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

Amit Jain¹, Pankaj Tantia², Kailash Saini¹, AA Sulemani³, P Sirohi⁴, Puneet Rizwani⁵, RP Agrawal⁶

Abstract

Aim: Diabetes is a well known risk factor for carotid atherosclerosis. However, screening of all diabetics by carotid ultrasonography is cumbersome and cost-effective. Search for anthropometric measures related to severity of disease has been relentless. It's a proposal for waist-calf ratio as a better marker of carotid atherosclerosis than traditional measurements as it is cost-effective and non-invasive.

Methods: This was a cross-sectional observational study. 100 patients were included. Detailed history, clinical examination, biochemical indices and anthropometric measurements were recorded. Carotid atherosclerosis was measured using a high resolution USG system with 10 MHz linear transducer. The carotid intima-media thickness (CIMT) was measured at 3 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 was used. CIMT → Distance between media-adventitia interface and lumen intima interface. Carotid Plaque → distinct area of hyperechogenicity and or protrusion into the lumen of vessel with at least 50% greater thickness than the surrounding area. Carotid atherosclerosis → Focal plaque or CIMT > 1.1 mm.

Results: Mean CIMT in quartiles of WCR in females and males are 1st (0.740, 0.674); 2nd (0.833, 0.726); 3rd (0.902, 0.814); 4th (1.005, 0.910) as well as mean WCR in quartiles of CIMT in males and females are 1st (2.292, 2.302); 2nd (2.473,2.443 ); 3rd (2.641, 2.671); 4th (3.177, 2.967). All the quartiles are statistically highly significant with p<0.001. Out of 100 patients 17 patients with carotid plaques, 12 had CIMT >1 and 14 had WCR >2.5. The difference was statistically significant with p<0.01

Conclusions: waist-calf ratio is a stronger anthropometric marker of carotid atherosclerosis and can be used in screening of high risk patients in diabetic population.

Introduction

Diabetes mellitus (DM) is a chronic metabolic condition characterized by persistent hyperglycemia with resultant morbidity and mortality related primarily to its associated microvascular and macrovascular complications.

Diabetes is a well known risk factor for cardiovascular diseases due to accelerated process of atherosclerosis. Carotid atherosclerosis (CA) is considered to be a non-invasive measure of generalized atherosclerosis and also a surrogate marker of coronary artery disease (CAD). Moreover there is an excellent agreement between histological examination and ultrasonography (USG) evaluation of carotid atherosclerosis. Duplex scanning allows efficient screening for carotid artery disease (CAD) but a trained physician or technologist is required and the equipment is still expensive. This routine screening of all diabetic patients for carotid atherosclerosis is cumbersome and not cost-effective.

Risk factors for carotid atherosclerosis include dyslipidemia, hypertension,
Table 1: Distribution of cases according to carotid plaques in relation to CIMT and waist calf ratio

<table>
<thead>
<tr>
<th>Carotid plaque</th>
<th>CIMT group</th>
<th>Waist-calf ratio group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1 (N=88)</td>
<td>≥1 (N=12)</td>
</tr>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Present</td>
<td>5 (5.7)</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Absent</td>
<td>83 (94.3)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

χ²: 66.578, p < 0.001

Material and Methods

**Study Design**

This was a cross-sectional observational study performed in patients of Type 2 DM

**Exclusion Criteria**

Patients with past history of cerebrovascular accident, PVD, muscular dystrophy, limb deformities and limb surgery were excluded.

100 patients were included. In the study. Detailed history, clinical examination, anthropometric measurements, biochemical indices were assessed for all the selected patients

**Anthropometric Measurements**

- Waist circumference → Midpoint between lower ribs and iliac crests at the end of normal expiration.
- Calf circumference → Point of highest circumference of calf with respondent standing straight, feet 20 cm apart, body weight equally distributed on both feet. One reading was taken from each leg and average of the two readings were taken.

**Carotid Ultrasound**

Carotid atherosclerosis was measured 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 was used.

CIMT → Distance between media-adventitia interface and lumen intima interface.

Carotid plaque → Distinct area of hyperechogenicity and or protrusion into the lumen of vessel with at least 50% greater thickness than the surrounding area.

**Statistical Analysis**

Quartiles of various anthropometric indices (WC, CC or WCR) were determined after stratifying by sex. The intergroup comparisons were performed using a one-way ANOVA test followed by a Scheffe Post Hoc test. In particular, comparisons of the prevalence of carotid atherosclerosis were made by means of a X² test. To estimate the Odds Ratio (OR) of carotid atherosclerosis in each quartile, logistic regression was performed and the lowest quartile was used as the reference category. Multivariate-adjusted Odds Ratio were be presented with 95% Confidence Intervals (CIs). For comparisons of CIMT, ANOVA and ANCOVA were used.

Results

In present study, out of the total 100 patients, only 17 patients had carotid plaque positive and out of them five had their CIMT <1 while three had their WCR ≤2.5 and the difference was statistically significant when compared to Carotid Plaque (p <0.001) and significant when compared to WCR with carotid Plaque (P<0.01) Table 1.

Table 2 shows association of CIMT and Quartiles of waist-calf ratio according to sex. All the quartiles were found statistically highly significant to have difference (p<0.001) in both female and males.

Table 3 shows multiple stepwise regression analysis showing variables independently associated with CIMT. Age alone had no significant difference and when we added waist circumference with age the difference was found to be statistically highly significant in both male and females. In addition
Peripheral subcutaneous fat has a protective effect on atherosclerosis. They favour coagulation and inhibitor and fibrinogen levels. Newly proposed mechanisms are dysfunctions in diabetic population. Peripheral subcutaneous fat is proposed; first is hypercoaguable or thrombogenic property. Firstly, insulin resistance. Secondly, there are differences in gene expression between visceral and subcutaneous adipocytes. This leads to a more proatherogenic pattern of gene expression in visceral fat. Thirdly, large amount of lean mass in the calf may offer protective effect on atherosclerosis.

In our study, calf circumference and carotid atherosclerosis showed an inverse relationship. Considering the above proposed mechanisms the following points favour our findings; firstly, the inverse association was graded. Secondly, this association is independent of age, gender, vascular factors, BMI and physical activity.

Debette et al. showed for the first time an inverse relationship between carotid plaques and calf circumference. Kim et al. showed that waist-calf ratio was a better indicator of carotid atherosclerosis. Park et al. concluded that waist circumference and waist to height ratio are better predictors of cardiovascular disease risk factors than BMI in Korean patients. Our results were consistent with their results.

Several limitations of this study should also be noted. Firstly, it low rate of lipolysis. Thus, it is more likely to take up free fatty acids from the circulation and less likely to release them. Increased peripheral fat stores may protect the liver and other organs from free fatty acid exposure. This reduces insulin resistance. Secondly, there are differences in gene expression between visceral and subcutaneous adipocytes. This leads to a more proatherogenic pattern of gene expression in visceral fat. Thirdly, large amount of lean mass in the calf may offer protective effect on atherosclerosis.

Weinberger et al. have demonstrated that diabetic patients have an increased risk of developing stroke. This is attributed to endothelial, platelet and vascular dysfunction in diabetic population. Newly proposed mechanisms are increased plasminogen activator and fibrinogen levels. They favour coagulation and impair coagulation thus creating a hypercoaguable or thrombogenic state.

Calf circumference is a surrogate marker of lean mass and subcutaneous fat, the relative importance of each component depending on the nutritional status. Several potential underlying mechanisms are proposed; first is the protective effect of peripheral subcutaneous fat on atherosclerosis. Peripheral subcutaneous fat has a

to this, calf, fasting blood sugar, glycated hemoglobin and waist-calf ratio the difference level had increased all the time and the significant range also increased.

Table 4 shows multiple stepwise regression analysis showing variables independently associated with waist-calf ratio.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS</td>
<td>0.390* 0.502*</td>
<td></td>
</tr>
<tr>
<td>FBS+TG</td>
<td>0.503* 0.863*</td>
<td></td>
</tr>
<tr>
<td>FBS+TG+HbA,C</td>
<td>0.717* 0.867*</td>
<td></td>
</tr>
<tr>
<td>FBS+TG+HbA,C+TC</td>
<td>0.725* 0.867*</td>
<td></td>
</tr>
<tr>
<td>FBS+TG+HbA,C+TC+LDL</td>
<td>0.787* 0.867*</td>
<td></td>
</tr>
<tr>
<td>FBS+TG+HbA,C+TC+LDL</td>
<td>0.802* 0.867*</td>
<td></td>
</tr>
<tr>
<td>FBS+TG+HbA,C+TC+VLDL</td>
<td>0.803* 0.868*</td>
<td></td>
</tr>
</tbody>
</table>

Correlation is significant at the 0.01 level (2-tailed); Correlation is significant at the 0.05 level (2-tailed)

Discussion

In our study it was found that waist circumference and waist-calf ratio correlated well with carotid atherosclerosis and calf circumference showed an inverse relation with carotid atherosclerosis. By multiple stepwise regression analysis it was proved that waist-calf ratio had the strongest association with carotid atherosclerosis than each circumference and the association was independent of multiple potential confounders; highest frequency being found in subjects of highest quarantile of waist calf ratio and lowest quarantile of calf circumference.

Variables (Male, Female)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.189</td>
<td>0.189</td>
</tr>
<tr>
<td>Age + WC</td>
<td>0.780* 0.857*</td>
<td></td>
</tr>
<tr>
<td>Age + WC + Calf</td>
<td>0.898* 0.960*</td>
<td></td>
</tr>
<tr>
<td>Age + WC + Calf+FBS</td>
<td>0.898* 0.962*</td>
<td></td>
</tr>
<tr>
<td>Age + WC + Calf+FBS + HbA,C</td>
<td>0.929* 0.962*</td>
<td></td>
</tr>
<tr>
<td>Age + WC + Calf+FBS + HbA,C + WCR</td>
<td>0.930* 0.974*</td>
<td></td>
</tr>
</tbody>
</table>

Correlation is significant at the 0.01 level (2-tailed)
is a cross-sectional study with a small sample size thus our results cannot establish cause and effective relationship between anthropometric indices and cardiometabolic risk. Secondly, study showed an independent association of waist-calf ratio with carotid atherosclerosis but did not observe the cardiovascular events and mortality. Thirdly, calf circumference is a marker of lean mass and peripheral subcutaneous fat. We could establish the inverse relation with cardiometabolic disease but could not determine whether it was due to protective effect of lean mass or peripheral subcutaneous fat or both.

Future studies should also test the association of calf circumference with plaque composition using more detailed measures like MRI instead of USG.

Studies must also test the association with plaque progression and vascular events. More research is required to unearth underlying mechanisms. Studies which establish the respective role of lean mass and peripheral fat mass are warranted.

References

1. Executive committee for the asymptomatic carotid atherosclerosis study. JAMA 1985; 273:1421-28


