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Cardiac Troponin I Predicts Myocardial Dysfunction in Aneurysmal Subarachnoid Hemorrhage

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OBJECTIVES We studied the incidence of myocardial injury in aneurysmal subarachnoid hemorrhage (SAH) using the more sensitive cardiac troponin I (cTnI) assay, correlated changes in cTnI with creatine kinase, MB fraction (CK-MB), myoglobin, and catecholamine metabolite assays, and examined the predictive value of changes in cTnI for myocardial dysfunction.

BACKGROUND Myocardial injury in aneurysmal SAH as evidenced by elevated CK-MB fraction has been reported. Little published data exist on the value of cTnI measurements in aneurysmal SAH.

METHODS Thirty-nine patients were studied for seven days. Clinical cardiovascular assessment, electrocardiographic (ECG), echocardiography, cTnI, CK, CK-MB and CK-MB index, myoglobin and 24-h urinary catecholamine assays were performed in all patients. The ECG abnormalities were defined by the presence of ST-T changes, prolonged QT intervals, and arrhythmias. An abnormal echocardiogram was defined by the presence of wall-motion abnormalities and a reduced ejection fraction. The severity of SAH was graded clinically and radiologically.

RESULTS Eight patients demonstrated elevations in cTnI (upper limit of normal is 0.1 μg/liter with the immunoenzymatic assay and 0.4 μg/liter with the sandwich immunoassay), while five had abnormal CK-MB levels (upper limit of normal is 8 μg/liter). Patients with more severe grades of SAH were more likely to develop a cTnI leak ($p < 0.05$). Patients with cTnI elevations were more likely to demonstrate ECG abnormalities ($p < 0.01$) and manifest clinical myocardial dysfunction ($p < 0.01$) as evidenced by the presence of a gallop rhythm on auscultation and clinical or radiological evidence of pulmonary edema as compared to those with CK-MB elevations. The sensitivity and specificity of cTnI to predict myocardial dysfunction were 100% and 91%, respectively, whereas the corresponding figures for CK-MB were 60% and 94%, respectively. Elevations in myoglobin levels (upper limit of normal <70 μg/liter) and urinary catecholamine metabolites (urinary vanilmandelate/creatinine ratio upper limit of normal, 2.6) are a nonspecific finding.

CONCLUSIONS Measurements of cTnI reveal a higher incidence of myocardial injury than predicted by CK-MB in aneurysmal SAH, and elevations of cTnI are associated with a higher incidence of myocardial dysfunction. Thus, cTnI is a highly sensitive and specific indicator of myocardial dysfunction in aneurysmal SAH. (J Am Coll Cardiol 2000;36:1328–35) © 2000 by the American College of Cardiology

Aneurysmal subarachnoid hemorrhage (SAH) has an estimated incidence of 6 to 7.5 cases per 100,000 persons per annum (1) and accounts for 6% to 10% of all strokes and 22% to 25% of cerebrovascular deaths. Cardiac abnormalities, as evidenced by release of cardiac enzymes, changes in electrocardiography (ECG) or clinical or echocardiographic evidence of left ventricular dysfunction, occurring in association with aneurysmal SAH, have been well described (2–5).

The etiology of the myocardial changes remains largely speculative. While the temporal profile and pattern of ECG changes suggest that myocardial ischemia may be contributory, regional myocardial dysfunction in association with ST segment elevation has been described in patients on whom subsequent coronary angiography showed no obstructive lesions (6). The weight of evidence points to a catecholamine-mediated damage based on histological lesions in the myocardium that resemble those of a catecholamine myocarditis (7,8) and the presence of elevated levels of catecholamines in the serum (9,10). It is possible that these patients are exposed to a catecholamine surge at the time of the bleed or subsequently during the course of the illness.

Despite a large body of evidence testifying to the development of myocardial injury in SAH (6,11–13), the true incidence in this population remains unknown. The ECG changes are often nonspecific and transitory (2). Several studies have examined cardiac enzyme release (typically creatine kinase, MB fraction, CK-MB), but interpretation can be difficult as CK-MB may be released from noncardiac muscle damage (14,15). Furthermore, some patients may develop clinically important myocardial dysfunction due to

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Abbreviations and Acronyms

cTnI	= cardiac troponin I
CK-MB	= creatine kinase MB fraction
EF	= Ejection fraction
Pa_{CO_2}	= Partial pressure of arterial carbon dioxide
SAH	= subarachnoid hemorrhage
VMA	= vanilmandelate

sublethal injury that does not result in CK-MB release (16). Echocardiography may detect left ventricular systolic dysfunction due either to transitory metabolic abnormalities or permanent ischemic damage.

In recent years, considerable investigative interest has been directed at the cardiac troponin I (cTnI), a new marker of myocardial injury. Cardiac troponin I is a regulatory protein highly specific for the cardiac muscle (17). Small amounts of cTnI may be released from a cytosolic pool due to sublethal myocyte injury, but larger amounts of cTnI release imply irreversible cell death and breakdown of the contractile apparatus. Troponin release is also accepted as the most specific marker of myocardial necrosis in patients with myocardial infarction (14). The major advantage of cTnI is its ability to detect myocardial cell damage that is undetectable by conventional enzyme methods, with high sensitivity and specificity (18). Although a number of studies demonstrate the greater specificity and sensitivity of cTnI as compared to CK-MB for the detection of myocardial damage from various etiologies (14,16,19,20), there is little published data with regard to cardiac troponins in patients with subarachnoid hemorrhage.

The aims of this study were:

1. to define the incidence of cardiac injury in patients with aneurysmal SAH as determined by cTnI release;
2. to compare the predictive value of elevations in cTnI, CK-MB mass and serum myoglobin in predicting myocardial injury in these patients; and
3. to investigate the relationship between urine catecholamine metabolite levels and cTnI and between elevated cTnI and neurological complications.

METHODS

The study was approved by the Royal Brisbane Hospital Research Ethics Committee. Informed consent was obtained from patients or the next of kin depending on the conscious state of the patient at the time of enrollment. The study period extended from April 1998 to April 1999.

Inclusion criteria. All patients with spontaneous, nontraumatic acute SAH confirmed on computed tomographic (CT) scan of the brain and presenting within 24 h of onset of symptoms were eligible for inclusion in the study.

Exclusions. Patients with a history of myocardial infarction, cardiac surgery, or trauma within the previous three months, cardiomyopathy and renal impairment defined as serum creatinine more than 0.12 mmol/liter were excluded from the study.

Following enrollment, the severity of subarachnoid hemorrhage (SAH) was graded clinically using the Hunt and Hess classification (21). Patients with grade I SAH were admitted to the neurosurgical ward, whereas those with grades II through V were managed in the neurosurgical intensive care unit (ICU). All patients in the ICU had continuous ECG monitoring and arterial cannulation for invasive pressure monitoring as part of standard clinical practice. When patients required sedation for intensive care procedures, facilitation of positive pressure ventilation or transport, propofol (1–3 mg/kg/hour) in combination with alfentanil (10–20 μg/kg/hour) or midazolam (0.1–0.2 mg/kg/hour) in combination with fentanyl (1–2 μg/kg/hour) were used.

Endotracheal intubation was performed and positive pressure ventilation initiated when clinically indicated. Four-vessel cerebral angiography was performed within 48 h of admission to the hospital to identify the location of the aneurysm. In all patients, intravenous (IV) nimodipine infusion was commenced at an initial infusion rate of 5 μg/kg/hour, which was progressively increased over a 5-h period to a maximum dose of 30 μg/kg/hour. All patients were then maintained on this dose for a week unless the presence of side effects such as hypotension dictated a reduction in the dose of, or total cessation of, nimodipine. Patients were monitored for evidence of vasospasm using daily Doppler flow measurements and, in select cases, cerebral angiography.

Clinical assessment. Patients were examined daily for evidence of cardiac dysfunction as evidenced by the presence of a gallop rhythm on auscultation and clinical or radiological evidence of pulmonary edema. Both the need for and the timing of commencement of inotropic and/or pressor therapy were recorded.

Biochemical measurements. Measurements of CK, CK-MB, CKMB index, and cTnI were performed daily for seven days on all patients. For estimation of CK, CK-MB and cTnI blood samples were collected in plasma separator tubes. Total CK activity (upper reference limit 210 U/liter, lower limit of detection 35, CV 3%) was measured on a Hitachi 747 analyzer. The CK-MB mass (upper reference limit of normal 8 μg/liter, lower limit of detection 0.1 μg/liter, CV 6.4%) was measured on the Beckman Access analyzer. In the first 29 patients, the serum cTnI levels were measured by an immunoenzymatic assay (reference range for upper limit of normal 0.1 μg/liter, lower limit of detection 0.01 μg/liter, CV 25%) using the Access analyzer. Owing to potential interference with this assay by mouse antibodies, an antibody test was performed in all patients with elevated troponin by this assay to exclude false positive rise in cTnI due to mouse heterophile antibodies. From December 1998, the method of assaying cTnI was changed to a sandwich immunoassay (reference range for upper limit of normal 0.4 μg/liter, lower limit of detection 0.2 μg/liter,

CV 10%), which incorporated two monoclonal antibodies specific for two different epitopes of cTnI. There is no reported interference with this assay by heterophile anti-mouse antibodies. The cTnI levels in the last 12 patients were measured using the new assay.

Because of the change of the troponin assay after patient number 29, a methods comparison was performed between the old and the new technique on blood samples (not belonging to the study) submitted to the laboratory for troponin analysis. Sixty-seven plasma samples from patients were analyzed by both methods. Samples that were positive by the immunoenzymatic assay (older method) were diluted with mouse serum to exclude heterophile interference, and if the samples were found to be positive on the reassay, they were excluded from comparison. Positive interference was found in nine samples that were reassayed. The data revealed a strong correlation ($r^2 = 0.8$) between the two methods.

Serum myoglobin and urinary vanilmandelate (VMA) were measured in the first 30 patients enrolled into the study. Serum myoglobin levels were measured every 6 h for the first 24 h of admission using latex-enhanced nephelometry (reference range for upper limit of normal 70 μg/liter, lower limit of detection 6.8 μg/liter, CV 9%) on a BN2 Analyzer. In addition, in the first 30 patients, urinary levels of VMA (reference range for upper limit of normal 25 μmol/liter, lower limit of detection 1 μmol/liter, CV 5%) were performed daily for three days using high-performance liquid chromatography.

ECG and echocardiography. Twelve-lead ECG with consistent chest leads positioning was performed daily for seven days. The ECGs were considered abnormal if the T wave was inverted or flattened, the S-T segment was elevated or depressed, the QT interval was prolonged, or if an arrhythmia was present (22). Echocardiography was performed within 24 h of symptom onset by a cardiologist blinded to the results of the cardiac clinical examination, ECG analyses, radiographic data and cardiac enzyme analysis. Transthoracic studies (TTE) were performed unless the patient was intubated and ventilated, in which case a transesophageal (TEE) study was undertaken. The echocardiograms were performed on Hewlett-Packard SONOS 1500 or 5000 machines, with multiplane imaging for the transesophageal studies. Ejection fraction (EF) was calculated by conventional algorithms from either parasternal M-mode measurements or the area-length method from the transthoracic apical two- and four-chamber views or the corresponding views from the transesophageal window. Using standard tomographic planes, the left ventricle was divided into 16 wall segments as defined by the American Society of Echocardiography (23). Wall motion was classified as normal, hypokinetic, akinetic, or dyskinetic in each of the myocardial segments. An echocardiogram was reported as abnormal if there was evidence of wall-motion abnormalities or a globally reduced EF (<50%) (24,25).

Table 1. Clinical Characteristics of the Study Patients

Total number of patients	39
Gender distribution	M 15, F 24
Mean age in years (range)	54 (31–78)
Grade of SAH (Hunt and Hess)	
1	13
2	12
3	6
4	3
5	5
Median Glasgow Coma score	13
Median Fisher scale score	4
Mean heart rate	90 ± 39
Mean arterial pressure in mm Hg	94 ± 29
Arterial oxygen saturation (%)	96 ± 4
$PaCO_2$ (torr)	37 ± 8
Number of survivors	34

Neurological assessment. At the end of the study, radiological grading of the severity of SAH was performed according to the Fisher scale (26) by a consultant radiologist who was blinded to the clinical and biochemical data.

Statistical analysis. Categorical variables were compared by the chi-square test, or the Fisher exact test for comparisons involving small cell sizes. Continuous variables were compared by linear regression analysis. An alpha value of 0.05 was accepted as the boundary for rejection of the null hypothesis. Alpha values were not adjusted for multiple comparisons. A $p < 0.05$ was taken as statistically significant.

RESULTS

Demographic and clinical data. Forty-one patients were enrolled into the trial, of whom 39 were considered suitable for analysis. Two patients had fewer than 24 h of data collection and did not have the full set of ECG, biochemical, and echocardiographic investigations. One of these patients died within 24 h of enrollment, and the other patient withdrew from the study in the first 24 h. The clinical characteristics of the study population are illustrated in Table 1.

Cardiac enzyme levels. Eight of the 39 patients demonstrated elevations of cTnI (20%). Five of the eight patients with elevated cTnI also had an elevated CK-MB, whereas no patient with a normal cTnI had elevation of CK-MB. The peak elevation in cTnI levels was seen on day 1 in six patients and on day 2 in two patients. The enzymatic and echocardiographic data of those patients who demonstrated elevated serum troponins are listed in Table 2. Serum myoglobin was elevated in 11 of the 30 patients in whom it was measured. Myoglobin release was not correlated with cTnI or CK-MB release.

Relation between urinary catecholamine release and enzyme abnormalities. Twenty-six of the 30 patients (87%) demonstrated elevated urinary VMA levels. Urinary VMA level was found to be highly sensitive (100%), but a nonspecific (17%) predictor of elevations in serum cTnI.

Table 2. Enzymatic and Echocardiographic Data of Patients With Elevated Troponin

Patient No.	Peak Troponin Levels	ECG Findings	EF	Other Findings on Echocardiography	Clinical or Radiological Myocardial Dysfunction
3	0.15†	Normal	84	Normal contractility	Absent
6	0.27	T-wave inversion inferior leads	25	Global reduction in LV contractility	Present
9	0.11	T-wave inversion anterior leads	40	RWMA of inferior, lateral and anterior wall	Absent
12	0.17	Global ST depression	69	Normal contractility	Present
14	0.19†	Prolonged QT, lateral wall ST-T changes	50	Circumferential hypokinesia at basal level and severe hypokinesia of anterior wall and septum at mid-cavity level	Present
19	0.78†	Prolonged QT, lateral wall ST-T changes	64	Normal contractility	Absent
30	1.54*†	T-wave inversion inferior leads	35	Global hypokinesia	Present
33	3.1*†	Global ST depression	50	Severe septal hypokinesia and moderate hypokinesia of the infero-apical segment	Absent

*cTnI assay in these patients was performed by the sandwich immunoassay using monoclonal antibodies (upper limit of normal 0.4 μcg/ml). †These patients also demonstrated an increase in CK-MB levels.
RWMA = regional wall motion abnormality.

Echocardiographic findings. Twelve patients underwent transesophageal echocardiography; 27 patients were investigated with a transthoracic echocardiogram. Five patients (13%) had abnormal echocardiograms. Five of the eight patients in the elevated cTnI group had impaired myocardial contractility on echocardiography ($p < 0.0001$). The sensitivity and specificity of cTnI to predict myocardial dysfunction as defined by echocardiography were 100% and 91%, respectively. Three of the 5 patients with elevated CK-MB and 2 of the 34 patients with normal CK-MB also had abnormal echocardiograms (CK-MB sensitivity 60%, specificity 94%). Only one of the 11 patients with abnormal myoglobin group demonstrated impaired myocardial contractility (p = NS). The mean EF of those patients with elevated troponin was 53% as compared to 72% with normal troponin ($p = 0.02$), whereas no significant differences were noted in the mean EF between patients with elevated CK-MB and normal CK-MB levels. The individual EF data for the cTnI and the CK-MB groups are illustrated in Figures 1 and 2.

Electrocardiographic abnormalities. Abnormal ECGs were detected in 23 (59%) patients. Twenty-five ECG abnormalities were detected in the 23 patients. The ST-T changes (17/39) were the most frequent, followed by prolonged QT intervals (6/39) and supraventricular arrhythmias (4/39). The ST-T abnormalities were observed mainly in the inferolateral leads (11/39). Patients with elevated troponin had a statistically higher proportion of ST-T changes (39%, $p < 0.01$) as compared to those with elevated CK-MB (22%, $p = 0.1$).

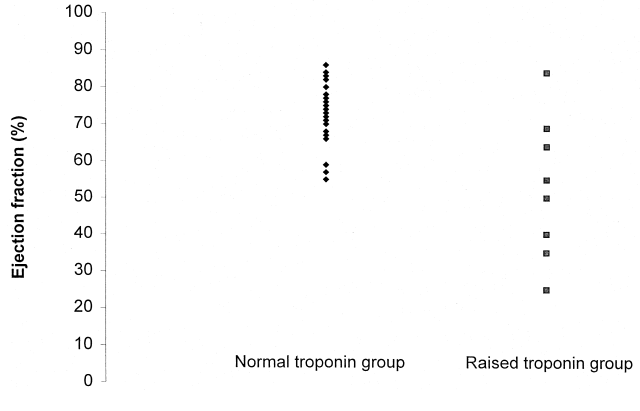

Figure 1. Individual echocardiographic data of patients with normal and abnormal cTnI.

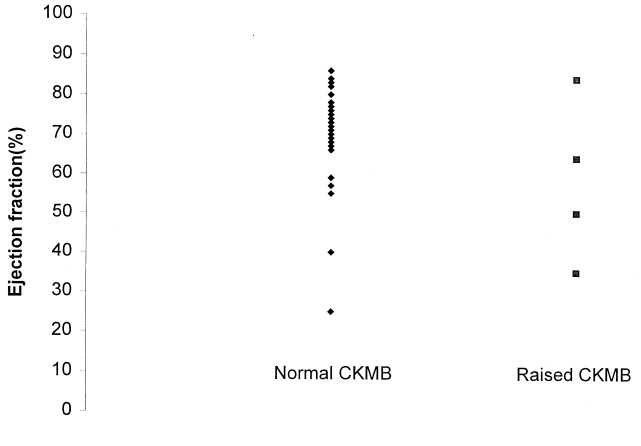

Figure 2. Individual echocardiographic data of patients with normal and abnormal CK-MB.

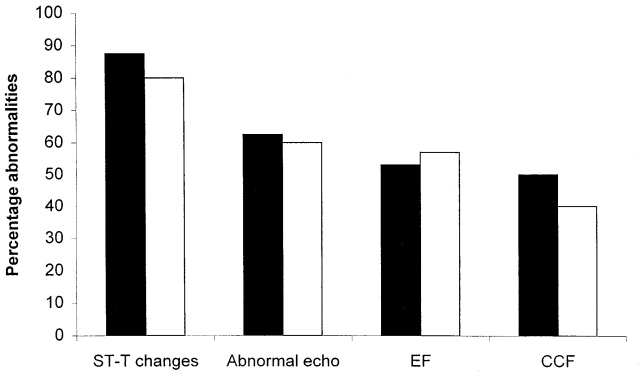

Figure 3. Cardiovascular data of both the cTnI and the CK-MB groups. **Solid bar** = raised cTnI; **open bars** = raised CK-MB.

Clinical outcomes. Six patients developed clinical signs of myocardial dysfunction based on clinical and radiological criteria. One patient required inotropic therapy with epinephrine to improve myocardial function and gas exchange. Four of the eight patients with raised troponin level developed clinical signs of myocardial dysfunction compared to two patients of those with normal troponin level ($p < 0.01$). Only 2 of the 5 patients with raised CK-MB developed clinical myocardial dysfunction, as compared to 3 of the 34 with normal CK-MB (p = NS). The cardiovascular data of both the cTnI and the CK-MB groups are summarized in Figure 3.

Relationship between clinical grade of SAH and biochemical abnormalities. Twenty-six of the 39 patients were categorized as grades 1–2 at the time of presentation; the remaining 13 were grouped as grades 3–5. The more severe grades of SAH (grades 3–5) were associated with a greater incidence of raised troponins (46%) ($p < 0.005$) and CK-MB (30%) ($p < 0.05$) values. Patients with less severe grades of SAH (grades 1–2) demonstrated a smaller incidence of both troponin (8%, $p < 0.005$) and CK-MB elevation (4%, $p < 0.05$).

Relationship between radiological grade of SAH and biochemical abnormalities. The brain CT scans of 37 patients were analyzed retrospectively for the radiological grade of SAH based on the Fisher score (scans of two patients were not available for analysis). All 7 patients who were grade 4 on the Fisher scale demonstrated an elevated cTnI as compared to the 30 patients who were grades 1–3 ($p = 0.04$). No statistically significant relationship was demonstrable between the radiological grading of SAH and CK-MB mass ($p = 0.08$), although the study was underpowered to exclude this relationship.

Relationship between biochemical abnormalities and the development of cerebral vasospasm. In all, 16 of the 39 patients (41%) demonstrated evidence of vasospasm, based on clinical examination, transcranial Doppler ultrasonography, and cerebral angiography. All five patients with a raised CK-MB mass demonstrated evidence of vasospasm ($p < 0.05$), whereas five of the eight patients with elevated troponin levels demonstrated vasospasm (p = NS). The relationship between biochemical changes and cardiac and neurological outcomes are shown in Tables 3 and 4.

DISCUSSION

The primary findings of this study are that cTnI is elevated in 20% of patients with SAH and that these patients are more likely to manifest echocardiographic and clinical evidence of left ventricular dysfunction. Patients with more severe grades of SAH were more likely to develop an elevated level of serum cTnI. Although five of the eight patients with elevated cTnI also had elevated CK-MB, cTnI was a more sensitive and specific indicator of left ventricular dysfunction assessed clinically or by echocardiography. However, there was no relationship between a raised cTnI and cerebral vasospasm.

Comparison with published literature. The CK-MB rise observed in this study is in keeping with the data of Rudehill et al. (2) and Mayer et al. (27). The lack of a significant relationship between elevations in myoglobin and cTnI are also in line with published data (28,29). The demonstration of a significant relationship between elevations in cTnI and myocardial dysfunction in SAH provides further evidence of the usefulness of cTnI as a marker of myocardial damage, irrespective of the etiology. The lack of correlation between the serum levels of other markers and myocardial dysfunc-

Table 3. Relationship Between Abnormal Troponin I and Clinical, Radiological, ECG, and Echocardiography Data

	Elevated Troponin	Normal Troponin	p Value
Number of patients	8	31	
ST-T changes on ECG	7/8*	11/31	< 0.01
Abnormal echocardiograph	5/8*	0/31	< 0.01
Clinical/radiological evidence of myocardial dysfunction	4/8*	2/31	< 0.01
Mean ejection fraction (%)	53*	72	0.02
Evidence of cerebral vasospasm	5/8	11/31	0.16
Clinical grade of SAH (grade 3 or >)	6/8*	8/31	< 0.01
Radiological grade of SAH Fisher scale 4	7/7*	18/30	0.04
Elevated urinary VMA	7/7	19/23	0.23

*Values reach statistical significance.

Table 4. Relationship Between Abnormal CK and Clinical, Radiological, ECG, and Echocardiography Data

	Elevated CK-MB/CK-MBI	Normal CK-MB/CK-MBI	p Value
Number of patients	5	34	
ST-T changes on ECG	4/5	14/34	0.1
Abnormal echocardiograph	3/5*	2/34	< 0.01
Clinical/radiological evidence of myocardial dysfunction	2/5	3/34	0.06
Mean ejection fraction (%)	57	70	0.18
Evidence of cerebral vasospasm	5/5*	11/34	< 0.01
Clinical grade of SAH (grade 3 or >)	4/5*	10/34	< 0.05
Radiological grade of SAH Fisher scale 4	5/5	20/32	0.09
Elevated urinary VMA	4/4	22/26	0.39

*Values reach statistical significance.

tion relate in part to their nonspecificity for the myocardium and in part to their inability to detect sublethal myocardial damage (16). The disparity in the incidence of myocardial injury in SAH reported in our study and those of others (2,3,30–32) 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. Only one published study (33) examined changes in cTnI in SAH and reported an incidence of myocardial injury of 17%, similar to what was observed in our trial (20%). However, owing to limited assessment of myocardial function in that study, other data are not comparable. The pattern of ECG abnormalities observed in our study are also consistent with previously published data (3,4,30,31). The lack of a statistically significant relationship between enzyme changes and development of cerebral vasospasm in our study is at variance with the data of Fabinyi et al. (32), who demonstrated clinical or angiographic evidence of cerebral vasospasm in all patients with elevated cardiac enzymes following a SAH.

Proposed mechanism of myocardial damage. An autopsy study in humans has suggested that SAH causes vascular damage to the hypothalamus with subsequent release of catecholamines, particularly noradrenaline, causing myocardial injury (34). Evidence to support the "catecholamine-mediated injury" hypothesis also exists in other studies (35,36), where it has been demonstrated that the histological lesions in the myocardium in SAH are similar to catecholamine-induced damage—that is, contraction band necrosis and myocytolysis (37,38).

Catecholamine-mediated myocardial injury is probably multifactorial: tachycardia, coronary spasm and vasoconstriction, toxic effects on the cardiac myocyte, and increased intracellular concentration of calcium (39,40). Although evidence for catecholamine-mediated damage is not substantiated by urinary VMA data in our study, urinary VMA is a reflection of serum catecholamines, and the serum catecholamines do not correlate with tissue catecholamines (9). These findings are also consistent with the data from Brouwers et al. (10), who could not demonstrate a relationship between ECG abnormalities in SAH and plasma noradrenaline concentrations. Myocardial catecholamine concentrations rise and fall rapidly after an intracranial catastrophe (41), and these may not be detectable by the use of urinary VMA. Hypoxia, hypocapnia, and hypotension were unlikely explanations for the myocardial changes as all patients were noted to maintain their blood pressure, arterial oxygen saturation and P_{CO_2} well within the clinically acceptable range. It is also important to recognize that the changes in ECG and echocardiography observed in these patients could be compatible with underlying coronary artery disease, although a previous study has demonstrated normal coronary anatomy in this cohort of patients (6).

The other variable to consider as an underlying etiological factor in the genesis of myocardial findings is the role of nimodipine. Nimodipine, a calcium channel blocker, is used as a cerebral vasodilator (42). Although nimodipine causes hypotension as a side effect, it has been shown to prevent ischemic injury in the myocardium (43,44). Maximum infusion rates of nimodipine were achieved in all our patients, and no significant episodes of hypotension were observed. Two of the four patients with clinical or radiological evidence of myocardial dysfunction in the elevated cTnI group had EFs of 50% or more on echocardiography. It is likely that in these patients there was a component of neurogenic pulmonary edema, which has been described in association with SAH (45).

Clinical implications of the study. The significance of this study is that it has demonstrated that more severe grades of SAH are associated with cTnI elevations, and a troponin leak in this setting is associated with myocardial dysfunction. This data are also consistent with and extend findings from previous work that identified both the superiority of cTnI over CK-MB as a marker of myocardial injury and the association of troponin leak with adverse outcome in a variety of conditions, including unstable angina (46), critically ill patients in intensive care (47), cardiac surgery (20), and doxorubicin therapy (48). The results from this study would also strengthen the case for monitoring more closely those patients with SAH who develop a troponin leak while in a high dependency unit or an ICU.

Patients with more severe grades of SAH may sometimes develop intractable intracranial hypertension and become brain dead. These patients can go on to become organ donors. Preliminary data from 19 pediatric patients suggest that elevated donor cTnI is a marker of acute graft failure in the cardiac recipient (49). Similar data have been published with regard to cTnT in adult patients (50). In the above studies, the cutoff values for donor cardiac troponins, above which there was a strong likelihood of graft failure, were very high. These data must be treated as preliminary, and a larger study is required to confirm these data. Nevertheless, the above studies raise important questions about the suitability of patients with significant elevations of cTnI from SAH becoming potential heart donors, and the combined assessment of cTnI and myocardial function may provide more useful information.

The presence of myocardial dysfunction raises the question of the follow-up studies to determine the duration of this phenomenon and the presence of any long-term sequelae. There is published data in a pediatric population to show that elevations in cTnI during cytotoxic chemotherapy predicted delayed ventricular dilatation and thinning (48). Although this study was not designed to address the question of long-term damage, this should be the subject of future studies to determine whether the myocardial dysfunction is a temporary or a more longer-lasting phenomenon as this has implications for future management and follow-up.

The presence of a troponin leak raises two anesthetic-management issues: first, the optimum timing of anesthesia and surgery and, second, the risk of perioperative cardiovascular deterioration. Recent myocardial injury and congestive cardiac failure have been consistently identified as risk factors for perioperative cardiac events in patients presenting for noncardiac surgery (51). Measures to minimize intraoperative cardiac risk could be considered, such as using a pulmonary artery catheter, avoiding myocardial depressant agents, and maintaining optimal myocardial oxygen supply and demand.

Study limitations. One of the limitations of the study was the exclusion of patients on the basis of preexisting cardiac disease based on history alone. It is possible that some patients may have had preexisting subclinical myocardial ischemia and dysfunction. We performed only one echocardiographic examination; serial assessment both during the acute illness and in the recovery phase may have given further insight into myocardial dysfunction. The use of inotropes in certain patients for inotropic and vasopressor support makes it difficult to interpret urinary catecholamine and biochemical data.

In conclusion, measurements of serum troponin I reveal a higher incidence of myocardial injury than predicted by CK-MB in patients with aneurysmal SAH. When SAH is accompanied by a raised serum cTnI, it is associated with a higher incidence of clinical and echocardiographic evidence of myocardial damage. The cTnI is a highly sensitive and specific indicator of myocardial dysfunction in aneurysmal SAH. Similar studies coupled with coronary angiography and long-term follow-up data are warranted in larger populations.

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