El Toony *et al.*
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The effect of non-invasively obtained central blood pressure on cardiovascular outcome in diabetic patients in Assiut University Hospitals

Lobna F. El Toony, Andrew N. Ramzy* and Mohamed A. A. Abozaid

Abstract

Background: The major cause of morbidity and mortality in diabetes is cardiovascular disease, which is exacerbated by the presence of hypertension. Therefore, proper control of BP in diabetic hypertensive patients is essential. Few studies have specifically investigated the prognostic significance of central BP in Egyptian populations with diabetes and hypertension and its relation with cardiovascular outcome. This study aims to evaluate relation between central BP and diabetic composite cardiovascular complications.

Results: Diabetic patients with CVD were significantly older (p value < 0.01), obese (p value < 0.01) with long duration of diabetes (p value < 0.001) and had significantly higher peripheral and central systolic and diastolic BP and higher AIx@75(p values < 0.01) than those without CVD. Regarding the metabolic parameters, they had significantly higher fasting blood glucose, HbA1c, and higher blood cholesterol levels (p values < 0.001), higher LDL (p value < 0.01), triglycerides levels (p value = 0.014), and microalbuminuria (p value = 0.028). Logistic regression analysis found increased BMI, central systolic BP, and AIx@75 were independent predictors of composite CVD (p values < 0.05).

Conclusions: There is a pattern of favorability towards central rather than peripheral BP indices to predict the occurrence of CVD in diabetic patients.

Keywords: Type 2 diabetes, Central blood pressure, Composite cardiovascular diseases, Assiut University Hospitals

Background

Type 2 diabetes accounts for 90–95% of all diabetes. This form encompasses individuals who have relative (rather than absolute) insulin deficiency and have peripheral insulin resistance [1]. According to IDF Diabetes Atlas 2019, The International Diabetes Federation (IDF) has identified Egypt as the ninth leading country in the world for the number of patients with T2D [2]. T2DM negatively affects the prognosis of patients by markedly increasing both hospitalization and mortality rate [3]. Beyond the inherent increase in mortality in diabetic subjects, when diabetes mellitus is combined with manifestations of CVD, such as myocardial infarction or stroke, the mortality rate is nearly doubled, leading to an estimated reduction in life expectancy of ≈ 12 years [4].

In Egypt, the prevalence of HTN has been increasing. Recently, it was estimated to be 29.5% according to the 2017 WHO STEPwise survey in Egypt [5]. Hypertension and type 2 diabetes are well known to be common comorbidities. Hypertension is twice as frequent in patients with diabetes in comparison with those who do not have diabetes. Moreover, patients with hypertension often experience insulin resistance and are at higher risk of diabetes developing than are normotensive individuals.

*Correspondence: Andrew_tamer@med.aun.edu.eg; Andrew_nader1993@yahoo.com
Assiut University Hospitals, Internal Medicine Department, Faculty of Medicine, Assiut University, Assiut, Egypt

The major cause of morbidity and mortality in diabetes is cardiovascular disease [6], which is exacerbated by hypertension. Accordingly, diabetes and hypertension are closely related because of similar risk factors, such as dysfunction of endothelial cells, vascular inflammation, arterial remodeling, atherosclerosis, dyslipidemia, and obesity. There is also substantial overlap in the cardiovascular complications of diabetes and hypertension related primarily to microvascular and macrovascular disease [7].

Therefore, proper control of blood pressure (BP) in diabetic patients with hypertension is essential. Yet, it is not the BP within the arm (brachial) artery that causes strokes and heart attacks, rather, it is the BP within the central arteries which directly interacting with the brain and the heart. Thus, while cuff BP is measured at a peripheral (brachial) artery, the goal is to estimate the pressure load experienced by the central organs (supplied by the aorta) as the best marker of risk from high BP [8].

A number of methods are now available for assessing central pressure. The most direct method involves cardiac catheterization and recording of the blood pressure in the ascending aorta using a pressure-sensing catheter. However, this is highly invasive, technically demanding, and clearly unsuitable for use in routine screening of large populations. More recently, a number of non-invasive methods have been developed, where pressure waveforms are recorded from sites distal to the aorta, such as the carotid, radial, or brachial arteries, and calibrated to blood pressure recorded by cuff sphygmomanometry. Each of these approaches has their own strengths and limitations [9].

Aim of the work

✓ Detection of the relation between central blood pressure and diabetic cardiovascular complications mainly coronary heart disease.

Methods

This study conducted in Internal medicine outpatient clinics, Assuit University Hospitals during the period from January 2018 to January 2020.

One hundred patients were included in the study and separated into two groups :

A- 49 patients were known to be diabetic and free from CVD.

B- 51 patients were known to be diabetic and with CVD.

Demographic data such as age, gender, cigarette smoking status, duration of diabetes and hypertension, previous medical history, and current medications usage (anti-hypertensive and anti-diabetic), history of cardiovascular disease were collected using questionnaire.

After that systemic examination was done for all patients including examination of the cardiovascular, chest, abdomen, and nervous systems.

Peripheral BP was measured based on the JNC8 guideline recommendation. Patients sit quietly for 10 min with their back supporting. Non-dominant arm was placed on the heart level and 3 BP readings were obtained with 1-min interval between each reading, and the last 2 readings were used to calculate the mean brachial BP level [10].

Central BP was measured using device called Mobil-o-graph which is a well validated non-invasive device made in Germany [11, 12]. This device uses a brachial based cuff and based on a transfer function, central pressure curves are obtained and processed. Central systolic and diastolic BP (cSBP/cDBP) and augmentation index adjusted for 75 beats per minute of heart rate (AIx@75), which is considered a reflection of arterial stiffness [13], were derived for analysis.

After central BP measurement, fasting venous blood was drawn for lipid profiles, fasting plasma glucose, glycated hemoglobin, CRP, and serum creatinine level. Urine analysis was done to detect albuminuria.

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Inclusion criteria

- Patients aged 40–60 years old
- Patients in groups A and B are documented to have type 2 DM
- Patients in group B are documented to have CVD with either ECG or echocardiography.
- Hypertensive patients enrolled must be compliant on their treatment for at least 1 month

Exclusion criteria

- Pregnancy or breastfeeding.
- Concomitant therapy of digoxin, lithium, non-depolarizing skeletal muscle relaxants, sex hormone.
- Documented connective tissue diseases such as systemic lupus erythematosus.

Consent for publication

Informed written consent was obtained from all the participants.

Statistical analysis

Statistical analysis was done by IBM SPSS statistics 20. Results were presented as means ± standard deviation (SD) for quantitative data and as numbers with percentages for qualitative data. Statistical associations between quantitative data were determined using one-way ANOVA test with Tukey HSD test and Student's *t* test. The chi-square test was used for qualitative data. To evaluate the relation between central blood pressure and diabetic hypertensive composite CVD, variables being significantly correlated with composite CVD in univariate analysis will be entered in a multivariate model using stepwise logistic regression. A *P* value < 0.05 was considered statistically significant, < 0.01 highly significant, and < 0.001 very highly significant.

Results

Among the hundred diabetic patients, there were 51 patients with composite CVD. They had been compared with the other patients without composite CVD to evaluate the association between central blood pressure and diabetic with composite CVD.

It was found that increasing age, BMI together with increasing duration of diabetes were statistically highly significant (*p* values 0.009, 0.002, and < 0.001 respectively) in those with composite cardiovascular diseases (CVD). Furthermore, both peripheral and central systolic and peripheral and central diastolic blood pressure in addition to Aix@75 were significantly higher in diabetic with CVD than those without CVD (*p* values < 0.01). Regarding the metabolic parameters, it was found that those with CVD had significantly higher fasting blood glucose, Hb A1c, total cholesterol levels (*p* values < 0.001each), LDL (*p* value < 0.01), triglycerides levels (*p* value 0.014), and microalbuminuria (*p* value 0.028) (Table 1).

Aspirin and statins were also significantly higher in those with CVD due to their related medical conditions.

Logistic regression analysis was performed to evaluate the independent predictors of the occurrence of composite CVD in diabetic patients showing that increased BMI, central SBP, and Aix 75 were significantly associated with composite CVD (*p* values < 0.05) (Table 2).

Discussion

Up to our knowledge, few studies have specifically investigated the prognostic significance of central BP among Egyptian populations with diabetes and hypertension. This study found that although there was no significant difference between central DBP and peripheral DBP in all studied cases, peripheral SBP was significantly higher than central SBP in each of the studied groups (*p* values < 0.001). This phenomenon of systolic pressure amplification arises principally due to an increase in the stiffness of the arterial walls moving away from the heart. As the pressure wave travels from the highly elastic central arteries to the stiffer brachial artery, the upper portion of the wave becomes narrower, the systolic peak becomes more prominent, and systolic pressure increases. Patients with type 2 diabetes (T2D) have vascular irregularities that affect blood pressure (BP) amplification and the indices of central BP [14].

In the present study, comparing between patients with composite CVD in our study and those without composite CVD, there was statistically significant difference between both groups as regards peripheral SBP, mean peripheral BP, and central SBP (*p* values < 0.001 each) (higher in those with composite CVD group), and there were high significant differences between the two groups in peripheral DBP, central DBP, and Aix 75 (*p* value < 0.01 each) (higher in those with composite CVD group). This goes in run with another study which revealed statistically significant difference between both groups as regards peripheral SBP and DBP, central SBP and DBP in addition to Aix 75 with (*P* value < 0.05) [15].

As regards metabolic parameters of the studied diabetic groups, there was statistically significant difference between patients with CVD and those without CVD as regards fasting blood glucose, Hb A1c, total cholesterol levels (*p* values < 0.001each), LDL (*p* value < 0.01), triglycerides levels (*p* value 0.014) and microalbuminurisa (*p* value 0.028). This results were also evident in Yeung et al. study where HbA1c was related to CAD [16] and Silbernagel et al. where there was a continuous positive association between LDL and triglycerides and cardiovascular mortality [17].

Logistic regression analysis displaying independent predictors of the occurrence of composite CVD in diabetic patients which showed that increased BMI, central SBP, and Aix 75 were significantly associated with composite CVD (*p* values < 0.05).

By using the heart-rate-corrected augmentation index (Aix75) and aortic pulse wave velocity (PWV), arterial stiffness, an important mechanical property of the arterial system, can be evaluated. Elevated stiffness increases the development of cardiovascular complications in hypertensive patients and normal individuals [13]. Data were analyzed from 11 longitudinal studies involving 5648 subjects followed for an average of 45 months. After correcting for CV risk factors that included brachial BP or history of hypertension in five studies, an absolute increase of 10% in central augmentation index corresponded to 31.8 and 38.4% relative risk increase for CV and all-cause mortality, respectively [18].

Table 1 Characteristics of diabetic with composite CVD and without composite CVD groups

	With composite CVD $n=51$	Without composite CVD $n=49$	*P* values
Gender no. (%)			
Male	15(29.4%)	18(36.7%)	0.436
Female	36(70.6%)	31(63.3%)	
Age Mean ± SD	54.78 ± 5.03	52.12 ± 4.96	0.009
BMI Mean ± SD	33.14 ± 7.79	28.82 ± 5.37	0.002
Smoking no. (%)	10(19.6%)	9(18.4%)	0.874
HTN No. (%)	28(54.9%)	22(44.9%)	0.317
Diabetic duration Mean ± SD	11.15 ± 6.54	6.54 ± 3.4	0.000
Peripheral SBP	137.12 ± 16.68	121.24 ± 13.91	0.000
Peripheral DBP	82.18 ± 13.25	76.33 ± 11.35	0.02
Mean peripheral BP	100.78 ± 12.85	90.96 ± 10.59	0.000
Central SBP	126.78 ± 16.26	112.73 ± 11.63	0.000
Central DBP	83.41 ± 13.45	76.96 ± 11.35	0.011
Aix 75	26.67 ± 11.57	20.57 ± 12.04	0.011
FBS (mg/dl)	295.88 ± 84.73	172.37 ± 77.19	0.000
HbA1c (%)	9.86 ± 1.71	6.92 ± 1.34	0.000
Creatinine (umol/L)	94.9 ± 57.08	88.18 ± 41.61	0.504
LDL (mg/dl)	144.37 ± 62.81	113.73 ± 28.72	0.002
TG (mg/dl)	209.22 ± 77.99	165.08 ± 98.36	0.014
Cholesterol (mg/dl)	206.65 ± 59.31	164.47 ± 47.94	0.000
Microalbuminuria no. (%)	14(27.5%)	5(10.2%)	0.028
Anti-diabetic medication no. (%)			
Insulin	23(45.1%)	18(36.7%)	0.395
Sulfonylurea	20(39.2%)	21(42.9%)	0.711
Metformin	11(21.6%)	12(24.5%)	0.729
DPP4I	5(9.8%)	2(4.1%)	0.437
SGLT2I	0(0%)	3(6.1%)	0.114
HTN medication no. (%)			
B-blocker	15(29.4%)	5(10.2%)	0.016
Diuretics	6(11.8%)	5(10.2%)	0.803
ACEI	6(11.8%)	11(22.4%)	0.155
ARBs	6(11.8%)	3(6.1%)	0.488
CCB	4(7.8%)	4(8.2%)	1
Other medication no. (%)			
Aspirin	26(51%)	1(2%)	0.000
Statin	9(17.6%)	1(2%)	0.016

Another study observed a strong association between cardiovascular outcomes and central, rather than brachial pressure [19]. In contrast, in the Framingham Heart Study Mitchell et al. show no additional value of carotid blood pressure [20].

The brain, the heart affected by central blood pressure more directly than peripheral, brachial blood

Table 2 Logistic regression analysis displaying independent predictors of the occurrence of composite CVD in diabetic patients

	B	S.E.	Wald	Sig.	Exp(B)	95% C.I. for EXP(B)	
						Lower	Upper
Age	0.102	0.094	1.183	0.277	1.107	0.921	1.331
BMI	0.179	0.089	4.035	0.045	1.197	1.004	1.426
Diabetic duration	0.071	0.105	0.456	0.500	1.073	0.874	1.317
Central systolic Bp	0.135	0.059	5.122	0.024	1.144	1.018	1.286
Augmentation index75	0.116	0.054	4.656	0.031	1.123	1.011	1.247
Fasting blood sugar FBS	0.010	0.006	2.509	0.113	1.010	0.998	1.022
LDL	0.012	0.013	0.877	0.349	1.012	0.987	1.038
HDL	0.076	0.052	2.168	0.141	1.079	0.975	1.195
TG	− 0.001-	0.008	0.033	0.856	0.999	0.984	1.014
Aspirin(1)	5.460	2.342	5.437	0.020	235.112	2.388	23145.827
Statin(1)	− 1.318-	2.333	0.319	0.572	0.268	0.003	25.888
Microalbuminuria(1)	− .440-	1.468	0.090	0.764	0.644	0.036	11.435
B blocker(1)	1.122	1.056	1.128	0.288	3.070	0.387	24.336
Constant	− 38.741-	11.656	11.047	0.001	0.000		

pressure. Thus, central blood pressure is more accurate and direct reflection of the pathophysiological outcomes of elevated blood pressure on the brain than peripheral blood pressure [21].

Recommendations

- Raising the awareness among health care providers of the importance of measuring central arterial blood pressure using the newer non-invasive devices and considering it as a guide of therapy to prevent composite cardiovascular complications of type 2 DM.
- More studies are needed with a large sample size aiming to assess the effect of anti-hypertensive and anti-diabetic drug classes on central arterial blood pressure.

Conclusions

This work clearly identified a pattern of favorability towards central BP indices being better than brachial BP in terms of their ability to predict the occurrence of composite cardiovascular diseases in diabetic patients.

Abbreviations

AIx@75: Augmentation index adjusted for 75 beats per minute of heart rate; BP: Blood pressure; cSBP/cDBP: Central systolic and diastolic BP; CVD: Cardiovascular diseases; DBP: Diastolic blood pressure; SBP: Systolic blood pressure; CBP: Central blood pressure; PBP: Peripheral blood pressure; DM: Diabetes mellitus.

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Authors' contributions

LFT, ANR, and MAA conceived and designed the research. LFT, ANR, and MAA recruited patients, carried out the clinical investigations, and collected patients' clinical data. ANR performed the experiment. LFT, ANR, and MAA prepared the original draft of the manuscript, participated in data analysis and writing, and read and agreed to the published version of the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available on reasonable request.

Declarations

Ethics approval and consent to participate

There was no risk during the application of the research. Privacy and confidentiality was maintained during all stages of assessment. Every patient subjected to this study was informed about the results of the research. The work is approved by Ethical Committee of Faculty of Medicine of Assiut University on 11 April 2018 (approval number 17100490). Informed written consent was obtained from all the participants in this study. Refusal would not affect medical services which are usually offered.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interest.

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