

## DOPPLER TISSUE VELOCITY SAMPLING FOR THE EARLY DETECTION OF MYOCARDIAL DYSFUNCTION IN DIABETIC PATIENTS

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**Summary.** *The aim of the study was to analyze the value of the Doppler tissue imaging (DTI) method in the early detection of myocardial dysfunction in diabetic patients.*

*Thirty-two patients with type 2 diabetes and twenty-five non-diabetic control subjects without clinical signs of coronary artery disease and with normal global left ventricular function by standard 2D echocardiography, were investigated with pulsed wave DTI at rest and after exercise stress echocardiography (ESE). Myocardial function was calculated as mean value from five basal left ventricular segments for the peak velocity at systole (Vs), early diastole (Ve), atrial contraction (Va) and ratio Ve/Va.*

*Compared to controls diabetic patients had a compromised Ve at rest ( $P < 0.01$ ). Their resting Va was higher ( $P < 0.02$ ), ratio Ve/Va lower ( $P < 0.001$ ) and Vs less (NS) than in the control group. After ESE in patients with diabetes Ve increased by 17.6%, Va by 11.8%, ratio Ve/Va by 6.6% and Vs by 14.6% compared to baseline values. In the control group changes in myocardial function induced by ESE were more pronounced: Ve increased by 34.3%, Va by 15.8%, ratio Ve/Va by 15.4% and Vs by 37.8%. Impaired response of myocardial function during ESE in diabetic patients resulted to more significant difference in Ve ( $P < 0.001$ ) and significant difference in Vs ( $P < 0.001$ ) between diabetic patients and controls after ESE.*

*In conclusion, patients with type 2 diabetes have early signs of predominant diastolic and also systolic myocardial dysfunction which are more expressed during ESE. Those signs can be identified by quantitative DTI before appearance of clinical signs of cardiovascular disease.*

**Key words:** *Diabetes mellitus, myocardial function, Doppler tissue imaging, stress echocardiography*

### Introduction

Diabetes is a chronic disease with high cardiovascular morbidity and mortality. Approximately 150 million worldwide are suffering from this condition and the number is expected to rise to 300 million by 2025 (1). Although there has been considerable improvement in managing patients with cardiovascular disease, rapid expansion of diabetes mellitus can increase incidence and prevalence of impaired cardiovascular function.

Myocardial dysfunction in patients with diabetes may be a consequence of diabetic cardiomyopathy and is an important factor for the poor prognosis. Accordingly early detection of myocardial dysfunction among diabetics is extremely important for implementing therapeutic strategies and to improve prognosis.

There are still many unresolved issues in the assessment of myocardial function through the progressive stages of diabetics heart disease and myocardial damage. During the past years, with rapidly evolving technologies in the area of non-invasive assessment of myocardial function Doppler tissue imaging (DTI) has gained broad acceptance. Doppler tissue imaging has the potential to analyze quantitatively the myocardial wall performance,

and can bring new insights into the understanding of the pathophysiology of heart disease (2).

This study analyzes the value of the DTI method in the early detection of myocardial dysfunction in diabetic patients.

### Methods

#### Patients

We studied 32 patients with type 2 diabetes (11 female and 21 males, mean age  $56.3 \pm 7.3$  years; mean duration of diabetes  $7.2 \pm 3.7$  years) and 25 non-diabetic control subjects (9 female and 16 males, mean age  $53.8 \pm 8.1$  years) without any clinical signs of coronary artery disease and with normal global left ventricular function. Arterial hypertension was present in 8 (25%) diabetic patients and in 5 (20%) non-diabetic control subjects. Left ventricular mass index was in normal range in both groups. Patients were instructed not to take medications, except for glycaemic control, 24 hours before investigation. The study protocol was approved by the hospital Ethics Committee and all patients gave informed consent.

**Exercise stress echocardiography.** After obtaining a baseline electrocardiogram and echocardiogram (Acuson-Sequoia C256, Mountain View, CA, USA, harmonic mode) in all subjects, sub-maximal or symptom limited bicycle exercise test was performed. Exercise was begun with a 25 W work-load that was then increased by 25 W every 4 min. Before, during and up to 10 min. after exercise continuous 12-lead electrocardiogram and two-dimensional echocardiogram in the apical 4-5 and 2 chamber views were monitored. At each stress step electrocardiogram, blood pressure and digital acquisition of echocardiographic images were recorded. Using side-by-side display on cine-loops before and after exercise stress echocardiography (ESE) left ventricular wall motion analysis was performed. Standard end points for ESE were used (3).

### Doppler tissue imaging

At baseline and at peak stress in all subjects pulsed wave DTI (PW-DTI) studies were performed using apical transthoracic echocardiographic Doppler spectrum. PW-DTI recording was obtained by positioning a sample volume in each basal left ventricle wall segment. Myocardial velocity was then detected throughout each cardiac cycle and displayed in the graphic format of Doppler spectrum. For each segment, a frozen image of the PW-DTI signals from three consecutive cardiac cycles was obtained at the end of datum acquisition sequence for off-line analysis. The peak myocardial velocity at systole (Vs), early diastole (Ve) and atrial contraction (Va) were measured and ratio Ve/Va was calculated. The final value of regional systolic and diastolic myocardial function, which also represent the global myocardial function, was calculated as a mean value from five basal left ventricular segments for the peak Vs, Ve, Va and ratio Ve/Va.

### Results

The standard M-mode and two-dimensional echocardiograms were normal in both groups. During ESE, electrocardiographic and/or echocardiographic markers of myocardial ischemia were not detected neither in diabetic patients nor in control subjects. Myocardial velocities were measured in 252 basal left ventricular segments: 140 (87.5%) segments in diabetic patients and 112 (89.6%) segments in control group.

Compared to controls diabetic patients had a compromised Ve at rest ( $P < 0.01$ ). Their resting Va was higher ( $P < 0.02$ ) and the ratio Ve/Va lower ( $P < 0.001$ ) than in the control group. Value of Vs at rest was lower in diabetic patients than in controls, but the difference was not significant (Table 1).

Table 1. Baseline values of PW-DTI parameters of basal left ventricular segments in diabetic patients and in control subjects

Parameters	Diabetic patients	Controls	P
Ve cm/s	$9.50 \pm 3.60$	$9.60 \pm 2.90$	0.01
Va cm/s	$9.30 \pm 3.40$	$8.20 \pm 3.30$	0.02
Ve/Va	$0.91 \pm 0.36$	$1.17 \pm 0.35$	0.001
Vs cm/s	$8.90 \pm 3.70$	$9.50 \pm 3.40$	NS

Ve – peak early diastolic velocity; Va – peak velocity during atrial contraction; Ve/Va ratio; Vs – peak systolic velocity

After ESE in patients with diabetes Ve increased by 17.6% Va by 11.8%, ratio Ve/Va by 6.6% and Vs by 14.6% compared to baseline values (Figure 1).

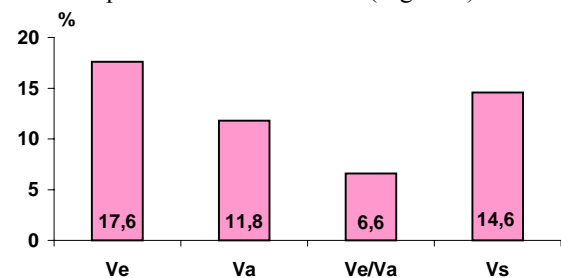


Fig. 1. Changes in myocardial velocities of basal left ventricular segments in diabetic patients induced by ESE

Ve – peak early diastolic velocity; Va – peak velocity during atrial contraction; Ve/Va ratio; Vs – peak systolic velocity

In the control group changes in myocardial function induced by ESE were more pronounced: Ve increased by 34.3%, Va by 15.8%, ratio Ve/Va by 15.4% and Vs by 37.8% (Figure 2).

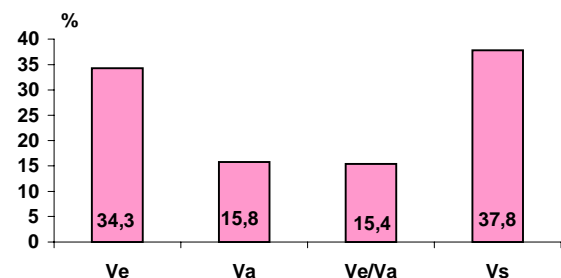


Fig. 2. Changes in myocardial velocities of basal left ventricular segments in controls induced by ESE

Ve – peak early diastolic velocity; Va – peak velocity during atrial contraction; Ve/Va ratio; Vs – peak systolic velocity

After ESE, difference in Vs between diabetic patients and controls become significant and the difference in Ve was more significant than before ESE (Table 2).

Table 2. Values of PW-DTI parameters after ESE of basal left ventricular segments in diabetic patients and in control subjects

Parameters	Diabetic patients	Controls	P
Ve cm/s	$10.00 \pm 3.50$	$12.90 \pm 3.70$	0.001
Va cm/s	$10.40 \pm 3.20$	$9.50 \pm 3.30$	0.05
Ve/Va	$0.97 \pm 0.39$	$1.35 \pm 0.40$	0.001
Vs cm/s	$10.20 \pm 4.20$	$13.10 \pm 3.90$	0.001

Ve – peak early diastolic velocity; Va – peak velocity during atrial contraction; Ve/Va ratio; Vs – peak systolic velocity

## Discussion

Patients with diabetes are at a greater risk of cardiovascular disease than individuals who are not diabetic, and they suffer significantly greater rates of cardiovascular mortality (4). Cardiovascular disease accounts for up to 80% of mortality in patients with type 2 diabetes and the age-adjusted relative risk of cardiovascular death is three times greater in these patients than in the general population (5). It has been demonstrated that cardiovascular risk increases before the onset of diabetes (6,7). Diabetes is associated, not just with increased cardiovascular disease, but also with a worse outcome. One reason for this appears to be enhanced myocardial dysfunction leading to diabetic cardiomyopathy which predispose patients to congestive heart failure (8). Several factors probably underline this condition: chronic hyperglycemia, severe coronary atherosclerosis, microvascular disease, prolonged hypertension, glycosylation of myocardial proteins and autonomic neuropathy. According to all, early detection of clinical and subclinical cardiovascular disease in diabetic patients has important therapeutic and prognostic implications.

Stress echocardiography and DTI are the most-effective imaging techniques for assessing myocardial function and ischemia in hyperglycaemic asymptomatic patients (9,10). Our results confirm that PW-DTI is a useful method in the quantification of regional myocardial velocity and that measurement of regional myocardial function can identify the presence of myocardial dysfunction in basal condition as well as during ESE. We showed significantly lower baseline values of  $V_e$  and ratio  $V_e/V_a$ ; higher  $V_a$  and lower  $V_s$  in diabetic patients than in control subjects. Our results for baseline peak myocardial velocity at early diastole and atrial contraction as well as for ratio  $V_e/V_a$  in diabetic patients reproduced values of the same parameters found by Thrainsdottir et al (10).

In our study the significantly lower basal  $V_e$  and ratio  $V_e/V_a$  in diabetic patients indicate the presence of diastolic myocardial dysfunction. Gustafsson and Hildebrandt have shown recently that diastolic filling abnormalities are common in patients with type 2 diabetes, which may represent early subclinical alterations in cardiac function (11).

In the present study we demonstrated increases in  $V_e$ ,  $V_a$ ,  $V_s$  and ratio  $V_e/V_a$  during ESE in both examined groups, but the rate of those changes was more favorable in controls than in diabetic patients. Impaired response of myocardial function during ESE in diabetic patients resulted to more significant difference in  $V_e$ , and significant difference in  $V_s$  between two examined groups, after ESE. Our results are similar to those reported by Thrainsdottir et al (10), who described the use of PW-DTI in diabetic patients during dobutamine/dipyridamole stress echocardiography.

The results of this study emphasized the value of Doppler tissue velocity sampling for the assessment of myocardial function in patients with type 2 diabetes mellitus. Early detection of impaired myocardial function using PW-DTI, signals the need for institution of more aggressive preventive measures in diabetic patients with subclinical cardiovascular disease.

## Conclusion

In the evaluation of myocardial function, PW-DTI is an important step in the effort to objectively assess early signs of myocardial dysfunction.

Quantitative PW-DTI in type 2 diabetic patients identified early signs of predominant diastolic and also systolic myocardial dysfunction.

Application of stress echocardiography with PW-DTI increases the diagnostic capacity of DTI in detection of myocardial impairment in diabetic patients with subclinical cardiovascular disease.

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## TKIVNI DOPPLER U RANOJ DETEKCIJI MIOKARDNE DISFUNKCIJE KOD BOLESNIKA S DIJABETESOM

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**Kratak sadržaj:** Cilj studije bio je analiza značaja metode tkivnog Dopplera (DTI) u ranoj detekciji miokardne disfunkcije kod bolesnika s dijabetesom tipa 2.

Tridesetdva bolesnika s dijabetesom tip 2 i dvadesetpet osoba bez dijabetesa, bez kliničkih znakova za koronarnu bolest i sa normalnom globalnom funkcijom leve komore na standardnom 2D ehokardiogramu, ispitivano je primenom pulsnog tkivnog Dopplera (PW DTI) pre i posle stres ehokardiografskog testa fizičkim opterećenjem (ESE). Miokardna funkcija izračunata je kao srednja vrednost maksimalne miokardne brzine iz pet bazalnih segmenata leve komore u sistoli ( $V_s$ ), ranoj diastoli ( $V_e$ ), tokom atrijalne kontrakcije ( $V_a$ ) i odnosa  $V_e/V_a$ .

U poredjenju sa kontrolnom grupom bolesnici s dijabetesom, pre ESE, imali su manju vrednost  $V_e$  ( $P < 0,01$ ), veću vrednost  $V_a$  ( $P < 0,02$ ), manji odnos  $V_e/V_a$  ( $P < 0,001$ ) i manju vrednost  $V_s$  (NS). Posle ESE, u bolesnika s dijabetesom registrovano je povećanje  $V_e$  za 17,6%,  $V_a$  za 11,8%, odnosa  $V_e/V_a$  za 6,6% i  $V_s$  za 14,6% u odnosu na vrednosti pre ESE. U kontrolnoj grupi, promene u miokardnoj funkciji tokom ESE bile su izraženije:  $V_e$  je povećano za 34,3%,  $V_a$  za 15,8%, odnos  $V_e/V_a$  za 15,4% i  $V_s$  za 37,8%. Smanjen odgovor miokardne funkcije tokom ESE kod bolesnika s dijabetesom, uslovio je povećanje značajnosti razlike u vrednosti  $V_e$  ( $P < 0,001$ ) i značajnu razliku u vrednosti  $V_s$  ( $P < 0,001$ ) između bolesnika s dijabetesom i ispitanika kontrolne grupe posle ESE.

Naša studija je pokazala da bolesnici s dijabetesom tip 2 imaju rane znake dominantno dijasolne, a takodje i sistolne disfunkcije miokarda, što se potencira tokom ESE. Ovi znaci mogu se detektovati kvantifikacijom miokardnih brzina primenom DTI, pre pojave kliničkih znakova kardiovaskularnog oboljenja.

**Ključne reči:** Dijabetes, miokardna funkcija, tkivni Doppler, stres ehokardiografija