Acute cerebral insults in the emergency department: epidemiology and predictive factors of highly sensitive troponin level's increase

Olfa Djebbi, Mariem Ben Abdellaziz, Dhikra Hamdi, Lilia Lotfi, Ons Khrouf, Mehdi Ben Lassoued, Khaled Lamine

Emergency Department, Military Hospital of Tunis, Tunisia

Corresponding author: *Olfa Djebbi; Email: olfa_urgence@yahoo.fr*

Abstract

Objectives : This study aimed to describe the clinical and epidemiological characteristics of acute neurological disease and to determinate the predictive factors of highly sensitive troponin elevation

Methods: this is a prospective and analytic study conducted at The Emergency Department of The Military Hospital of Tunis. It included 106 patients diagnosed with acute cerebral disease and having highly sensitive troponin measurement at admission over a period of 10 months. A multivariate analysis was conducted to identify the predictive factors of troponin elevation.

Results: The mean age of our patients was 62±19 years and the gender ratio was 1.4. Hypertension was the most common cardiovascular risk factor (46%). The most common acute neurological diseases were ischemic stroke (47%) followed by seizures (14%) and hemorrhagic stroke (13%). Thirty-six patients (35%) had a high troponin level, 18 patients (17%) had repolarization abnormalities and 8 patients (8%) had both troponin elevation and ST segment abnormalities. A high troponin level was found in 50% of patients with brain tumors, 47% of patients with seizures, 38% of patients with ischemic stroke and 33% patients with subarachnoid hemorrhage.

In this multivariate analysis, the independent predictive factors of troponin elevation in patients with acute neurological disease were: age greater than 65 (OR=2.75, CI: 2.801-5.456), diabetes (OR=1.47, CI: 1.546-3.956) and Glasgow Coma Scale (GCS) less than 15 (OR=0.53, CI: 2.213-4.329)

Conclusion: The troponin level was high in 35% of patients with acute neurological disease. Predictive factors of troponin elevation were: age greater than 65, diabetes, history of atrial fibrillation and a GCS under 15.

BACKGROUND

Acute brain insults are a frequent cause of patients presenting to the ED. It is also an important cause of functional disability and mortality among these patients. Numerous acute brain injuries such as stroke, subarachnoid hemorrhage, and seizures were associated with transitory heart malfunction with simultaneous troponin level increase [1]. Many studies showed that an increase in plasma catecholamine occurs after acute brain insults causing acute myocardial damage with elevated troponin levels. The increase in troponin levels could allow us to identify the patients having an acute brain insult with cardiovascular consequences. However, the cardiac repercussions of neurological insults are often unknown by the different stakeholders (emergency physician, neurologist, cardiologist). Also, increased troponin levels can occur in some conditions other than coronary artery disease whose symptoms can be atypical or hidden by the neurological signs. The challenge for the emergency physician is to recognize patients at high risk of myocardial repercussions because it is associated with poor prognosis.

Therefore, the management of these patients should be multidisciplinary. Our study aims to identify the epidemiological and clinical features of brain insults as well as to determine the predictive factors of troponin elevation among these patients.

METHODS

Patients and data acquisition: Consecutive patients admitted with acute brain insult were prospectively enrolled over 10 months in a database and followed during their hospitalization in the ED. We included 106 patients diagnosed with ischemic or hemorrhagic stroke, spontaneous or post-traumatic subdural and extradural hematoma, seizures, expansive intracranial process, and post-traumatic cerebral hematoma. Data prospectively collected included the following parameters: age, gender, medical history, clinical examination data, and laboratory data including cardiac Troponin I (cTNI) levels and brain imaging results. According to the final diagnosis, the patient was subsequently oriented towards the appropriate hospital department.

Blood samples: For the measurement of cTNI levels, the automated benchtop immunoanalyzer VIDAS based on the Enzyme Linked Assay (ELFA) technology was used. According to the local standards, a cTNI cut-off level of ≥ 19 ng/ml was considered a significant elevation; values of 19 ng/ml on admission were rated as increased when the second sample confirmed an elevation of ≥ 10 ng/ml.

Statistical analysis: We calculated the absolute frequencies and the relative frequencies (percentages) for the qualitative variables. We calculated means, medians, and standard deviations and determined the extreme values for the quantitative variable.

The comparisons of the percentages of independent series were carried out by the Chi-square test of Pearson, and in the event of invalidity of the previous test, we used the two-tailed Fisher test.

The comparisons of means of independent series were carried out with the student's t-test, and in the event of this test not being valid, we used the nonparametric test of Mann and Whitney.

To identify the factors of troponin elevation during acute brain insults, we compared two groups:

- G1: acute cerebral insults and positive troponin
- G2: acute cerebral insults and negative troponin

We conducted a multivariate, step-wise, decreasing logistic regression analysis. The multivariate analysis made it possible to calculate adjusted odds ratios, measuring the proper role of each factor.

For all statistical tests, the significance level "p" was fixed at 0.05.

RESULTS

Among the 106 patients who were included in the final analysis, the mean age was 62 years (SD ±19); the gender ratio was 1.4. The most common cardiovascular risk factor was hypertension (46%) followed by Diabetes (41%). Thirty-eight patients had at least two cardiovascular risk factors. In our study, 14% of patients had a medical history of coronary disease, and 5% had valvular disease with atrial fibrillation. A medical history of stroke was found among 23 patients. The reason for consultation was a motor deficit (41%) and an altered state of consciousness (34%). On admission, neurological examination showed a GCS of 9/15 in 11% of cases. The mean GCS was 14±3. A motor deficit was found in 49% of cases divided as follows: hemiparesis (49%), hemiplegia (36%), and monoparesis (15%). Ten patients had mental confusion and 7 patients had seizures. An ECG was performed for all patients showing: atrial fibrillation (21%), repolarization disorder (17%), tachycardia (27%), and bradycardia (2%). A cranial CT scan was also performed for all patients. It was normal for 34% of patients. Otherwise, it showed ischemic stroke (27%), hemorrhagic stroke (13%), subarachnoid hemorrhage (11%), extradural hematoma (3%), subdural hematoma (3%), intracranial hemorrhage (8%), and expansive intracranial process (1%).

Troponin levels were high for 36 patients. The average troponin value was 166±39 ng/l. High Troponin levels were found in patients with an expansive intracranial process (50%), seizures (47%), ischemic stroke (38%), and subarachnoid hemorrhage (33%).

Repolarization disorders were present in 22% of patients with ischemic strokes. These disorders were T-wave inversion in 6 patients and ST segment depression in 5 patients.

Table 1 resumes the different repolarization disorders associated with high troponin levels among patients with acute brain insults.

Table 1: the different repolarization disorders associated with high troponin levels among patients with acute brain insults.

Type of repolarization disorders	High troponin levels N (%)
T wave inversion	4 (11)
ST segment depression	4 (11)
T wave inversion with ST-segment depression	1 (3)

The duration of hospitalization was less than 12 hours for 90% of our patients. Seventy-six percent of patients diagnosed with ischemic stroke were hospitalized in the neurology department and 91% of those diagnosed with

subarachnoid hemorrhage were hospitalized in the neurosurgery department. The death rate in the ED was 3%. Troponin levels were normal among the patients who died.

Age over 65 and diabetes were significantly associated with high troponin levels (significance levels were respectively p=0,016 and p=0,032). Also, GCS under 15 was significantly associated with high troponin levels (p=0,04). Independent factors associated with the elevation in troponin levels among patients having brain insults were: age over 65, diabetes, atrial fibrillation, and GCS under 15 (Table 2).

Table 2: Independent factors associated with the elevation in troponin levels among patients having brain insults

	p	OR	CI
Age over 65	0,033	2,79	[2.801-5.456]
diabetes	0,048	1,47	[1.546-3.956]
GCS under 15	0,006	0,53	[2.213-4.329]
History of AF	0,04	0,05	[1,185-3,387]

DISCUSSION

In our study the mean age of patients having acute brain insults was 62±19 and the gender ratio of 1, 4. This is consistent with the findings of Sandhu and al [1]. who included 175 patients admitted for ischemic stroke, 107 patients admitted for brain hemorrhage, and 96 patients admitted for subarachnoid hemorrhage where the mean age was respectively 67, 61, and 51.

The most common cardiovascular risk factor in our study was hypertension (46%). It was also the case in the study of Tsivgoulis and al [2]. that included 703 patients for acute brain insults where hypertension was the first cardiovascular risk factor with a rate of 81%. Concerning atrial fibrillation, it was found among 27% of our patients while it was present among 28% of the patients included in Anders and al.'s study[3] that also found 17% of patients with ischemic stroke history.

In a prospective metacentric study conducted in Brazil by Carvalho and al (4), including 2407 patients for acute brain insults, motor deficit was the most frequent reason for consultation (71%) followed by headaches (27%). This result is close to our: motor deficit (41%) and headaches (25%). Ischemic stroke (47%) was the most common acute brain insult diagnosed among our study population preceding hemorrhagic stroke (13%). This finding is similar to both results from Carvalho and al [4] . and Tsivgoulis and al.'s works[2].

Troponin levels can rise without necrosis or ischemia but it always indicates the presence of acute or chronic myocardial injury. The importance of myocardial involvement during

brain injury is highlighted in autopsy studies in which the frequency of transmural myocardial injury is more important after death of neurological origin [5].

The nerve center controlling the cardiovascular system is located in the brainstem and hypothalamus. The right insula is involved in the cardiac sympathetic nervous activity while the left insula regulates the cardiac parasympathetic nervous activity. The damage in one of these areas causes an imbalance in the sympathetic/parasympathetic cardiac nervous activity [6]. The amygdala, located in the internal part of the temporal lobe, inhibits the Nucleus Tractus Solitarii and activates the lateral rostroventral segment of the brainstem leading to the decrease of parasympathetic activity and the increase of sympathetic activity [7].

The increase in troponin levels during stroke can be caused by an ischemic myocardial injury secondary either to the erosion of an atherosclerotic plate in coronary arteries or the imbalance between oxygen demand and supply. The myocardial injury during stroke can also be caused by a neurogenic myocardial cytolysis. Sympathetic hyperactivity occurs during stroke leading to a catecholamine discharge that causes myofibrillary degeneration which is responsible for non-ischemic myocardial injury and troponin liberation.

According to the literature, almost 19% of patients develop severe cardiac complications in the first few weeks following the ischemic stroke with a maximum frequency in the first 3 days. Cardiac-related death occurs in 4% of patients [8].

The rise in troponin levels is common after an ischemic stroke. It is found in 5 to 34% of patients. It predicts a poor prognosis for mortality and neurological outcomes [9]. In our study troponin levels were high in 38% of patients diagnosed with ischemic stroke.

The incidence of troponin level increase tends to vary across studies. It is influenced by the characteristics of the study population. Some studies excluded patients having renal failure or a history of heart disease. A literature review was conducted by Kerr and al [10]. including 15 studies that showed a high troponin level in 18% of cases. There was no significant difference between studies including or excluding patients with anterior renal failure.

Concerning hemorrhagic stroke, the physiopathological mechanism is similar to the ischemic stroke [11]. Hays and al [12] included 235 patients having hemorrhagic stroke in their study. 36% of them had high troponin levels. In another study including 208 patients with hemorrhagic stroke conducted by Tummala and al [13], the rate of cases with increased troponin levels was 49%. These outcomes are deemed to be higher than the results from our work where the rate of patients with hemorrhagic stroke associated with increased troponin level was 14%. The liberation of troponin in subarachnoid hemorrhage is the consequence of adrenergic myocarditis whose mechanism is very close to that observed in encephalic death [14]. The increase in troponin levels is frequently

observed among patients with hemorrhagic stroke secondary to ruptured aneurysm (68%). It is an early and specific marker of heart involvement. Its peak plasma concentrations occur in 2 days [15]. In a literature review that included 12 studies conducted on 2214 patients admitted for subarachnoid hemorrhage, troponin level increase was found in 21 to 25% of cases with a mean rate of 30% [16]. In our study, this rate was of 33%.

After a seizure, cytosolic troponin is liberated from the cardiomyocytes [17]. In our study increased troponin levels were found among 47% of patients with seizures. This outcome is considered to be higher than the results established by the literature where this rate was 8% [18] and 11% [19]. Namely in these studies, as in ours, patients with chronic renal failure and acute coronary syndrome were not included.

Traumatic brain injury generates an important catecholamine discharge that enhances the cardiac and cerebral oxygen requirements and causes an increase in troponin levels [20,21].

In the work of Prathep and al [22], troponin levels were high among 22% of patients hospitalized for post-traumatic brain injury. However, no patient with subdural, epidural, or cerebral hematoma was registered with high troponin levels in our study. This may be explained by the small number of cases included with these conditions.

Concerning the cases of intracranial expansive processes included in our study, the rate of high troponin levels was 50%. Unfortunately, the troponin level's increase in the intracranial expansive process has been poorly studied up to this point.

Cardiac electrical abnormalities are frequent after acute brain insults (90%) even in patients with no history of heart disease [23]

In our study, repolarization disorders were present in 22% of patients with ischemic stroke. They were represented by T wave inversion (12%) and ST segment depression (10%). Our results are close to those found by Faiz and al. (24) where T wave inversion and ST segment depression were observed in respectively 15% and 14% of the ischemic stroke cases included.

However, only 7% of cases with hemorrhagic stroke were registered with repolarization disorder which contrasts with the results from literature where this rate amounts to 64% [24]. Regarding subarachnoid hemorrhage, the most common repolarization disorder is T wave inversion (17%) followed by ST segment depression (14%). In our study, these rates were both of 8%. Other ECG modifications can be can be registered such as QT prolongation [25, 26].

Among our study population, 13% of seizure cases had T-wave inversion. This disorder was reported in 3 to 8% of cases in the literature [27,28].

We registered 33% cases of repolarization disorders among patients with epidural, subdural, and brain hematoma while Busl and al [29]. registered 11% of cases.

Concerning expansive intracranial process, repolarization disorders were registered in 13% of cases included in our study against 24% in the study of Povoa and al [30]. that excluded patients with hypertension, valvular, and coronary disease.

Table 3 summarizes the studies that analyzed the independent predictive factors of troponin levels increase in acute brain insults and compares them to our study.

Table 3: Independent predictive factors of troponin levels increase in acute brain insults in other studies compared to our study.

Study	Brain insult	Number of cases	Predictive factors of troponin levels increase
Abdi et al [62]	ischemic stroke	114	Age over 70, renal failure, repolarization disorder, NHISS score over 9
Batal et al [25]	ischemic stroke	1718	Advanced age, Hypertension, smoking, congestive heart failure, high NHISS score
Faiz et al [27]	Ischemic stroke	287	Age over 76, congestive heart failure, diabetes, renal failure, coronary disease
Tanabe et al [41]	Subarachnoid hemorrhage	103	Severe neurologic symptoms evaluated by Hunt Hess score
Miketic et al [42]	Subarachnoid hemorrhage	239	Severe neurologic symptoms evaluated by GCS
Sieweke et al [49]	seizures	741	Presence of cardiovascular risk factors
Chung et al [72]	Hemorrhagic stroke	253	Hypertension, masculine gender
Salim et al [58]	Brain Trauma	420	Severe neurologic symptoms evaluated by GCS
Our study	Stokes, subarachnoid hemorrhage, Brain trauma, intracranial expansive process	106	Age over 65, diabetes, history of atrial fibrillation, GCS under 15

According to the literature, the increase in troponin levels during acute brain insults is of bad prognosis leading to a higher mortality rate and severe neurological squeals. Early mortality (in less than 30 days) was significantly higher [31] as well as the mortality rate observed within a 5-year follow-up [9]. There is also an increase in the in-hospital deaths among these patients [1,12]. High troponin levels predict poor neurological recovery [32]and dependency on third parties [33].

CONCLUSION

In conclusion, assaying troponin levels is advisable in any patient admitted to the ED for acute brain insult. The different stakeholders (emergency physicians, neurologists, neurosurgeons, cardiologists, and radiologists) should be involved in the management of these patients for better evaluation and decision-making.

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