

## 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 weren't 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 Kolmogorov-Smirnov 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  $58,4 \pm 10,7$  year. The mean HbA1c values of the patients were  $8,6 \pm 2,03$  %. The mean cIMT values of the

patients were  $0,74 \pm 0,22$  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  $56,08 \pm 10,1$  and mean age of the cIMT =0,9 mm group was  $62,7 \pm 10,3$ . 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 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

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

The authors declare no competing interest.

## Authors' contributions

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

**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

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**Table 1:** 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

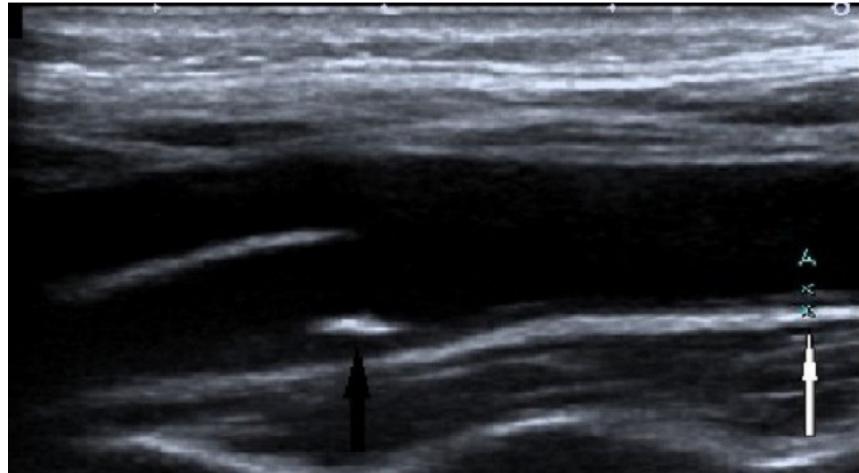
**Table 2:** relationship between cIMT and HbA1c

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>

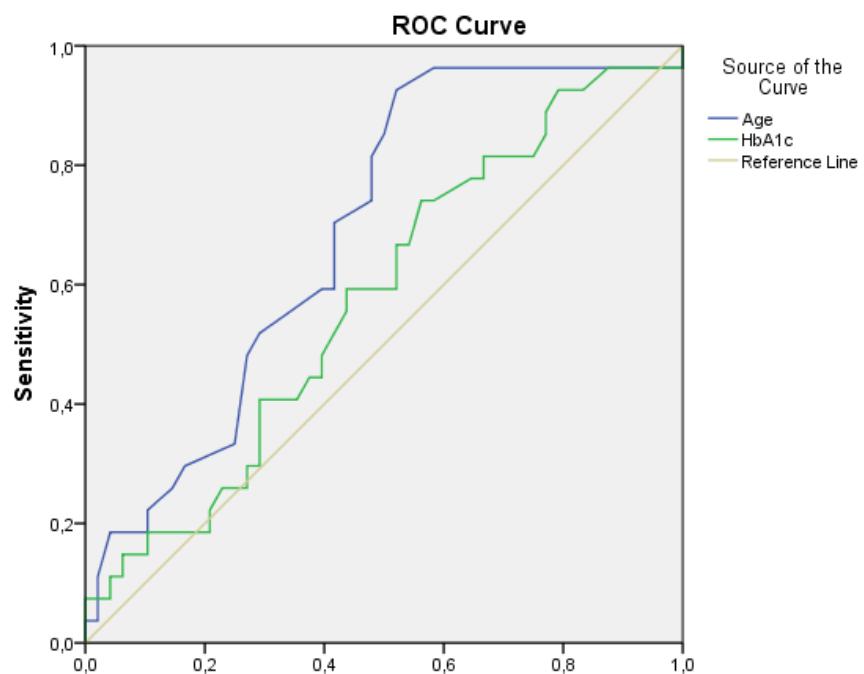
**Table 3:** result of the analysis of ROC curve\*

	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