CHARACTERISTICS OF CARDIO-ANKLE VASCULAR INDEX, DOPPLER ULTRASOUND IMAGE OF FEMORAL ARTERY AND PLASMA HOMOCYSTEINE LEVELS IN PATIENTS WITH T2D WITH FOOT ULCERS AT THE NATIONAL HOSPITAL OF ENDOCRINOLOGY

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SUMMARY

Objectives: To characterize the Cardio-ankle vascular index (CAVI), intima-media thickness (IMT) via Doppler ultrasound of the femoral vessels, and plasma homocysteine (Hcy) levels in patients with T2D at the National Hospital of Endocrinology. **Subjects and methods:** A cross-sectional descriptive study on 354 patients with T2D who met the inclusion criteria for the study. **Results:** The mean CAVI, IMT, Hcy in the diabetes group (DIA) with foot ulcer (FU) were higher than the DIA group without FU (CAVI: 9.34 ± 2.29 vs 8.59 ± 2.49; right IMT: 1.80 ± 1.04 vs 1.53 ± 0.96; left IMT: 1.82 ± 1.07 vs 1.45 ± 0.85; Hcy: 1.80 ± 1.04 vs 1.53 ± 0.96, $p < 0.05$). The average CAVI group with hypertension was higher than the group without hypertension. The mean Hcy was higher in men than in women and the hypertension group was higher than in the non-hypertension group (in the DIA group without FU, $p < 0.05$). **Conclusion:** The mean CAVI, IMT, Hcy in the DIA group had higher FU than the DIA group without FU. Blood pressure had an effect on the mean CAVI in both groups. Gender, hypertension have an effect on the average concentration of Hcy in both groups in the DIA group without FU.

* Keywords: Homocysteine; Cardio-ankle vascular index; CAVI; Intima-media thickness; Diabetes mellitus

INTRODUCTION

Over the past three decades, the global number of people with diabetes has quadrupled and it is the ninth leading cause of death. Diabetes and its complications pose a major threat to global health. The International Diabetes Federation (IDF) estimates that in 2015 there were 415 million adults with diabetes, more than 90% with T2D [2]. It is estimated that this may increase to 642 million by 2040 [2]. Early detection of complications, especially vascular complications, is a decisive factor in limiting the harmful effects of complications caused by diabetes.

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Doppler ultrasound of the lower extremity arteries has long been one of the methods of exploration and diagnosis of vascular complications. Ultrasound evaluation of femoral artery morphology examines intima-media thickening and atherosclerosis of artery.

In recent years, many domestic and foreign authors have paid attention to an independent factor that increases the risk of cardiovascular disease, which is plasma Hcy [1]. Cardio-Ankle Vascular Index (CAVI) is an index to evaluate the stiffness of blood vessels recommended by many authors around the world for clinical use because it is a non-invasive method. There have been studies showing that CAVI is increased in diabetic patients, especially those with T2D [3]. Therefore, we conducted this study: *To characterize the ankle vessel index, Doppler ultrasound images of the femoral artery and plasma Hcy levels in patients with T2D with foot ulcers treated at the National Hospital of Endocrinology.*

SUBJECTS AND METHODS

1. Subjects

354 patients diagnosed with T2D who were inpatient treatment at the National Hospital of Endocrinology from November 2014 to present agreed to participate in the study, without any acute illness (shock, stroke, heart attack...) and other chronic diseases, of which 176 patients had FU and 178 patients without FU.

2. Methods

* Study design: Cross-sectional descriptive study.

* Data analysis: Collected data will be cleaned, entered using Epidata 3.1 software and analyzed using SPSS 16.0 software. Statistics including frequencies and ratios are calculated for variables and indicators of interest.

* Study process:

+ Clinical examination, study records making, clinical symptoms of patients registration.

+ Patients were tested for blood count, blood biochemistry, measurement of heart-foot index, lower extremity vascular ultrasound, quantitative plasma Hcy.

+ Select study patients according to criteria. Eligible patients had blood drawn, plasma separated and samples stored at minus 70ºC until Hcy testing.

+ Information and medical records of each patient were recorded in the research medical record.

+ Prepare to summarize data, process and analyze data.

+ Evaluate results and write reports.

RESULTS AND DISCUSSION

In our study, subjects had an average age of 61.9 ± 11.1 years for the DIA group with FU vs. 60.0 ± 11.5 years for the DIA group without FU. The age group of 50 - 69 years old accounted for the highest percentage (60.6% for the DIA group with FU and 66.3% for the DIA group without FU), the lowest in the group under 40 years old.

The DIA group with FU was 40.3% female and 59.7% male; The DIA without FU group was 61.2% female and 38.8% male. Although there was a difference in gender, this was not statistically significant.

The proportion of DIA patients with FU tended to have a longer disease duration than the group of DIA patients without FU. The difference was statistically significant ($p < 0.05$).

DIA patients with FU has a higher rate of hypertension than the group of DIA patients without FU (65.3% vs. 42.1%), the difference was statistically significant.

Table 1: Average CAVI index, lower extremity intima-media thickness, Hcy concentration of 2 DIA groups with foot ulcer and without foot ulcer (n = 354).

Index	DIA with FU $\overline{X} \pm SD$	DIA without FU $\overline{X} \pm SD$	p
Mean CAVI	9.34 ± 2.29	8.59 ± 2.49	< 0.05
Right femoral IMT	1.80 ± 1.04	1.53 ± 0.96	< 0.05
Left femoral IMT	1.82 ± 1.07	1.45 ± 0.85	< 0.05
Hcy levels	11.12 ± 4.73	9.63 ± 5.10	< 0.05

In our study, the mean CAVI in the DIA group with FU was higher than in the DIA group without FU ($p < 0.05$). This result is similar to the study of Mehmet et al. [4] (8.22 ± 0.18 m/s in diabetes patients vs. 7.59 ± 0.17 m/s in the control group). In 2019, Park So Young et al. conducted a retrospective study on 219 patients with T2D, obtained an average CAVI result of 8.2 ± 1.4, in which the majority of patients had CAVI < 8 (47.0%); 28.3% of patients had a CAVI of 8 to less than 9 and 24.7% of patients had a CAVI of 9 or more [5].

According to our study result, the mean values of right femoral artery IMT and left femoral artery IMT were similar in each group of DIA with FU and DIA without FU, however there was a difference between the 2 groups. This result was similar to that of Nguyen Cong Hung in 66 patients with type 2 DIA at the Central Endocrinology Hospital, with right femoral IMT1.62 ± 0.74 mm, left femoral IMT 1.56 ± 0.68 mm, in a meta-analysis by Lorenz in which mean arterial thickness fluctuated from 0.72 to 0.97 mm in the DIA group [6].

According to the results of our study, the mean blood Hcy concentration in the DIA group with FU was higher than that in the DIA group without FU ($p < 0.05$). In 2017, Ala O.A research found that the Hcy concentration in patients with DIA type 2 was higher than that in the control group (DIA group 27.4 ± 12.1 vs control group 8.21 ± 3.2), and also indicated that the concentration Hcy level is a potential cardiovascular risk marker for patients with DIA [7]. In 2020, Alexander et al. [8] studied and found that the concentration of Hcy in the DIA group was 13.53 ± 6.6 at the time before the study and 13.87 ± 5.6 at the time of the study. In the same study, the authors found that elevated plasma Hcy level was a risk factor for cardiovascular disease, which seems to be the main cause of increased mortality in patients with type 2 DIA.

Table 2: Comparison of CAVI levels between study groups.

CAVI value	DIA with FU (n = 176)		DIA without FU (n = 178)		Comparision (p)
	n	%	n	%	
< 8	33	19.0	56	31.8	
8 ≤ CAVI < 9	31	17.8	38	21.6	p < 0.05
≥ 9	110	63.2	82	46.6	

In this study, the majority of patients had a CAVI index of 9 or higher. The proportion of subjects with CAVI ≥ 9 of the DIA group with FU (63.2%) was higher than that of the DIA group without FU (46.4%) (p < 0.001). Our results are higher than that of author Kim Kwang Joon, who studied 320 patients with DIA type 2; 20% of patients increased CAVI (≥ 9) [9].

Table 3: Average CAVI index by gender and hypertension of study subjects.

CAVI index	DIA with FU (n = 176)	DIA without FU (n = 178)
	$\overline{X} \pm SD$	$\overline{X} \pm SD$
Gender		
Male	9.41 ± 2.24	8.81 ± 2.35
Female	9.24 ± 2.37	8.46 ± 2.59
p	> 0.05	> 0.05
Hypertension		
Yes	9.85 ± 2.15	9.18 ± 2.27
No	8.37 ± 2.25	8.16 ± 2.58
p	< 0.05	< 0.05

In our study, the mean CAVI in men was not much different from that of women. Similar results were reported by author Yusuke Mineoka et al in 2012 on 371 DIA type 2 patients with clinical suspicion of coronary artery disease, showing that the mean CAVI in men was 8.9 ± 1.7 vs. 8.7 ± 1.5 in women, the difference was not statistically significant [10].

In this study, the mean CAVI in the group with hypertension was higher than the group without hypertension in both the DIA group with FU and the DIA without FU (p < 0.05). This result was similar to the study of Yusuke Mineoka et al., with the mean CAVI in hypertension and non-hypertension groups of 9.3 ± 1.6 vs 8.3 ± 1.5, respectively (p < 0.0001). Furthermore, correlation analysis demonstrated that age, systolic blood pressure, and fasting blood glucose were independent variables related to CAVI (age: r = 0.509, p < 0.001; systolic blood pressure: r = 0.392, p < 0.001; fasting blood sugar: r = 0.319, p = 0.001).

Table 4: Average Hcy concentrations by gender and hypertension of study subjects.

Homocysteine characteristics	DIA with FU (n = 176)	DIA without FU (n = 178)
	$\overline{X} \pm SD$	$\overline{X} \pm SD$
Gender		
Male	12.12 ± 5.43	11.09 ± 7.23
Female	9.63 ± 2.87	8.72 ± 2.74
p	< 0.001	< 0.01
Hypertension		
Yes	11.31 ± 4.82	10.79 ± 5.38
No	10.74 ± 4.55	8.79 ± 4.73
p	> 0.05	< 0.05

On average, Hcy concentrations were higher in men than in women in both groups: the DIA group with FU; DIA group without FU. This is consistent with the results reported by Cohen et al. [11]: the group of patients under 55 years of age, Hcy concentration in men was 12.6 ± 6.3 higher than in women with 9.4 ± 3.1; similar in the group of over 55 years old: Hcy concentration in men was 12.6 ± 4.5 higher than in women with 10.5 ± 3.2. This result may be due to the fact that men have some habits that are not common in women, such as smoking, alcohol abuse, coffee addictive, etc.., which are related factors that reduce folate absorption, which can increase blood Hcy by mediating effect on the balance of vitamins B6, B12, and folate in the body.

The relationship between Hcy levels and hypertension is still controversial. According to some studies, systolic BP showed a significant positive correlation with Hcy (r = 0.239, p = 0.007) [12] but some studies have not detected this correlation. In DIA group without FU, the average Hcy concentration in the hypertensive group was higher than in the non-hypertensive group.

CONCLUSION

The average CAVI index, femoral IMT, and Hcy concentration in the DIA group with FU were higher than those in the DIA group without FU.

The average CAVI index of the DIA with hypertension group was higher than that of the non-hypertension DIA group.

Homocysteine concentrations of men were higher than women's, and the DIA group with hypertension was higher than the DIA group without hypertension in the DIA group without FU.

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