TAJ December 2014; Volume 27 Number-2

ISSN 1019-8555
The Journal of
Teachers Association
RMC, Rajshahi

Original Article

Troponin I Changes in Patients with Subarachnoid Hemorrhage

Sarker A[1], Hoque MA[2], Khan MMR[3], Rahman MK[3], Alam SM[4], Majumder S[5], Sardar MAH[6], Hasan MA[7]

Abstract

Background : Subarachnoid hemorrhage (SAH) is a catastrophic neurological event. Aside from its neurological morbidities, SAH is associated with significant medical complications. Cardiac manifestations are common and can impact morbidity and mortality in SAH patients. Myocardial enzyme release occur frequently after Subarachnoid hemorrhage that reflect adverse intracranial events .These changes often are unrecognized or misinterpreted, potentially placing patients at risk for inappropriate management.

Objective : The aim of this study was to assess Troponin I changes after acute SAH and these changes were compared with neurological severity. The result of the study might be helpful for better understanding diagnostic and therapeutic implications of acute neurocardiogenic injury after SAH.

Patients and methods : This cross sectional descriptive study was conducted over 30 patients with SAH in medicine, neuromedicine and intensive care unit of Rajshahi Medical College Hospital during the period of January 2015 to December 2016. Predictor variables reflecting demographic (age, sex, occupation), hemodynamic (pulse, systolic and diastolic blood pressure) and neurological (WFNS score) informations were recorded. We evaluated their cTnI level, which had been measured at admission. A cTnI level above 0.12 ng/ml was defined as an indicator of cardiac injury following SAH.

Results : Out of 30 patients 26.7% were both in between 40-49 years and 60-69 years age group & 50% were male and 50% were female. Among the risk factors 60% of patient had history of hypertension, 40% smoking, 10% Diabetes mellitus and 3.3% alcohol abuse. On admission the mean GCS was 12.53±2.69,. The most frequently occurring WFNS grading were grade 1 and grade 4 (both were 43.3% of patients). Out of Thirty, 43.3% of patients demonstrated elevations of Troponin I. WFNS score ≥ 3 (92.3%, p = <0.001) significantly correlated with elevated Troponin I concentration.

Conclusion : serum troponin I reveal a higher incidence of myocardial injury in patients with SAH. The present study also demonstrates that raised serum cTnI is associated with more severe neurological injury. These findings support a neurocardiogenic cause of cardiac injury after SAH.

Key wards: Subarachnoid hemorrhage, Troponin I, ECG, WFNS grade.

TAJ 2014; 27: No-2: 39-43

[1] Emergency Medical officer, Rajshahi Medical College Hospital, Rajshahi.
[2] Professor, Department of Medicine, Rajshahi Medical College, Rajshahi.
[3] Associate professor, Department of Medicine, Rajshahi Medical College, Rajshahi.
[4] Senior consultant, Department of Medicine, Sadar Hospital, Pabna.
[5] Medical officer, Upazila Health Complex, Charghat, Rajshahi.
[6] Medical officer, Upazila Health Complex, Mohanpur, Rajshahi.
[7] Lecturer, Department of Biochemistry, Rajshahi Medical College, Rajshahi.

Introduction

SAH is defined as acute extravasation of blood into the subarachnoid space. It occurs primarily during young to mid adulthood in both sexes and approximately 30% of those affected die within 2 weeks of the initial event [1]. The most common cause of SAH is rupture of a congenital aneurysm in a blood vessel at the base of the brain. In addition to the classic clinical signs and symptoms of SAH, which include abrupt onset of severe headache, nuchal rigidity, nausea, vomiting and alteration in consciousness, ECG and Troponin changes often occur.

The connection between the central nervous system (CNS) and the heart was first described by Cushing at the turn of the previous century [2]. Cardiac abnormalities have since been described in the course of various CNS diseases. In 1954, Burch described "cerebral T wave" electrocardiographic (ECG) abnormalities in patients with stroke and noted that the findings were most marked in patients with subarachnoid hemorrhage [3]. Elevated cardiac enzyme levels and myocardial contraction band necrosis have been described after SAH and provide evidence that permanent cardiac damage may occur [4,5,6]. Cardiopulmonary complications after aneurysmal SAH negatively affect overall morbidity and mortality and have been linked to worsened clinical outcome, suggesting a role for cardiac monitoring and interventions [7].

The mechanisms of cardiac dysfunction after SAH used to be controversial until recently. Historically, cardiac necrosis after SAH has been attributed to coronary artery disease, coronary vasospasm or oxygen supply-demand mismatch. Experimental evidence, however, indicated that excessive release of norepinephrine from the myocardial sympathetic nerves was the most likely cause [8] .Now-a-days we know that acute left ventricular dysfunction associated with SAH can be the expression of a stress –related cardiomyopathy [9], ("catecholamine hypothesis" of neurogenic cardiac stunning causing non-ischemic myocardiac injury). Neurogenic stunned myocardium (also known as apical balloting syndrome or Takotsubo syndrome) is a frequent complication of aneurysmal SAH, with a significant impact on disease course. The presumed cause is catecholamine surge at the time of aneurysm rupture [10]. A possible mechanism is that hypothalamic ischemia causes increased sympathetic tone and resultant catecholamine surge producing subendocardial ischemia or coronary artery vasospasm[11]. The massive surge of catecholamines after SAH likely induces various degrees of cardiac injury, as evidenced by increased serum troponin levels, ECG changes and sometimes severe cardiac wall motion abnormalities [12].

In recent years, considerable investigative interest has been directed at the cardiac Troponin I, a new marker of myocardial injury. Cardiac Troponin I is a regulatory protein highly specific for the cardiac muscle[13]. SAH frequently results in myocardial necrosis with release of cardiac enzymes [8]. Cardiac Troponin I release occurs frequently after SAH and has been associated with a neurogenic form of myocardial injury [14]. Elevated Troponin I has been reported in up to 68% of SAH patients [15]. Troponin elevation, usually modest, is an early and specific marker for cardiac involvement after SAH [16,17] and its levels peak about two days after SAH. This study was designed to determine the incidence of cTnI changes in patients with SAH and those patients with abnormal findings on their electrocardiograms and elevated cTnI levels were evaluated to see relationship with SAH severity.

Material and Methods

This was cross sectional type of observational study carried out in Rajshahi Medical College Hospital, Rajshahi, Bangladesh. The duration of the study was two years. A systemic sampling technique was done. Every patient who admitted in Neuromedicine ward within the time frame of study was interviewed. Patients who were detected as acute Subarachnoid Hemorrhage and who fulfill the inclusion criteria was enrolled in this study.

With the consent of concerned authority the data was collected from the respondents according to questionnaire by face to face interview. All patients were admitted within 24 hours of onset of

symptoms. Complete history (including age, sex, occupation, history of hypertension, diabetes mellitus, smoking and other risk factors) was taken and thorough clinical examination with measurement of pulse, blood pressure was done by standard method. The World Federation for Neurosurgeons Score (WFNS) was calculated by observers who were blinded to the patient's ECGs. WFNS grade ≥ 3 was regarded as severe. cTnI was measured in all patients at admission. The serum cTnI levels were measured by Immulite 2000 (SIEMENS)/Vitros ECi system (j & j)/Abbott Architect i-1000-SR random access multibatch Immunoassay Analyzer. A cTnI level ≥ 0.12 ng/ml was considered as an indicator of cardiac injury. All relevant clinical examination findings and laboratory results were recorded in a case record form.

Results

30 patients were included in this study.

Table 1: Patient Characteristics

Age, Years ± SD	54.83 ± 12.8
Sex (%)	
M	15 (50)
F	15 (50)
Risk Factor (%)	
Hypertension	18 (60)
Smoking	12 (40)
Diabetes mellitus	3 (10)
Alcohol abuse	1 (3.3)
GCS ± SD	12.53 ± 2.69
WFNS	
1	13 (43.3)
2	1 (3.3)
3	3 (10)
4	13 (43.3)

Most of the patients in this study were in between 40-49 years and 60-69 years age group (26.7%). The mean age was 54.83±12.80 years (range 35-80 years).The gender distribution of the population was equal; 50% of the patients were male and 50% of the patients were female.Among the risk factors 60% of patient had history of hypertension, 40% smoking, 10% Diabetes mellitus and 3.3% alcohol abuse.On admission the mean GCS was 12.53±2.69. The lowest GCS score was 8 and highest was 15.The most frequently occurring World Federation of Neurosurgical Societies (WFNS) grading were grade 1 and grade 4 (both were 43.3% of patients). Others were grade 3 (10% of patients) and grade 2 (3.3% of patients).

Table 2: Percentage distribution of study patients by Troponin I level

	N (%)	Mean±SD	Minimum	Maximum
Normal	17 (56.7)	0.325 ±0.640	0.001	2.700
Elevated	13(43.3)			
Total	30			

Thirteen of the 30 patients demonstrated elevations of Troponin I (43.3%). Among the recorded Troponin I levels the lowest level was 0.001 ng/ml and highest level was 2.700 ng/ml. The mean Troponin I value was 0.325 ±0.640.

Table 3: Relationship between Troponin I changes and WFNS grade

Troponin I	WFNS (%)		χ^2,test (p value)
	Grade 1&2	Grade 3,4&5	
Elevated (≥0.12 ng/ml)	1 (7.7)	12 (92.3)	<0.001*
Normal (<0.12 ng/ml)	13 (76.5)	4 (23.5)	

*Values reach statistical significance.

Fourteen of the 30 patients were categorized as grades 1-2 at the time of presentation; the remaining 16 were grouped as grades 3-5. The

more severe grades of SAH (grades 3-5) were associated with a greater incidence of raised troponin (92.3%, p = <0.001) values.

Discussion

The age of SAH varies in different parts of the world. In our study, the mean age was 54.83±12.80 years. The age of the youngest patient was 35 years and the oldest was 80 years. Male-female ratio in our study was 1:1 Several risk factors found among SAH patients were discussed in many studies [18,16]. Our study revealed several risk factors such as hypertension (60%), smoking (40%), diabetes mellitus (10%) and alcohol abuse (3.3%). The most frequently occurring World Federation of Neurosurgical Societies (WFNS) grading in our study were grade 1 and grade 4 (both were 43.3% of patients); A study by Sakr et al.[18] showed that most frequently occurring WFNS grade was 1 (48.7%) followed by grade 4 (19.9%), grade 5 (13.5%), grade 2 (10.3%) and grade 3 (7.7%). This picture does not resemble our study. The possible explanation may be the difference of sample size between the studies.

The frequency of cTnI elevation (≥0.12 ng/ml) was 43.3% among the patients we tested, a result that is higher than the following studies by Horowitz et al.[5] (1998) – 17%, Parekh et al.[19] (2000) and Tung et al.[8] (2004) – 20%, In other studies, the reported frequency of cTnI elevation was higher than our study; Naidech et al.[14] (2005) – 68%, Ahmadian et al.[16] (2013)- 71.6%. Among the recorded Troponin I levels in our study, the lowest value was 0.001 ng/ml and highest value was 2.700 ng/ml. The mean Troponin I value was 0.325 ±0.640. Deibert et al.[20] (2003) showed that cTnI was 100% sensitive in detecting left ventricular dysfunction in patients with SAH. Similarly, in a study of 39 patients with Parekh et al.[19] (2000) found cTnI to be 100% sensitive in detecting myocardial dysfunction on echocardiograms. The disparity in the incidence of myocardial injury in SAH reported in our study and those of others could be attributed to the differing grades of SAH in the study population, differences in the timing and methodology of biochemical assays and the use of cTnI assay in our study.

The present study demonstrates that 92.3% patients of SAH with more severe WFNS grade (3-5) develop cTnI ≥0.12 ng/ml. A significant relationship was observed between the higher WFNS grade, which is widely used in assessing the severity of neurological injury after SAH and the raised Troponin I (p = <0.001). This finding is consistent with a study by Parekh et al.[19] (2000) that showed that patients with more severe grades of SAH had a higher incidence of cTnI release (46%, p < 0.005). Naidech et al.[14] (2005) and Tung et al.[8] (2004) also showed that significantly more patients with raised cTnI had greater SAH severity. But in these studies neurological severity was assessed by Hunt-Hess grade which has similarity with WFNS grade. The results of these studies indicate that the severity of neurological injury is strongly related to myocardial necrosis.

Conclusion

In conclusion, we found that measurements of serum troponin I reveal a higher incidence of myocardial injury in patients with SAH. The present study also demonstrates that raised serum cTnI is associated with more severe neurological injury. These findings support a neurocardiogenic cause of cardiac injury after SAH. So, it is useful to monitor cTnI level and ECG changes following SAH, especially to estimate cardiac complications and disease severity. However, further research is essential to evaluate the results of this study and to choose optimal management.

References

1. Brown RD Jr, Wiebers DO, 1998. Subarachnoid Hemorrhage and unruptured intracranial aneurysms. In: Ginsburg MD, Bogousslavsky J, eds. Cerebrovascular Disease: Pathophysiology, Diagnosis and Management. Vol 2. Malden, Mass: Blackwell Science; 1502-1531.

2. Cushing H, 1903. The blood pressure reaction of acute cerebral compression illustrated by cases of intracranial hemorrhage. Am J Med Sci, 125: 1017-44.

3. Burch GE, Meyers R, Abildskov JA, 1954. A new electrocardiographic pattern observed in cerebrovascular accidents. Circulation, 9: 719-723.

4. Fabinyi G, Hunt D, McKinley L, 1977. Myocardial creatine kinase isoenzyme in serum after subarachnoid hemorrhage. J Neurol Neurosurg Psychiatry, 40: 818-820.
5. Horowitz MB, Willet D, Keffer J, 1998. The use of cardiac troponin –I (cTnI) to determine the incidence of myocardial ischemia and injury in patients with aneurysmal and presumed aneurysmal subarachnoid hemorrhage. Acta Neurochir (Wien), 140 (1): 87-93.
6. Doshi R, Neil-Dwyer G, Stott A, 1977. Hypothalamic and myocardial lesions after subarachnoid hemorrhage. J Neurol Neurosurg Psychiatry, 40: 821-826.
7. Bruder N, Rabinstein A. 2011, Participants in the International Multi-Disciplinary Consensus Conference on the Critical Care Management of Subarachnoid Hemorrhage. Cardiovascular and Pulmonary complications of aneurysmal subarachnoid hemorrhage. Neurocrit Care, 15 (2): 257-269.
8. Tung P, Kopelnik A, Banki N, Ong K, Ko N, Lawton M T , 2004.Predictors of neurocardiogenic injury after subarachnoid hemorrhage. Stroke; 35 (2): 548-553.
9. Richard C, 2011. Stress-related cardiomyopathies. Ann Intensive Care, 1(1): 39.
10. Liang CW, Chen R, Macri E, Naval N, 2013. Preadmission beta –blockers are associated with decreased incidence of neurogenic stunned myocardium in aneurismal subarachnoid hemorrhage. J Stroke Cerebrovasc Dis, 22(5): 601-607.
11. Greenberg MS, 2006. Handbook of neurosurgery. 6th ed. New York: Thieme Medical Publishers, p.789.
12. Eddleman CS, Getch CC, Bendok BR, Batjer HH, 2012. Intracranial aneurysms. In: Ellenbogen RG, Abdulrauf SI, Sekhar LN, editors. Principles of neurological surgery. 3rd ed. Philadelphia: Saunders (Elsevier) p.214.
13. Collinson PO, 1998. Troponin T or troponin I or CK-MB (or none?). Eur Heart J, 19 (suppl N):N16-24.
14. Naidech AM, Kreiter KT, Janjua N, Ostapkovich ND, Parra A, Commichau C, et al.2005. Cardiac troponin elevation, cardiovascular morbidity and outcome after Subarachnoid Hemorrhage. Circulation, 112 (18): 2851-2856.
15. Spears J, Macdonald RL, Weir B, 2011. Perioperative management of Subarachnoid Hemorrhage. In: Winn HR, editor. Youmans Neurological Surgery. 6th ed. Vol. 4. Philadelphia: Saunders (Elsevier); p.3785-3786.
16. Ahmadian A, Mizzi A, Banasiak M, Downes K, Camporesi EM, ThompsonSullebarger J et al, 2013. Cardiac manifestations of Subarachnoid Hemorrhage. Heart, Lung and Vessel, 5 (3): 168-178.
17. Kumar PV, Vannemreddy P, Kumar D, Nanda A, Reddy P, 2011. Cardiac troponin I levels are a marker of myocardial dysfunction in subarachnoid hemorrhage and predicts poor neurologic outcome. J La State Med Soc 163 (5): 257-260.
18. Sakr Y L, Lim N, Amaral ACKB, Ghosn I, Carvalho FB, Renard M, Vincent JL, 2004. Relation of ECG changes to neurological outcome in patients with aneurysmal subarachnoid hemorrhage. International Journal of Cardiology, 96 (3): 369-373.
19. Parekh N, Venkatesh B, Cross D, Leditschke A, Atherton J, Miles W, Winning A, Clague A, Rickard C, 2000. Cardiac Troponin I predicts myocardial dysfunction in Aneurysmal Subarachnoid hemorrhage. J Am Coll Cardiol; 36 (4): 1328-35.
20. Deibert E, Barzilai B, Braverman AC, Edwards DF, Aiyagari V, Dacey R, Diringer M, 2003. Clinical significance of elevated troponin I levels in patients with nontraumatic subarachnoid hemorrhage. J Neurosurg 98:741-746.

All corresponds to
Dr. Ashoke Sarker
Emergency Medical Officer
Rajshahi Medical College Hospital, Rajshahi, Bangladesh
E-mail : Dr.ashoke.rmch@gmail.com