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● *Original Contribution*

LEFT VENTRICULAR ENERGY LOSS ASSESSED BY VECTOR FLOW MAPPING IN PATIENTS WITH PREDIABETES AND TYPE 2 DIABETES MELLITUS

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Abstract—The aim of this study was to assess left ventricular (LV) energy loss (EL) using vector flow mapping in patients with prediabetes (pre-DM) and type 2 diabetes mellitus (DM). Thirty pre-DM patients, 51 DM patients, and 38 controls were studied by transthoracic echocardiography. EL-total, EL-base, EL-mid and EL-apex climaxed at different phases. Compared with controls, pre-DM and DM patients showed increased EL-total during slow ejection, isovolumic relaxation, rapid filling and slow filling ($p < 0.05$). Similarly, EL-base, EL-mid and EL-apex increased during certain phases. Stepwise multiple regression analysis revealed that the early transmitral valve blood flow velocity E, the late transmitral valve blood flow velocity A, the ratio of E/A, LV peak torsion, diastolic untwisting velocity, vortex circulation and area were independently associated with EL during different phases (all $p < 0.05$). Our study suggests that LV EL is increased during diastole and certain phases of systole in DM patients compared with controls. The changes in LV vortex and deformation mechanics were correlated with EL. (E-mail: zhangmeidaixh@163.com) © **2016 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Diabetes mellitus, Energy loss, Left ventricle, Echocardiography, Vector flow mapping.**

INTRODUCTION

Cardiovascular disease is the leading cause of death among patients with diabetes mellitus. Elevated glucose levels are thought to induce hyperglycemia-mediated coronary microvascular dysfunction, resulting in myocardial injury (Di Carli et al. 2003; Selvin et al. 2014; Wallace et al. 2006). Previous studies have demonstrated that patients with prediabetes (pre-DM) or diabetes mellitus (DM) have an increased prevalence of atherosclerosis (Folsom et al. 1994; Moebus et al. 2009). However, impaired glucose metabolism often remains undiagnosed until a serious cardiovascular complication exposes the disease. Estimates predict that 40%–50% of individuals with pre-DM will develop type 2 DM within 10 years, highlighting the importance of early detection of abnormal glucose metabolism. Preventing the progression of pre-DM to type 2 DM can delay the occurrence of macrovascular and microvascular complications (Stratton et al. 2000). Most studies on this topic have focused on left ventricular (LV) function and mechanics in DM using tissue Doppler imaging or speckle-tracking imaging techniques (Ernande et al. 2014; von Bibra et al. 2015). However, blood flow dynamics in the left ventricle have not been quantitatively evaluated.

Blood flow patterns are shaped by the morphology and function of the cardiovascular system, and they reveal the exceptional adaptability of the cardiovascular system for maintaining relatively constant blood circulation under a wide range of workloads. Current approaches for blood flow visualization are primarily based on cardiac magnetic resonance (CMR), vector flow mapping (VFM) and contrast particle imaging velocimetry (PIV) (Sengupta et al. 2012). The temporal resolution of CMR is low because it requires a relatively long time for dataset collection. Compared with CMR, PIV exhibits superior temporal resolution, but high blood flow velocities can be underestimated, and the technique requires a contrast medium. By contrast, VFM is a novel technique for displaying velocity vectors of flow using color Doppler imaging, and the accuracy of velocity vectors computed using VFM has been

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verified relative to PIV values (Uejima et al. 2010). Energy loss (EL) is a flow dynamic parameter derived from the intraventricular flow velocity vector field, which can be calculated by VFM. The principles of how VFM measurements of blood flow velocity can be used to determine EL due to viscous friction have been described in detail (Stugaard et al. 2015). EL can be high if there are rapid changes in vorticity (high pulsatility) or if many small vortices interact (turbulence). In other words, a single large and steady vortex is an energetically favorable condition, whereas splitting the bloodstream into smaller rapidly changing vortices is unfavorable. Importantly, in the latter scenario, kinetic energy is lost, which needs to be replaced by the ventricular musculature (Batchelor 1953).

Recently, a study demonstrated that left ventricular deformation is significantly impaired in type 2 DM patients (Tadic et al. 2014). In the heart, blood flow patterns can be modified by valves, chamber geometry and the motions of the walls to produce hemodynamic environments that are either normal or pathological. Therefore, we hypothesized that blood flow patterns and EL due to viscous friction should be altered by changes in left ventricular geometry and myocardial mechanics.

The aim of this study was to use the new technique of VFM to quantify EL and early hemodynamic changes within the left ventricle in individuals with impaired glucose metabolism.

MATERIALS AND METHODS

This cross-sectional study included 30 normotensive subjects with pre-DM (blood pressure $<$140/90 mm Hg), 51 recently diagnosed normotensive patients with type 2 DM and 38 controls with similar age and sex distributions. Pre-DM was diagnosed if fasting plasma glucose levels were between 5.6 and 6.9 mmol/L (impaired fasting glucose, IFG), glycated hemoglobin (HbA1c) levels were between 5.7 and 6.4% or blood glucose levels during an oral glucose tolerance test (OGTT) after two hours were between 7.8 and 11.0 mmol/L (impaired glucose tolerance, IGT) (American Diabetes Association 2014). DM was diagnosed if fasting plasma glucose levels were $\geq$7 mmol/L, HbA1c levels were $\geq$6.5% OGTT plasma glucose levels after 2 hours were $\geq$11.1 mmol/L or a random plasma glucose level was $\geq$11.1 mmol/L (American Diabetes Association 2014). Subjects were classified into the control, pre-DM or DM categories if one or more criteria were satisfied. Exclusion criteria included arterial hypertension, angina pectoris, heart failure, myocardial infarction, significant valvular disease, atrial fibrillation, rheumatic diseases, congenital heart disease, obesity (body mass index $\geq$30 kg/m^2), asthma, chronic obstructive pulmonary disease, neoplastic disease, cirrhosis of the liver and kidney failure.

Body weight and height were measured, and body mass index was calculated as weight (kg) divided by height (m^2). Blood pressure was measured using a calibrated sphygmomanometer after the subject had rested in the supine position for at least 10 min. Laboratory analyses (fasting plasma glucose or OGTT plasma glucose levels after 2 hours, total cholesterol, triglycerides, high-density lipoprotein and low-density lipoprotein levels) were performed for all subjects. Venous blood samples were drawn from the antecubital vein the morning after an overnight fast. We were unable to measure HbA1c levels in every participant.

The study was approved by the medical Ethics Committee of Shandong Chest Hospital of Shandong University, and written informed consent was obtained from all participants.

Echocardiography

Conventional echocardiographic examinations were performed using a UST-52105 probe (1–5 MHz) mounted on a ProSound F 75 ultrasound device (Hitachi Aloka Medical Ltd., Tokyo, Japan) for all subjects. All echocardiographic readings were performed by experienced sonographers. The values for all 2-D echocardiographic parameters are the average of three consecutive cardiac cycles. Left ventricle morphology, conventional systolic parameters and diastolic parameters were also analyzed.

Left ventricular end-diastolic diameters, left ventricular posterior wall thickness and interventricular septal thickness were determined according to current recommendations (Lang et al. 2015). Left ventricular ejection fraction was calculated using biplane Simpson's method. Transmitral Doppler flow was recorded in apical four-chamber view by placing the sample volume at the tip of the mitral leaflets to measure early filling and late filling peak wave velocities and deceleration time. Isovolumic relaxation time was derived by placing the cursor of the pulse wave Doppler in the left ventricular outflow tract to simultaneously observe the end of aortic ejection and the onset of mitral inflow. Peak e, a and s waves were measured by Doppler tissue imaging on the lateral side in apical four-chamber view. We measured flow propagation velocity using color Doppler imaging with an M-mode cursor placed through the center of the transmitral flow. Aliasing velocity was set to 40%–50% of the early filling wave (Seo et al. 2004). The ratio of early filling to propagation velocity is directly proportional to left atrial pressure and can be used to predict left ventricular filling pressure (Nagueh et al. 2009).

Images for flow visualization were acquired in VFM mode in an apical three-chamber view, and the image width, depth and spatial-temporal settings were set to obtain the highest possible frame rate while including the entire left ventricle, mitral and aortic valves in the color-scan area. The Nyquist limit for 2-D color Doppler