Terminal QRS distortion versus serum levels of brain natriuretic peptide: Association with clinical prognosis in acute myocardial infarction

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Abstract: Background and Objective: To investigate the clinical significance of ECG terminal QRS distortion (TQRSD) in patients with acute myocardial infarction (AMI) and its relationship with plasma levels of brain natriuretic peptide (BNP); to explore the correlation of TQRSD with plasma BNP and compare their usefulness in determining short-term prognosis of patients. **Materials and Methods:** Eighty-three patients with AMI hospitalized from November 2007 to January 2009 were selected and divided into two groups: TQRSD(+) and TQRSD(-), according to their first electrocardiogram. The plasma BNP levels were measured 26.7 ± 10.8 hours after the onset of the symptoms. The mortality and the incidence of major adverse cardiac events (MACE), including cardiac death, reinfarction, recurrent angina, secondary heart failure, and rehospitalization composite endpoint, were recorded during hospitalization and followed up for 30 days after admission. **Results:** The plasma BNP levels in the TQRSD(+) group were significantly higher than in the TQRSD(-) group (t=2.416, P = 0.015). Multivariate logistic regression analysis showed : after correction for age, BNP and TQRSD to be independent separately of gender, hypertension, diabetes, hyperlipidemia, smoking status, non-emergency PCI, Killip class ≥ II, peak CPK enzyme levels>100U/L, and LVEF<40%, and BNP>357pg/ml predicted the 30-day incidence of MACE (r = 1.973, P = 0.011, OR=3.810), 95% CI(1.362,5.716) , TQRSD(+) predicted the 30-day incidence of MACE (r = 0.084, P = 0.014, OR=3.572), 95% CI(2.013,4.825) (figure 7 and 8); BNP and TQRSD was found to be independent separately of non-emergency PCI, Killip class ≥ II, peak CPK enzyme levels, and LVEF<40%, and BNP>357pg/ml predicted the 30-day mortality(r=1.174,P=0.004, OR=5.107), 95% CI(2.758,6.032). TQRSD(+) predicted the 30-day mortality (r=1.064,P=0.011, OR=1.783), 95% CI(1.251,2.713) (figure 9 and 10). **Discussions:** TQRSD (+) patients had higher plasma BNP level. TQRSD and BNP were found to be predictive value of the short-term incidence of MACE. BNP was found to be predictive of short-term mortality. BNP showed greater value than TQRSD in the prediction of short-term clinical prognosis in patients with AMI.

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INTRODUCTION

On admission, surface ECG changes are important predictors of infarct size, risk stratification and clinical prognosis in patients with acute myocardial infarction (AMI). Previous studies have largely focused on the number of leads with infarction Q wave and/or ST segment elevation and on corresponding ST-segment changes. In recent years, the prognostic significance of terminal QRS distortion (TQRSD) has attracted more and more attention. Clinical studies in different countries have also confirmed the prognostic value of TQRSD, which has been shown to perform better than the number and amplitude of ST-segment elevation. [1] Tamura et al observed that TQRSD (+) patients presented significantly altered cardiac function and reduced LVEF values compared to TQRSD (-) patients[2].

Recent studies have shown that plasma brain natriuretic peptide (BNP) can be an important independent prognostic factor in patients with AMI. Both TQRSD and BNP are important factors to the evaluation of myocardial ischemia, changes of cardiac function, and clinical prognosis for patients with AMI. This paper aims to explore the predictive value of admission electrocardiogram TQRSD and plasma BNP levels for the short-term clinical prognosis in patients with AMI and to evaluate the correlations between these two indicators.

MATERIALS AND METHODS

1. Subjects

This study selected 83 AMI patients who were hospitalized in the Department of Cardiology of the First Affiliated Hospital of Zhengzhou University within 24 hours of onset of symptoms. These patients were hospitalized as early as November 2007 or as late as January 2009. The AMI diagnosis was required to meet the following criteria: (1) persistent chest pain ≥

30 min; (2) admission ECG: at least two adjacent precordial leads with ST segment elevation ≥ 2.0 mm, or at least two adjacent limb leads with ST-segment elevation ≥ 1.0 mm; (3) serum creatine phosphokinase (CPK) ≥ 2 times the normal level or the isoenzyme (CK-MB) higher than normal level or positive troponin T (TnT) qualitative test. Exclusion criteria: previous myocardial infarction, bundle branch block or intraventricular conduction blockage, previous pacemaker surgery, previous CABG with coexisting valvular heart disease or cardiomyopathy, previous history of heart failure, severe liver or renal insufficiency, or chronic obstructive pulmonary disease capable of elevating BNP levels.

2. Research Methods

2.1 ECG analysis

According to the first 12-lead ECG on admission, the selected patients were divided into TQRSD (+) and TQRSD (-) groups. TQRSD (+) is here defined as follows: (1) On the basis of ST-segment elevation, the T wave remains upright, the S wave disappears in the leads, mainly with composite wave of rS; or J point ≥ 1/2R amplitude (measured from the equipotential lines) in the leads that were predominantly with composite qR waves; (2) the abnormality given above appeared in two or more contiguous leads. TQRSD (-) is here defined as follows: If the ST-segment was elevated, then the T wave remained upright with none of the aforementioned changes in the wave (Figure 1).

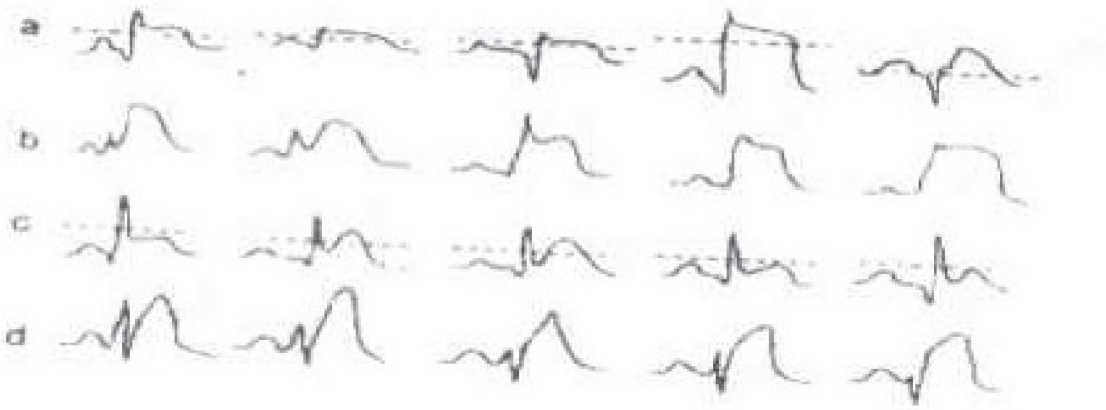

Figure1. a and b: TQRSD (+). The letter a represents the amplitude of R-waves when the J-point of qR waveform-based QRS complex is elevated ≥ 1/2. The letter b represents the disappearance of the S wave from the rS-based QRS complex. The letter c represents the amplitude of R-waves when the J point in qR wave-based QRS complex is elevated <1/2. The letter d represents the presence of S wave in rS-based QRS complex.

2.2 Determination of plasma BNP levels

Blood samples were collected from 83 patients with AMI within 24.71 ± 5.71 hours of the onset of symptoms. The plasma BNP levels were measured using rapid fluorescence immunoassay. The instrument and test plates were provided by the U.S. Biosite company, with normal reference value 0–100 pg/ml.

2.3. Medications

All patients admitted to hospital were given anti-anginal and anti-platelet therapy, the latter including enteric-coated aspirin 100 mg/day and clopidogrel 75 mg/day. Emergency patients who underwent PCI were given preoperative loading doses of enteric-coated aspirin (300 mg) and clopidogrel (600 mg) together, preventing coronary thrombosis caused by coronary atherosclerotic plaque rupture, preventing acute stent thrombosis after stent implantation. Anticoagulant therapy, such as low molecular weight heparin calcium 5000 U, was administered by subcutaneous injection every 12 hours, for 5–7 consecutive days. Patients with diabetes, hypertension, hyperlipidemia, and other diseases were given appropriate medications.

2.4 Coronary angiography and interventional treatment

All selected patients received coronary angiography and stent therapy within one week of admission. Of these, 68 patients received emergency PCI treatment within 24 hours of the onset of symptoms; 15 patients received coronary angiography and stent therapy within one week after admission. Coronary angiography was carried out using the Judkins method. The intervention therapy was performed by two experienced physicians. The stenosis was measured using QCA. Any major coronary artery or its major branches (> 2 mm) with > 50% stenosis was defined as an abnormal vessel.

2.5 Clinical follow-up

After discharge, patients were prescribed long-term oral enteric-coated aspirin at 100 mg/day. Patients implanted with bare metal stents (BMS) were given clopidogrel at 75 mg/day for 6–12 months. Patients implanted with drug-eluting stents (DES) were given clopidogrel for 12–18 months. Mortality and MACE (cardiac death, reinfarction, recurrent angina, secondary heart failure, and readmission composite endpoint) were observed and recorded during hospitalization and monthly follow-up, either through clinic visits or telephone interviews.

3. Statistical Analysis

SAS8.0 for Windows was used for statistical analysis. The measurement data are expressed as mean ± standard deviation, and the difference between groups was determined using t testing. The χ^2 test was used to determine the significant differences of count data. The correlation of TQRSD and BNP with mortality and the incidence of MACE over the course of 30 days was determined using logistic multivariate regression analysis.

RESULTS

1. Plasma BNP levels of the TQRSD (+) and TQRSD (-) groups

According to the first admission electrocardiogram, the patients were divided into two groups, a TQRSD (+) group containing 33 patients and a TQRSD (-) group containing 50 patients. There were no significant differences in age, sex, hypertension, diabetes, hyperlipidemia, smoking status, the part in AMI, emergency or non-emergency PCI, Killip class ≥ II, peak CPK enzyme level > 100U/L, or LVEF < 40%. The BNP levels in the TQRSD (+) and TQRSD (-) groups were 443.27 ± 280.74 pg/ml and 203.26 ± 164.05 pg/ml, respectively, and the difference was significant (t=2.416, P = 0.015) (Table 1).

Table 1. The correlation between plasma BNP and TQRSD

	The ECG character			
Group	TQRSD (+)	TQRSD (-)	t	p Value
The plasma BNP(pg/ml)	443.27 ± 280.74	203.26 ± 164.05	2.416	0.015

2. TQRSD and short-term clinical prognosis of AMI

The patients in the TQRSD (+) and TQRSD (-) groups were followed up for the occurrence of clinical events: The 30-day mortality rates were 24.24% and 6%, respectively(x^2=4.277, P=0.039) (Table 2). The MACE rates during the 30-day follow-up were 45.45% and 12%, respectively, with significant difference (x^2=11.71, P=0.001) (Table 3).

Table 2. The correlation between mortality and TQRSD

	Mortality		
Group	Occurrence	Non-occurrence	Total
TQRSD (+)	8(4.37%)	25(28.63%)	33
TQRSD (-)	3(6.63%)	47(43.37%)	50
Total	11	72	83

Table 3. The correlation between MACE and TQRSD

	MACE		
Group	Occurrence	Non-occurrence	Total
TQRSD (+)	15(8.35%)	18(24.65%)	33
TQRSD (-)	6(12.65%)	44(37.35%)	50
Total	21	62	83

3. Plasma BNP levels and short-term clinical prognosis of AMI

The patients were divided into three groups by plasma BNP level: BNP<136 pg/ml group (n=28), 136 <BNP≤357 pg/ml group (n=28), and BNP> 357 pg/ml (n=27). These three groups of patients were followed up for the occurrence of the clinical events: Mortality and incidence of MACE increased significantly with plasma BNP levels: the 30 day mortality rates of each group were 3.57%, 10.71%, and 25.93%, respectively (x^2=6.212 , P=0.045)(Table 4). The 30-day MACE rates were 7.14%, 14.29%, and 55.56%, respectively (x^2=19.75, P<0.001)(Table 5).

Table 4. The correlation between plasma BNP and mortality in 30 days

	Mortality		
Group (pg/ml)	Occurrence	Non-occurrence	Total
BNP<136	1	27	28
136 <BNP≤357	3	25	28
BNP> 357	7	20	27
Total	11	72	83

Table 5. The correlation between plasma BNP and MACE in 30 days

	MACE		
Group (pg/ml)	Occurrence	Non-occurrence	Total
BNP<136	2	26	28
136 <BNP≤357	4	24	28
BNP> 357	15	12	27
Total	21	62	83

Multivariate logistic regression analysis showed BNP and TQRSD to be independent separately of gender, hypertension, diabetes, hyperlipidemia, smoking status, non-emergency PCI, Killip class ≥ II, peak CPK enzyme levels, and LVEF<40%, and BNP predicted the 30-day incidence of MACE (r = 1.973, P = 0.011, OR=3.810), 95% CI(1.362, 5.716) , TQRSD predicted the 30-day incidence of MACE (r = 0.084, P = 0.014, OR=3.572), 95% CI(2.013, 4.825) (Table 6 and 7); BNP and TQRSD was found to be independent separately of non-emergency PCI, Killip class ≥ II, peak CPK enzyme levels, and LVEF<40%, and BNP predicted the 30-day mortality(r=1.174, P=0.004, OR=5.107), 95% CI (2.758, 6.032). TQRSD predicted the 30-day mortality (r=1.064, P=0.011, OR=1.783), 95% CI (1.251, 2.713) (Table 8 and 9).

Table 6. The clinical data analysis between occurrence of MACE and AMI within 30 days

	Occurrence of MACE (N=21)	Non-occurrence of MACE(N=62)	p Value
TQRSD (+), n	15	26	0.014
Age, n	64±12	58±12	0.057
Male, n	13	22	0.034
History of hypertension, n	14	25	0.037
History of diabetes, n	16	27	0.020
Hypercholesteremia, n	15	23	0.013
History of smoking, n	14	24	0.049
Non-emergency PCI, n	17	25	0.001
Peak value of CPK >100, n	13	19	0.011
LVEF<40%, n	16	23	0.004
Killip classification≥Ⅱ, n	15	20	0.004
CHD family history, n	13	30	0.284
The part in AMI	--	--	--
Antetheca, n	10	28	0.845
inferior wall/paries	--	--	--
Posterior, n	7	23	0.756
lateral wall, n	4	11	0.893
Level of plasma BNP (pg/ml)	--	--	--
BNP≤136	10	43	0.073
136 < BNP≤357	6	15	0.690
BNP > 357	5	3	0.011

Table 7. The risk factors of MACE occurrence within 30 days of AMI by Logistics regression analysis

	P Value	OR	95%CI
Male	0.034	2.015	(1.107,3.251)
History of diabetes	0.020	3.048	(1.875,5.364)
LVEF<40%	0.004	4.107	(2.316,6.037)
Peak value of CPK>100	0.011	2.103	(1.503,3.726)
Hypercholesteremia	0.013	2.416	(1.472,4.016)
TQRSD (+)	0.014	3.572	(2.013,4.825)
History of smoking	0.049	2.735	(1.205,3.741)
History of hypertension	0.037	1.504	(1.030,3.018)
Killip classification≥ Ⅱ	0.004	4.539	(2.573,6.837)
BNP > 357	0.011	3.810	(1.362,5.716)
Non-emergency PCI	0.001	3.172	(2.308, 4.253)

Table 8. The clinical data analysis between mortality and AMI within 30 days

	Occurrence of death (N=11)	Non-occurrence of death (N=72)	p Value
TQRSD (+) , n	9	26	0.011
Age(years)	67±12	55±12	0.057
Male, n	6	41	0.920
History of hypertension, n	7	35	0.353
History of diabetes, n	8	19	0.007
Hypercholesteremia, n	8	45	0.748
History of smoking, n	6	28	0.325
Non-emergency PCI, n	8	14	0.001
Peak value of CPK>100, n	10	37	0.033
LVEF<40%, n	8	11	0.001
Killip classification≥ Ⅱ , n	6	15	0.017
CHD family history, n	4	18	0.426
The part in AMI	--	--	--
Antetheca, n	6	41	0.881
inferior wall/paries	--	--	--
posterior, n	3	17	0.791
lateral wall, n	2	14	1.000
Level of plasma BN(pg/ml)	--	--	--
BNP≤136	1	42	0.007
136 < BNP≤357	3	17	0.933
BNP > 357	7	13	0.004

Table 9. The risk factors of mortality within 30 days of AMI by Logistics regression analysis

	P Value	OR	95%CI
LVEF<40%	0.001	4.135	(2.015,6.351)
Peak value of CPK >100	0.033	2.056	(1.143, 3.581)
TQRSD (+)	0.011	1.783	(1.251, 2.713)
Killip classification≥ Ⅱ	0.017	3.502	(1.726, 4.051)
History of diabetes	0.007	2.235	(1.375, 3.821)
BNP > 357	0.004	5.107	(2.758,6.032)
Non-emergency PCI	0.001	2.573	(1.205, 2.931)

DISCUSSION

Changes in surface ECG play important roles in predicting the prognosis of AMI. The prognostic significance of TQRSD was first reported by Birnbaum et al. in 1993, and it has attracted more attention since. A number of clinical studies have confirmed the prognostic value of TQRSD, which is even better than that of the number and amplitude of ST-segment elevation events[3]. Studies have shown that TQRSD(+) patients with early onset of symptoms who receive primary PCI tend to have lower mortality rates than those who receive thrombolysis therapy. No association has been found between the incidence of reinfarction and TQRSD. Primary PCI has been shown to reduce the incidence of reinfarction more effectively than thrombolysis[4]. TQRSD reflects the presence of severe myocardial ischemia and irreversible myocardial damage in AMI patients. Severe myocardial ischemia is present in TQRSD(+) patients, with poorer cardiac function, higher incidences of cardiac events, and relatively poorer clinical prognosis compared to TQRSD (-) patients.

Brain natriuretic peptide (BNP) is a natriuretic peptide. It is mainly secreted by ventricular myocytes. It has a strong natriuretic, diuretic, and vasodilative functions, thereby inhibiting renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system to regulate body fluids and blood vessels. Previous studies have shown that plasma BNP level is a valid indicator of left ventricular dysfunction. In case of left ventricular insufficiency, the increased ventricular pressure, expanded ventricular muscle, and increased ventricular wall tension prompt the release of BNP[5]. As reported in recent years, myocardial ischemia is an important stimulus of BNP release. In this way, BNP levels can indicate the extent and severity of ischemic injury[6]. Richards et al. analyzed plasma BNP levels in patients with AMI episodes within 1 to 4 days of onset. They found that patients with elevated plasma BNP levels have a higher rate of major cardiovascular adverse events than those with normal plasma BNP levels during the three-year follow-up. The clinical prognostic value of BNP was found to be independent of the well-proven prognostic factors, such as LVEF, peak value of CPK, and diabetes[7]. The mortality rate among patients with myocardial infarction increased as their BNP levels increased, and they experienced more complications after the intervention than patients with normal BNP levels[8]. The blood flow reperfusion level after AMI was found to be negatively correlated with plasma BNP levels. The higher the BNP level, the lower the level of reperfusion[9]. Studies have shown that the incidence of no-reflow after coronary angiography to be significantly higher in TQRSD(+) patients than in TQRSD(-) patients[10,11]. TQRSD was found to be an independent predictor of no-reflow, suggesting that it may reflect the widespread destruction of microcirculation caused by severe ischemia[10].

The results of the present study indicated a good correlation between plasma BNP levels and TQRSD. The plasma BNP levels in TQRSD(+) group were higher than those in the TQRSD(-) group ($t=2.416$, $P = 0.015$). BNP was found to reflect changes in cardiac function after ischemia, including systolic function, diastolic function, and the degree of myocardial ischemic injury. In previous studies, impaired cardiac function and myocardial ischemia were always being predictors of adverse events directly. In this way, the level of plasma BNP was found to directly predict clinical prognosis in patients with AMI. For this reason, myocardial ischemia was more severe in TQRSD(+) patients, and the higher the plasma BNP concentration, the poorer the prognosis.

In summary, TQRSD(+) patients have higher plasma BNP concentrations during AMI. TQRSD(+) and plasma BNP are closely correlated with the severity of AMI clinical events. BNP can predict short-term mortality and MACE incidence, and TQRSD can predict short-term MACE incidence. BNP showed greater value than TQRSD in predicting short-term clinical prognosis in patients with AMI.

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