



SONOGRAPHIC EVALUATION OF SUPERFICIAL FEMORAL ARTERIAL CALCIFICATION IN DIABETIC PATIENTS WITH AND WITHOUT NEPHROPATHY IN BANGLADESHI POPULATION.

Radiology

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ABSTRACT

Type-2 diabetes mellitus is a common metabolic disease associated with many co-morbidities including nephropathy. Diabetic nephropathy is one of the most serious complications leading to end stage renal failure (ESRD) and leading cause of morbidity and mortality among diabetic patients in Bangladesh. Vascular calcification is a well known complication of ESRD and one of the main predictors for increased cardiovascular morbidity and mortality in these patients. Arterial disease in diabetic patients with nephropathy is characterized by extensive medial arterial calcification (MAC). The aim of the study to evaluate the presence of calcification & to compare the severity of calcification in tunica media of Superficial femoral arteries (SFA) in diabetic patients with and without nephropathy. This cross sectional study was carried out in Radiology & Imaging department of BIRDEM Hospital, Dhaka during July 2013 to June 2014. For this purpose, a total number of 111 Type-2 diabetic subjects with and without nephropathy were considered as group I (diabetic subjects with nephropathy) and group II (diabetic subjects without nephropathy). Ultrasonogram was done in all these patients. From the findings of present study it can be concluded that sonographically detected tunica medial arterial calcification of superficial femoral arteries is significantly higher in patients with diabetic nephropathy in compare to patients without nephropathy. Ultrasonography (USG) is capable of detection of subtle & early medial arterial calcification which allows early detection of vascular abnormalities, so that intensive treatment can be started early and timely to modify the subsequent clinical course.

KEYWORDS

Superficial femoral artery (SFA), Ultrasonography (USG), Diabetes mellitus (DM).

Introduction:

Diabetes mellitus is the most prevalent metabolic, non communicable disorder in the world. Diabetic nephropathy is one of the dreaded complications of diabetes. DN is a type of progressive kidney disease that occurs in people who have type 1 or type 2 diabetes. The University of Washington estimates that 20 to 40 percent of people with diabetes will get nephropathy at some point in their lives.¹ It is prevalent that approximately 20-30% of patients with type 2 diabetes develop evidence of nephropathy.² DN is a clinical syndrome characterized by persistent albuminuria (>300mg/day or >200ug/min) that is confirmed on at least 2 occasions 3-6 months apart, progressive decline in glomerular filtration rate (GFR), elevated arterial blood pressure.³ There are five stages of diabetic nephropathy. The fifth and final stage is end stage renal disease (ESRD). Diabetes is responsible for 30-40% of all ESRD cases in the United States. Although both type-1 and type-2 DM lead to ESRD, the great majority of patients are those with type 2 diabetes.⁴ According to the University of Rochester Medical Center, the average time it takes to progress from the beginning stage of kidney failure to the fifth stage is 23 years.² Arterial calcification occurs in two sites: the tunica intima and tunica media. Intimal calcification is a marker of atherosclerotic disease & associated with arterial stenosis.⁵ Medial arterial calcification (MAC), also known as Monckeberg arteriosclerosis, is a condition that leads to stiffening of the elastic layer of the arterial wall, but in contrast to intimal calcification, it does not obstruct the arterial lumen.⁶ MAC is a very common condition in subjects with diabetes & chronic renal failure.^{7,8} The presence of uniform, smooth, linear and nonstenotic calcified arterial wall in the ultrasonographic assessment is diagnostic of medial arterial calcification. The discrete, plaque like and stenotic calcified wall is regarded as intimal wall calcification. The presence of both medial and intimal wall calcifications is regarded as a mixed calcification.⁹ USG is the imaging method that can directly aid visualization of the arterial lumen of the peripheral arteries and can potentially be used to detect MAC. It is widely used to assess arterial wall abnormalities such as intima-medial wall thickening^{10,11} and endothelial dysfunction¹². The arterial wall calcification is defined as hyperechogenicity in the arterial wall as compare with the surrounding tissues, which also disrupts the normal intima-medial wall configuration.⁹ Exact mechanism or pathogenesis of MAC has not been fully explored. It has been found that hyperglycemia and duration of

diabetes are associated with MAC. Some researchers suggest that loss of autonomic innervations may result in trophic disturbances in the smooth muscle cells of the tunica media of the vessels.⁶ This changes in smooth muscle structure and function¹³ may lead to abnormal calcium metabolism result in formation of medial calcification.⁷ MAC may also be a consequence of age related accumulation of glycosylated proteins, which is exacerbated in diabetes. The presence of MAC may signify loss of arterial elasticity, which can result in impairment of blood flow to cause further injury to the endothelium and increase the risk of vessel thrombosis.⁶ In previous studies for assessment of medial arterial calcification, conventional radiography was used. However, conventional radiography has the disadvantages of radiation exposure to subjects and possible underestimation of MAC severity.⁶ The latter might limit its sensitivity. US was found to be much more sensitive than the traditional conventional radiography for detection of MAC, particularly the early or mild form of MAC in type 2 diabetes patients. The incidence of diabetes mellitus (DM) and diabetic nephropathy have risen rapidly in the past few decades and have become an economic burden to the healthcare system.¹⁴ Monitoring of type 2 patients for nephropathy becomes vital to avoid ESRD. The regular monitoring of these patients should delay the onset of this comorbidity.¹⁵

Materials and methods:

This cross sectional study was carried out with an aim to find out the presence of calcification in the tunica media of SFA by USG in study groups and to compare the presence of medial arterial calcification of SFA in diabetic patients with and without nephropathy. A total of 111 Type-2 diabetic subjects with and without nephropathy (considered as group I & group II) referred to Radiology and Imaging department of BIRDEM, Dhaka for USG, during July 2013 to June 2014 were included in this study. Hypertensive patients, subjects with cardiovascular, cerebrovascular & peripheral vascular disease and patients had been treated with chemotherapy for cancer were excluded from the study. USG was performed by linear transducer of 6-10 MHz (SIEMENS SONOLINE ANTARES). All patients were examined in supine position. SFA of both thighs were scanned in the cross sectional plane from their origins at the groin to their distal parts at the entrance of the adductor canal to have an overall view of the blood vessels. Then the Superficial femoral arteries were

longitudinally scanned and the degree and type of calcifications are assessed on the longitudinal US images.

Ultrasound scoring of medial arterial calcification (MAC)-The MAC was assigned a score from 0 to 4 according to severity of the calcification within a 4cm scanned area(which is usually the approximate size of the transducer).The definitions are as follows:

Score 0, no MAC.

Score 1, extent of MAC less than 1 cm in length.

Score 2, extent of MAC between 1 and 2cm in length.

Score 3, extent of MAC between 2 and 3 cm in length.

Score 4, extent of MAC more than 3 cm in length.

There may be calcifications in both anterior and posterior walls of the arterial lumen. The calcifications in anterior and posterior walls at the same level were regarded as the same calcification, while those at different levels were summed in the MAC scoring. The highest MAC score in any one of the 4 cm scanned areas was used as the score for that side in analysis. The MAC scores of both sides were summed to have the final score with the range from 0 to 8. The MAC group then was classified into mild (scores 1-4) and severe (scores 5-8) groups for analysis. A value of $p < 0.05$ was considered as statistically significant. Difference between two groups was analyzed by the unpaired t test and Chi-square test. The total study was summarized as per the standard procedures and unbiased conclusion will be drawn. Data was analyzed by SPSS computer program if needed.

Observation and results:

This study included total 111 type2 diabetic subjects with and without nephropathy considered as group I & group II respectively. It was observed that majority 37(60.7%) patients were age belonged to 61-70 years in group I and 28(56%) in group II. The mean age was found 63.0±6.02 years in group I & 60.06±5.56 years in group II. Duration of diabetes shows that almost half 28(45.9%) patients were duration of diabetes belonged to 6-10 years in group I and 34(68%) in group II. The mean duration of diabetes was found 10.48±3.33 years in group I and 7.9±2.32 years in group II. It was observed that almost half 29(47.5%) were serum creatinine belonged to >4.5 mg/dl in group I and 36(72%) patients were serum creatinine belonged to 1.3-3 mg/dl in group II. The mean serum creatinine was 4.63±1.8 mg/dl in group I and 1.69±0.43mg/dl in group II. Urinary albumin of the study patients shows majority 28(45.9%) patients had moderate (+++) in group I and 28(56%) had no urinary albumin in group II. The differences was statistically significant ($p < 0.05$) between two groups in above mentioned variables. It was observed that majority 52(85.2%) patients had tunica medial arterial calcification in group I and 22(44%) in group II. Mean distribution of serum creatinine level according to severity of calcification evaluated by USG of 111 patients are shown in following table.

Severity of calcification evaluated by USG	Serum creatinine(mg/dl)		P value		
	Serum creatinine(mg/dl)				
	Group I(n=61)	Group II(n=50)			
	n	mean±SD	n	mean±SD	
No calcification Range	9	3.33± 0.98 1.6-4.3	28	1.65± 0.431,1-2.3	0.001*
Mild calcification Range	23	2.94±0.54 1.9-3.9	22	1.75± 0.45 1.1-2.7	0.001*
Severe calcification Range	29	6.26± 0.88 4.3-7.5	0	0.0± 0.0 0.0	0.0-

It was observed that patients having no calcification evaluated by USG, the mean serum creatinine was found 3.33±0.98 mg/dl in group I and 1.65±0.43 mg/dl in group II. Patients having mild calcification evaluated by USG, the mean serum creatinine was 2.94±0.54 mg/dl in group I and 1.75±0.45 mg/dl in group II. Patients having severe calcification evaluated by USG, the mean serum creatinine was 6.26±0.88 mg/dl in group I but not observed in group II. The mean serum creatinine level was significantly ($p < 0.05$) higher in group I, in patients with no calcification and mild calcification.

Discussion:

Medial arterial calcification (MAC) may be a consequences of age related accumulation of glycosylated proteins, which is exacerbated in

diabetes obtained by Lehto et al.(1996).In this series it was observed that majority (60.7%) of the patients in group I and 56.0% in group II were in 7th decade. The mean age was found 63±6.02 years varied from 40-75 years in group I and 60.06±5.56 years varied from 46-69 years in group II. The mean age difference was significantly higher in group I. Liu et al(2012) showed the mean age of the patients with type 2 DM 59.8±12.2 years and Agarwal et al.(2011) mentioned that incidence of nephropathy increased significantly with increase in age and was 30% in age group >60 years, which are comparable with the current study. Fox et al. (2006) study demonstrated that the combination of both CKD and MAC was associated with a threefold increased risk of death compared with those with neither CKD nor MAC($p=0.0004$) In this present series it was observed that almost half (45.9%) patients had duration of diabetes belonged to 6-10 years in group I and 68% in group II. On the other hand, 47.6% and only 12% had duration of diabetes more than 10 years in group I and II respectively. The mean duration of diabetes was 10.48±3.33 years varied from 2-20 years and 7.9±2.32 years varied from 4-12 years in group I and II respectively. The mean duration of diabetes was significantly higher in group I. Liu et al.(2012) showed the mean duration of diabetes was 11.9±8.2 years, which are comparable with the current study. In this current series, it was observed that almost half(47.5%) of the patients had serum creatinine level belonged to more than 4.5 mg/dl in group I and 72.0% patients had serum creatinine level belonged to 1.3-3.0 mg/dl in group II. In Liu et al (2012) study obtained that serum creatinine level was associated with nephropathy but not with the other diabetes related complications. The ultrasound detection of MAC of the lower limb was found to be more sensitive method than traditional radiography, with a much higher percentage of diabetic patients found to have MAC(65.8% vs 12.2%) reported by Liu et al(2012).

Conclusion:

Ultrasonography is a simple and sensitive imaging technique to evaluate association of MAC with diabetes related complications as diabetic nephropathy. It is also cheap, available, painless & nonhazardous imaging tool. So, it can be routinely used in diabetic patients for assessment of vascular calcification as a complication of diabetes, thus may help the doctors for treating and follow up the patients.

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