The predictive role of electrocardiographic abnormalities in ischemic stroke patients with intravenous thrombolysis

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ABSTRACT

Background/Objectives: The association between electrocardiographic abnormalities and the outcomes in acute ischemic stroke patients after intravenous thrombolysis remains unclear. We sought to assess the predictive value of electrocardiographic abnormalities in stroke patients after thrombolysis.

Methods: Consecutive acute stroke patients with thrombolysis from Feb 2008 to Jun 2013 were included. Electrocardiographic abnormalities during hospitalization were retrospectively reviewed. Outcomes were 90-day modified Rankin’s Score. Multivariate logistic regression was used to analyze the association of electrocardiographic abnormalities with 90-day outcome.

Results: From Feb 2008 to Jun 2013, 95 acute stroke patients (median age of 67 and 64.2% male) with electrocardiographic before/after thrombolysis and 90 day modified Rankin’s Score were recruited in our study. Increased age (p = 0.027), higher baseline National Institutes of Health Stroke Scale (p < 0.001) and T-wave changes (p = 0.030) were significantly associated with worse functional outcome. T-wave changes (odds ratio 5.54, 95% confidence interval 1.37-22.37, p = 0.016) were independently associated with unfavorable outcome.

Conclusions: T-wave changes can be useful markers to predict the outcome in stroke patients after thrombolysis.

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1. Introduction

Ischemic stroke is one of the leading causes of mortality and morbidity in the world. Cardiac comorbidities account for almost 20% of deaths after ischemic stroke [1]. Standard 12-lead electrocardiography (ECG) is a routine and mandatory cardiovascular examination in the evaluation of stroke patients. ECG abnormalities, frequently seen in acute ischemic stroke (AIS), are proved to be associated with long-term outcome [2]. However, that association has not been established in patients who receive intravenous thrombolysis (IV-tPA). We sought to assess whether cardiac abnormalities on ECG can independently influence the outcome in AIS patients after IV-tPA.

2. Methods

2.1. Patients

We identified acute ischemic stroke patients presenting to our institution between Feb 2008 and Jun 2013 within 4.5 h of stroke symptom onset who received IV-tPA from our prospectively recorded stroke database. Baseline National Institutes of Health Stroke Scale (NIHSS), 90-day modified Rankin’s Score (mRS), blood pressure, onset to treatment time (OTT) and risk factors were obtained from the database.

2.2. ECG

ECGs were performed after admission and analyzed by one investigator (FW), blinded to the clinical data of the patients. ECG abnormalities were defined according to the guidelines of the European Society of Cardiology [3]. ST deviation was considered to represent myocardial ischemia when ST elevation occurred at the J point in 2 contiguous leads with the cutoff points of ≥0.2 mV in men or ≥0.15 mV in women in leads V2 to V3 and/or ≥0.1 mV in other leads. Horizontal or
downsloping ST depression ≥0.05 mV in 2 contiguous leads, was also considered ST ischemic changes (STIC). T-wave changes (TWC) included T-waves that were of low voltage or are flat or inverted in leads that were normally upright or that are abnormally tall and peaked; a T-wave less than 0.1 mV in depth was defined as inverted [4]. QTc was considered as prolonged if longer than 0.44 s (≥0.45 s) [5].

2.3. Statistical analysis

Statistical analyses were performed using SPSS, Version 21 (SPSS Inc., Chicago, USA). p < 0.05 was considered to indicate statistical significance. Patients were dichotomized by using the 90-day mRS score into good (mRS score 0–2) versus poor outcome (mRS score 3–6). Differences of patients’ characteristics between outcomes were tested by Chi-square or Fishers exact test for categorical and Mann–Whitney for continuous variable. Multivariate logistic regression (including age, sex and variables with p-value < 0.15) was used to assess the association of variables with unfavorable outcome.

3. Results

From Feb 2008 to Jun 2013, there were 152 patients within 4.5 h of stroke symptom onset received IV-tPA in our institution. Of those 95 with both ECG after admission and 90 day mRS were recruited in our study. Median onset to ECG time is 1 day (IQR 0, 3). Patient characteristics in total and stratified by outcomes are listed in Table 1. Increased age (p = 0.027), higher baseline NIHSS (p < 0.001) and TWC (p = 0.030) were significantly associated with worse functional outcome.

Age, sex and other factors with “p < 0.15” were put into multivariate logistic regression analysis. We found that TWC odds ratio (OR) 5.54, 95% confidence interval (CI) 1.37–22.37, p = 0.016), and baseline NIHSS (OR 1.39, 95% CI 1.19–1.62, p < 0.001) were significantly associated with functional outcome after adjustment for the age, sex, smoking, atrial fibrillation history and previous stroke (Table 2).

4. Discussion

This study found considerable variability in the ECG abnormalities in patients treated with thrombolytic therapy for AIS. The main finding is that TWC is an independent predictor for adverse clinical outcome in AIS patients after IV-tPA.

Neurohumoral mediated cardiac damage has been proposed to be bad signs in acute ischemic stroke, which can manifest as elevated troponin [6,7] and brain natriuretic peptides [8,9]. ST and T wave changes, as nonspecific ECG abnormalities, occur nearly 40% of the stroke patients [10] and are associated with increased risk of stroke [11].

5. Conclusions

TWC on ECG, can be useful markers to predict outcome in AIS patients after IV-tPA.

Conflicts of interests

The authors declared no conflicts of interest.

References

[1] Bounds IV, Wiebers DO, Whisnant JP, Okazaki H. Mechanisms and timing of deaths from cerebral infarction. Stroke 1981;12:474–7.
[2] Dogan A, Tunc E, Düztrur M, Kerman M, Akhan G. Electrocardiographic changes in patients with ischemic stroke and their prognostic importance. Int J Clin Pract 2004;58:436–40.
[3] Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. J Am Coll Cardiol 2012;60:1581–98.
[4] Goldstein DS. The electrocardiogram in stroke: relationship to pathophysiological type and comparison with prior tracings. Stroke 1979;10:253–9.
[5] Hjalmarsson C, Bokemark L, Fredriksson S, Antonsson J, Shadmehr A, Andersson B. Can prolonged QTc and cTNT level predict the acute and long-term prognosis of stroke? Int J Cardiol 2012;155:214–7.
[6] James P, Ellis CJ, Whittlock RM, McNeil AR, Henley J, Anderson NE. Relation between troponin T concentration and mortality in patients presenting with an acute stroke: observational study. BMJ 2000;320:1502–4.

Those are unlikely related with wall motion abnormalities in echocardiogram among AIS patients [12]. The univariable association between ECG abnormalities and mortality has been described in patients with subarachnoid hemorrhage [13]. Our study provides further evidences of the association between TWC and the outcome in AIS after IV-tPA. Notably, we found TWC, with an incidence rate of 41.4%, independently associated with unfavorable outcome that has never been reported in the prior studies. These findings suggest ECG abnormalities, reflecting underlying arteriosclerotic degree not only in cardiac vascular disease but also in cerebrovascular diseases, can be good markers to predict the outcome after thrombolysis.

T-wave represents ventricular repolarization. Besides T-wave, repolarization changes in ECG affecting ST segment or the duration of QTc can frequently be diagnosed in AIS patients [14,15]. Prolonged QTc was reported to be a predictor of mortality during the first 30 days after stroke [5]. However, we didn’t find it significantly influence the 3-month outcome in our study (p = 0.765). Only one study investigated the association between ECG abnormalities in AIS patients with IV-tPA, which demonstrated that changes of QT dispersion (QTD) were correlated with short-term neurological functional outcome [16]. Weakness of that study is that due to the small sample size (only including 30 subjects) they were not able to reveal the independently predictive value of QTD. The highlight of our study was to find an independent association between TWC and functional outcome after the adjustment of age, sex, baseline NIHSS, smoking, AF and previous stroke. Those results increase the power of ECG abnormalities in predicting the outcome after IV-tPA.

Limitations of our study are due to the small sample size and derived from a single center experience. Secondly, ECGs were not limited in those performed before IV-tPA may possibly influence the results. Further study needs to validate our findings in a prospective cohort.

Table 1

| Patient characteristics in total and stratified by outcomes. |
|---------------------|---------------------|---------------------|
|                     | Total             | mRS 0–2             | mRS 3–6             |
| N                   | 95                | 54                  | 41                  |
| Age (yr)            | 67(59, 75)        | 65(53, 73)          | 71(62, 78)          | 0.027 |
| Male                | 64.2%(61/95)      | 70.4%(38/54)        | 56.1%(23/41)        | 0.151 |
| HBP                 | 64.2%(61/95)      | 68.5%(37/54)        | 58.5%(24/41)        | 0.315 |
| DM                  | 30.5%(29/95)      | 27.8%(15/54)        | 34.1%(14/41)        | 0.504 |
| Dyslipidemia        | 18.9%(18/95)      | 23.3%(10/43)        | 15.6%(6/41)         | 0.903 |
| Smoking             | 42.1%(40/95)      | 50.0%(27/54)        | 31.7%(13/41)        | 0.074 |
| AF                  | 33.7%(32/95)      | 29.5%(15/54)        | 43.9%(19/41)        | 0.066 |
| Previous stroke     | 16.8%(16/95)      | 11.1%(6/54)         | 24.4%(10/41)        | 0.087 |
| IHD                 | 13.7%(13/95)      | 13.0%(7/54)         | 14.6%(6/41)         | 0.814 |
| Baseline NIHSS      | 10.5(14)          | 8.3(10)             | 14.1(17)            | 0.003 |
| OTT (min)           | 165(135, 170)     | 170(139, 165)       | 129(29)             | 0.860 |
| QTc ≥ 0.45 s prolongation | 219(233)       | 217(217)            |                    | 0.765 |

Table 2

| Multivariate logistic regression for unfavorable functional outcome (mRS 3–6). |
|---------------------|---------------------|---------------------|
| OR                   | 95% CI              | p value              |
| Age                  | 1.00                | 0.93–1.06            | 0.798 |
| Sex                  | 1.25                | 0.35–4.53            | 0.730 |
| Smoking              | 0.49                | 0.12–2.00            | 0.322 |
| AF                   | 0.21                | 0.04–1.02            | 0.054 |
| Previous stroke      | 2.20                | 0.52–9.30            | 0.282 |
| Baseline NIHSS       | 1.39                | 1.19–1.62            | <0.001 |
| TWC                  | 5.54                | 1.37–22.37           | 0.016 |
[7] Di Angelantonio E, Fiorelli M, Toni D, Sacchetti ML, Lorenzano S, Falcou A, et al. Prognostic significance of admission levels of troponin I in patients with acute ischaemic stroke. J Neurol Neurosurg Psychiatry 2005;76:76–81.

[8] Nakagawa K, Yamaguchi T, Seida M, Yamada S, Inae S, Tanaka Y, et al. Plasma concentrations of brain natriuretic peptide in patients with acute ischemic stroke. Cerebrovasc Dis 2005;19:157–64.

[9] Makikallio AM, Makikallio TH, Korpelainen JT, Vuolteenaho O, Tapanainen JM, Ylitalo K, et al. Natriuretic peptides and mortality after stroke. Stroke 2005;36:1016–20.

[10] Togha M, Sharifpour A, Ashraf H, Moghadam M, Sahraian MA. Electrocardiographic abnormalities in acute cerebrovascular events in patients with/without cardiovascular disease. Ann Indian Acad Neurol 2013;16:66–71.

[11] Ohira T, Iso H, Imano H, Kitamura A, Sato S, Nakagawa Y, et al. Prospective study of major and minor ST–T abnormalities and risk of stroke among Japanese. Stroke 2003;34:e250–3.

[12] Darki A, Schneck MJ, Agrawal A, Rupani A, Barron JT. Correlation of elevated troponin and echocardiography in acute ischemic stroke. J Stroke Cerebrovasc Dis 2013;22:559–61.

[13] van der Bilt I, Hasan D, van den Brink R, Cramer MJ, van der Jagt M, van Kooten F, et al. Cardiac dysfunction after aneurysmal subarachnoid hemorrhage: relationship with outcome. Neurology 2014;82:351–8.

[14] Christensen H, Fogh Christensen A, Boysen G. Abnormalities on ECG and telemetry predict stroke outcome at 3 months. J Neurol Sci 2005;234:99–103.

[15] Khechinashvili G, Asplund K. Electrocardiographic changes in patients with acute stroke: a systematic review. Cerebrovasc Dis 2002;14:57–76.

[16] Lazar J, Busch D, Wikowski E, Clark LT, Salischioli L. Changes in QT dispersion after thrombolysis for stroke. Int J Cardiol 2008;125:258–62.