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Original Research Article.

Relationship between Waist-To-Calf Circumference Ratio and Carotid Atherosclerosis in Patients of Type 2 Diabetes Mellitus

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ABSTRACT

Background: Obesity and Diabetes mellitus are well known risk factors for cardiovascular diseases (CVD). Though body fat appears to play important role in insulin resistance, the way body fat is distributed is also significant. Waist circumference (WC), calf circumference (CC), and wait to calf ratio (WCR) can be used as predictors of risk of CVD. This study aims to evaluate the utility of WCR as a simple non-invasive, cheaper, easy to use and non-instrumental modality which can be used as screening tool and as an indicator of coronary atherosclerosis and resulting cardiovascular risk in patients (OPD as well as Inpatients) with Diabetes mellitus by correlating WCR with Carotid Intima Media Thickness (CIMT) which itself is an established indicator for risk of CVD.

Methods: 100 adult patients with Type-2 diabetes were diagnosed on the basis of latest ADA criteria. Detailed history, clinical examination, anthropometric measurements, biochemical indices were assessed for all the selected patients. Carotid atherosclerosis was measured by scanning the bilateral common carotid arteries using a high resolution USG system with 10 MHz linear transducer. The carotid intima-media thickness (CIMT) was measured at three points on far wall of mid and distal CCA and 1 cm proximal to dilation of carotid bulb. Mean value of six measurements from right and left CCA were used.

Results: There is an expected negative correlation between calf circumference and prevalence of abnormal CIMT ($p<0.011$). WCR correlated with CIMT more strongly than the independent measures with ($p<0.001$) and is a good predictor of CIMT abnormality as AUC (area under the curve) is 97.7%

Conclusion: Waist to calf circumference ratio is a simple non-invasive, cheaper, easy to use and non-instrumental modality which can be used as screening tool in assessment of atherosclerotic burden of the vasculature at an early stage in type 2 diabetic OPD as well as in patients. WCR will serve as surrogate marker of coronary artery disease.

Keywords: Diabetes Mellitus; Waist Circumference; Calf Circumference; Waist to Calf Ratio; Carotid Intima Media Thickness; Cardiovascular Disease; Atherosclerosis.

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INTRODUCTION

Diabetes mellitus is a disorder of carbohydrate metabolism characterized by impaired ability of the body to produce or respond to insulin and thereby maintain proper levels of glucose in the blood.[1,2] Diabetes is a major cause of morbidity and mortality mostly related to the diseases that develop as a result of chronic diabetes mellitus.[3] These include diseases of large blood vessels (macrovascular disease, including coronary heart disease and peripheral arterial disease) and small blood vessels (microvascular disease, including retinal and renal vascular disease), as well as diseases of the nerves.[4]

One of the main macrovascular changes associated with diabetes include aggravated atherosclerosis[5] and there are several vascular beds which carry this atherosclerotic burden i.e. abdominal aorta, coronary arteries, carotid arteries and popliteal arteries.[6] Estimation of arterial atherosclerotic burden is being investigated as a surrogate marker for evaluation of risk of Coronary Artery Disease (CAD) and also as a screening tool.[7] Carotid atherosclerosis may be a surrogate for coronary risk, as carotid and coronary diseases occur simultaneously.[8] An increased carotid intima media thickness IMT was found to be an independent risk factor for CAD, and it correlated with the coronary vessel IMT.[9] Carotid intima-media thickness (IMT) has been associated with the presence of Cardiovascular Disease (CVD) in subjects with Diabetes mellitus and is considered a measure of atherosclerotic burden in patients with clinically manifest CVD.[10]

While central adiposity is crucial to the risk of CVD, Peripheral adiposity also has a role to play in overall metabolic profile of the

patient and it is essential to look for its relation to the risk of CVD and overall atherosclerotic burden in the major arteries. Although the atherogenic role of central fat mass (CFM) is well established[11], there is a limited data to address the specific role of peripheral fat mass (PFM). Calf Circumference is a simple anthropometric measure that is highly correlated with muscle mass. The layer of subcutaneous fat is generally thin at the calf and, in contrast to the arm, hip or thigh, no correction for this fat layer is made.[12] Therefore, Calf circumference is a surrogate marker of lean mass and peripheral subcutaneous fat, the relative importance of each component depending on the nutritional status, and the global body mass.[13,14] Among anthropometric measures, the calf circumference best reflects lean body mass, and weight-adjusted calf circumference negatively correlates with metabolic abnormalities and insulin resistance indices.[15] Also, the magnitude of protective effect of calf circumference against all-cause mortality in both men and women is fairly robust as is evidenced by its significant prediction of mortality when compared to WC, BMI and all other covariates.[16]

Carotid Ultrasound provides quantitative measurements of carotid intima-media thickness (CIMT) that can be used to assess cardiovascular disease (CVD) risk in individuals and monitor ongoing disease progression and regression in clinical trials.[17] It is non-invasive, rapid, reproducible, and carries no risk.[18] Numerous epidemiological studies have established that CIMT is a marker of subclinical atherosclerosis and is associated with established CVD risk factors and with both prevalent and incident CVD.[19] The use of CIMT in outcome trials as a surrogate or predictor of CVD outcomes is widespread.[20,21] Carotid ultrasound is being employed to test the efficacy of CVD treatment in order to identify potential useful drugs earlier and to possibly speed regulatory approval.[22]

MATERIALS AND METHODS

Source of Data: The study was be conducted in the Department of Medicine, Sri Guru Ram Dass institute of Medical Sciences and Research, Vallah, Sri Amritsar, in close collaboration with Department of Radio-diagnosis and Imaging and Department of Biochemistry of the institution

Study Design: This was a cross-sectional observational study performed in Type 2 Diabetes mellitus patients of both sexes. The study involved 100 subjects.

Exclusion Criteria

1. Patients with past history of cerebrovascular accident,
2. PVD
3. Muscular dystrophy
4. Limb deformities
5. Lower limb surgery; were excluded.

Inclusion Criteria

1. Adult Type-2 diabetic patients, diagnosed by latest ADA Criteria.[23] According to American Diabetes Association Criteria (2016)[23] patients were considered having Diabetes Mellitus if:
   a) Fasting plasma glucose (FPG**)** >126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h. or
   b) 2-h plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT (75 gm anhydrous glucose dissolved in water). Or
   c) HbA1C ≥6.5% (48 mmol/mol). Or
   d) In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).
2. Detailed history, clinical examination, anthropometric measurements, biochemical indices were assessed for all the selected patients

Anthropometric Measurements

Weight and height were measured for all the subjects. Waist circumference was measured at midpoint between lower ribs and iliac crests at the end of normal expiration. Calf circumference was measured at the point of highest circumference of calf with respondent standing straight, body weight equally distributed on both feet. One reading was taken from each leg and average of the two readings was taken. Waist-to-calf ratio (WCR) was calculated as the ratio of the waist circumference (WC) and calf circumference (CC).

Carotid Ultrasound

Carotid atherosclerosis was measured by scanning the bilateral common carotid arteries using a high resolution USG system with 10 MHz linear transducer. Scanning was performed at mid and distal common carotid artery (CCA) by lateral longitudinal projection. The carotid intima-media thickness (CIMT) was measured at three points on far wall of mid and distal CCA and 1 cm proximal to dilation of carotid bulb. Mean value of six measurements from right and left CCA were used.

CIMT is defined as the distance between the media-adventitia interface and the lumen-intima interface.

Carotid plaqueis defined as a distinct area of hyper-echogenicity and/or protrusion into the lumen of the vessel with at least 50% greater thickness than the surrounding area.

Carotid atherosclerosis defined as having a focal plaque or diffuse thickening of the carotid wall (CIMT ≥1.1 mm).

RESULTS

The mean age of study sample was 60.08±11.96 years in females and 58.43±10.64 years in males. Average duration of diabetes was 11.4±6.32 years in male patients and 13.69±7.63 years in female patients with 9.48±1.90 and 9.21±1.89 as mean HbA1c in males and females respectively. Fasting blood sugar as measured over the first encounter and/or over the course of stay at the hospital averaged at 240.67±79.64 mg/dl for females and 244.55±86.61mg/dl for males. Study group had disease duration and deranged control of blood sugar sufficient to predict a considerable atherogenesis. Waist circumference as a measure of central adiposity was recorded to be 100.35±11.38 cm and 97.88±12.10 cm of females and males respectively. Waist circumferences were fairly above the normal guidelines of "The Diabetes Canada 2018 Clinical Practice" for Asian population, which is in itself suggestive of a high risk of association with Type 2 diabetes and heart disease. Mean calf circumference of the group came out to be 30.85±3.77cm and 30±3.15cm for females and males respectively which are below the accepted cut off as a measure of lean muscle mass in elderly. This decreased calf circumference amongst the study subjects also supported the inverse relationship between the risk of diabetes, atherosclerotic diseases and peripheral adiposity of which calf circumference is an indicator. As the basic metabolic indicators and anthropometric measurements were in accordance with what has been suggestive of a chronic metabolic disease like diabetes mellitus.

These findings, which were strongly pointing towards underlying atherosclerosis and risk of heart disease, encouraged us to investigate further correlations. CIMT measurements in the study group were assessed as being normal and abnormal and correlated with WC, CC individually and with WCR. Data was analyzed by grouping patients into 5 categories of waist circumference i.e. <80, 81-100, 101-120, 121-140 and >40 cm. The mean waist circumference of patients with abnormal CIMT was 97.31±12.08. Similar analysis was performed with 5 groups of Calf circumferences i.e. 20-25, 26-30, 31-35, 36-40, >40 cm and the mean Calf Circumference of patients with abnormal CIMT was 31.05± 3.75. With both the WC and CC available, the WCR was also grouped into 5 ranges to correlate with CIMT i.e. <03, 03- 3.5, 03.6- 40, 04- 4.5, >4.5 where the mean WCR amongst those with abnormal CIMT was found to be 3.10±21. These values suggest a positive correlation between increasing waist circumference and prevalence of abnormal CIMT (p<0.007). There is an expected negative correlation between calf circumference and prevalence of abnormal CIMT (p<0.011). WCR correlated with CIMT more strongly than the independent measures with (p<0.001) and is a good predictor of CIMT abnormality as AUC (area under the curve) is 97.7%

Table 1: Mean of Age and Diabetes Duration in Males and Females

	Female		Male		t	p-value	95% Confidence Interval of the Difference	
	Mean	SD	Mean	SD			Lower	Upper
Age	60.08	11.96	58.43	10.64	0.730	0.467	-2.839	6.139
Diabetes duration (years)	13.69	7.63	11.14	6.32	1.828	0.071	-0.219	5.333

Mean age of male patients 58±10.64; Mean age of female patients 60±11.96;
Mean diabetes duration in male patients 11.14±6.32; Mean diabetes duration in female patients 13.69±7.63

Table 2: Mean of Fasting Blood Glucose and Glycosylated HbA1c Both Males and Females

	Female		Male		t	p-value	95% Confidence Interval of the Difference	
	Mean	SD	Mean	SD			Lower	Upper
FBS	240.67	79.64	244.55	86.61	-0.233	0.817	-36.931	29.180
HbA1c	9.21	1.89	9.48	1.90	-0.709	0.480	-1.020	0.483

Mean of FBS in males and females 244.55±86.6 and 240.6±79.6 respectively;
Mean of HbA1C in males and females 9.48±1.90 and 9.21±1.89 respectively

Table 3: Mean of WC, CC and WCR in Both Males and Females

	Female		Male		t	p-value	95% Confidence Interval of the Difference	
	Mean	SD	Mean	SD			Lower	Upper
Waist Circumference (cm)	100.35	11.38	97.98	12.10	1.008	0.316	-2.294	7.035
Calf Circumference (cm)	30.85	3.77	30.00	3.15	1.228	0.222	-0.525	2.229
Waist to Calf Circumference	3.26	0.34	3.24	0.35	0.311	0.756	-0.117	0.160

Mean of WC in males and females 97.97±12.1 and 100.35±11.3; Mean of CC in males and females 30.00±3.11 and 30.85±3.77; Mean of WCR in males and females 3.24±0.35 and 3.26±0.34

Table 4: Association of Gender and CIMT

Sex	CIMT				Total	
	Abnormal		Normal			
	No.	%	No.	%	No.	%
Female	16	32.7	33	67.3	49	49
Male	9	17.6	42	82.4	51	51
Total	25	25.0	75	75.0	100	100

X^2: 3.001; p=0.083

Table 5: Association of Diabetes Duration and CIMT

Duration of diabetes	CIMT				Total	
	Abnormal		Normal			
	No.	%	No.	%	No.	%
1-5	1	5.3	18	94.7	19	19
6-10	3	8.8	31	91.2	34	34
11-15	5	29.4	12	70.6	17	17
16-20	8	44.4	10	55.6	18	18
>20	8	66.7	4	33.3	12	12
Total	25	25.0	75	75.0	100	100
Mean ± SD	10.80±6.27		17.16±7.32		12.39±7.07	

P=0.001

Table 6: Association of ECG and CIMT

ECG	CIMT				Total	
	Abnormal		Normal			
	No.	%	No.	%	No.	%
Normal	5	8.2	56	91.8	61	61
Abnormal	20	51.3	19	48.7	39	39
Total	25	25.0	75	75.0	100	100

X^2: 23.55; p=0.001

Table 7: Association of Waist Circumference and CIMT

Waist circumference	CIMT				Total	
	Abnormal		Normal			
	No.	%	No.	%	No.	%
≤80	0	0.0	3	100.0	3	3
81-100	11	17.2	53	82.8	64	64
101-120	13	44.8	16	55.2	29	29
121-140	1	33.3	2	66.7	3	3
>140	0	0.0	1	100.0	1	1
Total	25	25.0	75	75.0	100	100
Mean ± SD	97.31±12.08		104.60±8.84		99.13±11.75	

P=0.007

Table 8: Association of Calf Circumference and CIMT

Calf circumference	CIMT				Total	
	Abnormal		Normal			
	No.	%	No.	%	No.	%
20-25	1	33.3	2	66.7	3	3
26-30	19	35.2	35	64.8	54	54
31-35	5	13.9	31	86.1	36	36
26-40	0	0.0	4	100.0	4	4
>40	0	0.0	3	100.0	3	3
Total	25	25.0	75	75.0	100	100
Mean ± SD	31.05±3.75		29.00±2.11		30.53±3.52	

P=0.011

Table 9: Association of Waist to Calf Circumference Ratio and CIMT

Waist to Calf circumference	CIMT				Total	
	Abnormal		Normal			
	No.	%	No.	%	No.	%
<3	0	0.0	23	100.0	23	23
3.0-3.5	8	14.0	49	86.0	57	57
3.6-4.0	13	81.3	3	18.8	16	16
4.0-4.5	3	100.0	0	0.0	3	3
>4.5	1	100.0	0	0.0	1	1
Total	25	25.0	75	75.0	100	100
Mean ± SD	3.10±0.21		3.68±0.28		3.24±0.34	

P=0.001

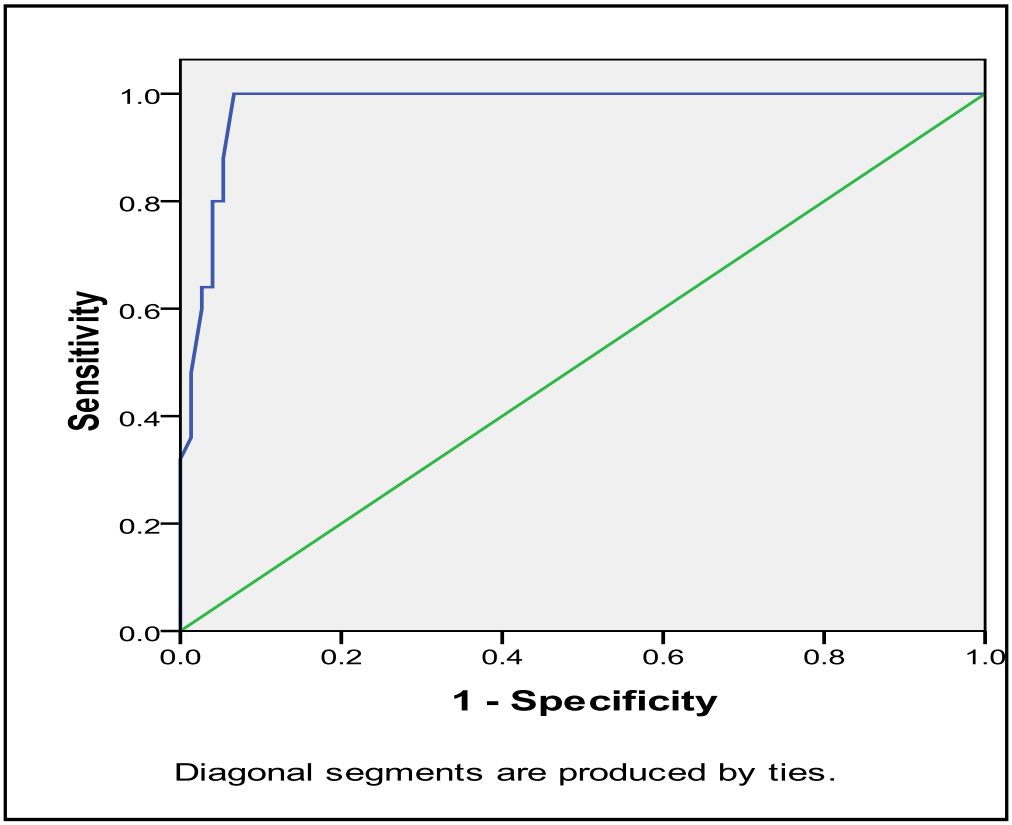

Figure 1: ROC Curve

DISCUSSION

In the present study, WC, CC, and WCR were compared to carotid atherosclerotic burden (CIMT).

These results demonstrate that CC is negatively and WC is positively associated with carotid atherosclerotic burden. Furthermore, the WCR has the strongest association with carotid atherosclerosis compared with each circumference alone, and that association was independent of multiple potential confounders. Simultaneously measuring both WC and CC could provide more specific information for sarcopenic phenotype compared with either a WC or CC measurement. Our analysis demonstrated an opposite and multiplicative relationship of WC and CC with the frequency of carotid atherosclerosis in both sexes. The number of patients with abnormal CIMT increased with increasing WCR and WC and decreasing CC in both sexes. Our study establishes WCR as a useful tool for out-patient determination of the risk of CAD, severity of atherosclerosis in patients with Diabetes Mellitus in a non-invasive, easy, and cost-effective manner.

Waist to calf circumference ratio is a simple non-invasive, cheaper, easy to use and non-instrumental modality which can be used as screening tool in assessment of atherosclerotic burden of the vasculature at an early stage in type 2 diabetic OPD as well as in patients. WCR will serve as surrogate marker of coronary artery disease.

CONCLUSION

The present study concluded that waist to calf circumference ratio is a simple non-invasive, cheaper, easy to use and non-instrumental modality which can be used as screening tool in assessment of atherosclerotic burden of the vasculature at an early stage in type 2 diabetic OPD as well as in patients. WCR will serve as surrogate marker of coronary artery disease.

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