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Diabetes & Metabolism 42 (2016) 256–262

Original article

Bone mineral density is associated with left ventricular diastolic function in men with type 2 diabetes

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Received 9 October 2015; received in revised form 4 February 2016; accepted 15 February 2016
Available online 10 March 2016

Abstract

Aims. – Type 2 diabetes (T2DM) is associated with chronic heart failure and cardiomyopathy. Furthermore, low bone mineral density (BMD) predicts incident heart failure. Abnormal diastolic function reflects early changes in cardiac function and plays a key role in the development of heart failure. The purpose of this study was to investigate the association between BMD with left ventricular (LV) diastolic function in men with T2DM.

Methods. – In all, 344 men with T2DM and 331 age-matched control subjects were enrolled. BMD measurements were performed. LV diastolic function and structure were assessed by echocardiographic evaluation.

Results. – BMD was lower in men with T2DM than in controls. There were significant differences in the level of parameters reflecting cardiac structure and LV diastolic function between two groups. Moreover, LV diastolic function and structure parameters also showed significant differences as BMD reduced in T2DM group. BMD at femoral neck was correlated with LV diastolic function parameters in T2DM after adjusting for confounding factors. Multivariable logistic analysis revealed that osteopenia and osteoporosis were associated with diastolic dysfunction compared to the control in men with T2DM. However, no association between BMD and LV diastolic function was found in subjects without T2DM.

Conclusion. – Osteoporosis may be an independent factor for LV diastolic dysfunction in men with T2DM. Our data suggested that early detection of abnormal BMD should warrant for early search of undetected LV diastolic dysfunction in diabetic men.

Keywords: Bone mineral density; Brachial-ankle pulse wave velocity; Left ventricular diastolic function; Type 2 diabetes

1. Introduction

Type 2 diabetes (T2DM) is associated with ischemic heart disease and chronic heart failure. Moreover, individuals with T2DM may develop cardiomyopathy independent of hypertension and coronary artery disease. Abnormal diastolic function reflects early changes in cardiac function and plays a key role in the development of heart failure. Recent studies have shown that left ventricular (LV) diastolic dysfunction is associated with cardiovascular outcomes and mortality [1,2].

In parallel, osteoporosis has been suggested as an independent risk factor for cardiovascular disease [3]. Low bone mineral density (BMD) increased cardiovascular mortality [4].

Abbreviations: T2DM, type 2 diabetes; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; eGFR, estimated glomerular filtration rate; FN, femoral neck; BMD, bone mineral density.

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http://dx.doi.org/10.1016/j.diabet.2016.02.001
1262-3636/

Furthermore, subjects with cardiovascular disease have a higher risk of bone loss and fracture [5]. Currently, literature has emerged that shows common underlying biological processes might contribute to vascular calcification and bone mineralization [5].

The conclusions on the relationship between BMD and LV diastolic dysfunction were inconsistent. A study reported that BMD is associated with LV diastolic dysfunction in men with hypertension [6]. Another study found that BMD is not an independent determinant of left ventricular mass index in men [7]. This inconsistency may be due to small sample sizes and selected populations.

Recently, a study demonstrated that low BMD predicts incident heart failure in healthy individuals [8]. On the basis of these observations, we hypothesized that low BMD might be an index for diastolic dysfunction in T2DM. However, some of above studies used ultrasound of the calcaneum as a measure of osteoporosis, yet dual energy X-ray absorptiometry (DEXA) is the standard method recommended to diagnose osteoporosis [6–8]. In this study, we aim to evaluate the association between BMD measured by DEXA and LV diastolic function in men with T2DM.

2. Methods

2.1. Participants

Between January 2013 to December 2013, 344 men with T2DM were enrolled in the cross-sectional study. A total of 331 age-matched control subjects were also studied. All participants were recruited from the International Physical Examination and Healthy Center in Harbin. Male subjects with type 2 diabetes aged 50–80 y were recruited. Control subjects were randomly selected from the International Physical Examination and Healthy Center and were age matched in 5-year age groups. We combined sequential recruitment strategy and opportunistic recruitment strategy in this study. The recruited subjects were free of complications linked to diabetes (retinopathy, neuropathy, and arterial disease) except incipient nephropathy. Exclusion criteria were cancer, autoimmune diseases, chronic obstructive pulmonary disease, chronic inflammatory disease, chronic renal failure, chronic heart failure, Cushing disease, thyroid disease, hypogonadism, fractures, coronary heart disease, stroke, atrial fibrillation, and medical treatment with glucocorticoid, any sex hormones, glitazone, bisphosphonates, vitamin D or calcium. Our institutional ethics committee approved the study protocol, and all study subjects gave written informed consent.

2.2. Clinical examination

Clinical data include medical history, alcohol consumption, smoking status, current use of medication, physical examination, and laboratory test. Cigarette smoking was defined as having smoked at least 100 cigarettes in one's lifetime. Alcohol drinking was defined as the consumption of at least 30 g of alcohol per week for 1 year or more. Regular leisure-time physical activity was defined as participation in moderate or vigorous activity for 30 minutes or more per day at least 3 days a week. Blood pressure was measured using a mercury-gravity sphygmomanometer in the sitting position after a 15-min rest. Systolic and diastolic blood pressures were determined twice with a 10-min interval and mean values were used in the analysis. Body mass index was calculated as weight/height squared (kg/m^2).

2.3. Biochemical analyses

All blood samples were drawn after subjects had fasted over-night. Serum total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), fasting plasma glucose (FPG), calcium, phosphorus, albumin, and prealbumin were determined by standard laboratory methods (Modular Analytics, Roche, Mannheim, Germany). The glycated hemoglobin (HbA_{1c}) level was measured using high-performance liquid chromatography method (Variant^{TM} II; Bio-Rad, Hercules, CA, USA). All measurements were conducted within 2 h of sampling.

Diagnosis of type 2 diabetes (T2DM) was based on American Diabetes Association criteria such as fasting plasma glucose $\geq$ 7.0 mmol/L, current treatment with a hypoglycaemic agent, or casual glucose $\geq$ 11.1 mmol/L.

The Modification of Diet in Renal Disease (MDRD) equation was used to estimate glomerular filtration rate (eGFR). MDRD equation was: $eGFR = 186.3 \times (SCr)^{-1.154} \times (age)^{-0.203}$.

2.4. BMD measurement

BMD at lumbar spine (L2–L4) and femoral neck (FN) was measured using dual-energy X-ray absorptiometry (DPX-MD; LUNAR, GE, Madison, WI, USA). BMD was expressed as g/cm^2 and as *T*-score. Osteopenia or osteoporosis was defined according to lowest measured *T*-score value in either spine or femoral neck. The method was validated in a previous report [9]. Diagnostic classification was based on the World Health Organization criteria: BMD *T*-score ≥ -1.0 is normal; > -2.5 and < -1.0 is low bone mass (osteopenia); and ≤ -2.5 is osteoporosis.

2.5. Echocardiographic examination

Echocardiography was performed by standardized procedures with Philips iE33 (Philips Ultrasound, Bothell, WA). LV linear dimensions were measured according to the American Society of Echocardiography's recommendations [10]. LV mass was calculated with a validated formula and indexed for $height^{2.7}$ [11]. LV ejection fraction was calculated by biplane modified Simpson's rule. The peak early diastolic transmitral flow velocity (E), peak late diastolic transmitral flow velocity (A), and E/A ratio were measured using pulsed-wave Doppler imaging of the mitral valve inflow from the apical 4-chamber view. Peak early diastolic mitral annular velocity (e′) was measured in the septal position using spectral Doppler imaging. The e′ wave velocities from the septal and lateral walls were averaged and the E/e′ ratio