Correlation of Brain Natriuretic Peptide and Microalbuminuria in Patients with Heart Failure

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ABSTRACT

Objective: *To evaluate the changes of plasma levels of N-terminal pro-brain natriuretic pepide (NT-proBNP) and microalbuminuria (MAU) in patients with heart failure and the correlation between them.*
Methods: *Ninety-one patients with heart failure were divided into different groups according to different stages of heart failure. Plasma levels of NT-proBNP were measured by microsome enzyme immuno-assay (MEIA). Plasma levels of MAU were determined by immune scattering turbidimetry (ICTM). Simultaneously, left ventricular ejection fraction (LVEF) and left ventricular end diastolic diameter (LVEDD) were measured by Doppler echocardiography for all patients. The correlation of NT-proBNP and MAU was evaluated at different stages of heart failure.*
Results: *The plasma levels of NT-proBNP and MAU increased with the severity of heart failure. There was a high correlation between NT-proBNP and MAU (*$r = 0.885$, $p < 0.001$*).*
Conclusion**:** *Both NT-proBNP and MAU levels were closely associated with the severity of heart failure.*

Keywords: Heart failure, microalbuminuria, N-terminal pro-brain natriuretic pepide

Correlación del Péptido Natriurético Cerebral y la Microalbuminuria en Pacientes con Insuficiencia Cardíaca

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RESUMEN

Objetivo: *Evaluar los cambios en los niveles de plasma de la fracción N-terminal del propéptido natriurético cerebral (NT-proBNP), y la microalbuminuria (MAU) en pacientes con insuficiencia cardíaca y la correlación entre ambas.*
Métodos: *Noventa y un pacientes con insuficiencia cardíaca fueron divididos en diferentes grupos de acuerdo con las diferentes etapas de insuficiencia cardíaca. Los niveles de plasma de NT-proBNP fueron medidos mediante inmunoensayo enzimático microsomal (MEIA). Los niveles plasmáticos de MAU se determinaron mediante turbidimetría inmune de difusión (ICTM). Simultáneamente, a todos los pacientes se les midió la fracción de eyección ventricular izquierda (FEVI) y el diámetro de fin de diástole del ventrículo izquierdo (DFDVI), mediante ecocardiografía Doppler. La correlación de NT-proBNP y MAU fue evaluada en diferentes etapas de la insuficiencia cardíaca.*
Resultados: *Los niveles de plasma de NT-proBNP y MAU aumentaron con la severidad de la insuficiencia cardíaca. Hubo una alta correlación entre NT-proBNP y MAU (*$r = 0.885$, $p < 0.001$*).*
Conclusión: *Tanto los niveles de NT-proBNP como los de MAU estuvieron estrechamente asociados con la severidad de la insuficiencia cardíaca.*

Palabras claves: Insuficiencia cardíaca, microalbuminuria, N-terminal del propéptido natriurético cerebral

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BACKGROUND

Measurable B-type natriuretic peptides (BNPs) which are largely produced by the left ventricle, include BNP and N-terminal proBNP (NT-proBNP). These proteins are released from cardiomyocytes in response to wall tension and neurohumoral signals. These proteins are used as the tools for the diagnosis and prognosis of heart failure (HF). Microalbuminuria (MAU) is a common indicator of diagnosis of early complications in Type 1 diabetic patients. It has been known that albuminuria is associated with atherothrombotic events and is the cause of mortality in patients with or without diabetes. Increases of excretion of MAU might also be a marker of the various pathophysiological changes that arise in patients with heart failure (1, 2). Both plasma levels of NT-proBNP and MAU increased in patients with heart failure. The costs of monitoring MAU and NT-proBNP are different. Therefore, measurement of MAU instead of NT-proBNP in inpatients and outpatients with heart failure may be an economic and easy way to monitor the progress of heart failue. Hence, the correlation between NT-proBNP and MAU were investigated in the present study.

SUBJECTS AND METHODS

The 91 patients in the study came from inpatients with primary heart failure (3) [NYHA stage I~IV, NT-proBNP > 450 pg/ml, LVEF < 50% and LVED > 55 mm] a normal renal function (GFR > 90 ml/min/1.73 m^2), and MAU (> 30 mg/L). All enrolled subjects were without diabetic symptoms and signs of liver dysfunction, other causes of dyspnoea or dyslipoproteinaemia. All subjects were enrolled without any acute illness. The study protocol was approved by the ethics committee of Shandong University Qilu Hospital. A written informed consent was obtained from all patients who participated in the study.

Ninety-one patients with heart failure were divided into different groups according to different stages of heart failure. As per standard guidelines (4), left ventricular ejection fraction (LVEF) and left ventricular end diastolic diameter (LVEDD) by Doppler echocardiography (HP Sonos 5500) were measured in all patients. Serum creatinine was also determined. Glomerular filtration rate (GFR) was calculated by using the Modification of Diet in Renal Disease (MDRD) (5). Plasma levels of NT-proBNP were determined at baseline by microsome enzyme immunoassay (MEIA) on AxSYM [sensitivity 10 pg/ml] (6) and MAU at baseline by immune scattering turbidimetry [ICTM](sensitivity 2 mg/L).

Data were expressed as mean ± SD. Statistical analysis was evaluated using SPSS for Windows 11.0 software, followed by one-way analysis of variance and the *q*-test to assess the significance of the differences among the various groups. Correlation analysis were assessed by linear regression analysis. Significance was accepted at $p < 0.05$.

RESULTS

Characteristics of the patients enrolled in the study are seen in Table 1. In all the groups, significant differences at every stage of heart failure were noted from the last baseline values of NT-proBNP and MAU among the subjects with the progress of heart failure [$p < 0.05$] (Table 2). For all enrolled subjects with heart failure, there was a significant negative correlation in MAU and LVEF [r = -0.733, $p < 0.001$] (Figure). There were all positive correlation for MAU with

Table 1: Characteristics of patients

stage	n	age (y)	male	duration of disease (m)
I	21	53 ± 7.8	10	1.1 ± 0.5
II	25	60 ± 11.1	12	1.9 ± 0.6
III	23	65 ± 10.3	12	2.6 ± 1.0
IV	22	72 ± 6.5	11	3.1 ± 0.8

($\bar{x}$ ± SD)

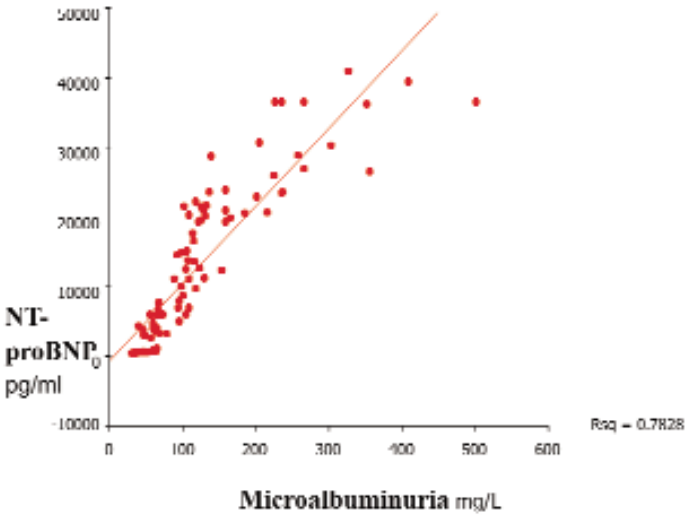

Figure: Correlation of N-proBNP and microalbuminuria

Table 2: Changes in NT-proBNP, MAU, LVEF, LVEDD in all subjects

stage	n	age (y)	NT-proBNP (pg/ml)	MAU (mg/L)	LVEF(%)	LVEDD (mm)
I	21	53 ± 7.8	639.8 ± 187.6	46.9 ± 12.4	46.2 ± 2.5	57.6 ± 2.0
II	25	60 ± 11.1	5772.8 ± 2432	76 ± 24.6	42.6 ± 2.6	59.6 ± 1.3
III	23	65 ± 10.3	19071 ± 4814	130.6 ± 36.6	38 ± 2.8	63.9 ± 2.4
IV	22	72 ± 6.5	27008 ± 8887	242 ± 101	32.6 ± 3.6	69.3 ± 1.8

($\bar{x}$ ± SD)

LVEDD and NT-proBNP. The values of r and *p* were 0.704, < 0.001, 0.885 and < 0.001, respectively (Table 3). The

Table 3: Correlation of MAU and NT-proBNP, LVEF, LVEDD

	NT-proBNP	LVEF	LVEDD
MAU	0.885, < 0.001	- 0.733, < 0.001	0.704, < 0.001

(*r, p*)

levels of NT-proBNP and MAU at every stage of heart failure and in all patients were not normally distributed.

DISCUSSION

The level of NT-proBNP, a biomarker of cardiac function and heart failure (3, 7–9), has become an important diagnostic tool for assessing patients who present acutely with dyspnoea (10, 11), and provides important prognostic information in both acute and chronic heart failure. Also, monitoring NT-proBNP plasma level is expected to improve patient care and outcomes. Secretion and plasma level of NT-proBNP respond to intracardiac distending pressures, with other modulating influences including age, sex, renal function and other aspects of neurohormonal status. Single measurement of NT-proBNP shows promise in diagnosis of heart failure. NT-proBNP at cutpoints > 450 pg/ml was highly sensitive and specific for the diagnosis of heart failure and NT-proBNP level < 300 pg/ml was optimal for ruling out acute chronic heart failure (CHF), with a negative predictive value of 99% (12).

Minor increase in urinary albumin excretion (MAU) is known to predict adverse renal and cardiovascular events (13–15) in diabetic and hypertensive patients. Recent findings show that MAU is an early and sensitive marker of future cardiovascular events even in healthy subjects. Albumin excretion is indicative of a disturbance of the barrier function of endothelial cells (16), and vascular alterations are not confined to the kidney but can also be observed in the myocardium (17). Microalbuminuria is now considered to be an atherosclerotic risk factor and predicts future cardiovascular disease risk in diabetic patients, in elderly patients, as well as in the general population. Microalbuminuria is associated with increased heart failure risk (2, 18). Lowering of MAU using renin angiotensin aldosterone system (RAAS) inhibitors and other drugs appear to lower the risk for heart failure.

This present study indicates that the plasma levels of NT-proBNP and MAU increased synchronously in pace with the aggravation of heart failure; at the same time there was positive correlation for MAU with NT-proBNP (r = 0.885, $p < 0.001$). For all enrolled subjects, there was a significant negative correlation between MAU and LVEF (r = - 0.733, $p < 0.001$). These phenomena indicated that a disturbance of the barrier function of vascular endothelial cells gradually increased with the aggravation of heart failure. Very likely, generalized endothelial dysfunction plays an important role in the mechanisms, thus linking MAU and NT-proBNP with end-organ damage.

As explained above, the plasma levels of NT-proBNP and MAU increased synchronously with the aggravation of heart failure. Monitoring MAU might take the place of monitoring NT-proBNP in patients with heart failure. The cost of monitoring MAU is low, but it is expensive for monitoring NT-proBNP in a laboratory or hospital. Therefore, measurement of MAU instead of NT-proBNP in inpatients and outpatients with heart failure is an economic and easy way to monitor the progress of heart failue.

This study was limited by the small sample size and the short duration of the study.

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