Editorial

Carotid Intima-Media Thickness in Type 2 Diabetes Mellitus

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Asian Indians are known to have very high rates of diabetes[1,2] and premature coronary artery disease.[3] Diabetes leads to both macro and microvascular complications. For assessment of macrovascular complications, carotid intima media thickness (CIMT), is a well-standardized surrogate marker for assessing cardiovascular risk, and it is well accepted as a parameter of subclinical atherosclerosis. CIMT is a strong predictor of future cardiovascular events and is associated with conventional markers of cardiovascular risk such as age, hypertension and dyslipidemia.[4] Earlier studies have documented a significant role of CIMT in cardiovascular disease prediction in both non-diabetic and diabetic populations.[5] Studies have shown that in Asian Indians there is an association between increased CIMT and type 2 diabetes, CIMT significantly higher in diabetic patients than in non diabetic subjects[6,7] and also demonstrated that subclinical atherosclerosis increases with increasing degrees of glucose intolerance.[8] This underscores the need for detecting early changes of atherosclerosis in type 2 diabetic subjects. Consequently, assessment of carotid atherosclerosis by means of CIMT ultrasound measurement is rapidly becoming an accepted way to detect generalized atherosclerosis. In addition, studies have shown that microvascular complications including retinopathy, nephropathy and neuropathy are independently associated with atherosclerosis in type 2 diabetes.[9-11] However, there have so far been very few studies demonstrating the association between cardiac autonomic neuropathy (CAN) and atherosclerosis in Asian type 2 diabetic subjects.

The article by Sinha et al[12] in this issue of the Journal asks the question whether there is any correlation between CAN and CIMT in type 2 diabetic patients. The authors studied 84 diabetic patients admitted in medical wards of Medical College, Kolkatta in western India. The study shows that nearly 43% of the study patients were detected to have CAN, assessed by five clinical tests. The investigators use mutilpe logistic regression analysis and conclude that duration of diabetes, high LDL cholesterol, low HDL cholesterol, fasting blood sugar and CIMT (≥0.69 mm) influence the development of CAN. The finding that CIMT is significantly higher in subjects with CAN compared with those without CAN is not surprising as their duration of diabetes is significantly high compared to those without CAN. This is similar to studies conducted by Gottsäter et al[13,14] in people with type 2 diabetes. The authors also conclude that CIMT ≥0.69 mm had a sensitivity of 94% and specificity of 87.5% for detecting development of CAN and this cut point was associated with development of various CAN function tests in their diabetic population. This study has thus shown that a relationship does exist between CAN and CIMT. Further studies are needed to see if CAN has a role in the occurrence and progression of CIMT in diabetic patients.

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Another article by Gayathiri et al,[15] in this issue of the journal, was carried out to study the correlation between CIMT with risk factors for atherosclerosis and atherosclerotic events in 44 type 2 diabetes mellitus patients at the Department of General Medicine, Calicut Medical College in south India. The authors report that CIMT was significantly higher in those type 2 diabetic patients who had atherosclerotic events than in those patients who had no atherosclerotic events. It was also reported that waist hip ratio was significantly higher among those with increased CIMT compared with those who had normal CIMT, emphasizing the emerging concept of central obesity. The risk factors for increased CIMT in patients with diabetes seem to be variable in various studies. In this study age, smoking and dyslipidemia did not show any association with CIMT. However, the findings that diabetic patients with atherosclerotic events had significantly higher CIMT compared to those who had only risk factors for atherosclerosis are of great concern. Though, the results of this study may not be novel, as they are well known and widely documented in larger and better powered studies,[16,17] they still add to the body of knowledge on the factors associated with increase in CIMT in type 2 diabetes mellitus.

From the above two studies it can be inferred that CIMT measurement is an effective, noninvasive tool which can assist in identifying people with diabetes who are at higher risk of developing microvascular and macrovascular complications. The results emphasize the possible common or interacting pathogenetic mechanisms in the onset/progression of microvascular and macrovascular complications. The main limitations of the two studies are their small sample size and that they are not representative of the general population. Studies with large sample sizes and more importantly prospective longitudinal follow-up studies are needed to confirm such associations.

References

1. International Diabetes Federation, Diabetes Atlas . Unwin N, Whiting D, Guariguata L, Ghyoot G, Gan D (eds). Fifth Edition, International Diabetes Federation, Brussels, Belgium, 2011;11–74.
2. Anjana RM, Pradeepa R, Deepa M, Datta M, Sudha V, Unnikrishnan R, et al. Prevalence of diabetes and prediabetes (impaired fasting glucose or/and impaired glucose tolerance) in rural and urban India: Phase 1 results of the Indian Council of Medical Research-INdiaDIABetes (INDIAB) study. *Diabetologia* 2011;54:3022-3027.
3. Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation* 1998;97:596–601.
4. Mannami T, Konishi M, Baba S, Nishi N, Terao A. Prevalence of asymptomatic carotid atherosclerotic lesions detected by high-resolution ultrasonography and its relation to cardiovascular risk factors in the general population of a Japanese city: the Suita study. *Stroke* 1997;28:518–525.
5. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M. Prediction of clinical cardiovascular events with carotid intima media thickness: a systematic review and meta-analysis. *Circulation* 2007;115:459-467.

6. Mohan V, Ravikumar R, Shanthi Rani S, Deepa R. Intimal medial thickness of the carotid artery in south Indian diabetic and nondiabetic subjects: the Chennai Urban Population Study (CUPS). *Diabetologia* 1998;433:494–499.
7. Ravikumar R, Deepa R, Shanthirani CS, Mohan V. Comparision of carotid intima-media thickness, arterial stiffness and brachial artery flow medicated dilatation in diabetic and non-diabetic subjects. (The Chennai Urban Population Study [CUPS, 9].) *Am J Cardiol* 2002;90:702–707.
8. Mohan V, Gokulakrishnan K, Sandeep S, Srivastava BK, Ravikumar R, Deepa R. Intimal media thickness, glucose intolerance and metabolic syndrome in Asian Indians--the Chennai Urban Rural Epidemiology Study (CURES -22). *Diabet Med* 2006;23:845-850.
9. de Kreutzenberg SV, Coracina A, Volpi A, Fadini GP, Frigo AC, Guarneri G, Tiengo A, Avogaro A. Microangiopathy is independently associated with presence, severity and composition of carotid atherosclerosis in type 2 diabetes. *Nutr Metab Cardiovasc Dis* 2011;21:286-293.
10. Rema M, Mohan V, Deepa R, Ravikumar R. Association of carotid intima media thickness and arterial stiffness with diabetic retinopathy: the Chennai Urban Rural Epidemiology Study (CURES-2). *Diabetes Care* 2004;27:1962–1967.
11. Yokoyama H, Yokota Y, Tada J, Kanno S. Diabetic neuropathy is closely associated with arterial stiffening and thickness in Type 2 diabetes. Diabet Med. 2007 ;24:1329-35
12. Sinha PK, Santra G, De D, Saha A, Biswas K, Bhattacharya P, Ghosh P. Carotid intima-media thickness un type 2 diabetes mellitus patients with cardiac autonomic neuropathy. *J Assoc Physicians India* 2012;60:14-18.
13. Gottsäter A, Rydén-Ahlgren A, Szelag B, Hedblad B, Persson J, Berglund G, Wroblewski M, Sundkvist G. Cardiovascular autonomic neuropathy associated with carotid atherosclerosis in Type 2 diabetic patients. *Diabet Med* 2003;20:495-499.
14. Gottsäter A, Szelag B, Berglund G, Wroblewski M, Sundkvist G. Changing associations between progressive cardiovascular autonomic neuropathy and carotid atherosclerosis with increasing duration of type 2 diabetes mellitus. *J Diabetes Complications* 2005;19:212-217.
15. Gayathiri R, Chandni R, Udayabhaskaran V. Carotid artery intima media thickness in relation with atherosclerotic risk factors in patients with type 2 diabetes. *J Assoc Physicians India* 2012;60:20-24.
16. Chambless LE, Folsom AR, Davis V, Sharrett R, Heiss G, Sorlie P, Szklo M, Howard G, Evans GW. Risk factors for progression of common carotid atherosclerosis: the Atherosclerosis Risk in Communities Study, 1987–1998. *Am J Epidemiol* 2002;155:38–47.
17. Brohall G, Oden A, Fagerberg B. Carotid artery intima-media thickness in patients with Type 2 diabetes mellitus and impaired glucose tolerance: a systematic review. *Diabet Med* 2006;23:609–616.