Tei Index and B-Type Natriuretic Peptide in Assessment of High-risk Patients with Acute Coronary Artery Syndromes

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ZHANG ET AL.: ***Tei Index and B-Type Natriuretic Peptide in Assessment of High-risk Patients with Acute Coronary Artery Syndromes.*** *In order to assess the value of Doppler echocardiographic Tei index and B-Type natriuretic peptide (BNP) in evaluating high-risk patients with acute coronary artery syndromes and their relationship with myocardial ischemia. Eighty-three consecutive patients and eighty controls were included, according to ACC/AHA directions, patients were divided into low-risk group and high-risk group, all participants had undergone echocardiography, neurohormonal analysis, coronary angiography, Gensini score were recorded. All data were analyzed by SPSS 13.0 software. The results showed that tei index and BNP were higher in patients with acute coronary artery syndromes (0.32±0.06, 0.48±0.09, 0.68±0.11, p<0.05; median 29.2, IQR 11.5-48.6, median 94.5, IQR 39.1-168.2, median 458.8, IQR 183.8-1295.2, p<0.05), and the difference between low-risk group and high-risk group was still significantly (0.48±0.09 vs. 0.68±0.11, p<0.05; median 94.5, IQR39.1-168.2 vs. median 458.8, IQR183.8-1295.2, p<0.05). They were independent predictors of myocardial ischemia (r=0.52, p<0.01; r=0.32, p<0.01), and were useful in assessing high-risk patients with acute coronary artery syndromes. (J HK Coll Cardiol 2009;17:4-10)*

Acute coronary artery syndromes, B-Type natriuretic peptide, Tei index

摘要

探討超聲多普勒指標－Tei指數與血漿腦利鈉肽（BNP）評估急性冠脈綜合徵高危患者及二者與心肌缺血的關係。連續入選83例急性冠脈綜合徵患者，80例健康者作爲對照組，根據ACC/AHA指南，將急性冠脈綜合徵患者分爲低危組和高危組，所有入選者均進行超聲心動圖檢查，血漿BNP濃度測定，冠狀動脈造影，並記錄Gensini積分。所有資料採用SPSS13.0統計軟體進行分析。結果顯示：Tei指數和BNP在急性冠脈綜合徵患者顯著升高（0.32±0.06，0.48±0.09，0.68±0.11，p<0.05；中位數29.2，四分位間數11.5-48.6，中位數94.5，四分位間數39.1-168.2，中位數458.8，四分位間數183.8-1295.2，p<0.05），且低危組與高危組之間也有顯著差別（0.48±0.09 vs. 0.68±0.11，p<0.05；中位數94.5，四分位間數39.1-168.2 vs.中位數458.8，四分位間數183.8-1295.2，p<0.05），二者是心肌缺血的獨立預測因數（r=0.52，p<0.01；r=0.32，p<0.01），對評估急性冠脈綜合徵高危患者一定價值。

關鍵詞：急性冠脈綜合徵　血漿腦利鈉肽　Tei指數

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Introduction

Acute coronary artery syndromes were urgent events of coronary artery diseases, including unstable angina, non-ST elevation myocardial infarction and ST elevation myocardial infarction, the mortality was high, early diagnosis and assessment of high-risk patients were very important.

Doppler echocardiographic Tei index[1] was an index that could reflect both systolic and diastolic function of myocardium, defined as the summation of the isovolumic contraction and relaxation times divided by ejection time. Myocardial ischemia could influence both the systolic and diastolic function of the heart, so it was reasonable for Tei index to assess acute coronary artery syndromes.

B-Type natriuretic peptide (BNP) was cardiac hormone secreted mainly from cardiac ventricles. It was related to myocardial function, a lot of studies have demonstrated its value in assessing heart failure patients, recent studies had found that myocardial ischemia could result in higher plasma BNP level too.[2,3]

The aims of this study were to elucidate: 1) The value of Tei index and BNP in diagnosing high-risk patients with acute coronary artery syndromes; 2) their correlation with myocardial ischemia.

Materials and Methods

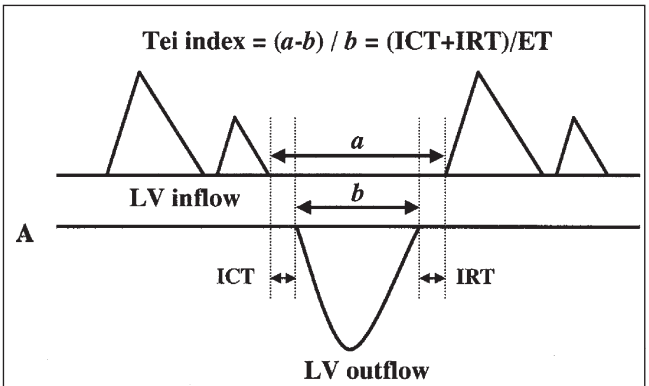
Study Population

The study population consisted of a consecutive series of 83 patients (43 men and 40 women, mean age 60.2±9.8 years) with acute coronary artery syndromes admitted to our hospital from February 2007 to February 2008, according to the direction of ACC/AHA,[4,5] the patients were divided into low-risk group and high-risk group, 80 age- and gender-matched normal subjects (42 men and 38 women, mean age 58.7±11.1 years) who had undergone physical examination, X-ray, echocardiography and electrocardiograph to excluded primary or secondary heart disease were included as controls. These patients were excluded from the present study: (1) arrhythmia patients; (2) heart-pacemaker transplanted patients; (3) serious valve heart disease patients; (4) patients with renal, hepatic or thyroid dysfunction; (5) patients with chronic pulmonary hypertension and chronic obstruction pulmonary disease; (6) obesity patients (BMI≥30 kg/m^2). The study was approved by regional scientific ethic committee. All participants gave informed written consent.

Echocardiography

Echocardiography was performed by a single investigator in the morning to exclude potential influence of circadian variation. A Hewlett Packard Sonos 5500 ultrasound instrument with a 3.5-MHz transducer was used. Three cardiac cycles were stored digitally. LV dimensions were measured as proposed by the American Society of Echocardiography. LV systolic function was estimated using ejection fraction (EF) by Simpson's modified biplane method.[6,7] Trans-mitral flow was recorded from the apical four-chamber view with a 1-2 mm sample volume placed at the tips of the mitral valve leaflets during diastole. Peak E velocity (cm/s), peak A velocity (cm/s), E/A ratio, deceleration time (DT) (ms) were obtained.[8]

Tei index was assessed from Doppler recordings of LV inflow and outflow. From mitral inflow, the time interval from cessation to onset of mitral inflow was measured (A-interval). Ejection time (B-interval) was measured from LV outflow velocity curve recorded from an apical long-axis view. Tei index was calculated as (A-B)/B (Figure 1).[9]



ICT: isovolumic contraction time
IRT: isovolumic relaxation time
ET: ejection time

Figure 1. *Tei index measurement.*

Reproducibility

Intraobserver variability was assessed in 10 patients by repeating the measurements on two occasions (1 to 12 days apart) under the same basal conditions. To test the interobserber variability, the measurements were performed off-line from video recordings by a second observer who was unaware of the results of the first examination. Variability was calculated as the mean percent error, derived as the difference between the two sets of measurements, divided by the mean of the observations.

Measurement of Plasma BNP Level

Venous blood sample for hormone analyses were taken in the morning after 30 min of rest in supine position. Blood was put into prechilled EDTA tubes. Plasma was immediately separated by centrifugation in 4 hours, BNP concentration was measured with the commercially available AxSYM BNP assay. This fully automated micro-particle enzyme immunoassay used two monoclonal antibodies in a two-step format. Being harmonized to the Biosite BNP assay, it had a dynamic range of 0-4000 pg/ml. An evaluation including 70 consecutive patients with a clinical indication for BNP measurement showed an excellent correlation between the AxSYM BNP and the Biosite BNP assay at our institution: AxSYM BNP=1.0104 × Biosite BNP+ 0.2017.

Gensini Scores

Two cardiology doctors who were unaware of the results of the level of plasma BNP and Tei index read the coronary angiographic pictures, the number of stenosis vessels and degree of coronary artery stenosis were recorded, The degree of coronary artery stenosis was evaluated by Gensini score system,[10] which was a measure of the extent and severity of coronary artery disease and was computed by assigning a severity score to each coronary segment according to the degree of luminal narrowing and its geographic importance. Reduction in the diameter of the lumen and the roentgenographic appearance of concentric lesions, as well as eccentric plaques, were evaluated (reductions of 25, 50, 75, 90 and 99%, and complete occlusion values were given Gensini scores of 1, 2, 4, 8, 16, and 32, respectively). For each principal vascular segment, a multiplier was assigned based on the functional significance of the myocardial area supplied by the segment: left main coronary artery, × 5; Proximal segment of the left anterior descending coronary artery (LAD), × 2.5; proximal segment of the circumflex artery, × 2.5; mid-segment of the LAD, × 1.5; right coronary artery, distal segment of the LAD, posterolateral artery, and obtuse marginal artery, × 1; and others, × 0.5.[11]

Statistic Analysis

Continuous variables were summarized as mean±SD, the plasma BNP levels and Gensini score were summarized as median and inter quartile range (IQR). Comparisons between groups for continuous variables were made using student's t-test. The Kruskal-Wallis test was used to compare differences in BNP levels and Gensini score between groups. Count data was analyzed by X^2 test, correlations between logGensini score and echocardiographic variables, logBNP were analyzed using linear regression analysis. To define the value of echocardiographic variables, plasma BNP level to predict Gensini score, multivariate stepwise regression analysis were conducted using variables statistic significant in univariate analysis. A probability value of <0.05 was considered significant. All statistic analysis was performed by SPSS version 13.0.

Results

General Clinical Data

There were no difference as to age, sex, body weight index between low-risk, high-risk patients with acute coronary syndromes and the controls (p>0.05). In high-risk group, more patients were involved in multiple-vessel stenosis, the level of TnT were high, blood pressure were low, heart dysfunction were worse as assessed by NYHA class, the mortality during in hospitals was high (p<0.05) (Table 1). Besides, there were 25 diabetes patients, 6 patients with acute pulmonary edema, 5 patients with heart shock, 9 patients

with acute heart failure, 23 patients with TnT>20 ng/ml in high-risk group.

Echocardiographic Analysis

Compared to the control group, Tei index were much higher in low-risk and high-risk patients with acute coronary artery syndromes ($p<0.05$), and there was still difference between low-risk and high-risk groups ($p<0.05$). EF which reflect the systolic function of LV, was lower in high-risk group when compared to the control group ($p<0.05$), However, there was no difference between low-risk group and the controls ($p>0.05$). Deceleration time (DT) was shorter in high-risk group compared to control group ($p<0.05$), while there was no difference between low-risk group and the controls ($p>0.05$). In the control group, E/A>1, in low-risk group, E/A<1, in high-risk group, E/A>1, There were no statistic difference in the three groups. Compared to the controls and the low-risk group, LV dimensions were bigger in high-risk group, while there were no difference between the controls and low-risk group ($p>0.05$) (Table 2).

Intraobserver variability for measurement of the Tei index was 3.2±1.1%, interobserver variability was 3.3±1.8%.

Table 1. General clinical data

	Control group	Low-risk group	High-risk group
Age	58.7±11.1	61.8±10.1	59.7±11.8
Sex (man/women)	42/38	22/21	21/19
BMI (kg/m^2)	24.6±2.3	25.1±3.1	24.9±2.8
Systolic pressure (mmHg)	128±14	124±8	82±7†‡
Diastolic pressure (mmHg)	75±11	76±9	56±12†‡
TnT (ng/ml)	0	5.2±2.4†	21.3±9.8†‡
One-vessel stenosis	0	30	2
Two-vessel stenosis	0	8	10
Multiple-vessel stenosis	0	5	28†‡
NYHA class			
NYHA I	80	40	0
NYHA II	0	3	5
NYHA III	0	0	20
NYHA IV	0	0	15
Mortality	0	0	3

$^{\dagger}p<0.05$ compared to the control group, $^{\ddagger}p<0.05$ compared to low-risk group.

Table 2. Echocardiographic variables

	Control group	Low-risk group	High-risk group
LVESD (mm)	29.4±4.2	29.7±9.5	39.4±9.1†‡
LVEDD (mm)	49.3±5.9	54.2±4.0	62.1±8.2†‡
EF	75.1±6.8	69.4±11.7	42.2±6.7†‡
E/A	1.24±0.26	0.86±0.33	1.16±0.57
DT (ms)	191±35	186±38	142±45†‡
Tei	0.32±0.06	0.48±0.09†	0.68±0.11†‡

$^{\dagger}p<0.05$ compared to the control group, $^{\ddagger}p<0.05$ compared to low-risk group.

Plasma BNP Level

Compared to the control group, plasma BNP levels were much higher in low-risk group and high-risk group ($p<0.05$), and the differences between low-risk and high-risk groups was also significant ($p<0.05$) (Table 3).

Gensini Score

Compared to the control group, Gensini Score were much higher in low-risk group and high-risk group ($p<0.05$), and the differences between low-risk and high-risk groups was also significant ($p<0.05$) (Table 3).

Correlation between Gensini Score and Echocardiographic Variables, Plasma BNP Level

There were significant correlation between logGensini score and LV dimensions, EF, DT, E/A, Tei index, logBNP, NYHA class, TnT level, the number of coronary artery stenosis in liner regression analysis ($p<0.01$), there were no correlation between logGensini and age ($p>0.05$). Multiple stepwise regression analysis showed that only Tei index and logBNP were independent predictors of higher Gensini score ($r=0.52$, $p=0.01$; $r=0.32$, $p=0.01$) (Table 4).

Discussion

The present study found that Tei index, the plasma BNP level were higher in patients with acute coronary artery syndromes, the high-risk group had the highest Tei index and plasma BNP concentration. Using Gensini score system to evaluate myocardial ischemia, we found that Tei index and BNP could independently predict myocardial ischemia.

Tei Index

We found Tei index increased in patients with acute coronary artery syndromes, maybe it was because acute coronary artery syndromes could induce

Table 3. Plasma BNP level and Gensini score

	Control group	Low-risk group	High-risk group
BNP (pg/ml)	29.2 (11.5-48.6)	94.5 (39.1-168.2)†	458.8 (183.8-1295.2)†‡
Gensini score	0	10.8 (9.2-18.4)†	68.2 (46.5-101.2)†‡

†$p<0.05$ compared to the control group, ‡$p<0.05$ compared to low-risk group.

Table 4. Correlation between Gensini score and Echocardiographic variables, plasma BNP level

	Univariate		Multivariate	
	r	p	Standardized regression coefficient	p
AGE	0.12	>0.05	0.02	0.64
LVESD	0.48	<0.01	0.13	0.19
LVEDD	0.37	<0.01	0.04	0.54
EF	-0.58	<0.01	-0.12	0.17
E/A	0.29	<0.01	0.10	0.24
DT	-0.45	<0.01	-0.09	0.28
NYHA class	0.42	<0.01	0.08	0.30
TnT	0.52	<0.01	0.21	0.11
Vessel stenosis	0.39	<0.01	0.05	0.50
Tei	0.68	<0.01	0.52	0.01
BNP	0.62	<0.01	0.32	0.01

myocardial ischemia, while myocardial ischemia resulted in systolic or diastolic dysfunction of the heart, so Tei index increased. Besides, Tei index was highest in high-risk patients, properly because in high-risk group, coronary artery stenosis index was high, myocardial ischemia and myocardial dysfunction were more serious, so Tei index increased significantly. Further analysis found that EF decreased in low-risk group and high-risk group, but there was no difference between low-risk group and the controls, indicating that systolic function of the herat had some reserve capacity, only when myocardial ischemia reached to some extent, EF decreased, maybe there was only diastolic dysfunction in low-risk group patients, while in high-risk group, myocardial ischemia was more serious, resulted to systolic dysfunction of the heart, so EF decreased. One more question need to mention, E/A decreased in low-risk group (<1), while increased in high-risk group (>1), indicated the pseudo-normalization phenomenon about E/A, and this was in accordance with the past studies.[12] So there were some limitation using either EF or E/A to evaluating myocardial function, Tei index could assess global function of the heart more accurately and sensitively.

Plasma BNP Level

BNP was cardiac hormone that secreted mainly from the cardiac ventricles in response to increased pressure and volume, there were only a little BNP in the circulation of healthy people, it kept the micro-circulation stability of the heart, regulated the balance of system blood and water and sodium.[13]

In the present study, we found that compared to the control group, BNP was higher in patients with acute coronary artery syndromes, this was in accordance with past studies,[11,14] maybe because acute coronary syndromes resulted in myocardial ischemia, while ischemia contributed to transitorily or permanently myocardial dysfunction, stimulated myocardium synthesize and release BNP to the blood, and there were nerve-hormone activation in patients with acute coronary artery syndromes, contributed to the rise of plasma BNP level. Plasma BNP level were highest in high-risk patients, properly because myocardial ischemia area was bigger in high-risk patients, so BNP concentration increased. Suggesting BNP could diagnose acute coronary artery syndromes, and it was valuable in evaluating high-risk patients.

Actually, BNP could be affected by many conditions, such as sex, age, heart rate, renal function, and so on, besides, in one day, plasma BNP level could be different at different time, medications could affect plasma BNP level too, ACEI increased plasma BNP level, while β-blockers decreased plasma BNP level. In the present study, plasma BNP level were measured in the morning, after 30 min of rest in supine position, and no drugs were taken, so the factors affecting BNP could be excluded.

In the present study, we used the universal Gensini score to assess myocardial ischemia. Multiple stepwise regression analysis showed only Tei index, BNP were independent predictors of myocardial ischemia, while LV dimensions, EF, DT, E/A had no value. We proposed that 1) Ischemia could influence both systolic and diastolic function of left ventricular, not just systolic or diastolic function, so Tei index and BNP as makers of "global cardiac function", could reflect ischemia more accurately. 2) Ischemia may stimulate the secretion of BNP, the more serious was myocardial ischemia, and the higher was plasma BNP concentration. Therefore, as indexes that could evaluate both systolic and diastolic function of the heart, Tei index and BNP could reflect myocardial ischemia indirectly; they had some value in assessing high-risk patients with acute coronary artery syndromes. Further research found that, there was significant positive correlation between Tei index and logBNP ($r=0.75$, $p=0.01$). There was one more question need to mention, past studies had proved that both Tei index and BNP had positive correlation with NYHA class, in the present study, most high risk patients were within NYHA class III and IV, contributed to the higher Tei index and BNP, these were in accordance with past studies, however, we had proved NYHA class was not independent predictors of myocardial ischemia.

Conclusions

Tei index, plasma BNP concentration were higher

in patients with acute coronary artery syndromes, and they were highest in high-risk patients, they were independent predictors of myocardial ischemia, had some value in assessing high-risk patients with acute coronary artery syndromes in clinical practice.

References

1. Tei C. New non-invasive index for combined systolic and diastolic ventricular function. J Cardiol 1995;6:135-6.
2. D'Souza SP, Baxter GF. B-type natriuretic peptide: a good omen in myocardial ischemia? Heart 2003;89:707-9.
3. Pascual-Figal DA, Antolinos MJ, Bayes-Genis A, et al. B-type natriuretic peptide release in the coronary effluent after acute transient ischemia in humans. Heart 2007;93:1077-80.
4. Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: summary article: A report of the American College of Cardiology / American heart Association Task Force on practice guidelines (committee on the management of patients with unstable angina). Circulation 2002;106:1893-900.
5. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction-executive summary. J Am Coll Cardiol 2004;44:671-719.
6. Sahn DJ, Demaria A, Kisslo J, et al. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072-83.
7. Shiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989;2:358-67.
8. Khouri SJ, Maly GT, Suh DD, et al. A practical approach to the echocardiographic evaluation of diastolic function. Am Soc Echocardiogr 2004;17:290-7.
9. Tei C, Ling LH, Hodge DO, et al. New index of combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function-a study in normals and dilated cardiomyopathy. J Cardiol 1995;26:357-66.
10. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol 1983;51: 606.
11. Hong SN, Yoon NS, Ahn Y, et al. N-terminal pro-B-type natriuretic Peptide predicts significant coronary artery lesion in the unstable angina patients with normal electrocardiogram, echocardiogram, and cardiac enzymes. Circ J 2005;69:1472- 6.
12. Hui Z, Yutaka O, Keiko M, et al. Noninvasive differentiation of normal from pseudo-normal/ restrictive mitral flow using Tei index combining systolic and diastolic function. Circ J 2002; 66:831-6.
13. Cameron VA, Ellmers LJ. Minireview: Natriuretic peptides during development of the fetal heart and circulation. Endocrinology 2003;144:2191-4.
14. Morrow DA, de Lemos JA, Sabatine MS, et al. Evaluation of B-type natriuretic peptide for risk assessment in unstable angina/ non-ST-elevation myocardial infarction: B-type natriuretic peptide and prognosis in TACTICSTIMI 18. J Am Coll Cardiol 2003;41:1264-72.