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N-terminal pro-brain natriuretic peptide (NT-proBNP) in Type 2 diabetes with left ventricular dysfunction

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Abstract

Plasma N-terminal proBNP (NT-proBNP) is released in response to pressure overload, intravascular volume expansion and myocardial ischemia from cardiac ventricles. We studied the relationship between NT-proBNP levels and left ventricular dysfunction and urinary albumin excretion in Type 2 diabetes. The study group consisted of 130 diabetic patients referred for echocardiography. They were divided into four groups according to echocardiographic finding and into three groups according to urinary albumin excretion. NT-proBNP levels were measured by electrochemiluminescence. There were significant differences in NT-proBNP levels among four groups ($P = 0.012$), with a highly significant difference between normal and other groups with left ventricular dysfunction. NT-proBNP levels in diastolic dysfunction were significantly higher than normal group (1491.1 pg/mL versus 232.3 pg/mL, $P = 0.01$), even though there was no difference in ejection fraction (EF) ($61.2 \pm 7.9\%$ versus $60 \pm 8.4\%$, $P = 0.773$). NT-proBNP levels showed positive correlation with age (Rs = 0.37, $P < 0.001$), creatinine (Rs = 0.38, $P = 0.001$), LVIDS (Rs = 0.56, $P = 0.001$) and LVIDD (Rs = 0.34, $P = 0.04$) and negative correlation with EF (Rs = −0.66, $P = 0.001$). NT-proBNP levels significantly differed among three groups according to urinary albumin excretion ($P = 0.031$). These results suggest that NT-proBNP could be used to identify any impairment of left ventricular function in diabetes.

Keywords: NT-proBNP; Left ventricular dysfunction; Urinary albumin excretion

1. Introduction

Diabetes is important as a cause of cardiovascular disease (CVD) and involves a wide spectrum, ranging from asymptomatic ischemia to clinically evident heart failure [1]. The prognosis of CVD in diabetic patients is worse than non-diabetic subjects, and over two-thirds of patients with diabetes will die of CVD [2]. Also macrovascular complications including CVD seem to increase gradually in patients with prediabetes such as impaired glucose tolerance and impaired fasting glucose. Therefore, early identification of CVD in diabetic patients may be particularly important in leading to early initiation of treatment. Diagnostic methods need to

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cover screening patients with high risk, as well as identification of patients with symptoms. Recent years have seen activity directed towards the search for clinically useful circulating markers of CVD [3]. Until recently, while echocardiography is the diagnostic tool of evaluating left ventricular dysfunction in general population, screening is difficult in all diabetic patients.

NT-proBNP, a 76 amino acid peptide, is the second remnant after cleavage from the 108 amino acid preprobrain natriuretic peptide with BNP, which is rapidly released in response to pressure overload, intravascular volume expansion and myocardial ischemia from the myocytes of cardiac ventricles mainly [4]. However, it has a longer half-life than BNP which is degraded by neutral endopeptidase and therefore, more stable in plasma [5] and may be a good marker for the cardiac status.

NT-proBNP has been less investigated in patients with Type 2 diabetes. We assessed the relationship between plasma NT-proBNP levels and left ventricular function in Type 2 diabetes. Furthermore, we investigated the relationship between NT-proBNP and urinary albumin excretion as a marker of angiopathy.

2. Subjects and methods

2.1. Subjects

The study group consisted of 130 diabetic patients (65 males and 65 females) referred for echocardiography at the Samsung Medical Center in Korea from July 2003 to December 2003. The patients were diagnosed by the American Diabetes Association criteria. This study was approved by the Internal Review Board (IRB) of Samsung Medical Center and informed consent was obtained from all subjects before their participation. We excluded patients with valvular heart disease, abnormal thyroid function, and serum creatinine >133 μmol/L. The mean age of all patients at examination was 63.9 ± 13.1 years and mean duration of disease was 9.2 ± 7.1 years. The diabetes was controlled with diet alone in 23 patients, with oral hypoglycemic agents in 81 patients, and with insulin in the remaining 26. 130 diabetic patients were divided into four groups according to left ventricular dysfunction by echocardiographic classifications: normal ($n = 30$), diastolic ($n = 27$), systolic ($n = 42$), systolic and diastolic dysfunction ($n = 31$).

2.2. Echocardiography

Two-dimensional, M-mode, and color flow Doppler echocardiograms were done at 2.0–3.5 MHz. Two-dimensional imaging was performed in the standard fashion in parasternal long and short axis views and apical four and two chamber views and apical views. Left ventricular systolic and diastolic volumes and ejection fractions were derived from two and four chamber views using a modified Simpson's rule algorism [6]. The transmitral pulsed Doppler velocity recordings from three consecutive cardiac cycles were used to derive measurements as follows: E and A velocities as the peak early and late diastolic transmitral flow velocities, respectively. Experienced cardiologists interpreted all echocardiograms and they were blinded to patients' NT-proBNP level.

2.3. Classification of echocardiography

Normal ventricular function was defined as EF $\geq$ 50%, normal left ventricular end diastolic and end systolic dimension, and no major wall motion abnormalities. Systolic dysfunction was defined as EF $<$ 50% or global hypokinesia or discrete wall motion abnormalities. Diastolic dysfunction was defined as impaired relaxation and restrictive and pseudonormal pattern. Systolic and diastolic dysfunction was defined as EF $<$ 50% with global hypokinesia or discrete wall motion abnormalities along with diastolic dysfunction.

2.4. Measurement of NT-proBNP levels and metabolic parameters

Before echocardiography, blood samples were collected into tubes containing heparin. NT-proBNP was measured by a double antibody sandwich technique using electrochemiluminescence as signal (Elecsys 2010, Roche Diagnostics, USA). The sensitivity of assay was <50 pg/mL and intra- and inter-assay coefficients of variation were 3.0% and 5.8%, respectively. There is no detectable cross-reaction with ANP, NT-proANP, and BNP. Normal reference values are dependent on age and sex.

Blood was collected after overnight fasting for determination of the fasting plasma glucose (FPG), HbA1c, total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol levels. FPG was measured in duplicate by the glucose oxidase method using an autoanalyzer (Hitachi, Tokyo, Japan) and HbA1c was measured by high-performance liquid chromatography (TosohG7, Japan). Total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol were measured by enzymatic methods using an automated multi-analyzer (7600; Hitachi, Tokyo).

2.5. Classification of abnormalities in urinary albumin excretion

130 diabetic patients collected urine for 24 h twice. Urinary albumin excretion was measured using a quantitative RIA kit (Immunotech, Prague, Czech). According to average urinary albumin excretion, it was categorized into normal (<30 mg/24 h), microalbuminuria (30–299 mg/24 h), and macroalbuminuria (≥300 mg/24 h).

2.6. Statistical analysis

Data were expressed as mean ± S.D. or median (interquartile range). Statistical analysis was performed using SPSS