ORIGINAL ARTICLE

The Assosiation of Carotid Intima-Media Thickness and Ankle Brachial Index with SPECT Myocardial Perfusion Imaging in Asymptomatic Diabetic Patients

Seyed Mohamad Hossein Sadr Bafghi[1], Seid Kazem Razavi Ratki[2], Hassan Haghaninejad[7], Seyed Ali Sadr Bafghi[3], Seid Hossein Razavi[4], Alireza Mardanshahi[5], Nasim Namiranian[6], Naser Hossein Sartipzadeh[7], Mohamad Ali Jelodari[8], Reza Nafisi Moghadam[9*]

1. MD, Shahid Sadoughi University of Medical Sciences Yazd, Iran.
2. MD, Assistant Professor of Nuclear Medicine, Department of Radiology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
3. MD, Cardiologist, Afshar Hospital, Shahid Sadoughi University of Medical Sciences Yazd, Iran.
4. DDH, Assistant Professor of Maxilo Facial Radiology Dental Factuly Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
5. Nuclear Medicine Specialist, Department of Radiology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
6. MD, Assistant Professor Community Medicine. Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
7. MD, Department of Cardiology, Afshar Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
8. Nuclear Medicine Technologist. Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
9. MD, Associated professor, Department of Radiology, Shahid Sadooghi University of Medical Sciences, Yazd, Iran.

***Correspondence:**
Reza Nafisi Moghadam, MD, Associated professor, Department of Radiology, Shahid Sadooghi University of Medical Sciences, Yazd, Iran.
Email: Nafisi.moghadam@gmail.com
Tel: (98) 353 822 4000

Received: 12 June 2016

Accepted: 01 August 2016

Published in November 2016

Abstract

Objective: The risk of cardiac death in diabetic patients is 3 times more than non-diabetics. But it is not determined who need cardiac screening. About 41% of diabetic patients with silent ischemia are missed. the carotid intima-media thickness (CIMT) and ankel brachial index are two independent,simple and non invasive method in vascular complications diagnosis in diabetic patients.The aim of this study was to evaluate the assosiation of CIMT and ABI in prediction of silent myocardial ischemia in myocardial perfusion scintigraphy in Asymtomatic diabetic papulation.

Materials and Methods: This was an analytic cross-sectional study. The convenient sampling was used. About 114 patients with diabetics and no history and symptom of coronary artery disease (CAD) were included. Myocardial perfusion scan (MPI), CIMT and ABI were done. All of statistical analysis was done by SPSS-20.

Results: Totally114 diabetic patients without cronary artery disease symptoms were included .About 66.7% were female. The mean age of patients was 53.8± 8.6 years old. About 50% (57) of patients were normal. The mean of CIMT was 0.93 ± 0.21 and mean ABI was 0.97 ± 0.11. Regarding the anlysis of variance (ANOVA) there were significant differences of mean CIMT and ABI between normal and moderate to severe ischemia in MPI.

Conclusion: Our findings showed that CIMT and ABI is significantly different between patients with and without ischemia. The CIMT and ABI are simple, non-invasive, and inexpensive tests that may be used to identify individuals who are at high risk of developing cardiovascular disease (diabetic patients).

Keywords: Carotic intima media thickness, Ankel brachial index, Silent ischemia, Myocardial perfusion scan, Diabetes.

Introduction

Diabetes mellitus (DM) is an independent risk factor of cardiovascular disease (CAD) (1-3). CAD is the leading cause of death in DM patients (4). Myocardial infarction (MI), Angina and sudden death rates in diabetic patients are higher than normal population (5).

Also silent ischemia and CAD prognosis are more sever in diabetic patients (6).

Silent myocardial infarction (SMI) is defined as "the presence of objective evidence of myocardial ischemia in the absence of chest discomfort or other angina equivalent symptom" (7-8). Diabetic patients are at risk of SMI about 2-4 times more than normal population (9-11). The prevalence of SMI in diabetic patients is 10-20% but in non-diabetic population is 1-4% (12-16).

In 1998, American Diabetes Association (ADA) recommended that diabetic patients with at least two cardiovascular disease risk factors need cardiovascular screening (20). Non-invasive techniques for cardiovascular screening in diabetic patients are more recommended, such as (21): Exercise tolerance testing (ETT), myocardial perfusion imaging (MPI), Stress echocardiography, Single photon emission computer tomography (SPECT), Electron beam computed tomography (EBCT),Magnetic resonance angiography (MRA), Multislice computed tomography (MSCT) and Ankle-Brachial Index (ABI) (20-24).

CIMT is a surrogate marker of atherosclerosis (25-27). CIMT is a marker of CAD and further cardiovascular events (28). A marked association between CIM and cerebrovascular or coronary artery disease is showed in recent studies. Carotid ultrasonography revealed carotid wall and lumen surfaces which is quantified severity of atherosclerosis. Carotid IMT is non-invasive and inexpensive diagnostic surrogate test for CAD and CIMT could useful for prediction of CAD. (26-27)

ABI is a non-invasive method used to diagnose peripheral artery disease (PAD) but suggested as a CAD screening method in diabetic patients (29-30). The screening tests should be available, acceptable, non-invasive, inexpensive, reliable and valid (31). ABI fulfills the screening tests criteria. ABI lower than 0.9 in diabetic patients indicates CAD and cerebrovascular disease (CVD) risk (32).

The aim of this study was to evaluate the association of CIMT and ABI in prediction of SMI in MPI in Asymptomatic diabetic population.

Materials and Methods

This was an analytic cross-sectional study conducted in Shaheed Sadoughi hospital on 104 diabetic patients during 2015-2016. All patients received information about the study and signed an informed consent. The study inclusion criteria was: type 2 diabetes mellitus and no history of CAD, Percutaneous coronary intervention (PCI) and no symptom of CAD. Exclusion criteria was: Lower limb trauma, Deep vein thrombosis (DVT), Amputation or surgery, Foot ulcers, lower limb swelling , Type I diabetes mellitus.

For assessing of CIMT, the study was down in supine position and mildly head hyperextension. By B-mode ultrasonography 7.5-10 MHz linear transducer, with an automatic boundary detection system, the carotid arteries were evaluated. The origins of the common carotid arteries, internal and external carotid arteries as well as carotid sinus were scanned. Mean CIMT was evaluated throughout 10-mm segments. The mean of four segments was used to determine mean CIMT.

ABI was calculated with continuous wave Doppler using a hand-held sensor Smartart model 450 Hz instrument for all patients.

Duplex Colour Doppler and blood pressure was measured in all four limbs at brachial and posterior tibial artery. ABI was calculated as ankle pressure/ brachial pressure and the lower ratio amongst the two was chosen. All patients were examined by physician. Selected patients were included. The ABI and dipyridamole or Exercise stress test were done for all patients. Finally Myocardial Perfusion SPECT was done and the ischemic findings in Myocardial Perfusion SPECT were correlated by ABI.

All statistical analysis was done by the SPSS software (Statistical Package for the Social Sciences, version 20; SPSS Inc, Chicago, Illinois). The normal distribution of data was checked. Mean, standard deviations (SD), minimum and maximum were calculated.

Analysis of variance (ANOVA) and Pearson correlation were used. The statistical significances considered as 0.05.

Results

Totally 114 patients were studied. About 66.7% of patients were female and 33.3% were male. The baseline characteristics of patients were presented in table 1.

Differences between the group means of continuous variables were tested for significance by ANOVA. In post hoc ANOVA analyses, the mean CIMT, ABI, age and diabetes duration values were significantly associated within groups with moderate to severe ischemia in SPECT but in groups with normal MPI and mild ischemia no statistically significant mean deference is noticed .Also between groups with Mild ischemia and moderate to severe ischemia significant mean deference was not seen. Table 2 shows differences between the group means of CIMT, ABI, age, Diabetes duration with MPI results.

Spearman's correlation coefficients revealed statistically significant correlation between CIMT, ABI, and age and diabetes duration. But In this partial Spearman's correlation analysis (adjusted for age), correlations between CIMT with ABI and diabetes duration was not still statistically significant. (table 3).

Discussion

SPECT prognostic values were confirmed in diabetic patients (41). But, the important question remains exactly how diabetic patients without symptom of ischemic heart disease should be excluded in general diabetic population. Our findings showed that age, CIMT and ABI are significantly different between patients with and without ischemia. The previous studies suggested, diabetic patients suffer from SMI and the prevalence of SMI differs from 6-59% (2-5). The prevalence of SMI in our study was 48.5%.

The validity of SPECT in patients without

Table 1. The baseline characteristics of patients

Variable	No ischemia	Mild ischemia	Moderate to severe ischemia
Sex (Female/male %)	66.7/33.3	71.4/28.6	57.7/42.3
Age (Mean ± SD)	53.87 ± 8.6	58.82 ± 8.7	60.81 ± 9.2
Hypertension (%)	41.7	71.4	91.3
Hyperlipidemia (%)	46.7	75	69.2
Diabetes duration (Mean ± SD)	5.1 ± 4.3	7.3 ± 5.7	8.3 ± 6.6
Mean IMT	0.85 ± 0.18	0.96 ± 0.18	1.06 ± 0.23
ABI (Mean ± SD)	1.01 ± 0.06	0.96 ± 0.12	0.91 ± 0.16
MPI (%)	52.5	25	22.8
Smoking (%)	14	16	19

Table2. Mean age, ABI, diabetes duration and CIMT in patients with normal myocardial perfusion scan, Mild ischemia and moderate to severe ischemia (analysis of variance)

Variable	MPI		Mean Difference	Std. Error	Sig.
Age	Normal	Mild ischemia	-4.955	2.022	.054
		Moderate/severe	-6.941*	2.075	.005
	Mild	Moderate ischemia	-1.986	2.407	.712
ABI	Normal	Mild ischemia	.050262	.024946	.136
		Moderate/severe	.099795*	.025592	.001
	Mild	Moderate/severe	.049533	.029685	.253
Duration	Normal	Mild ischemia	-2.266	1.207	.176
		Moderate/severe	-3.244*	1.238	.036
	Mild	Moderate/severe	-.978	1.436	.793
IMT	Normal	Mild ischemia	-.10579	.04504	.068
		Moderate/severe	-.20996*	.04621	.000
	Mild	Moderate /severe	-.10418	.05360	.156

Table 3. Spearman's and partial (adjusted for age) correlation coefficients between carotid intima-media thickness, ABI, age and diabetes duration.

Correlations					
Variables		**ABI**	**IMT**	**Duration**	**Age**
ABI	Correlation	1.000	-0.280	-0.195	- 0.215
	P-value	0.000	0.003	0.038	0.022
IMT	Correlation	-0.280	1.000	0.219	0.731
	P-value	0.003	0.000	0.019	0.000
Duration	Correlation	- 0.195	0.219	1.000	0.184
	P-value	0.038	0.019	0.000	0.049
Age	Correlation	- 0.215	0.731	0.184	1.000
	P-value	0.022	0.000	0.049	0.000
Partial Correlations age adjusted					
ABI	Correlation	1.000	-0.184	0.162	
	P-value		0.051	0.087	
IMT	Correlation	- 0.184	1.000	0.125	
	P-value	0.051		0.186	
Duration	Correlation	- 0.162	0.125	1.000	
	P-value	0.087	0.186		

cardiac symptoms was reported between 59-69% which is influenced by type of stress and imaging technique (2). In our study the prevalence of Ischemia in SPECT was about 48.5%. But one of understandable limitation of our study was absence of angiography which is recommended for future studies.

The PAD are simply diagnosed by ABI (31-32). Also ABI can be as a diagnostic prognostic factor of CAD in diabetic patients (34-35). Previous studies documented the association between CAD, CVD and PVD (36-38) which was according with our findings.

ABI is a simple, non-invasive, inexpensive, available and sensitive method in diagnosis of CAD (39-40) ABI is an acceptable screening method before any other invasive and expensive modalities.

Lack of gold standard in CAD diagnosis should be noticed as the major limitations of our study. Valuation of CIMT has been previously suggested for this Question (42). Relationship between CIMT and CAD has not been fully recognized in asymptomatic diabetic patients. In our study, increased CIMT was revealed to be a predictor of the degree of severity in MPI. Lower CIMT values were related with a low risk MPI. In current study the analysis showed significance correlation between ABI, IMT, Diabetes duration and age but in additional analysis partial correlation suggests that age is a confounding factor. Also, Diabetic patients who referred to diabetes center with CAD risk more than the general asymptomatic Diabetic population, current study results recommend that CIMT for initial risk stratification.

Many study limitation should be deliberated. Small number of cases and therefore gender imbalance of the participants. Furthermore, the age of participant was a confounding factor .As a result, the clinical usefulness of IMT as a screening method for CAD should be verified in studies with larger sample size. Especially, the cut-off level of maximum IMT should be confirmed by further studies.

Conclusion

Our findings showed that ABI is significantly different between patients with and without ischemia. The ABI is a simple, noninvasive, and inexpensive test that can be used to identify individuals who are at high risk of developing cardiovascular disease (diabetic patients).

References

1. Baral N, Koner BC, Karki P, Ramaprasad C, Lamsal M, Koirala S. Evaluation of new WHO diagnostic criteria for diabetes on the prevalence of abnormal glucose tolerance in a heterogeneous Nepali population-the implications of measuring glycated hemoglobin. Singapore Med J 2000;41(6):264-7.
2. Babes EE, Babes VV. University Oradea, Faculty of Medicine and Pharmacy Romania. Detection of Silent Ischemia in Patients with Type 2 Diabetes. Recent Advances in the Pathogenesis, Prevention and Management of Type 2 Diabetes and its Complications. Chapter 9.
3. Dolat-Abadi Farahani V, Razavi-ratki S K, Namiranian N, Emami-Meybodi M, Nough H, Razavi H et al . Transient Ischemic Dilatation Ratio in Stress Myocardial Perfusion SPECT in Diabetic Patients-A Systematic Review and Meta-Analysis. IJDO. 2013;5(3):132-13
4. Cryer PE. Management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2007;30:190-2.
5. Fox CS, Coady S, Sorlie PD. Trends in cardiovascular complications of diabetes. JAMA 2004; 292: 2495-2499.
6. Young LH, Chyun DA: Heart disease in patients with diabetes. In Ellenberg and Rifkin's Diabetes Mellitus: Theory and Practice. 6th ed. Porte DJ, Baron A, Sherwin RS, Eds. New York, McGraw-Hill, 2002;823–44.
7. Nesto RW, Phillips RT, Kett KG. Angina and exertional myocardial ischemia in diabetic and nondiabetic patients: assessment by exercise thallium scintigraphy. Ann Intern Med 1988; 108:170–5.
8. Razavi Ratki SK, Amelshahbaz A, Nafisi-Moghadam R, Sartipzadeh NH. Application of Anatomical and Functional Modalities in Detection of Silent Myocardial Ischemia in Asymptomatic Diabetic Patients- A Review Article. IJDO. 2015;7(2):73-81A,
9. Janand-Delenne B, Savin B, Habib G, Bory M, Vague P, Lassmann-Vague V. Silent myocardial ischemia in patients with diabetes: who to screen. Diabetes Care1999;22:1396-400.
10. Cosson E, Guimfack M, Paries J, Attali JR, Valensi P. Are silent coronary stenosis predictable in diabetic patients and predictive of cardiovascular events? Diabetes Metab 2003;29:470-6.
11. Nesto RW, Watson FS, Kowalchuk GJ. Silent myocardial ischemia and infarction in diabetics with peripheral vascular disease: assessment by dipyridamole thallium-201 scintigraphy. Am Heart J 1990;120:1073-7.
12. Doobay AV, Anand SS. Sensitivity and specificity of the ankleebrachial index to predict future cardiovascular outcomes: a systematic review. Arterioscler ThrombVascBiol 2005;25:1463-9.
13. Golomb BA, Dang TT, Criqui MH. Peripheral arterial disease: morbidity and mortality implications. Circulation 2006; 114:688-99.
14. Bhatt DL, Steg PG, Ohman EM. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. JAMA 2006;295:180-9.
15. Pedersen F, Sandre E, Laerkeborg A. Prevalence and significance of an abnormal exercise ECG in asymptomatic males. Outcome of thallium myocardial scintigraphy. Eur Heart j 1991;12(7):766-9.
16. Almeda FQ, Kason TT, Nathan S, Kavinsky CJ. Silent Myocardial Ischemia: concepts and controversies.AM J Med 2004;16:112-8.
17. Janand-Delenne B, Savin B, Habib G, Bory M, Vague P, Lassaman-Vague V. Silent myocardial ischaemia in patients with diabetes. Who to screen. Diabetes Care 1999;22:1396-400.
18. Mariano-Goulart D. Myocardial perfusion imaging and cardiac events in asymptomatic patients with diabetes.Heart Metab. 2007;35:1–4.
19. Bacus HB, Motala AA, Pirie FJ.Screening for asymptomatic coronary artery disease in type 2 diabetes mellitus. April 2008;13(1).
20. Wackers FJT, Zaret BL. Detection of myocardial ischaemia in patients with diabetes mellitus. Circulation 2002;105:5-7.
21. Hendel RC, Patel MR, Kramer CM. criteria for cardiac computed tomography and cardiac magnetic resonance imaging. J Am CollCardiol 2006;48:1475–97.
22. Grundy SM, Howard B, Smith S Jr, Eckel R, Redberg R, Bonow RO. Prevention conference VI: Diabetes and cardiovascular disease. Circulation 2002;105:2231-9.
23. Grundy SM, Benjamin IJ, Burke GL. Diabetes and cardiovascular disease. A statement for health care professionals from the American Heart Association. Circulation 1999;100:1134-46.
24. Chiariello M, Indolfi C. Silent myocardial ischaemia in patients with diabetes mellitus. Circulation 1996;93:2089-91.
25. Nafisi-Moghadam R, Namiaranian N, Karbasi M, Hojat H, Razavi Ratki S K. Assessment of Carotid Intima-Media Thickness and Infra-Renal Abdominal Aorta Diameter in Women with and Without Gestational Diabetes Mellitus-A case Control Study. IJDO. 2015;7(2):50-4

26. Irie Y, Katakami N, Kaneto H. Maximum carotid intima-media thickness improves the prediction ability of coronary artery stenosis in type 2 diabetic patients without history of coronary artery disease. Atherosclerosis 2012;221:438-44.
27. Consensus development conference of the diagnosis of coronary heart disease in people with diabetes. Miami, Fla. Diabetes Care 1998;21(9):1551-9.
28. Oren A, Vos LE, Uiterwaal CS, Grobbee DE, Bots ML. Cardiovascular risk factors and increased carotid intima-media thickness in healthy young adults: the Atherosclerosis Risk in Young Adults (ARYA) Study. Arch Intern Med. 2003;163(15):1787–92
29. Wilson RF, Laughlin DE, Ackell PH, Chilian WM, Holida MD, Hartley CJ. Transluminal, subselective measurement of coronary artery blood flow velocity and vasodilator reserve in man. Circulation 1985;72(1):82-92.
30. Amjad Al Mahameed. Peripheral Arterial Disease. J Vasc Surg 2000;31(l):1-296.
31. Mostaza JM, González-Juanatey JR, Castillo J, Lahoz C, Fernández-Villaverde JM, Maestro-Saavedra FJ. Prevalence of carotid stenosis and silent myocardial ischemia in asymptomatic subjects with a low ankle-brachial index.J VascSurg 2009;49:104-8.
32. Wackers FJ, Young LH, Inzucchi SE. Detection of silent myocardial ischemia in asymptomatic diabetic subjects: the DIAD study. Diabetes Care 2004;27:1954–61.
33. Scognamiglio R, Negut C, Ramondo A. Detection of coronary artery disease in asymptomatic patients with type 2 diabetes mellitus. J Am CollCardiol 2006;47:65–71.
34. Khammash MR, Obeidat KA, El-Qarqas EA. Screening of hospitalized diabetic patients for lower limb ischemia: is it necessary? Singapore Med J 2008;49(2):110-13.
35. Khan TH, Farooqui FA, Niazi K. Critical Review of the Ankle Brachial Index.Current Cardiology Reviews 2008;4(2):101-6.
36. Jue L, Yingyi L, Yawai X, Jingang Y, Liqiang Z, Buaijiaer H et al. Risk factors of peripheral arterial disease and relationship between low Ankle-Brachial Index and mortality from all-cause and cardiovascular disease in Chinese patients with type 2 diabetes. Circ J 2007;71:377-81.
37. Maeda Y, Inoguchi T, Tsubouchi H, Sawada F, Sasaki S, Fujii M et al. High prevalence of peripheral arterial disease diagnosed by low Ankle-Brachial Index in Japanese patients with diabetes, The Kyushu prevention study for atherosclerosis. Diabetes Res ClinPract 2008;17:378-82.
38. Sillesen H, Falk E. Peripheral Artery Disease (PAD) Screening in the Asymptomatic Population: Why, How, and Who?Current Atherosclerosis Reports 2011;13(5):390-5.
39. Tabibiazar R, Steven V. Silent ischemia in people with diabetes: A condition that must be heard. Clinical Diabetes 2003;21:5-9.
40. Yoon JK, Lee KH, Park JM. Usefulness of Diabetic Retinopathy as a Marker of Risk for Thallium Myocardial Perfusion Defects in Non-Insulin-dependent Diabets mellitus. American
41. Valensi P, Parie`s J, Brulport-Cerisier V, Torremocha F, Sachs RN, Vanzetto G, et al. Predictive value of silent myocardial ischemia forcardiac events in diabetic patients: influence of age in a French multicenter study. Diabetes Care 2005;2:2722–7
42. Raggi P, Bellasi A, RattiC. Ischemia imaging and plaque imaging in diabetes: complementary tools to improve cardiovascular risk management. Diabetes Care 2005;28:2787–94