50% with 1.4 and 78% with 1.6).

No Anthropometric CVRP was significant in ROC Curve (all = p > 0.05).

In the anthropometric predictors, for Hecht's and Blaha's classifications, a lower value in score 0 was observed, being BMI the exception (tables 3 and 4).

Table 3 – Cardiovascular predictors according to CCS (Hecht's classification)

	CCS OF HECHT				
	0	1	2	3	p
Body Mass Index	29.9 ± 5.1	31.1 ± 4.7	29.6 ± 4.6	31.6 ± 7.1	0.32 [1]
Neck Circumference	36.7 ± 3.6	38.7 ± 4.1	37.5 ± 3.7	38.6 ± 4.4	0.02 [1a]
Waist Circumference	98.0 ± 12.3	105.4 ± 10.4	101.1 ± 10.5	105.8 ± 14.4	< 0.01 [1a]
Waist Height Ratio	0.61 ± 0.07	0.65 ± 0.06	0.64 ± 0.07	0.65 ± 0.09	< 0.01 [1a]
A Body Shape Index Risk	0.99 ± 0.25	1.16 ± 0.41	1.07 ± 0.34	1.11 ± 0.39	0.06 [1b]
Conicity Index	1.29 ± 0.07	1.36 ± 0.06	1.35 ± 0.07	1.36 ± 0.07	< 0.001 [1c]
Castelli Index	3.8 (3.3 - 4.9)	4.1 (3.5 -0.0)	4.1 (3.4 - 4.7)	3.5 (2.7 - 4.5)	0.33 [1]
Castelli Index II	2.2 (1.6 - 3.1)	2.3 (1.8 - 3.1)	2.1 (1.6 - 2.7)	2.0 (1.4 - 2.8)	0.38 [1]
Triglyceride to High-Density Lipoprotein Ratio	3.0 (1.7 - 5.4)	3.6 (2.4 - 5.1)	3.6 (1.9 - 5.0)	2.6 (1.8 - 3.9)	0.37 [1]
Framingham Score Risk- Low Risk	49 (51.6 %)	2 (26.3 %)	6 (6.3 %)	15 (15.8 %)	< 0.001 [2]
Score Score Risk- Low Risk	10 (76.9 %)	3 (23.1 %)	0 (0.0 %)	0 (0.0 %)	< 0.001 [2]
Global Risk Score/Lifetime Score Risk- Low Risk	20 (80.0 %)	3 (12.0 %)	0 (0.0 %)	2 (8.0 %)	< 0.001 [2]
Ankle Brachial Index	1.04 ± 0.12	1.08 ± 0.14	1.05 ± 0.12	1.10 ± 0.15	0.17 1
Central Pressure	125.3 ± 16.5	125.3 ± 17.9	127.3 ± 23.2	132.6 ± 16.7	0.30 [1]
Augmentation Index	20.0 (9 - 31)	27.0 (12 - 34.5)	27.0 (14 - 39)	26.0 (9.5 - 38.5)	0.66 [1]
Augmentation Pressure	6.0 (4 - 15)	8.5 (4 - 17.5)	10.0 (5 - 28)	9.0 (3.5 - 20.5)	0.41 [1]
Vascular Resistance	1.28 ± 0.20	1.34 ± 0.25	1.41 ± .27	0.37 ± 0.27	0.12 [1]
Reflection Coefficient	67.6 ± 9.3	62.0 ± 12.0	62.0 ± 11.3	66.8 ± 9.1	<0.01 [1a]
Pulse Wave Velocity	8.2 ± 1.7	9.1 ± 1.5	10.0 ± 1.7	9.7 ± 1.7	<0.001 [1c]

NOTE: 1: Anova one-way with Duncan *post-hoc* test; 2: Chi-square of Pearson test. [a] classification 0 < classification 1 and 2 [b] classification 0 < classification 1 [c] classification 0 < classification 1, 2 and 3. Source: Authors

Table 4 – Cardiovascular risk predictors according to CCS (Blaha's classification).

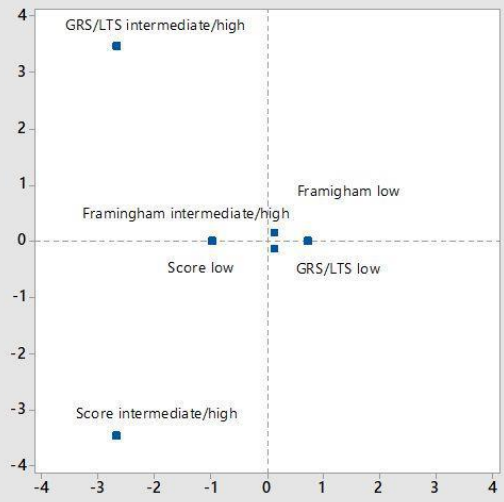
	CCS OF BLAHA			
	0	1	2	p
Body Mass Index	29.9 ± 5.1	31.1 ± 4.7	30.6 ± 6.0	0.45 [1]
Neck Circumference	36.7 ± 3.6	38.7 ± 4.1	38.0 ± 4.1	0.01 [1a]
Waist Circumference	98.0 ± 12.3	105.4 ± 10.4	103.4 ± 12.7	< 0.01 [1b]
Waist Height Ratio	0.61 ± 0.07	0.65 ± 0.06	0.64 ± 0.08	< 0.01 [1b]
A Body Shape Index Risk	0.99 ± 0.25	1.16 ± 0.41	1.09 ± 0.36	0.02 [1a]
Conicity Index	1.29 ± 0.07	1.36 ± 0.06	1.36 ± 0.07	< 0.001 [1b]
Castelli Index	3.8 (3.3 - 4.9)	4.1 (3.5 - 5.0)	3.6 (2.9 - 4.5)	0.32 [2]
Castelli Index II	2.2 (1.6 - 3.0)	2.3 (1.8 - 3.1)	2.1 (1.4 - 2.7)	0.23 [2]
Triglyceride to High-Density Lipoprotein Ratio	3.0 (1.7 - 5.4)	3.6 (2.4 - 5.1)	3.0 (1.9 - 4.8)	0.45 [2]
Framingham Score Risk- Low Risk	49 (51.6 %)	25 (26.3 %)	21 (21.1 %)	< 0.001 [3]
Score Score Risk- Low Risk	10 (76.9 %)	3 (23.1 %)	0 (0.0 %)	< 0.001 [3]
Global Risk Score/Lifetime Score Risk – Low Risk	20 (80.0 %)	3 (12.0 %)	2 (8.0 %)	< 0.001 [3]
Ankle Brachial Index	1.04 ± 0.12	1.08 ± 0.14	1.07 ± 0.14	0.29 [1]
Central Pressure	125.3 ± 16.5	125.3 ± 17.9	129.9 ± 20.3	0.30 [1]
Augmentation Index	20.0 (9 - 31)	27.0 (12 - 34.5)	27.0 (11 - 39)	0.23 [1]
Augmentation Pressure	6.0 (4 - 15)	8.5 (4 - 17.5)	10.0 (4 - 21)	0.24 [1]
Vascular Resistance	1.28 ± 0.20	1.34 ± .25	1.39 ± 0.27	0.06 [1]
Reflection Coefficient	67.6 ± 9.3	62.0 ± 12.0	64.4 ± 10.5	0.01 [1a]
Pulse Wave Velocity	8.2 ± 1.7	9.1 ± 1.5	9.9 ± 0.7	< 0.001 [1b]

NOTE: 1: Anova one-way with Duncan *post-hoc* test; 2: Anova of Kruskal-Wallis test; 3: Chi-square of Pearson test. [a] classification 0 < classification 1 [b] classification 0 < classification 1 and 2. Source: Authors

Clinical Predictors

When the multiple correspondence analyses model was applied to identify the clinical variables correlated with CAC, the GRS/LTS intermediate/high and the SS intermediate/high were the most associated with the indicated outcome, as noticed (Graph 1).

GRAPH 1 – MULTIPLE CORRESPONDENCE ANALYSIS FOR CORONARY CALCIFICATION ACCORDING TO CLINICAL VARIABLES



NOTE: Multiple Correspondence Analysis: p < 0.001. GRS / LTS: Global Risk Score / Lifetime Score

Considering the clinical scores, in the multivariate logistic regression model, the GRS/LTS intermediate/high was more intensely associated with cardiovascular risk (OR = 2.65, 95% CI = 1.20 - 5.87, p = 0.01) than others (OR = 1.18, 95% CI = 0.69 - 2.02, p = 0.52 for FS and OR = 0.75, 95% CI = 0.75 - 2.35, p = 0.32 for SS).

For the CCS, the frequency of clinical indexes classified as low was higher in the 0 classification for Hecht's and Blaha's (tables 3 and 4, previously showed).

ABI and arterial stiffness predictors

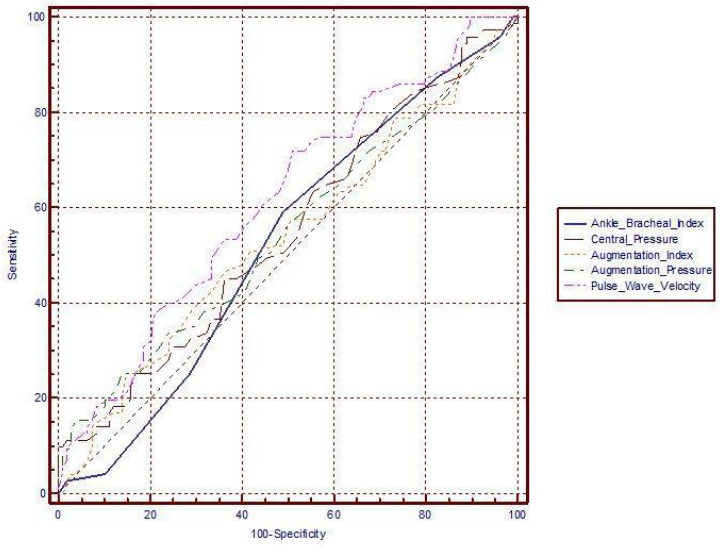
No association of ABI (p = 0.89), CtP (p = 0.10), VR (p = 0.09), AP (p = 0.10), RC (p = 0.46) or AI (p = 0.42) with the probable increase of CAC was noticed.

There was a significant increase, about 20%, of CAC probability, to PWV = 6, rising to practically 50% when = 10, and 80% when = 16.

Neither ABI nor arterial stiffness predictors presented significance in the ROC Curve (all = p > 0.05), PWV showed the major sensitivity on the ROC curve (AUC 0.61, with a sensitivity of 72.2, graph 2).

Considering CCS, the PWV and the RC were significantly lower with a rating of 0 for Hecht and Blaha (tables 3 and 4, previously showed), on the other hand for the multivariate logistic regression, PWV, GRS/LTS and age represented significant risks to CAC, estimated at 28%, 265% and 4%, respectively. In the back wise multivariate logistic regression model, considering all variables studied, the A Body Shape Index Risk increased the risk for CAC by 3.5 times (OR = 3.50, 95% CI = 1.38-1.64, p = 0.001) and PWV by 36% (OR = 1.36, 95% CI = 1.13 - 1.64, p < 0.01), being the two main variables selected considered as a meaningful predictive of the outcome.

GRAPH 2– ROC CURVES OF ANKLE BRACHIAL INDEX, CENTRAL PRESSURE, AUGMENTATION INDEX, AUGMENTATION PRESSURE AND PULSE WAVE VELOCITY ACCORDING TO CORONARY ARTERY CALCIFICATION



NOTE: ROC Curve ROC: p > 0.05.
AUCs: Ankle Bracheal Index=0.52; Central Pressure= 0.54; Augmentation Index= 0.53; Augmentation Pressure=0.54; Pulse Wave Velocity= 0.61.

4. Discussion

Age and sex were predictive factors for CAC, following the literature (Mohan *et al*., 2020; Oliveira, 2015). Meanwhile, men scored higher to all clinical predictors (FS, GRS/LTS and SS) and higher cardiovascular risk by FS and SS which is according to a study (Galvão *et al*., 2003) that found a higher frequency of FS for men rather than for women (32% vs 9%). Another research (Mcclelland & Blaha, 2017) also observed a higher CCS, as well as a higher risk for Blaha classification (CCS = 0, CCS = 1 - 99 and CCS > 100) for men.

This study found no significant association between BMI and CAC (Kommuri *et al*., 2019; Passos *et al.,* 2019), as well as between NC and CAC (Passos et al. 2019; Pokharel et al., 2014), which also matches the results found by other authors.

The association observed between WC (Passos *et al*, 2019) and WHtR (Oh et al., 2016) and the CAC follows to other results

The research investigated 33 432 Korean adults and the association between WC and CAC, finding that WC, in the obese group (according to BMI), presented a higher risk for CAC, OR = 1 235 (1 194 – 1 461, 95% CI) (Park *et al*., 2016). For the CCS classified by Hecht and Blaha, a significant association with WC was noticed, agreeing with published papers (Yu *et al*., 2013). A study investigated 6 745 individuals and concluded that WC was significantly related to CCS (CCS = 0; CCS = 1 - 99; CCS = 100 - 299; CCS ≥ 300), $p<0.001$ for all groups, when considering age, sex and race in adjusted model (model 1); and for groups with CCS=1-99 ($p=0.032$) and groups with CCS 100-299 ($p=0.025$) for model 1 plus tobacco, blood pressure, antihypertensive use, HDL-c, total cholesterol, other lipid-lowering therapy use, diabetes and PCR (Kommuri *et al*., 2019).

The same was observed for the WHtR, corroborating to other results (Yu *et al*., 2013). In the analysis of the CCS by Blaha and Hecht, a significant association was noted. A study with 6 814 patients found that the WHtR was associated with increased CAC in the 3 categories evaluated (CAC = 1 - 99, 100 – 299; CAC > 300): 11.2 (5.44 - 23.2; 95% CI, $p < 0.001$); 27.1 (9.44 - 79.1; 95% CI, $p < 0.001$); 41.7 (13.8 - 125.8; 95% CI, $p < 0.001$) respectively, adjusted for sex, age and race

(Model 1) and 2.73 (1.18 - 6.31; 95% CI, p = 0.019); 5.52 (1.61 - 18.9; 95% CI, p = 0.006); 4.59 (1.24 - 16.9; 95% CI, p = 0.022) correspondingly, adjusted for model 1 plus smoking, systolic blood pressure, HDL, antihypertensive medication, cholesterol, other lipid-lowering therapy, diabetes and PCR (Kommuri *et al*., 2019).

The probability of CAC has also increased significantly by ABSI and ABSIR. Some studies refer to cardiovascular risk, analyzed by other parameters, despite not finding any literature relating CCS or CAC to ABSI or ABSIR. The study monitored 7,011 individuals over 24 years old and observed the results of the ABSI Z score, comparing it to the BMI, WC, waist to hip ratio and WHtR, concluding that ABSI was a strong predictor of mortality from all causes and its rates extended in 1.13 (1.09 - 1.16; IC 95%) due to enlarged standard deviation in ABSI, and a risk rate of 1.61 (1.40 - 1.86), between the 20% highest ABSI scores and the 20% lowest ABSI scores (Krakauer & Krakauer, 2014). Meta-analysis with 38 studies showed that ABSI standard deviation had been associated with an increase in the chances of hypertension (13%), diabetes type 2 (35%) and risks of CVD (21%) and mortality from all causes (55%) (Ji *et al*., 2018).

Similarly, there was a higher probability of CAC related to the C Index, and when analyzing Blaha or Hecht's CCS a significant suggestion was found, accessing other work where C Index was associated with increased CAC in the 3 categories evaluated (CAC = 1 - 99, CAC = 100 - 299; CAC > 300): adjusted for sex, age and race (Model 1) - 8.83 (4.66 - 16.7; CI = 95%, p < 0.001); 18.3 (7.17 - 46.9; CI = 95%, p < 0.001); 14.2 (5.4 - 37.5; CI = 95%, p = 0.001) for model 1 plus smoking, systolic blood pressure, HDL, antihypertensive medication, cholesterol, other lipid-lowering therapy, diabetes and PCR - 3.29 (1.65 - 6.57; CI = 95%, p = 0.001); 6.27 (2.26 - 17.4; CI = 95%, p < 0.001); 3.0 (5.4 -8.78; CI = 95%, p = 0.044) (Kommuri *et al.*, 2019).

The anthropometric predictors (WC, WHtR, ABSIR and C Index) presented association with the CAC and are indicators of central obesity, which is a recognized risk factor for atherosclerosis, since several authors have shown the relationship among visceral fat, insulin resistance and high cardiovascular risk, even in non-obese individuals, but with elevated visceral fat content. The hormonal issue also seems to be related to the differences in body composition between men and women (Passos *et al*., 2019; Park *et al*., 2016; Mathieu *et al*., 2008).

No significance was established for biochemical predictors in any of the analyses conducted which are partially or integrally after other findings (Choi *et al*., 2010; Allison & Wright, 2004).

Intermediate/high GRS/LTS and SS have been the most associated with CAC, reinforcing the importance of more adequate classification of cardiovascular risk for intermediate scores and the importance of appropriate predictors to help it and improve clinical intervention and prevent cardiovascular events.

Regarding the non-association between ABI and CAC, other work also investigated the connection of CAC with ABI in 1 775 healthy individuals, finding a correlate coefficient of -0.003 (-0.011 to 0.004; 95% CI; p > 0.05), without significant association (Aboyans *et al*., 2007).

For the measures of arterial stiffness, the positive association between PWV and CAC, as demonstrated is in line with the other findings (Cecelja *et al*., 2013), one of them, which observed 213 asymptomatic patients and found that PWV had an independent association with CCS, β=0.18 (0.01 - 0.35; 95% CI; p = 0.04), and arterial calcification seemed to mediate atherosclerosis and increase arterial stiffness (Roos *et al*., 2014).

5. Conclusion

The identification of subclinical atherosclerosis is valuable for the effective prevention of cardiovascular events. Proper stratification of cardiovascular risk can optimize treatments and health costs, relieving health systems.

After performing those set of analyses the results showed that the predictor used to evaluate central obesity (mainly ABSIR) and arterial stiffness, more specifically the PWV, were the ones which obtained the best predictive value for

cardiovascular risk. Mainly the ABSIR has proven to be a reliable, easy and inexpensive method to assess CAC and consequently cardiovascular risk, and its use in Public Health is of great value.

Limitations

a) Selection bias: patients coming from outpatient clinics linked to cardiology, therefore with higher aggregate cardiovascular risk.

b) The sample was composed of a reduced number of patients.

c) The high use of statin in the studied population may have affected the results found, since it has an atherosclerotic plaque stabilization effect, but increases the CAC.

Data accessibility statements

All data are available on request to the first author.

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Conflict of interest

The authors report no conflicts of interest related to this article.

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