Original Article

Relationship of Cardiac Troponin and Creatine Kinase-MB Fraction at Admission in Acute Ischemic Stroke and outcome in a Tertiary Hospital in Nigeria

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Abstract

Background: Stroke has been a global burden, with increasing morbidity and mortality. Studies had reported elevated levels of serum cardiac troponin T (cTnT) and creatine kinase-MB (CK-MB) fraction in patients with acute ischemic stroke. Therefore, the aim of this study is to relate the serum levels of these biomarkers and outcome in acute ischemic stroke as seen in a tertiary hospital in Nigeria. **Subjects and Methods:** This study was conducted in Ahmadu Bello University Teaching Hospital, Zaria. One hundred acute ischemic stroke patients were recruited into the study from December 2013 to February 2015. Blood samples were collected within the first 24 h of admission for cTnT and CK-MB concentration measurement using enzyme-linked immunosorbent assay method. Patients' outcome either dead or alive was recorded at 1 month (discharge) and at 24 months. Data were analyzed using SPSS version 20 and $P < 0.05$ was considered statistically significant. **Results:** The mean age of stroke patients was 59 years and 38% were women. Forty-one percent of patients had a raised cTnT concentration with mean ± standard deviation (SD) of 108.31 ± 7.82 ng/ml while 59% had normal cTnT with mean ± SD of 79.91 ± 15.64 ng/ml ($P = 0.000$). Furthermore, 43% had raised CK-MB concentration with mean ± SD of 35.01 ± 8.70 ng/ml and 57% had normal CK-MB with mean ± SD of 17.41 ± 2.06 ng/ml ($P = 0.000$) on admission. Twenty-two patients signed discharge against medical advice and left the hospital before 1 month. Twenty patients died in hospital within 1 month of admission with cTnT mean ± SD of 100.4 ± 15.5 ng/ml while the 58 patients who survived 1 month had a mean ± SD of admission cTnT of 88.2 ± 21.5 ng/ml ($P = 0.009$). Similarly, mean ± SD CK-MB of dead patients was 32.6 ± 25.5 ng/ml compared to the live patients who had a mean ± SD of 25.5 ± 11.1 ng/ml ($P = 0.04$). After 24 months of follow-up, a total of 31 patients died and their mean ± SD cTnT was found to be 97.0 ± 19.2 ng/ml while the live 47 patients had mean ± SD cTnT of 87.6 ± 21.1 ng/ml ($P = 0.047$). Furthermore, the mean ± SD of CK-MB concentration of dead patients was 29.8 ± 13.0 ng/ml as against live patients who had 25.6 ± 11.2 ng/ml ($P = 0.151$). **Conclusion:** Admission serum cTnT concentration is a powerful predictor of mortality outcome in patients admitted with an acute ischemic stroke.

Keywords: Cardiac, ischemic stroke, troponin

Introduction

Stroke is defined as an abrupt onset of neurological deficit that is attributable to pathology of brain vascular system that temporarily or permanently affects brain functions as a result of ischemia or hemorrhage.[1] Due to consequent high mortality and morbidity rates, stroke is to become a major community health problem for whole world[2] and it is the top most common cause of death in most Western industrialized countries.[3] The identification of predictors of morbidity and mortality of stroke may contribute to reducing mortality and increasing functional outcome by allowing adaptation of prompt therapeutic management strategies to patients at risk. Heart–brain connections have been described and showed that changes in central nervous system metabolism influence cardiac function;[4] thus, this could result in elevated concentrations of serum cardiac troponin T (cTnT) and creatine kinase MB fraction (CK-MB) during the acute phase of ischemic stroke.[5] Some studies have shown that higher

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levels of both cTnT and CK-MB are associated with increased severity and poor outcome and are predictors of early death in patients with acute ischemic stroke[6,7] while some do not show any link.[6] This study aims at determining if there is any relationship between these analytes and outcome of stroke.

Subjects and Methods

This is a prospective study were all patients who presented to the Accident and Emergency and General Outpatient Department of Ahmadu Bello University Teaching Hospital (ABUTH), Zaria with an acute ischemic stroke were recruited and followed up from January 2, 2013, to February 2017 (n = 100) where recruited. ABUTH is a tertiary health-care institution that receives referral from neighboring state hospitals though some patients also come on self-referral. The hospital is equipped with neurodiagnostic facilities including computed tomography scan and magnetic resonance imaging. These patients were followed until hospital discharge and for 2 years after stroke. Hemorrhagic stroke patients with recent history of myocardial infarction within 3 weeks and with diagnosis of long-standing hypertension, myopathies, muscular dystrophy, renal disease, previous stroke, recent surgery, or trauma were ruled out of the study appropriately. Blood samples were collected 12–72 h after admission. The antecubital fossa was cleaned with methylated spirit and allowed to dry. Blood sample was taken using sterilized 5 ml syringe and 21G needle from the brachial vein in the antecubital fossa. This was transferred into a plain bottle and allowed to stand to clot and retract. This was then centrifuged for 5 min at 10,000 rpm. The serum was separated from the cells and transferred into plain (sample) bottles and then frozen at −80°C in the deep freezer in President's Emergency Plan for AIDS Relief laboratory until the time for analysis that is when the last sample was collected. These specimens were used for analysis of serum cTnT and CK-MB fraction. The severity of stroke was assessed using the National Institute of Health Stroke Score.[7] Patient outcomes were recorded as death in hospital, return home, or discharge home within the first 1 month and after 24 months of stroke.

Serum cTnT and CK-MB fraction concentration was measured using the enzyme-linked immunosorbent assay using Bio-Rad PR-5100, Vamed Engineering Nigeria Limited, L10000-ZR-002, microplate reader. The chemicals and kits used for measurements of serum cTnT and CK-MB were procured from Wkea Medical Supplies Corporation, Changchum China, and Labkit, Chemlex S.A. Barcelona Spain, respectively.

Concentrations above 100.36 ng/ml and 19.61 ng/ml for cTnT and CK-MB are regarded as elevated and were termed as raised, respectively.

Informed consent was obtained from the patient, or their relations and ethical clearance were obtained from Health and Research Ethical Committee of ABUTH Zaria before embarking on the study. The investigation was at no cost to the patients.

Statistical analysis

Data recorded were analyzed using Statistical Program for Social Sciences 22.0 (SPSS 22.0) for Windows (SPSS Inc. Chicago 22). The mean values of serum cTnT and CK-MB of the two groups were compared using Student's t-test. Categorical data were reported as frequencies and percentages while continuous data were summarized as mean ± standard deviation (SD). $P < 0.05$ was considered statistically significant.

Results

One hundred patients (mean age: 59 years; 38% women) presented with an acute ischemic stroke, but only 78 were analyzed because 22 discharged themselves against medical advice.

Tables 1 and 2 show that there is no significant difference between the stroke patients with high and normal cTnT and CK-MB in terms of age, mean systolic pressure, and diastolic blood pressure, respectively. Forty-one (41%) patients had a raised cTnT concentration with a mean ± SD of 108.31 ± 7.82 ng/ml while 59% had normal cTnT concentration with mean ± SD of 79.91±15.64 ng/ml (P = 0.000). Furthermore, 43% had raised CK-MB concentration with mean ± SD of 35.01 ± 8.70 ng/ml, and 57% had normal CK-MB concentration with mean ± SD of 17.41 ± 2.06 ng/ml with P = 0.000.

Table 3 shows that twenty patients died in hospital within 1 month of admission and their mean ± SD of admission cTnT concentration was 100.4 ± 15.5 ng/ml while 58 patients were alive who had mean ± SD cTnT concentration of 88.2 ± 21.5 ng/ml (P = 0.009). Similarly, mean ± SD of CK-MB of patients who died was 32.6 ± 25.5 ng/ml as compared to those who were alive who had mean ± SD of 25.5 ± 11.1 ng/ml (P = 0.04).

At 24 months after the stroke follow-up, 31 patients died,had a mean ± SD cTnT of 97.0 ± 19.2 ng/ml while 47 patients who were still alive, had mean ± SD cTnT of 87.6 ± 21.1 ng/ml (P = 0.047). Furthermore, the mean ± SD of CK-MB concentration of patients who died was 29.8 ± 13.0 ng/ml compared to the alive had 25.6 ± 11.2 ng/ml (P = 0.151) as shown in Table 4.

Discussion

We investigated the serum levels of cTnT and CK-MB in acute ischemic stroke in relation to short- and long-term mortality. This study has shown that a raised serum concentration of cTnT

Table 1: Mean±standard deviation of age and cardiac troponin T and systolic and diastolic blood pressure based on level of cardiac troponin T at admission

Level of cTnT	*n*	Age	cTnT	Systolic BP	Diastolic BP
Normal cTnT	59	58.3±14.1	79.91±15.64	153.9±29.7	90.4±20.1
High cTnT	41	59.6±14.0	108.31±7.82	184.3±161.6	98.17±18.8
P		0.63	0.000	0.24	0.054

cTnT: Cardiac troponin T, BP: Blood pressure

Table 2: Mean±standard deviation of age and creatine kinase-MB and systolic and diastolic blood pressure based on level of creatine kinase-MB at admission

Level of CK-MB	*n*	Mean±SD			
		Age	CK-MB	Systolic BP	Diastolic BP
Normal CK-MB	43	60.84±13.09	17.41±2.06	157.7±31.41	93.16±22.60
High CK-MB	57	57.3±14.01	35.01±8.70	172.88±138.21	93.91±17.60
P		0.225	0.000	0.484	0.553

CK-MB: Creatine Kinase-MB, BP: Blood pressure, SD: Standard deviation

Table 3: Relationship between admission cardiac troponin T and creatine kinase-MB and 1-month ischemic stroke outcome

Hospital admission outcome after 1 month	*n*	cTnT	CK-MB
Dead	20	100.4±15.5	32.6±13.41
Alive	58	88.2±21.5	25.5±11.1
P		0.009	0.04

CK-MB: Creatine kinase-MB, cTnT: Cardiac troponin T

Table 4: Relationship between admission cardiac troponin T and creatine kinase-MB and 24-month ischemic stroke outcome

Hospital admission outcome after 24 months	*n*	cTnT	CK-MB
Dead	31	97.0±19.2	29.8±13.0
Alive	47	87.6±21.1	25.6±11.2
P		0.047	0.151

CK-MB: Creatine kinase-MB, cTnT: Cardiac troponin T

above reference limit is a major predictor of death after an acute ischemic stroke. The use of the cTnT assay has shown a greater and more predictive of death than studies using CK-MB.[8] It has been suggested that the elevated levels of cardiac markers in acute ischemic stroke patients could be related to cardiac myocytolysis that occurred as a result of activation of the sympathetic nervous system.[8] The presumed cause for this elevation in acute neurologic disease is related to an increase in systemic catecholamines.[6] It is also possible that the secondary rise in CK-MB seen might represent brain damage since the B subunit also exists in the brain as creatine kinase B isoenzyme brain[8] that shows that the CK-MB rise is not purely cardiac in origin, and thus, CK-MB was not a predictor of long-term mortality.

Our results are consistent with this mechanism although there are other possible explanations, including that a prior cardiac event resulted in the subsequent stroke. This review reinforces the view that elevated troponin is associated with poor outcomes but has not fully established if elevated troponin is an independent prognostic factor. However, two of the four studies that did a multivariate analysis[9] and included a measure of stroke severity in that analysis found that troponin was an independent predictor of death. The variable exclusion of patients with preexisting cardiac/renal disease is still in support of the above.

The results of these studies have raised the debate as to whether cTnT should be routinely checked in patients with acute ischemic stroke. Recent UK acute stroke guidelines from the National Institute of Clinical Excellence[10] and the Scottish Intercollegiate Guidelines Network[11] do not recommend the routine checking of cardiac enzymes. However, the American Stroke Association[12] does recommend this. More research is required to determine the clinical utility of routine serum cTnT measurement after acute ischemic stroke so as to intensify management which might reduce mortality of patients.

Conclusion

If a combined end point of death and survival was considered, cTnT was still a powerful predictor of outcome.

In summary, elevated troponin after acute ischemic stroke appears to be common in patients and is associated with an increased risk of death.

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Conflicts of interest

There are no conflicts of interest.

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