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Central Blood Pressure and Vascular Aging in Patients with Type 2 Diabetes Mellitus

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Abstract

Background Structural modifications of conduit arteries in diabetes mellitus substantially contribute to subclinical changes including increased arterial stiffness, which is recognized as one of the dominant hemodynamic manifestations of vascular aging, and a determinant of central systolic blood pressure (cSBP). However, it remains unclear whether elevated cSBP might be an independent contributor to arterial stiffness. The present study aimed to evaluate the contribution of central blood pressure calculated via an Arteriograph (TensioMed, Hungary) to the identification of patients with impaired vascular function.

Methods This observational cross-sectional study included 125 obese/overweight patients aged 22–72 years, with type 2 diabetes mellitus (T2DM), on antidiabetic medication. Patients may have hypertension as a concomitant disease. Pulse wave analysis was conducted via an Arteriograph. Correlation analysis was performed between the brachial augmentation index (AIx), pulse wave velocity (PWV), cSBP, systolic (SBP), diastolic BP (DBP), and central aortic pulse pressure (cPP). In the case of significant partial correlation coefficients and after the exclusion of multicollinearity, multiple linear regression was performed, adjusted for age, heart rate and height. According to these models, ROC curves were prepared with cutoff values of PP = 60 mmHg used as classifiers of impaired vascular function.

Results The values of the evaluated parameters were, as follows: AIx -23.6 ± 32.7%, PWV 9.1±2.3 m/s, cSBP 127.4± 21.7 mmHg, SBP 133.1± 18.5 mmHg, DBP 80.9± 10.5 mmHg, and cPP 49.97 ± 12.9 mmHg. Significant correlations were obtained between cSBP and AIx ($r = 0.65$, $p<0.05$), cSBP and PWV ($r = 0.48$, $p<0.05$), PWV and AIx ($r = 0.50$, $p<0.05$), and cPP and cSBP ($r = 0.75$, $p<0.05$).

Significant models were obtained for PWV with PP = 60 mmHg as a classifier: cSBP and age (AUROC = 0.824 ($R2 = 0.28$, $p<0.05$)); for AIx with PP = 60 mmHg as a classifier: cSBP and age (AUROC = 0.773 ($R2 = 0.44$, $p<0.05$)); cSBP, age and height (AUROC = 0.776 ($R2 = 0.53$, $p<0.05$); cSBP, age and heart rate (AUROC = 0.699 ($R2 = 0.59$, $p<0.05$); cSBP, age, height and heart rate (AUROC = 0.658 ($R2 = 0.70$, $p<0.05$).

Conclusion Our results revealed strong correlations between cSBP and other measures of vascular function assessed by the Arteriograph. Our models demonstrated that cSBP determined by the Arteriograph is identifying patients with arterial stiffening independently of potential confounders, and, therefore, the Arteriograph may serve as a screening tool for patients with diabetes mellitus.

Keywords Vascular aging, Pulse wave velocity, Central blood pressure, Pulse pressure, Arterial stiffening

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1 Introduction

Diabetes mellitus (DM) has been implicated in the development and progression of arterial stiffness (AS) at several levels. Structural modifications of conduit arteries in DM substantially contribute to subclinical changes related to increased AS, which is recognized as one of the dominant hemodynamic manifestations of vascular aging, and is a determinant of central systolic blood pressure (cSBP) [1]. The clinical importance of the measurement of cSBP was first demonstrated in a large cohort which revealed substantial overlap in cSBP between different levels of brachial SBP (SBP) in all age groups [2]. According to this cohort, more than 70% of individuals with high-normal SBP had cSBP in common with patients with stage 1 hypertension [3]. Many studies have evaluated the ability of the cSBP to predict the risk of future CV events.

The traditional view characterizes AS as a phenomenon affecting predominantly large arteries, which is a consequence of long-standing hypertension, however, the post hoc analysis of the Framingham Heart Study revealed that in middle-aged and older-aged individuals it is a cause rather than a consequence of hypertension [4]. On the other hand, evidence of the consequences of long-lasting hypertension regarding the progression of AS suggests that the relationship is bidirectional [5].

Abnormally fast propagation of the pressure wave reflection with its arrival at early systole caused by arterial stiffening shifts the point of summation of the forward and antegrade pressure waves more centrally which results in boosting of the cSBP and a decrease in pulse pressure amplification to the periphery, whereas central diastolic BP falls, resulting in increased central PP [6]. The elevation of cSBP increases cardiac afterload whereas a decrease in cDBP impedes coronary blood flow [7]. However, it remains unclear whether the increase in cSBP might be an independent contributor to arterial stiffness [8, 20]

This study evaluated the relationships between cSBP determined by the Arteriograph and vascular aging parameters in patients with T2DM. The novelty of our analysis is that we examined the ability of central blood pressure (cSBP) measured by an Arteriograph (TensioMed, Hungary) to determine impaired vascular function, as assessed by pulse wave velocity (PWV) and the brachial augmentation index (AIx). Thus, multivariate regression models were prepared to assess the contribution of cSBP measured by the Arteriograph, to the identification of patients with arterial stiffness, independently of confounding factors. Besides that, we evaluated the differences between cSBP and SBP concerning pulse pressure amplification.

2 Patients and Methods

2.1 Data Collection

In this cross-sectional observational study data from 125 patients (69 females (55.2%) and 56 males (44.8%) were analyzed. The average age of the sample was 49.8 ± 10.3 years, with 49.1 ± 11.3 years in the male group and 50.4 ± 9.4 years in the female group. We also recruited a control group consisting of 45 individuals without a diagnosis of DM, matched for age, treated for hypertension, and with a BMI of less than 25 and a HOMA index of less than 2.5. The average age of the control group was 48.3 ± 14.1 years.

All patients were of Caucasian origin according to self-assigned as well as observer-assigned ethnicity and lived in the Eastern-Slovakian region. Patients were recruited during their regular control examinations, which were performed once every three months and were involved in the study after providing informed consent. They signed the informed consent form after an explanation of the aim of this type of noninvasive BP measurement and the study. Each patient underwent a basic clinical examination in terms of internal medicine and measurement of anthropometric parameters. The questionnaire concerning the participants´ characteristics was self-administered and regularly updated during each visit, in terms of the biometric values of patients. Access to data is possible only for persons authorized by the University Hospital Ethical Committee, Nr. of approval is 529–165/EK/21.

2.1.1 Inclusion and Exclusion Criteria

The inclusion and exclusion criteria are listed in the data supplement (Table 1).

2.2 Evaluation of Hemodynamic Parameters

The invasively and noninvasively validated instrument Arteriograph Tensiomed Ltd. (H-1103 Budapest, Hungary) was used for the evaluation of parameters of peripheral and central hemodynamics. Arteriograph is based on the methodology of high-sensitivity cuff oscillometry, which uses only one cuff for both BP measurement and waveform detection for pressure wave analysis (single-point analysis), in which an ensemble waveform is generated during a period of constant suprasystolic cuff pressure of at least 35 mm Hg over the actual SBP and then the late systolic wave amplitude is analyzed [9]. By creating a stop-flow condition in this suprasystolic condition a small diaphragm develops at the level of the upper edge of the overpressurized cuff.

Simultaneously with the change in the central pressure the direct systolic wave (P1), the reflected systolic wave (P2) and the diastolic wave arrive at this point and cause a beat on the diaphragm. In this situation, the conduit arteries above this point act like a cannula to transfer changes in the central pressure. Because of the occlusion of the artery, the local impact of the characteristics of the arterial wall is practically eliminated. As the surrounding tissues are incompressible, this energy propagates to the cuff edge and causes a subtle volume/pressure change, which is detected by a high-fidelity piezoelectric pressure sensor in the device. The process starts with an oscillometric measurement of actual systolic and diastolic BP-s, which is followed by decompression of the cuff. The inflation of the cuff then starts again, first to the level of the diastolic pressure, and then to the suprasystolic level (systolic + 35 mmHg). The detection of the signals lasts 8 s at both levels [10].

The pressure waves are automatically calibrated to absolute BP readings, using the brachial pressure during the same cycle of measurement, which lasts 2–3 min. The measurement is operator independent and the results depend solely on the device.

The Arteriograph provides measurements of several parameters, and the patients were analyzed for brachial systolic pressure (SBP), brachial diastolic blood pressure (DBP), central systolic blood pressure (cSBP), central aortic pulse pressure (cPP), aortic pulse wave velocity (PWV) and the brachial augmentation index (AIx).

The software of the device calculates AIx-brachial via the following formula:

$$AIx\,(\%)\,:\,P2{-}P1/\,PP\,\times\,100$$

where P1 is the amplitude of the first (direct) wave, P2 is the amplitude of the late (reflected) systolic wave and PP is the pulse pressure. The device determines the time interval between the peaks of the direct and systolic reflected waves (return time—RT).

The distance used in the PWV calculation was between the jugulum and symphysis, suggesting a fixed reflection point above the aortic bifurcation.

PWVAo is then calculated via the following formula:

$$PWVAo\,(m/s)\,=\,Jug\,(m){-}Sy\,(m)\,/\,RT\,/2\,(s)$$

Validation studies comparing Arteriograph and the gold standard methods and an invasive validation study are available [9, 11, 12].

Measurements were performed after 15 min of rest in the horizontal position, using an appropriate upper arm cuff, considering the arm circumference. In accordance with the user´s manual, the cuff was tightly fastened on the dominant arm above the elbow.

2.3 Statistical Analysis

The normality of the distribution of continuous variables was tested via the Shapiro––Wilk test, and the homogeneity of variances was tested via the Levenes test. In the case of a normal distribution, the two-sample Student´s t-test was used to determine the difference between the analyzed groups. In the case of the nonparametric distribution of values, the Mann––Whitney *U*-test was applied to compare the differences between the two groups. For the whole group, as well as the sex groups the Pearson correlation test was applied for the assessment of relationships between outline variables and explanatory variables. In the case of a nonparametric distribution, Spearman´s correlation test was used. To assess the contribution of cSBP as an explanatory variable to the value of PWV and Aix, multiple linear regression models were prepared. The relationships between predictor variables in the models were checked for potential multicollinearity via a correlation matrix. Before fitting the models, all variables were checked for normal distribution and homogeneity. To simplify the model, stepwise selection was performed. The models were adjusted for age, heart rate and height. According to these models, ROC curves were prepared with a cutoff value of PP = 60 mmHg, which was used as a classifier of impaired vascular function [13–15].

The AUC was determined for all the models to evaluate their performance. The significance of the ROC curves at the determined cutoff values was tested via McNemar´s test.

Only p-values lower than 0.05 were considered statistically significant. All tests were two-tailed, and analyses were performed via the SAS statistical package version 9.4 (SAS Institute Inc., Cary, CA).

3 Results

Basic descriptive statistics of the evaluated variables are presented in Table 1.

Seventy-six percent of patients were diagnosed with hypertension as a concomitant disease that preceded the diagnosis of diabetes.

We compared the results of the evaluated group with those of the control group consisting of 45 individuals who were diagnosed with hypertension, without a diagnosis of diabetes mellitus, and with a BMI of less than 25. There was no significant difference in any BP parameter between the patient and control group.

Table 1 Basic descriptive statistics of the whole group and sex-stratified groups

Parameter	Patients´ gr Mean ± SD Nr. = 125	Range	Male patients Mean ± SD Nr. = 56	Range male	Female patients Mean±SD Nr. = 69	Range female	Male/ Female Significance of differences
Age	49.82 ± 10.3	50	49.12± 11.3	50	50.37± 9.41	44	**p = 0.50**
BMI	27.24 ± 35	24	28.55± 4.40	22	26.17± 4.04	20	**P = 0.002**
SBP	133.08 ± 18.49	115	136.67±17.09	101	130.16±19.18	100	**P = 0.049**
DBP	80.88± 10.49	55	83.28± 9.80	50	78.92± 10.68	55	**P = 0.020**
cSBP	127.41± 21.66	124	127.82± 19.29	114	127.08± 23.55	115	**p = 0.72***
cPP	49.97±12.89	55	49.93±11.70	50	50.02±14.11	55	**P = 0.277**
AIx%	−23.58 ± 32.67	143	−35.38 ± 24.86	103	−13.69± 35.23	143	**p = 0.001***
PWV	9.11 ± 2.25	11.7	8.90± 2.04	11.7	9.27± 2.41	11.6	**p = 0.36**

* Non-parametric Mann-–Whitney *U* test

Table 2 Basic descriptive statistics of age-stratified groups

Parameter	Patients ≤ 50y Mean ± SD Nr. = 59	Range	Patients >50y. Mean ± SD Nr. = 66	Range	Patients ≤ 50y/>50y Significance of differences
Age	41.13 ± 7.31	28	57.57± 5.01	21	**p = 0.0.001**
BMI	26.18± 3.93	16	28.18± 4.52	23	**P = 0.01**
SBP	127.59±14.52	73	137.98±20.30	107	**P = 0.001**
DBP	78.40± 8.93	38	83.09± 11.32	55	**P = 0.01**
cSBP	118.88± 16.08	70	135.04± 23.22	114	**p = 0.001**
cPP	49.97±12.89	45	54.89±12.23	65	**P = 0.003**
AIx%	−37.52± 29.53	140	−11.39± 30.64	120	**p = 0.001**
PWV	8.38± 2.40	11.7	9.75± 1.90	10.9	**p = 0.001**

When comparing parameters between males and females, we found significant differences in BMI, cSBP, DBP and AIx. The two sex groups did not differ in age, cSBP or PWV.

We aimed to compare the differences between cSBP and SBP in the whole group, as well as in the age-stratified groups, therefore we divided patients into two subgroups with a cutoff value of 50 years.

Basic descriptive statistics of the age-stratified groups are presented in Table 2.

In the whole group, only thirty-three of the 125 patients had greater cSBP values than SBP values, 26 in females and 7 in males. In the group of patients younger than 50 years, only six patients and in the group of patients older than 50 years 27 patients had greater cSBP values than SBP values. When we assessed the whole group, SBP was significantly greater than cSBP. In the group of patients younger than 60 years, this difference was significant but in the group of patients older than 60 years, this difference was not significant.

Basic descriptive statistics of patients with diabetes compared with patients with hypertension but without diabetes are presented in Table 2 in the data supplement.

After baseline characteristics, we prepared correlation matrixes in the whole group, and separately, in males and females, to assess linear relationships between different BP values and indices of arterial stiffness.

Significant correlations between parameters of vascular function in the overall and sex-stratified cohorts are shown in Table 3 in the data supplement.

To determine whether cSBP measured by Arteriograph can reliably predict vascular dysfunction in the form of elevated PWV or AIx present or absent in a particular patient, we used multivariable regression modelling.

Accordingly, we prepared ROC curves to determine the specificity and sensitivity of the calculated PWV or AIx as a predictor of vascular dysfunction in our models, where the cut-off value for PP of 60 mmHg was considered as a classifier of vascular dysfunction.

Receiver-operating characteristic curve (ROC) is a graphical representation for evaluating the performance of binary classification models like our one in which the

Table 3 Basic outputs of the stepwise linear regression models with PP = 60 mmHg as a classifier

Model Nr	Dependent variable	Independent variable	Adjustment for	AUC (95% CI)	Sensitivity of the model (%)	Specificity of the model (%)	Cutoff value of the dependent variable
Model 1	PWV (m/s)	cSBP (mmHg)	Age	0.824 (0.72—0.92)	81.81	68.93	9.43 m/s
Model 2	AIx (%)	cSBP (mmHg)	Age	0.773 (0.67—0.87)	74.07	65.30	−20.90%
Model 3	AIx (%)	cSBP (mmHg)	Age + Height	0.776 (0.66—0.89)	72.72	73.78	−13.50%
Model 4	AIx (%)	cSBP (mmHg)	Age + Heart rate	0.699 (0.57—0.82)	68.18	67.96	−15.90%
Model 5	AIx (%)	cSBP (mmHg)	Age + Height + Heart rate	0.658 (0.52—0.79)	72.72	60.19	−22.59%
Model 6	AIx (%)	cSBP (mmHg)	PWV	0.777 (0.67—0.87)	72.72	67.96	−18.60%

positive class represented the presence of a condition (vascular dysfunction) and the negative class represented its absence.

Key Terms in ROC:

TPR (True Positive Rate): The ratio of correctly predicted positive vascular dysfunction.

FPR (False Positive Rate): The ratio of incorrectly predicted negative vascular dysfunction.

Specificity: The proportion of actual negatives correctly recognized by the model (inverse of FPR).

Sensitivity/Recall: The proportion of actual positives correctly recognized by the model (same as TPR).

ROC projects the TPR against the FPR at different thresholds (in practice at selected intervals). In short, it shows the trade-off between the sensitivity and specificity of the calculated values of the models (PWV or AIx).

The area under the ROC curve (AUC) demonstrates the probability (chance) at which the model if given a randomly chosen positive and negative example, will scale the positive one higher than the negative one. In short, the AUC gives an overall idea of how well our model, which is a calculation of PWV or AIx, is doing at sorting positives and negatives, in terms of vascular dysfunction, without being affected by the threshold we set for classification. A higher AUC value shows better model performance, demonstrating a greater ability to distinguish between classes. An AUC value of 1.0 indicates perfect performance while 0.5 demonstrates that the model is random guessing, representing a 50% chance of correctly ranking a random positive and negative example. Low AUC (close to 0) indicates that the model struggles to differentiate between the two classes.

A perfect model, which at some threshold has a TPR of 1.0 and an FPR of 0.0, can be depicted by either a point at „0 " or „1 " if all other thresholds are ignored. This perfect model with sides of length 1, has an AUC of 1.0. This means there is a 100% chance that the model will correctly scale a randomly chosen positive example higher than a randomly chosen negative example.

On the basis of sensitivity and specificity and the Akaike information criterion, only the variants of our models with the highest performance and significant explanation of the variation in the outcome (vascular dysfunction) were further taken into consideration.

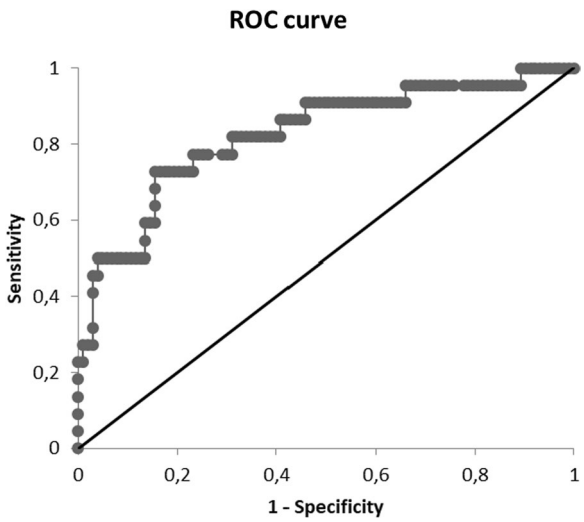

Fig. 1 The ROC curve of the model for PWV calculated from cSBPAo and adjusted for age The AUC for PWV in the model calculated from SBPAo, and adjusted for age was 0.824 (95% CI 0.72 to 0.92, $p \leq 0.05$) with a sensitivity of 81.81% and specificity of 68.93%. The cut-off value of PWV was 9,43 mmHg. The ROC curve is depicted in Fig. 1

3.1 Significant Models with PP = 60 mmHg as a Classifier Were Obtained as Follows

Basic outputs of the stepwise linear regression models are shown in Table 3.

Significant model was obtained for PWV calculated from cSBP after adjustment for age as follows (model 1):

PWV = 1.45 + 0.03 (cSBP) + 0.05 (Age) $p < 0.05$ F = 23.82 $R^2 = 0.28$.

The ROC curve is depicted in Fig. 1.

The relationships between PWV and height ($r = -0.08$, $p = 0.33$) and between PWV and heart rate ($r = 0.14$, $p = 0.11$) were not significant, therefore, the model could not be adjusted for height or heart rate. Although PWV was significantly correlated with BMI ($r = 0.21$, $p = 0.01$), the model adjusted for BMI lost significance.

Significant model was obtained for AIx calculated from cSBP after adjustment for age as follows (model 2):

AIx = −163.03 + 0.84 (cSBP) + 0.64 (Age) $p < 0.05$ F = 49.97 $R^2 = 0.44$.

The ROC curve is depicted in Fig. 2

Significant model was obtained for AIx calculated from cSBP after adjustment for age and height as follows (model 3):

AIx = 35.47 + 0.82 (cSBP) + 0.36 (Age)—1.07 (height) $p < 0.05$ F = 46.37 $R^2 = 0.53$.

The ROC curve is depicted in Fig. 3

Significant model was obtained for AIx calculated from cSBP after adjustment for age and heart rate as follows (model 4):

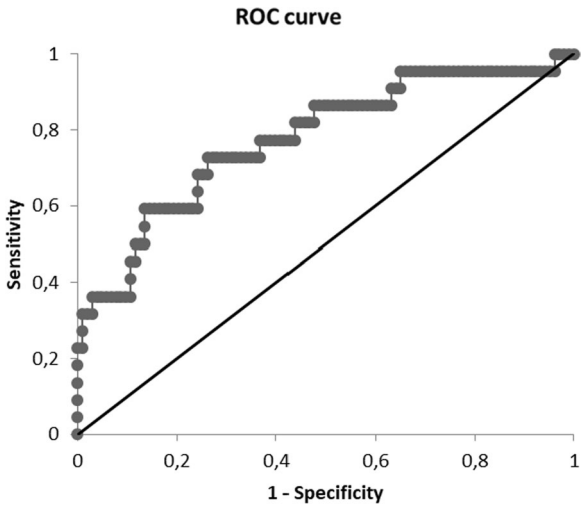

Fig. 3 The ROC curve of the model for Aix calculated from cSBPAo, and adjusted for age and height. The AUC for Aix in the model calculated from cSBPAo and adjusted for age and height was 0.776 (95% CI 0.66 to 0.89, $p \leq 0.05$) with a sensitivity of 72.72% and specificity of 73.78%. The cut-off value of Aix was -13.50%. The ROC curve is depicted in Fig. 3

AIx = −86.98 + 0.84 (cSBP) + 0.66 (Age) − 1.11 (heart rate) $p < 0.05$ F = 57.47 $R^2 = 0.59$.

The cutoff value of AIx was -15.90%. The ROC curve is depicted in Fig. 4

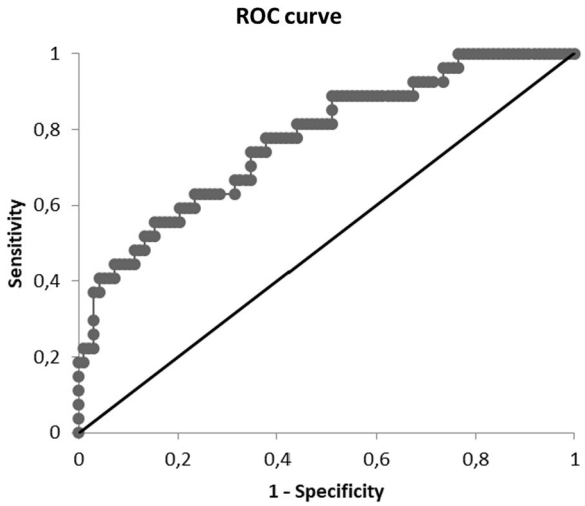

Fig. 2 The ROC curve of the model for Aix calculated from cSBPAo and adjusted for age The AUC for Aix in the model calculated from cSBPAo, and adjusted for age was 0.773 (95% CI 0.67 to 0.87, $p \leq 0.05$) with a sensitivity of 74.07% and specificity of 65.30%. The cut-off value of Aix was −20.90%. The ROC curve is depicted in Fig. 2

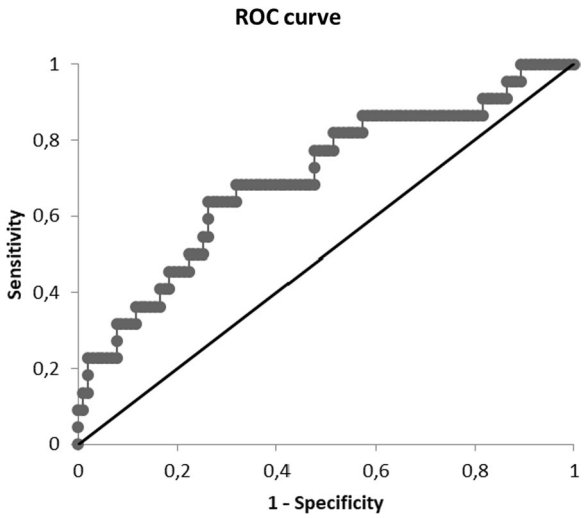

Fig. 4 The ROC curve of the model for Aix calculated from cSBPAo and adjusted for age and heart rate. The AUC for Aix in the model calculated from cSBPAo, and adjusted for age and heart rate was 0.699 (95% CI 0.57 to 0.82, $p \leq 0.05$) with a sensitivity of 68.18% and specificity of 67.96%. The cut-off value of Aix was −15.90%. The ROC curve is depicted in Fig. 4

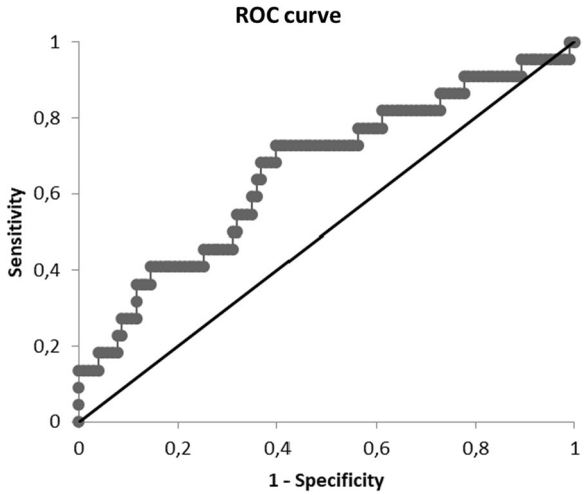

Fig. 5 The ROC curve of the model for Aix calculated from cSBPAo and adjusted for age and height and heart rate. The AUC for Aix in the model calculated from cSBPAo, and adjusted for age, height and heart rate was 0.658 (95% CI 0.52 to 0.79, $p \leq 0.05$) with a sensitivity of 72.72% and specificity of 60.19%. The cut-off value of Aix was −22.59%. The ROC curve is depicted in Fig. 5

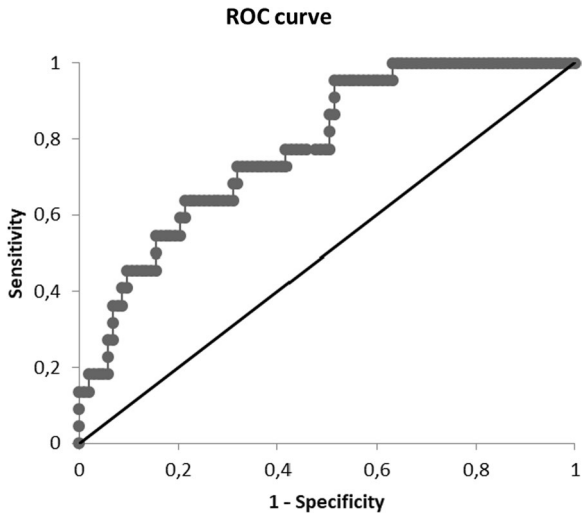

Fig. 6 The ROC curve of the model for Aix calculated from cSBPAo, and adjusted for PWV. The AUC for Aix in the model calculated from cSBPAo, and adjusted for PWV was 0.777 (95% CI 0.67 to 0.87, $p \leq 0.05$) with a sensitivity of 72.72% and specificity of 67.96%. The cut-off value of Aix was −18.60%. The ROC curve is depicted in Fig. 6

Significant model was obtained for AIx calculated from cSBP after adjustment for age, height and heart rate as follows (model 5):

AIx = 165.34 + 0.82 (cSBP) + 0.32 (Age) − 1.30 (height) − 1.27 (heart rate) $p < 0.05$ $F = 73.43$ $R^2 = 0.70$.

The ROC curve is depicted in Fig. 5

Significant model was obtained for AIx calculated from cSBP after adjustment for PWV as follows (model 6):

AIx = −157.33 + 0.79 (cSBP) + 3.59 (PWV) $p < 0.05$ F = 52.77 $R^2 = 0.46$.

The ROC curve is depicted in Fig. 6

4 Discussion

The aim of this study was to evaluate the contribution of central blood pressure calculated via an Arteriograph (TensioMed, Hungary) for the determination of measures of arterial stiffness and vascular function, i.e. pulse wave velocity (PWV) and the brachial augmentation index (AIx). As we expected, we found significant relationships between parameters of vascular function in the whole group, as well as in the sex-stratified subgroups.

The best capability to identify patients with arterial stiffness was in the case of the model which determined PWV from cSBP (AUC 0.824) adjusted for age. As shown in this model, the relationship between PWV and cSBP remained significant after adjustment for age. Age is a well-recognized confounding factor of arterial stiffness, however, cSBP has been shown to be an independent contributor. We also determined the AUC for the relationship without the inclusion of age, and it had a slightly lower value (AUC 0.819), which demonstrates that considering age as a contributor does not decrease the ability of cSBP to diagnose patients with arterial stiffness. The relationships between PWV and cSBP could not be adjusted for height or heart rate because of the nonsignificant relationships of these parameters with PWV.

In contrast, in the case of the equations used to evaluate changes in AIx from cSBP and the addition of age, the value of AUC decreased from 0.819 to 0.773, however, the relationship maintained significance. The same applied to the inclusion of height together with age (AUC 0.776). When heart rate was included in the equation, the relationship remained significant, however, the AUC decreased under 0.70, which was 0.699 without the additional inclusion of height and age, and 0.658 with the additional inclusion of height and age. These findings show that cSBP also makes an independent contribution to the magnitude of AIx after adjustment for height and heart rate. The authors who evaluated the relationships between heart rate and PWV reported disparate findings, demonstrating positive correlations, no correlations or even negative correlations. On the other hand, height influences AIx by affecting arterial diameter and wall properties, and most of the authors have reported, in line with our results, inverse relationships between these parameters [16].

Moreover, it is well documented that AIx, which is defined by the proportion of the difference between the peak of the reflected pulse wave and the forward systolic pulse wave and the percentage of PP, is also affected by PVW and systemic vascular resistance [6]. Therefore, the age-related increase in AIx is partially a manifestation of increased arterial stiffness, which causes an earlier return of the reflected wave. For that reason, despite high collinearity between PWV and cSBP ($r=0.48$, $p < 0.001$,), we also prepared a model including both of these parameters, which had an AUC of 0.777.

Despite high collinearity between these indices, central hemodynamic indices and aortic stiffness do not necessarily change to the same extent or in the same direction since they represent different hemodynamic characteristics of the vasculature [17] The magnitude and direction of the association between cSBP and PWV could change with age, and differ by sex [18]. SardiNIA data from the examination of the concomitant trajectories of PWV and cSBP demonstrated a striking dissociation in the trajectories of these parameters with advancing age by the fifth decade which was characterized by accelerated rates of increase in PWV at higher cSBP values and was more pronounced in men [19]. Moreover, because cSBP is a common scaling variable in the calculation of other variables, these relationships, in addition to statistical interference, also include a large extent of expected confounding [6]. This fact makes it difficult to perform a multivariate regression analysis because the application of more than one explanatory variable in the models is redundant in these cases. Besides that, the dependency of AS on blood pressure is complex because all of these variables, i.e. PWV, cSBP and AIx are affected by age [20]. Furthermore, arterial stiffening is associated with other risk factors, such as low birth weight, chronic inflammation and inherited conditions related to CVS risk, among others, that are independent of BP elevation, DM and aging [21].

Notably, relationships between DM and vascular aging have been implicated at more levels: the overexpression of angiotensin type I receptors caused by hyperinsulinemia and chronic hyperglycemia, which promotes fibrosis of the vascular wall; reduced capillary surface area caused by insulin resistance, which increases peripheral vascular resistance, and in this way AIx; and a higher heart rate for different reasons which, in contrast, decreases Aix [22]. Accordingly, the timing of cSBP elevation concerning increased arterial stiffness varies from case to case [23]. In addition, this nonlinear relationship does not capture all cardiovascular risks associated with arterial stiffness [24]. Takahashi et al. [25] recently reported in a prospective study that a positive relationship between cSBP and baPWV may be independent of peripheral BP. These findings may also indicate that factors other than peripheral vascular damage may contribute to the accelerated progression of arterial stiffness by increasing cSBP.

When we compared the values of SBP and cSBP, and evaluated the whole group, we found that SBP was significantly greater than cSBP. However, when we compared the age-stratified groups, in the group with patients older than 50 years this difference lost significance, which is in accordance with the decrease in PPA developing in parallel with aging. If we consider patients with lower SBP than cSBP as those with missing pulse pressure amplification (PPA), we conclude that only 26.4% of our patients were identified with this pattern, and 78.8% of them were females. These findings partially contrast with the results of Bulas et al., who also evaluated patients measured with Arteriograph [26]. The cross-sectional study of these authors revealed a relatively equal proportion of the two groups.

However, PPA has shown high within- and between-subject variability, and depends on many variables including age, sex, height and heart rate. Aging is associated with a disproportionate elevation of cSBP in relation to SBP and thus a decrease in PPA. Thus, central and brachial systolic pressures tend to equalize with the duration of hypertension and aging because of increased wave reflection rather than diminished transfer of the forward wave [27]. Because PPA differs strongly in different circulatory regions depending on branching patterns the question of whether PPA in one circulatory bed can represent PPA traits in others has not yet been clarified. Notably, only approximately 70% of the variability in PPA can be explained in multivariable regression models [28].

We explain that there was no significant difference in any of the evaluated parameters between the diabetes group and the control group because both groups consisted of patients with long-term antihypertensive treatment, most of whom were treated with ACE inhibitors and calcium channel blockers.

The main limitation of the study is that the Arteriograph, like all current oscillometric devices uses brachial blood pressure as a means to calibrate the central pressure waveform, which implies that the estimation of cSBP is critically dependent on the concomitant measurement of peripheral BP. Second, the cross-sectional design of the study makes it impossible to draw conclusions regarding the cause-effect relationships between AS indices and BP parameters. Third, we did not investigate the group according to the duration of diabetes, and we do not know which of the two conditions was the first in the patients´ history in patients

with concomittant hypertension and diabetes. We also did not consider other medications used by patients.

5 Conclusion

Our results demonstrate strong correlations between cSBP assessed by an Arteriograph and variables related to vascular aging in a group of patients with TDM2 and prove that cSBP is an indirect measure of vascular aging. Our models demonstrated that the cSBP determined by an Arteriograph is capable of identifying patients with arterial stiffening independently of potential confounders.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1007/s44200-025-00078-8.

Below is the link to the electronic supplementary material.Supplementary file1 (DOC 119 KB)

Author contributions

Emil Fraenkel conceived the idea, determined the study design, collected the data, and drafted and revised the manuscript.Ioana Mozos drafted and revised the manuscript.

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Data Availability

No datasets were generated or analysed during the current study. Access to data is possible only for persons authorized by the University Hospital Ethical Committee, Nr. of approval is 529-165/EK/21.

Declarations

Conflict of Interest

The authors have no conflicts of interest.

Ethics Approval and Consent to Participate

Patients signed the informed consent form after an explanation of the aim of this type of noninvasive BP measurement and of the study.

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References

1. Jia G, Sowers JR. Hypertension in diabetes: An update of basic mechanisms and clinical disease. Hypertension. 2021;5:1197–205.
2. McEniery CM, Cockcroft JR, Roman MJ, Franklin SS, Wilkinson IB. Central blood pressure: current evidence and clinical importance. Eur Heart J. 2014;35:1719–25.
3. CM McEniery McDonnell B Yasmin M Munnery SM Wallace CV Rowe JR Cockcroft IB Wilkinson Anglo-Cardiff Collaborative Trial Investigators. Central pressure: variability and impact of cardiovascular risk factors: the Anglo-Cardiff Collaborative Trial II. Hypertension. 2008;51:1476–82.
4. Kaess BM, Rong J, Larson MG, Hamburg NM, Vita JA, Levy D, Benjamin EJ, Vasan RS, Mitchell GF. Aortic stiffness, blood pressure progression, and incident hypertension. JAMA. 2012;308:875–81.
5. Dernellis J, Panaretou M. Aortic stiffness is an independent predictor of progression to hypertension in nonhypertensive subjects. Hypertension. 2005;45:426–31.
6. Izzo JL Jr. Brachial vs. central systolic pressure and pulse wave transmission indicators: a critical analysis. Am J Hypertens. 2014;27:1433–42.
7. Kass DA, Saeki A, Tunin RS, Recchia FA., 1996 Kass DA, Saeki A, Tunin RS, Recchia FA. Adverse influence of systemic vascular stiffening on cardiac dysfunction and adaptation to acute coronary occlusion. Circulation. 1996;93:1533–41.
8. Boutouyrie P. Estimating is not measuring: The lessons about estimated pulse wave velocity. J Am Heart Assoc. 2022;11:e025830.
9. Horváth IG, Németh A, Lenkey Z, Alessandri N, Tufano F, Kis P, Gaszner B, Cziráki A. Invasive validation of a new oscillometric device (Arteriograph) for measuring augmentation index, central blood pressure and aortic pulse wave velocity. J Hypertens. 2010;28:2068–75.
10. László A, Reusz G, Nemcsik J. Ambulatory arterial stiffness in chronic kidney disease: a methodological review. Hypertens Res. 2016;39:192–8.
11. Nemcsik J, Egresits J, El Hadj OT, Fekete BC, Fodor E, Szabó T, Járai Z, Jekkel C, Kiss I, Tislér A. Validation of arteriograph - a new oscillometric device to measure arterial stiffness in patients on maintenance hemodialysis. Kidney Blood Press Res. 2009;32:223–9.
12. Rossen NB, Laugesen E, Peters CD, Ebbehøj E, Knudsen ST, Poulsen PL, Bøtker HE, Hansen KW. Invasive validation of arteriograph estimates of central blood pressure in patients with type 2 diabetes. Am J Hypertens. 2014;27:674–9.
13. Mancusi C, Losi MA, Izzo R, Canciello G, Carlino MV, Albano G, De Luca N, Trimarco B, de Simone G. Higher pulse pressure and risk for cardiovascular events in patients with essential hypertension: The Campania Salute Network. Eur J Prev Cardiol. 2018;25:235–43.
14. Yu D, Simmons D. Association between pulse pressure and risk of hospital admissions for cardiovascular events among people with Type 2 diabetes: a population-based case-control study. Diabet Med. 2015;32:1201–6.
15. Winston GJ, Palmas W, Lima J, Polak JF, Bertoni AG, Burke G, Eng J, Gottesman R, Shea S. Pulse pressure and subclinical cardiovascular disease in the multi-ethnic study of atherosclerosis. Am J Hypertens. 2013;26:636–42.
16. Hughes AD, Park C, Davies J, Francis D, McG Thom SA, Mayet J, Parker KH. Limitations of augmentation index in the assessment of wave reflection in normotensive healthy individuals. PLoS ONE. 2013;8(3):e59371.
17. AlGhatrif M, Lakatta EG. The conundrum of arterial stiffness, elevated blood pressure, and aging. Curr Hypertens Rep. 2015;17:1–15.
18. Najjar SS, Scuteri A, Shetty V, Wright JG, Muller DC, Fleg JL, Spurgeon HP, Ferrucci L, Lakatta EG. Pulse wave velocity is an independent predictor of the longitudinal increase in systolic blood pressure and of incident hypertension in the Baltimore Longitudinal Study of Aging. J Am Coll Cardiol. 2008;51:1377–83.
19. Scuteri A, Morrell CH, Orrù M, Strait JB, Tarasov KV, Ferreli LA, Loi F, Pilia MG, Delitala A, Spurgeon H, Najjar SS, AlGhatrif M, Lakatta EG. Longitudinal perspective on the conundrum of central arterial stiffness, blood pressure, and aging. Hypertension. 2014;64:1219–27.
20. Cheng HM, Park S, Huang Q, Hoshide S, Wang JG, Kario K, Park CG, Chen CH; Characteristics on the Management of Hypertension in Asia - Morning Hypertension Discussion Group (COME Asia MHDG). Vascular aging and hypertension: Implications for the clinical application of central blood pressure. Int J Cardiol. 2017;230:209–13.
21. Battistoni A, Michielon A, Marino G, Savoia C. Vascular aging and central aortic blood pressure: from pathophysiology to treatment. High Blood Press Cardiovasc Prev. 2020;4:299–308.
22. Townsend RR et al., 2015 RR Townsend IB Wilkinson EL Schiffrin AP Avolio JA Chirinos JR Cockcroft KS Heffernan EG Lakatta CM McEniery GF Mitchell SS Najjar WW Nichols EM Urbina T Weber, American Heart

Association Council on Hypertension. Recommendations for improving and standardizing vascular research on arterial stiffness: A scientific statement from the american heart association. Hypertension. 2015;66:698–722.
23. Mitchell GF. Does measurement of central blood pressure have treatment consequences in the clinical praxis? Curr Hypertens Rep. 2015;17:1–8.
24. Terentes-Printzios D, Gardikioti V, Vlachopoulos C. Central over peripheral blood pressure: An emerging issue in hypertension research. Heart Lung Circ. 2021;30:1667–74.
25. Takahashi T, Nakano H, Shiina K, Fujii M, Matsumoto C, Satomi K, Yamashina A, Tomiyama H, Chikamori T. Central systolic blood pressure as a risk factor for accelerated progression of arterial stiffness. J Atheroscler Thromb. 2024;31:180–7.
26. Bulas J, Potocarova M, Kupcova V, Gaspar L, Wimmer G, Murin J. Central systolic blood pressure increases with aortic stiffness. Bratisl Lek Listy. 2019;120:894–8.
27. Nichols WW, O'Rourke MF, Vlachopoulos C. McDonald's Blood Flow in Arteries: Theoretic, Experimental, and Clinical Principles. (6th ed.), CRC Press, London, UK (2011).
28. Camacho F, Avolio A, Lovell NH. Estimation of pressure pulse amplification between aorta and brachial artery using stepwise multiple regression models. Physiol Meas. 2004;25:879–89.

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