

## Research

### The relationship between HbA1c and carotid intima-media thickness in type 2 diabetic patients

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#### Abstract

**Introduction:** The aim of this study was to investigate the relationship between HbA1c and carotid intima-media thickness (cIMT) which is noninvasive marker of atherosclerosis in type 2 diabetic patients. **Methods:** 81 type 2 diabetic patients were enrolled in this study. Demographic, clinical and laboratory features of the patients were obtained from hospital records. cIMT values were measured by high resolution B-mode ultrasound. Patients were divided into two groups according to cIMT values: cIMT < 0,9 mm group and cIMT ≥ 0,9 mm group. Increased cIMT values were accepted as ≥ 0,9 mm. Then we compared HbA1c and other collected features between normal and increased cIMT groups. **Results:** 69,2% of the patients were female, 30,8% were male. The mean age of the patients were 58,4±10,7 year. The mean HbA1c values of the patients were 8,6±2,03%. The mean cIMT values of the patients were 0,74±0,22 mm. Result with Student T test and ROC curve analysis HbA1c values were'nt different between the groups (p >0.05). **Conclusion:** in this present study we demonstrated that HbA1c could not be a marker for subclinical atherosclerosis in diabetic patients.

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## Introduction

Atherosclerosis is a disease of the arteries that characterized by deposition of plaques of fatty material on their inner walls. It develops over many years. Both micro and macrovascular diabetic complications are associated with atherosclerotic vascular changes. Carotid intima-media thickness (cIMT) is a non invasive indicator of subclinical atherosclerosis that is measured by B-mode ultrasonography and the association between cIMT and atherosclerosis has been showed in many studies [1, 2]. HbA1c is an important glycemic control indicator which demonstrate average three month blood glucose prediction [3]. It shows fluctuating progress in most diabetic patients. For instance it may keep on high for along time and it can return to normal levels with a tight glycemic control in a short time. Thus, while complications occur we can see HbA1c levels in normal range. Thus we established a hypothesis that instant measured HbA1c values should not be related with subclinical atherosclerosis. In this present study we aimed to investigate whether HbA1c values are associated with cIMT which is a non invasive indicator of subclinical atherosclerosis, or not, in type 2 diabetic patients.

## Methods

**Study design:** the study population consisted of 81 patients with type 2 diabetes mellitus. We collected demographic, clinical and laboratory features of 81 patients with diabetes mellitus from hospital records between April 2015 and December 2015. HbA1c values were documented from the hospital records. cIMT were measured by high-resolution real-time ultrasonography (Toshiba Aplio 500). cIMT involves a high-resolution ultrasound imaging of the distance between the lumen-intima interface and the media-adventitia interface, reflecting the arterial wall characteristics. cIMT measurements were carried out from the central part of both common carotid artery and taken of the mean value (Figure 1). Because it can be measured in a relatively simple and noninvasive way, it is well suited for use in large-scale population studies [4]. Normal values for CIMT are difficult to provide because the absolute value also depends on the location of the measurement (segments, near, or far wall), the ultrasound equipment used, and the off-line reading system employed (automated or manual tracings). Generally, more than 0,9 mm values of cIMT are considered abnormal [5]. In this present study we accepted the increased cIMT values as = 0,9 mm. Patients were divided into two groups according to cIMT values: cIMT < 0,9 mm group and cIMT 0,9 mm group. Then we compared collected parameters between these groups.

**Statistical analysis:** all the analyses were performed using the SPSS for Windows (version 21,0;SPSS/IBM, Chicago, IL). Normality was tested by the Kolmogrow-Smirnow Test. The Descriptive statistics, T-test and ROC curve regression analysis were used when suitable. The statistical significance level was accepted as a p value of less than 0.05.

**Ethics and consent:** the patients were screened after the permission was received from Adiyaman University Clinical Research Ethics Committee (2015/3-6; Adiyaman, Turkey).

## Results

69,2% of the patients were female, 30,8% were male. The mean age of the patients were 58,4±10,7 year. The mean HbA1c values of the patients were 8,6±2,03 %. The mean cIMT values of the

patients were 0,74±0,22 mm. The baseline characteristics of the patients are shown in Table 1. The collected parameters were compared between cIMT <0.9 mm group and cIMT =0.9 mm group. The results with the Student's t test no significant correlation was found between cIMT and HbA1c (p >0,05). Mean age of the cIMT <0,9 mm group was 56,08±10,1 and mean age of the cIMT =0,9 mm group was 62,7±10,3. Increased age was significantly associated with increased cIMT values (p <0,01). The results are shown in Table 2. The results with the ROC curve regression analysis no significant correlation was found between cIMT and HbA1c (p >0,05). Increased age was significantly associated with increased cIMT values (p <0,01). The results are shown in Table 3 and Figure 2.

## Discussion

HbA1c, shows presumed blood sugar levels for the last 3 months which is used worldwide as a parameter that determines the level of glycemic control. Complications of diabetes mellitus generally occurs after a long period of 10-15 years. Thus, while complications occur we can see HbA1c levels in normal range. Thus we established a hypothesis that instant measured HbA1c values should not be related with subclinical atherosclerosis. cIMT is accepted as a non-invasive marker of atherosclerosis in recent years [6-13]. Many epidemiological studies established that CIMT is a marker of subclinical atherosclerosis associated with conventional cardiovascular disease (CVD) risk factors. An important condition to use CIMT to predict CVD is to demonstrate that it is associated with both prevalence and incidence of clinical vascular events. A number of longitudinal studies examined the relationship between CIMT and future events, most frequently the incidence of cardiac events (myocardial infarction (MI) and angina pectoris) and cerebrovascular events (stroke or transient ischemic attacks) [5]. Currently over 20 cohort studies performed among subjects with or without previous vascular disease, and with and without CVD risk factors, showed consistently that increased CIMT values is related to increased cardiovascular risk [14]. Although there is a significant association between HbA1c and microvascular complications in diabetic patients, there are very few publications in the literature investigating the relationship between HbA1c levels and atherosclerotic macrovascular complication. In a study conducted on patients with diabetes mellitus by Brohall G et al. they found significantly increased cIMT values in patients with diabetes mellitus compared to healthy subjects [15]. In the studies conducted on on patients with diabetes mellitus by Mukai N et al [16] Huang Y et al [17] Venkataraman et al [18] and Ma X et al [19] they found significant correlation between high HbA1c and increased cIMT. In a study conducted on patients with diabetes mellitus by Du HW et al. they found no significant relationship between HbA1c and cIMT values [20]. Atherosclerotic complications develop after a long period of time in the patients with diabetes mellitus. HbA1c shows presumed blood sugar levels for the last 3 months. Therefore, it may be assumed that correlation between HbA1c and atherosclerosis is unlikely. Indeed, in our study we found no significant relationship between cIMT which is noninvasive marker of atherosclerosis and HbA1c values which is marker of glycemic control. Increased age is the major determinant factor for the macrovascular complications in diabetic patients. So we expect that it also should be associated with cIMT values which is a indirect indicator of the atherosclerosis. As we expect increased age was significantly associated with increased cIMT values in this present study.

## Conclusion

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Our results demonstrated that HbA1c values wasn't associated with subclinical atherosclerosis and increased age was significantly related to the developing atherosclerosis.

### What is known about this topic

- The investigations have demonstrated that HbA1c is associated with the diabetic microvascular complications including nephropathy, retinopathy and neuropathy;
- Carotid intima media thickness is a indicator of the subclinical atherosclerosis;
- The association of the HbA1c and diabetic macrovascular complications including atherosclerosis of the coronary arteries and carotis arteries is controversial.

### What this study adds

- While complications occur we can see HbA1c levels in normal range;
- Macrovascular diabetic complications wasn't associated with HbA1c values in this present study.

## Competing interests

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The authors declare no competing interest.

## Authors' contributions

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SO designed the study. SO, MS and AHB supervised data collection and handling. SO, MS and AHB were responsible for data analysis. SO, MS and AHB assisted with questions and comments throughout the entire process. All authors approved the final version of the manuscript prior to submission.

## Tables and figures

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**Table 1:** Baseline characteristics of the diabetic patients

**Table 2:** Relationship between cIMT and HbA1c

**Table 3:** Result of the analysis of ROC curve

**Figure 1:** Increased intima-media thickness (1,1 mm) at Common Carotid Artery (white arrow) and calcified plaque formation proximal segment of Internal Carotid Artery (black arrow)

**Figure 2:** ROC curve regression analysis for cIMT

## References

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1. Ryden L, Standl E, Bartnik M, Van den Berghe G, Betteridge J, de Boer MJ et al. Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary; The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology ESC and of the European Association for the Study of Diabetes EASD. *Eur Heart J.* 2007; 28(1):88-136. [PubMed](#) | [Google Scholar](#)
2. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. N Engl J Med Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. 1999; 340(1):14-2. [PubMed](#) | [Google Scholar](#)
3. Musenge EM, Manankov A, Mudenda B, Michelo C. Glycaemic control in diabetic patients in Zambia. *Pan Afr Med J.* 2014; 19:354. [PubMed](#) | [Google Scholar](#)
4. 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(4):459-67. [PubMed](#) | [Google Scholar](#)
5. Onut R, Balanescu AP, Constantinescu D, Calmac L, Marinescu M, Dorobantu PM. Imaging Atherosclerosis by Carotid Intima-media Thickness in vivo: How to, Where and in Whom? *Maedica (Buchar).* 2012; 7(2):153-62. [Google Scholar](#)
6. Kota SK, Mahapatra GB, Kota SK, Naveed S, Tripathy PR, Jammula S et al. Carotid intima media thickness in type 2 diabetes mellitus with ischemic stroke. *Indian J Endocrinol Metab.* 2013; 17(4):716-22. [PubMed](#) | [Google Scholar](#)
7. Chen Y, Li YJ, Bian K. Relationship of stroke and carotid intima-media thickness and traditional Chinese medicine intervention progress: a review. *Zhongguo Zhong Yao Za Zhi.* 2014; 39(5):759-64. [PubMed](#) | [Google Scholar](#)
8. Cobble M, Bale B. Carotid intima-media thickness: knowledge and application to everyday practice. *Postgrad Med.* 2010; 122(1):10-. [PubMed](#) | [Google Scholar](#)
9. Zielinski T, Dzielinska Z, Januszewicz A, Rynkun D, Makowiecka Ciesla M, Tyczynski P et al. Carotid intima-media thickness as a marker of cardiovascular risk in hypertensive patients with coronary artery disease. *Am J Hypertens.* 2007; 20(10):1058-64. [PubMed](#) | [Google Scholar](#)
10. Hodis HN, Mack WJ, LaBree L, Selzer RH, Liu CR, Liu CH et al. The role of carotid arterial intima-media thickness in predicting clinical coronary events. *Ann Intern Med.* 1998; 128(4):262-9. [PubMed](#) | [Google Scholar](#)
11. Held C, Hjemdahl P, Eriksson SV, Björkander I, Forslund L, Rehnqvist N. Prognostic implications of intima-media thickness and plaques in the carotid and femoral arteries in patients with stable angina pectoris. *Eur Heart J.* 2001; 22(1):62-72. [PubMed](#) | [Google Scholar](#)
12. Johnsen SH, Mathiesen EB. Carotid plaque compared with intima-media thickness as a predictor of coronary and cerebrovascular disease. *Curr Cardiol Rep.* 2009; 11(1):21-7. [PubMed](#) | [Google Scholar](#)
13. Johnsen SH, Mathiesen EB, Joakimsen O, Stensland E, Wilsgaard T, Løchen ML. Carotid atherosclerosis is a stronger predictor of myocardial infarction in women than in men: a 6-year follow-up study of 6226 persons: the Tromsø Study. *Njølstad I, Arnesen E. Stroke.* 2007; 38(11):2873-80. [PubMed](#) | [Google Scholar](#)
14. O'Leary DH, Bots ML. Imaging of atherosclerosis: carotid intima-media thickness. *Eur Heart J.* 2010; 31(14):1682-9. [Google Scholar](#)

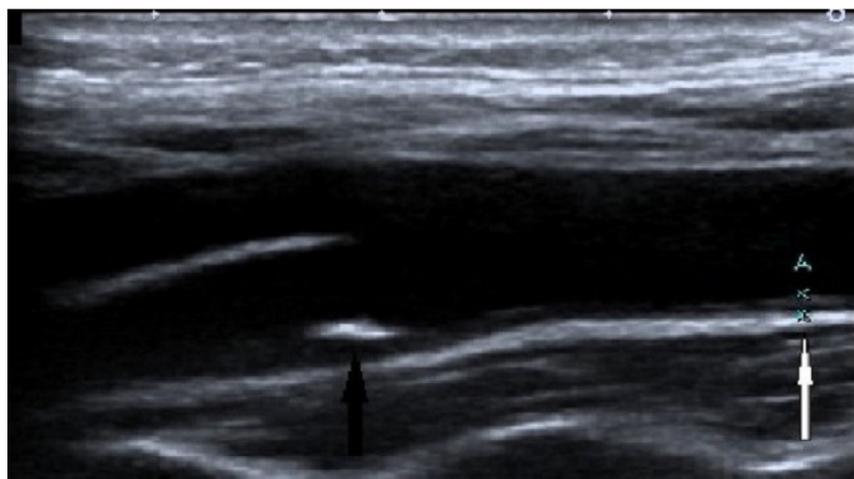
15. Brohall G, Odén A, Fagerberg B. Carotid artery intima-media thickness in patients with Type 2 diabetes mellitus and impaired glucose tolerance: a systematic review. *Diabet Med.* 2006; 23(6):609-16. **PubMed | Google Scholar**
16. Mukai N, Ninomiya T, Hata J, Hirakawa Y, Ikeda F, Fukuhara M et al. Association of hemoglobin A1c and glycated albumin with carotid atherosclerosis in community-dwelling Japanese subjects: the Hisayama Study. *Cardiovasc Diabetol.* 2015; 14:84. **PubMed | Google Scholar**
17. Huang Y, Bi Y, Wang W, Xu M, Xu Y, Li M et al. Glycated hemoglobin A1c, fasting plasma glucose, and two-hour postchallenge plasma glucose levels in relation to carotid intima-media thickness in chinese with normal glucose tolerance. *J Clin Endocrinol Metab.* 2011; 96(9):1461-5. **PubMed | Google Scholar**
18. Venkataraman V, Amutha A, Anbalagan VP, Deepa M, Anjana RM, Unnikrishnan R, Vamsi M, Mohan V. Association of glycosylated hemoglobin with carotid intimal medial thickness in Asian Indians with normal glucose tolerance. *J Diabetes Complications.* 2012; 26(6):526-30. **PubMed | Google Scholar**
19. Ma X, Shen Y, Hu X, Hao Y, Luo Y, Tang J et al. Associations of glycosylated haemoglobin A1c and glycosylated albumin with subclinical atherosclerosis in middle-aged and elderly Chinese population with impaired glucose regulation. *Clin Exp Pharmacol Physiol.* 2015; 42(6):582-7. **PubMed | Google Scholar**
20. Du HW, Li JY, He Y. Glycemic and blood pressure control in older patients with hypertension and diabetes: association with carotid atherosclerosis. *J Geriatr Cardiol.* 2011; 8(1):24-30. **PubMed | Google Scholar**

<b>Table 1:</b> baseline characteristics of the diabetic patients	
Age Mean±SD	58,4± 10,7
Gender Male/Female n%	25 (30,8%)/56 (69,2%)
HbA1c % Mean±SD	8,6±2,03
cIMT [mm] Mean±SD	0,74±0,22

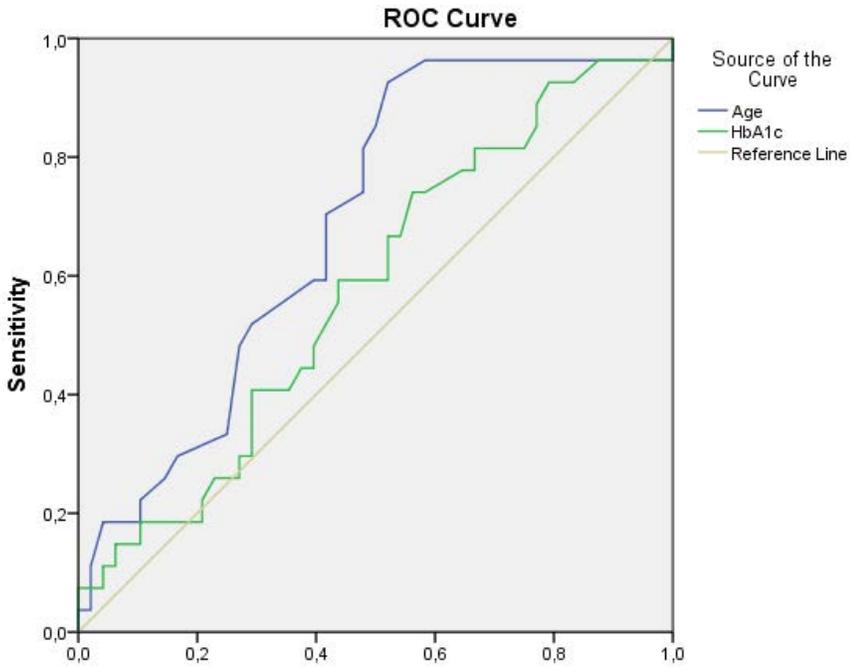
<b>Table 2:</b> relationship between cIMT and HbA1c			
HbA1c %	8,37±1,95	9,03±2,16	0,18
Age	56,08±10,1	62,7±10,3	<b>&lt;0,01</b>

<b>Table 3:</b> result of the analysis of ROC curve*			
	P value	Asymptotic 95% Confidence Interval	
		Lower Bound	Upper Bound
Age	<b>0,007</b>	0,567	0,809
HbA1c%	0,267	0,444	0,711

\*Reference line is <0,9 mm and >0,9 mm for cIMT



**Figure 1:** Increased intima-media thickness (1,1 mm) at Common Carotid Artery (white arrow) and calcified plaque formation proximal segment of Internal Carotid Artery (black arrow)



**Figure 2:** ROC curve regression analysis for cIMT