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Research Article

Type 2 Diabetes Mellitus, Hypertension, and HbA1c, as Risk Factors for Arterial Stiffness

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ABSTRACT

Studies in a healthy and diabetic population have shown that there is a correlation between the disease and arterial stiffness, and consequently an increase in Pulse Wave Velocity (PWV). Little is known about risk factors of arterial stiffness particularly regarding the prediction of type 2 diabetes mellitus. We investigate predictors laboratory and clinical associated with arterial stiffness, validated by the increase in PWV. All patients of BioCor Cardiology Center, in the city of Maringa, Parana, Brazil, were subject to a cross-sectional study in the period from 2010 to 2016. A non-invasive oscillometric device, the Mobil®-o-graph, was used to measure the central pressure and pulse wave velocity. The analyses were conducted using Stata 9.0 (StataCorp, College Station, TX 77845 USA). This research was approved by the Local Ethics Committee (Permanent Ethics Committee in Human Research of the State University of Maringá), approval number 1.664.157/2016. The population was 1197 patients, mean age of 60.1 [SD ± 14.6], and 341 (28.5%) of these patients had altered PWV. The variables impacting for PWV ≥ 10, with statistical significance for p<0.001 were: Type 2 diabetes mellitus (D2M), hypertension, HbA1c ≥ 5.7, total cholesterol ≥ 190 mg/dl, LDL cholesterol ≥ 130 mg/dl, and HDL cholesterol ≤ 40 md/dl, besides the known factor hypertension. The final model showed a positive association for PWV ≥10 for the presence of DM (OR 1.5, CI 1.0-2.3, p=0.040), hypertension (OR 2.7, CI 1.9-3.9, p<0.001), HbA1c 5.7-6.4 (OR 2.1, 1.5-2.9, p<0.001), HbA1c ≥ 6.5 (OR 3.6, 2.2-2.8, p<0.001), and HDL cholesterol ≤ 40 md/dl (OR 1.4, IC 1.0-1.8, p=0.031). Our findings showed that the predictor for D2M, hypertension, glycated hemoglobin ≥ 5.7, confirmed the significant association for increased arterial stiffness, validated by the increase in PWV.

Keywords: Hypertension; Diabetes mellitus; Pulse wave velocity; Vascular stiffness; Risk factors

INTRODUCTION

Cardiovascular Disease (CVD) is the leading cause of death in diabetic patients [1]. Diabetes Mellitus (DM) is an independent predictor for cardiovascular adverse events [2]. Their mechanisms are still not fully understood, but it is believed that increased arterial stiffness is an important mechanism linking diabetes to increased cardiovascular risk [3]. Studies have shown that factors related to diabetes and hypertensions are associated with a stiffer artery [4,5].

A systematic review regarding diabetes, 52% of the studies had a positive association with increased PWV [6]. In another study, the conclusions regarding risk factors and blood pressure were inconsistent or showed low correlation, as these factors would explain only 1% of the PWV variation [7]. In parallel, another research reports that there was no correlation between the variables HbA1c and blood sugar levels in fasting diabetic participants, with arterial stiffness. Concomitantly diabetes and hypertension significantly increased the risk of arterial stiffness [8]. Diabetes mellitus is independently associated with increased arterial stiffness and carotid atherosclerosis [9].

Currently, great attention is being drawn to the investigation of arterial stiffness, probably due to the evidence that this stiffness, measured by Pulse Wave Velocity (PWV), is an important predictor of cardiovascular events, especially in hypertensive individuals and with other comorbidities [10,11]. In view of the conflicting results, we investigate predictor's laboratory and clinical associated with

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arterial stiffness, validated by the increase in PWV.

MATERIALS AND METHODS

All patients of BioCor Cardiology Center, in the city of Maringá, Paraná, Brazil, were subject to a cross-sectional study in the period from 2010 to 2016, using data from a secondary medical records source containing the information of the central pressure of each patient. This research was approved by the Local Ethics Committee (Permanent Ethics Committee in Human Research of the State University of Maringá), approval number 1.664.157/2016.

A non-invasive oscillometric device, the Mobil®-O-Graph, was used to measure the central pressure and pulse wave velocity. Three measurements were performed over a 15-minute period, with the subsequent average of these values.

The Mobil®-O-Graph uses a cuff-based method to estimate cf-PWV from single point pressure wave recording. After obtaining Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP), the brachial cuff is inflated to the DBP level and held for 10 seconds to record pulse waves. Using a transfer function, central pressure curves are obtained and processed using the ARCSolver algorithm (Austrian Institute of Technology, Vienna, Austria); various parameters from pulse wave analysis to wave separation analysis are incorporated in a mathematical model, that combines age, central pressure and aortic characteristic impedance [12-15]. The advantages of this method are that is easy to perform, the method is validated invasively and with another non - invasive method, such as pulse tonometry using the Sphygmocor device, and it is also the only device approved for clinical use in our country, and with reference values for our population [16-18]. The limitation of this device is that it estimates the pulse wave velocity.

A structured instrument with the independent clinical and laboratory variables: diabetes mellitus-DM (Yes/No), glycated hypertension-SAH (Yes/No), total cholesterol (<190, ≥ 190 mg/dl), low-density lipoproteins-LDLc (<130, ≥ 130 mg/dl), high-density lipoproteins-HDLc (<40, ≥ 40 mg/dl), triglycerides (<150, ≥ 150 mg/dl) was used to collect data [19,20]. The PWV was considered as an outcome variable with two cuts,<10 and ≥ 10 m/s.

The analyses were conducted using Stata 9.0 (StataCorp, College Station, TX 77845 USA). The statistical analysis for variables was validated with p-value <0.05 by the chi-square test, and an Odds Ratio (OR) measure and a 95% confidence interval were used. In the logistic model construction for the primary outcome of PWV, all variables regardless of the p-value were considered in the analysis and adjusted for D2M, hypertension, HbA1c, total cholesterol, LDLc, HDLc d LDL and Triglycerides.

RESULTS

The population considered in this study was 1197 patients with a range of 18 to 100 years, with mean age of 60.1 [SD ± 14.6], and 341 (28.5%) of these patients had altered PWV and 856 (71.5%) not had altered PWV. Table 1 shows the univariate analysis of the risk factors for pulse wave velocity between the two PWV groups <10 and ≥10, using association effect measures, estimated by the Odds Ratio. The variables impacting for PWV ≥ 10, with statistical significance for p<0.001 were: D2M, hypertension, HbA1c ≥ 5.7, total cholesterol ≥ 190 mg/dl, LDL cholesterol ≥ 130 mg / dl, and HDL cholesterol ≤ 40 md/dl (Table 1).

Next, a logistic regression analysis tried to verify the association of independent variables adjusted for <0.05 and the outcome variable PWV. The final model showed a positive association for PWV ≥10 for the presence of D2M (OR 1.5, CI 1.0-2.3, p=0.040), hypertension (OR 2.7, CI 1.9-3.9, p <0.001), HbA1c 5.7-6.4 (OR 2.1, 1.5-2.9, p<0.001), HbA1c ≥ 6.5 (OR 3.6, 2.2-2.8, p<0.001), and HDL cholesterol ≤ 40 md/dl (OR 1.4, IC 1.0-1.8, p=0.031).

Table 1: Logistic regression of clinical and laboratory risk factors for arterial stiffness.

Variables	PWV**<10	PWV** ≥ 10	OR (CI 95%)	p-value	OR (CI 95%)	p-value
	N (%)	N (%)	Unadjusted		Adjusted	
D2M*** (Yes)	258 (30.1)	141 (41.4)	1.6 (1.3-2.1)	<0.001*	1.5 (1.0-2.3)	0.040*
Hypertension (Yes)	594 (69.4)	300 (87.9)	3.2 (2.3-4.6)	<0.001*	2.7 (1.9-3.9)	<0.001*
HbA1c (%) 5.7–6.4	311 (36.3)	147 (43.1)	2.2 (1.6-2.9)	<0.001*	2.1 (1.5-2.9)	<0.001*
HbA1c (%) ≥6.5	138 (16.1)	106 (31.1)	3.5 (2.5-5.0)	<0.001*	3.6 (2.2-2.8)	<0.001*
Total cholesterol (≥ 190 mg/dl)	589 (68.8)	281 (82.4)	2.1(1.6-2.9)	<0.001*	1.3 (0.6-2.5)	0.535
LDL cholesterol (≥ 130 mg/dl)	546 (63.8)	268 (78.6)	2.1 (1.6-2.8)	<0.001*	1.6 (0.8-3.1)	0.183
HDL cholesterol (< 40 mg/dl)	516 (60.3)	216 (60.4)	1.0 (0.8-1.3)	0.967	1.4 (1.0– 1.8)	0.031*
Triglycerides (≥ 150 mg/dl)	331 (38.7)	145 (42.5)	1.2 (0.9-1.5)	0.219	1.1 (0.8-1.5)	0.459

Note: *Statistical association (p<0.05), CI (confidence interval), SD (standard deviation). The variable outcome pulse wave velocity (PWV)**, was adjusted in the logistic model by type 2 diabetes mellitus (D2M)***, hypertension, glycated hemoglobin (HbA1c), total cholesterol, LDLc, HDLc and Triglycerides

DISCUSSION

In our cross-sectional analysis, diabetes mellitus and elevated glycated hemoglobin emerged as risk factors of arterial stiffness, besides the known factor arterial hypertension, validated by the increase in PWV. Our study values ≥ that 5.7% of HbA1c showed an estimated risk gradient increasing between 110% to 260% for PWV alteration than patients with values lower than 5.7%. Studies show a strong relationship between high levels of glycated hemoglobin and an increased risk of cardiovascular diseases [20,21]. This result could also be observed in another study where elevated glycated hemoglobin was positively associated with elevated PWV, that is, lousy diabetes control would lead to greater arterial stiffness [22,23]. Recent studies reveal that clinical findings and comorbidities, such as hypertension, glucose, poor glycemic control, dyslipidemia, and diabetes duration were associated with arterial stiffness in D2M [24,25].

In individuals with primary HA, the risk for any Cardiovascular (CV) complication increases in parallel to the elevation of the PWV, as vessel stiffening is accelerated in the presence of the disease [26,27]. The results obtained demonstrate that hypertension patients are approximately two times more likely to increase PWV than patients with no hypertension. The most important modification that occurs in the vessel wall of a hypertensive patient is the hypertrophy of the middle layer associated with reduced arterial compliance and distensibility regardless of the BP level [28,29].

Arterial stiffness in diabetics patients could be attenuated and even treated with lifestyle modifications, such as diet and exercises. Besides lifestyle modifications, glycemic controls, and recent medications, such as SGLT2 inhibitors, have shown an impact on arterial stiffness, and monitoring through oscillometric devices could help in the assessment of vascular damage that occurs in this population [30]. The demonstration of an objective data of vascular damage during the medical consultation, could aware the patient of his condition, and the need for a better adherence to treatment. It is important to educate health professionals and patients about the importance of assessing the vascular damage that has clinical implications for cardiovascular outcomes [10,31].

The study has both strengths and limitations. The primary limitation is the size of patient sample. While 1197 patients were included, larger samples would provide more precise evidence, especially regarding diabetes mellitus prediction. Another limitation is that the study was conducted in a single ambulatory service, which may have faced challenges in assessing PWV due to technical difficulties and limitations. It's important to note that the research spanned six years, adding significance to the findings. Finally, the cross-sectional nature of our analysis prevents us from establishing causal relationships. Despite the limitations, the findings hold relevance for medical clinics and health services, helping them focus on parameters to prevent arterial stiffness progression and cardiovascular mortality.

CONCLUSION

Hypertension and diabetes mellitus are alterations that have been widely studied due to their association with the increased risk of cardiovascular diseases. Current evidence suggests that arterial stiffness is an essential component in the pathophysiology of diabetes and that endothelial dysfunction can occur in the early stages of the disease, or even earlier, in the phase of altered fasting glucose. In our research, the predictor`s type 2 diabetes mellitus, hypertension, glycated hemoglobin ≥5.7 beside the known factor hypertension, adjusted logistic regression analysis, confirmed a significant association with increased arterial stiffness, validated by the increase of pulse wave velocity. Future studies are necessary to better assess the role of arterial stiffness in the pathophysiology of diabetes and to evaluate the impact of treatment of arterial stiffness on cardiovascular outcomes.

CONFLICT OF INTERESTS

Authors declared no conflict of interests.

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