# The relation of arterial blood pressure and serum lipids to carotid intima-media thickness in patients with type II diabetes mellitus

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*Microvascular and macrovascular complications are the most important causes of the mortality and morbidity in patients with diabetes mellitus. Atherosclerosis is the main mechanism in the genesis of those complications. The diabetes itself causes a risk for atherosclerosis and diabetics may also own a high incidence of other risk factors for atherosclerosis. Thickening of the intima-media complex in great vessels is the first morphologic feature of the atherosclerosis. Thickness of the carotid intima-media serves as an indicator of the carotid atherosclerosis. On the other hand, it gives an useful information about atherosclerotic course at the other regions, too. We evaluated common carotid arteries, because aorta and its branches are the first region which are affected by atherosclerosis and it can be examined easily and non-invasively by B-mode ultrasonography. In this study, we investigated the relation of the arterial blood pressure and serum lipids to the thickness of the carotid intima-media complex in 79 non-insulin-dependent diabetics. We established that the thickness of the carotid intima-media complex increases with the arterial blood pressure and hypertriglyceridemia. In conclusion, the thickness of the carotid intima-media complex can be claimed as a parameter of the atherosclerotic status of diabetics. So, we may recommend that carotid ultrasonography should be performed routinely in all diabetics. [Turk J Med Res 1997; 15(1):32-35]*

**Key Words:** Diabetes mellitus, Diabet complications, Atherosclerosis, Carotid artery intima-media thickness

Diabetes mellitus is a heterogeneous primary disorder of carbohydrate metabolism with multiple etiologic factors that generally involve absolute or relative insulin deficiency or insulin resistance or both. Non-insulin-dependent diabetes mellitus (NIDDM) may be the most rapidly growing chronic disease in the world. Its long-term complications, including retinopathy, nephropathy, neuropathy, and accelerated macrovascular disease causes major morbidity and mortality. Atherosclerosis is the main mechanism in the genesis of the microvascular and macrovascular complications. The diabetes itself causes a risk for atherosclerosis and diabetics may also own a high incidence of other risk factors for atherosclerosis.

Nonenzymatic glycosilation of the proteins play an important role in the genesis of macrovascular complications. Other factors, such as increased oxidative modification of the lipoproteins, dyslipidemia and hyperinsulinemia also can facilitate the development of the macrovascular complications (1-3).

Diabetic macrovascular complications occur gradually and insidiously during course of the disease, and they can be described as accelerated atherosclerotic events. Myocardial infarction, cerebrovascular events or peripheral arterial occlusions in the range of claudication to lower extremity amputation, all of are undesirable outcomes of macrovascular disease (4).

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Because of the aorta and its branches are the first regions affecting from atherosclerosis, thickness of the carotid intima-media is a good indicator for atherosclerotic progression. Thus, thickness of the carotid intima-media is also gives useful information about atherosclerotic course of the other regions.

The purpose of our study is to determine the relation of arterial blood pressure and serum lipids to carotid intima-media thickness (IMT) and to establish whether the IMT is an useful parameter for evaluating peripheral vascular disease or not.

## MATERIALS AND METHODS

This study was carried out between October 1995 and July 1996, and included 79 patients with non-insulin dependent diabetes mellitus (NIDDM). Patients whose fasting blood glucose higher than 140 mg/dl were accepted as diabetic. Those patients have been treating either by oral antidiabetic drugs or insulin. Diabetic patients were accepted as NIDDM according to these criteria:

1- Onset of symptoms after age 30.

2- Positive family history of diabetes mellitus.

3- Clinical background of onset of diabetes.

Patients who were receiving hypolipidemic drugs or calcium channel blockers were excluded from our study.

Carotid ultrasonography (CUS) were performed to all patients with Acuson 128 XP *15* US, before determination of clinical risk factors and complications. Carotid artery was visualised both in transverse and longitudinal planes. In images made in the longitudinal plane, the intima-media complex was seen as a hyperechogenic line separated by the pair of parallel echogenic lines. Distance between the hyperechogenic lines were measured as the IMT. Measurements were done from far-wall of common carotid and 2 cm proximal to bulb. Three measurements (anterolateral, lateral and posterolateral) were done for each common carotid artery, and mean of these values accepted as IMT.

Following CUS, detailed medical history including age, family history of diabetes, duration of diabetes, medications, smoking, symptoms of coronary heart disease were taken and patients underwent complete physical examination. Arterial blood pressure measurement was performed after 20 minutes resting period with the same sfigmomonometer for each patient. Standard 12 leads electrocardiogram were recorded and ishchemia findings noted. Venous blood was drawn from a cubital vein after 12 hour fasting period. Serum cholesterol and triglyceride levels were tested in the same laboratory.

The data were processed by computer using SPSS (Statistical Program for the Social Sciences, Release 6.00). Stem-and-leaf plot was used the normal probability analysis. Results were compared by using a two-sample t-test, variance analysis and Mann-Whitney U test.

### Definition of risk factors

Hyperlipemia: Serum cholesterol and triglyceride levels were evaluated separately and patients divided into subgroups according to cholesterol and triglyceride levels (higher than 200 mg/dl, lower than 200 mg/dl and higher than 150 mg/dl, lower than 150 mg/dl, respectively).

Hypertension: Patients were classified according to systolic and diastolic blood pressures. Systolic blood pressure was divided into 3 groups (lower than 140 mmHg, between 140-159 mmHg and higher than 160 mmHg) and diastolic blood pressure divided into 4 groups (lower than 90 mmHg, between 90-104 mmHg, between 105-114 mmHg and higher than 115 mmHg).

## RESULTS

Patient group was consisted of 47 females (mean age 64.4 ± 9.5 years (range 48 to 88)) and 32 males (mean age 59.7± 6.8 years (range 48 to 70)). The mean age of the all patients were 62.5± 8.8 years (range 48 to 88). Patient distribution according to risk factors was presented in Table 1.

Sixty-eight percent of patients were at the age of 55 to 74 years old. 74.7% were non-smoker. Cholesterol level was up to 200 mg/dl in 57% and triglyceride level up to 150 mg/dl in 50.6%. Systolic blood pressure in 48.1% and diastolic blood pressure in 65.8% were within normal ranges. BMI was within the range of 25 to 30 kg/m$^2$ in 45.6%.

Mean IMT of left and right common carotid arteries according to plasma cholesterol and triglyceride levels were shown in Table 2.

The mean IMT values were about the same and statistically insignificant (p>0.05) in the cholesterol groups But, results were statistically significant in the triglyceride groups for both right IMT (p<0.05) and left IMT (p<0.05).

The relation of systolic and diastolic blood pressure to IMT values was summarised in Table 3.

As shown in table-3, while the relation of systolic blood pressures to mean IMT values were statistically significant (p<0.05), the relation according to diastolic blood pressures were not (p>0.05).

**Table 1.** Patient distribution according to risk factors

| Risk factors | Number of patients (n) | % |
|---|---|---|
| Cholesterol (mg/dl) | | |
| <200 | 34 | 43.0 |
| >200 | 45 | 57.0 |
| Triglyceride (mg/dl) | | |
| < 150 | 39 | 49.4 |
| > 150 | 40 | 50.6 |
| Systolic BP (mmHg) | | |
| <140 | 38 | 48.1 |
| 140-159 | 27 | 34.2 |
| >160 | 14 | 17.7 |
| Diastolic BP (mmHg) | | |
| < 90 | 52 | 65.8 |
| 90-104 | 12 | 15.2 |
| 105-114 | 11 | 13.9 |
| >115 | 4 | 5.1 |
| BMI (kg/m$^2$) | | |
| <25 | 27 | 34.2 |
| 25-30 | 36 | 45.6 |
| >30 | 16 | 20.2 |

**Table** 2. Mean IMT of left and right common carotid arteries according to plasma cholesterol and triglyceride levels

| | IMT of right common carotid | | | IMT of left common carotid | | |
|---|---|---|---|---|---|---|
| Cholesterol levels | Mean + SD | t | P | Mean + SD | t | P |
| < 200 mg/dL. | 0.72 + 0.13 | | | 0.74 + 0.14 | | |
| > 200 mg/dL. | 0.76 + 0.14 | -1.45 | >0.05 | 0.79 + 0.14 | -1.41 | > 0.05 |
| Triglyceride levels | | | | | | |
| < 150 | 0.71 +0.13 | | | 0.73 + 0.14 | | |
| > 150 | 0.78+_0.14 | -2.09 | <0.05 | 0.81+0.13 | -2.45 | < 0.05 |

**Table** 3. The relation of systolic and diastolic blood pressures to mean IMT values

| | IMT of right common carotid | | | IMT of right common carotid | | |
|---|---|---|---|---|---|---|
| Systolic BP(mm Hg) | Mean + SD | Khi-square | P | Mean + SD | Khi-square | P |
| < 140 | 0.73 + 0.15 | | | 0.74 + 0.15 | | |
| 140-160 | 0.70 + 0.09 | | | 0.74 + 0.11 | | |
| >160 | 0.84 + 0.13 | 6.7 | <0.05 | 0.90 + 0.10 | 14.1 | <0.05 |
| Diastolic BP(mm Hg) | | | | | | |
| < 90 | 0.75 + 0.14 | | | 0.76 + 0.14 | | |
| 90-104 | 0.75 + 0.13 | | | 0.79 + 0.13 | | |
| 105-114 | 0.73 + 0.20 | | | 0.76 + 0.16 | | |
| >115 | 0.76 + 0.04 | 0.99 | >0.05 | 0.92 + 0.07 | 5.14 | >0.05 |

## DISCUSSION

Since microvascular complications are responsible for morbidity, the macrovascular complications play the most important role in the increment of mortality in diabetic patients. Macrovascular complications can be described as an accelerated atherosclerosis. Thickness of the intima-media complex in large vessels is the first evidence of atherosclerosis. Thus, measurement of IMT is a useful method to establish the atherosclerosis at subclinical stages. This measurement can be performed easily from common carotids by using B mode US.

We could not establish significant differences between the IMT values of hypercholesterolemic and normocholesterolemic patients. However, Fabris et al had shown that common carotid IMT increases parallel to serum cholesterol levels (7). Of course, increased cholesterol level leads to augmentation of the coronary atherosclerosis risk (8,9). In addition, reduction of cholesterol level, decreases the ischaemic heart disease (IHD) risk in hypercholesterolemic patients (1). On the other hand, a weak relationship between serum cholesterol and transient ischaemic attack and stroke has been established in several studies. In a 8 years duration prospective study, Morris et al established that serum total cholesterol levels and recent myocardial infarction are closely related in diabetic patients. But, in Framingham Study, results were not concordant with Morris et al's findings, and were shown interest to other lipoprotein fractions (10).

In one other study consisting with diabetics, Pujia et al had shown that, patients with carotid atherosclerosis have lower HDL levels than patients without carotid atherosclerosis (6). In addition, Salonen et al. established that, carotid atherosclerosis accelerates with the high level of LDL in patients without diabetes (11). LDL cholesterol is related with both carotid and coronary atherosclerosis (12).

In our study, carotid IMT values in hypertriglyceridemic patients were significantly higher than normotriglyceridemics. Hypertriglyceridemia had been shown as a risk factor of IHD for both IDDM and NIDDM, in several studies (13,14). The increased tendency to atherosclerosis in hypertriglyceridemic diabetics may be related to presence of smaller and dens VLDL particles and to easy penetrance of these particles to subendothelial space (15)

Hypertriglyceridemia or hypercholesterolemia, in general hyperlipidemia is an important risk factor for atherosclerosis. The close relationship between hyperlipidemia and carotid atherosclerosis had been reported by Nauba et al and it is certain that the same result is valid in diabetic patients (5).

The relation of systolic blood pressures to mean IMT values were statistically significant, but the relation according to diastolic blood pressures were not significant. Salonen et al reported the positive correlation between IMT and systolic and diastolic blood pressures (11). Pujia et al have also been established the same results in patients with NIDDM. Hypertension is more commonly seen in diabetics. The increased incidence of hypertension in diabetics may be the result of hyperinsulinemia via increasing sodium reabsorption, sympathetic activity and vascular resistance, etc. (16). On the other hand, insulin also has a vasodilator effect and, this probably, may be explained by the less common combination of hypertension and hyperinsulinemia than expected (17).

In conclusion, the thickness of the carotid intima-media complex can be claimed as a parameter of the atherosclerotic status of diabetics. So, we may recommend that carotid ultrasonography should be performed routinely in all diabetics.


**Tip II diabètes mellitusta vasküler komplikasyonlar ile karotis intima-media kalınlığı arasındaki ilişki**

*Diabetli hastalarda mortalité ve morbiditenin en önemli nedeni mikro ve makrovasküler komplikasyonlardır. Bu vasküler komplikasyonların gelişmesinde temel mekanizma aterosklerozdur. Diabetik kişilerde hem diabetin kendisi bir ateroskleroz risk faktörüdür, hem de diabetiklerde aterosklerozun diğer risk faktörleri daha sık görülmektedir. Büyük damarlarda intima-media kompleksinin kalınlaşması aterosklerozun ilk morfolojik belirtisidir. Karotis intima-media kalınlığı hem karotis aterosklerozu için bir gösterge, hem de diğer bölgelerdeki ateroskleroz için bir habercidir. Çalışmamızda carotis arterlerinin seçilme nedeni aortun dalları olması ve bu arterin B mod US ile kolayca ve non-invaziv bir şekilde görüntülenebilmesidir. Çalışmamızda, 79 NIDDM'li hastada ateroskleroz risk faktörleri ve vasküler komplikas-*

*yonlar ile karotis intima-media kalınlığı arasındaki ilişkiyi inceledik. Çalışmamız sonucunda, mikrovasküler komplikasyon varlığı ile ve vasküler komplikasyon sayısının artışı ile, karotis İMK'nın da arttığını tesbit ettik. Bu sonuçlara göre, karotis İMK diabetik kişilerde kişinin ateroskleroz açısından durumunu belirlemede kullanılabilir bir parametredir ve bu sonuçlarla biz tüm diabetiklere rutin olarak karotis US yapılmasını öneriyoruz. [T Klin Araştırma 1997; 15(1):32-35]*

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