Correlation of Troponin-I with Angiographic Profile in Patients of Unstable Angina

Md. Akteruzzaman[1]
Aminur Rahman[2*]
Md. Nurul Amin Miah[3]
Afzalur Rahman[1], Johurul Hoque[1]
Anisur Rahman Khan[1], Zahed Ali[2]

1. Department of Cardiology, Sir Salimullah Medical College & Mitford Hospital, Dhaka, Bangladesh

2. Department of Neurology, Sir Salimullah Medical College & Mitford Hospital, Mitford, Dhaka, Bangladesh

3. Department of Medicine, Sir Salimullah Medical College, & Mitford Hospital, Mitford, Dhaka, Bangladesh

*Correspondence to:

Dr. Aminur Rahman,
Registrar, Department of Neurology,
Sir Salimullah Medical College & Mitford Hospital, Mitford, Dhaka,
Bangladesh
Phone: +8801711180902
E-mail: draminur@yahoo.com

Abstract

Objective: The study was intended to determine the angiographic profile (severity, site, and type of lesion) based on the level of cardiac troponin-I (cTn-I) in patients of unstable angina. **Methods:** The present cross-sectional study was conducted in the Department of Cardiology, Sir Salimullah Medical College & Mitford Hospital (SSMCH). Data were collected at Ibrahim Cardiac Hospital & Research Institute and SSMCH. A total of 81 patients with unstable angina were selected over a period of 1 year. Based on the level of cTn I at admission, the patients were divided into high risk (troponin-I level 0.06–0.6) and low-risk (0–<0.06) groups. Thus 47patients fell into high risk group (Group-I) and 34 patients into low-risk group (Group-II). The angiographic characteristics of the two groups of patients were then compared. **Results**: Over three-quarter (77%) of the patients in Group-I had significant coronary lesions compared to 26% in Group-II. Significant stenosis was commonly observed in Group-I than that in Group-II ($p < 0.001$). Number of vessels involved like single vessel (SVD), double vessel (DVD), and triple vessel diseases (TVD) were higher in Group-I compared to Group-II (30% vs. 20%; 34% vs. 3% and 12% vs. 3%). Site of lesions in LAD (left anterior descending) were compared between the study groups, proximal and mid lesions were found significantly higher in Group-I (45% vs. 9% and 49% vs. 18%, respectively), while distal lesion was almost identically distributed (5% vs. 6%). Type-B land type C lesions were higher in Group-I (30% vs. 3.0%) and (47% vs. 14%) while type-A lesion was higher in the Group-II (20% vs.8%). Majority (77%) of the patients who developed significant coronary artery lesion had raised cTnI. **Conclusions:** Patients of unstable angina with raised serum troponin-I had more severe coronary lesions (in terms of number of vessels significantly affected and site and type of lesions) than those with low serum troponin-I.

Key words: Tropnin-I; Angiographic profile; Low-risk patients; High-risk patients.

INTRODUCTION

Unstable angina is very common and often quite serious and is responsible for more than 750,000 hospitalizations annually in the United States and thus ranks among the most frequent causes of hospitalization in this country.[1] More than 70,000 of these hospitalized patients develop myocardial infarction and some die suddenly.[2,3] In Bangladesh, atherosclerotic disease is increasing gradually. National data on incidence and mortality of coronary heart disease are few in Bangladesh. The prevalence of coronary heart disease was estimated as 3.3/1000 in 1976 and 17.2/1000 in 1986 indicating 5 fold increase of the disease in 10 years.[4] Since

the unstable coronary artery disease (CAD) population is heterogeneous both regarding the severity of the underlying CAD and prognosis early risk stratification is essential.[5–7] The pathophysiologic mechanism involve rupture or erosion of atherosclerotic plugs, with activation of platelets and of the clotting system followed by local thrombus formation.[3,8] Coronary arteriographic examinations have revealed that rapid progression of coronary stenosis often precedes the development of unstable angina.[9] This stenosis is frequently caused by eccentric, irregular lesion often associated with filling defects thought to be caused by coronary thrombi.[10,11] Minor myocardial injury is detected in 20–40% of patients with unstable angina by the measurement of serum troponin-T or troponin-I, but rarely by measurement of serum creatine kinase.[12,13] Thus the introduction of cardiac troponin-I (cTn-I) into daily routine practice allows for highly accurate, sensitive, and specific determination of myocardial injury in patients with unstable angina. Any increase in these markers implies extent of myocardial injury and an adverse outcome for these patients, with increased risk of death.[13]

Raised serum levels of both cTn-I and troponin-T in patients with clinically unstable angina had more type B2 or C lesions with similar sensitivity.[14] Patients with unstable CADs and elevated troponin-I or troponin-T had more widespread CAD than those without elevated and more often had complex lesion characteristics and visible thrombus in the culprit vessels.[15–17] Elevated values of serum cTn-I is to be evenly associated with the severity and extent of coronary lesion.[18] Recently a study on 50 consecutive patients of chest pain at rest with cTn-I above normal level and normal creatine-kinase shown to have significant CAD.[19]

Although previous studies showing elevated troponin-I and normal creatinine kinase level predicted the prognosis and severity of CADs in NSTEMI patients but coronary angiography has not been systematically performed and the angiographic characteristics have not been well determined in patients of unstable angina with border line raised troponin-I level.[20] The present study is, therefore, intended to find the correlation between borderline raised troponin-I level and extent and severity of CAD in patients with unstable angina.

PATIENTS AND METHODS

The present cross-sectional study was conducted in the Department of Cardiology, Sir Salimullah Medical College & Mitford Hospital (SSMCMH). Data were collected at Ibrahim Cardiac Hospital & Research Institute and SSMCMH. On the basis of inclusion and exclusion criteria, a total of 81 patients of unstable angina were selected over a period of 1 year between 1 September 2009 and 31 August 2010. Based on the level of cTn-I at and 8 hours after admission, the patients were divided into high normal (troponin-I level 0.06–0.6) and low-normal (0–<0.06) groups. Thus 47 patients fell into high normal group (Group-I) and 34 patients into low-normal group (Group-II). The angiographic characteristics of the two groups of patients were then compared.

RESULTS

The present study was intended to determine cTn-I at admission and 8 hours apart, the patients were divided into high normal (Group-I, $n = 47$) and low-normal (Group-II, $n = 34$) groups. The findings obtained from data analyses are presented in Table 1.

Chi-square (χ^2) test reveals that most of unstable angina occurs in patients with high troponin-I level particularly during rest ($p < 0.001$).

Table 1: Comparison of type of unstable angina between groups

Type of unstable angina	Group		p-value
	Group-I ($n = 47$)	Group-II ($n = 34$)	
Rest angina	30(63)	8(23)	
New onset angina	5(10)	14(41)	<0.001
Cresendo angina	12(25)	10(29)	
Post MI angina	0	2(5.8)	

Figures in the parenthesis denote corresponding percentage.

More than three-quarter (77%) of the patients in Group-I had significant lesion and 23% insignificant and normal lesion compared to 26% and 74% respectively in Group-II ($p < 0.001$) (Table 2).

Table 2: Comparison of stenosis between groups

Stenosis	Group		p-value
	Group-I ($n = 47$)	Group-II ($n = 34$)	
Normal (<20%)	6(12.8)	21(62.5)	
Insignificant (20%–50%)	5(10.2)	4(11.8)	< 0.001
Significant (≥50%)	36(77)	9(26)	

#Chi-square (χ^2) test was employed to analyze the data.

Table 3: Comparison of no. of vessels involved between groups

No. of vessels involved	Group		p-value
	Group-I (*n*= 47)	Group-II (*n* = 34)	
None	11(23.0)	25(73.0)	
SVD	14(30)	7(20.0)	
DVD	16(34)	1(3)	<0.001
TVD	6(12)	1(3)	

#Chi-square (χ^2) test was employed to analyze the data.

Table 4: Comparison of site of lesions in LAD between groups

Site of lesion in LAD	Group		p-value
	Group-I (*n* = 47)	Group-II (*n* = 34)	
Proximal	21(44.68%)	3(8.82)	<.001
Mid	23(48.93%)	6(17.64)	<.001
Distal	2(4.25%)	2(5.88)	0.455

Chi-square (χ^2) test was employed to analyze the data.

Table 5: Comparison of site of lesions between groups

Site of lesion	Group		p-value
	Group-I (*n* = 47)	Group-II (*n* = 34)	
Proximal	31(65.95)	3(8.82)	<0.001
Mid	24(51.06)	4(11.76)	<0.001
Distal	10(21.27)	6(17.64)	0.455

Chi-square (χ^2) test was employed to analyze the data.

Number of vessels involved like single vessel (SVD), double vessel (DVD), and triple vessels (TVD) were all higher in Group-I compared to Group-II ($p < 0.001$) (Table 3).

As site of lesions were compared between the study groups, proximal, and mid lesions were found significantly higher in Group-I than those in Group-II (44.68% vs. 8.82%, $p < 0.001$ and 48.93% vs. 17.64%, $p < 0.001$, respectively), while distal lesion was almost identically distributed between groups (4.25% vs. 5.88 %, $p = 0.455$) (Table 4).

As site of lesions were compared between the study groups, proximal and mid lesions were found significantly higher in Group-I than those in Group-II (65. % vs. 8.8%, $p < 0.001$ and 51% vs. 11%, $p < 0.001$, respectively), while distal lesion was almost identically distributed between groups (21% vs. 17 %, $p = 0.455$) (Table 5).

A significantly higher proportion of patients in Group-I exhibited Type-B and Type-C lesion than that in Group-II (p <.005), and Type-A lesion was higher in Group-II than Group-I (20% vs 8.5, $p = 0.117$) (Table 6).

Presence of collateral circulation was observed to be significantly higher in Group-I (40.5%) than that observed in Group-II (8.8%) ($p = 0.002$) (Table 7).

Table 8 shows the risk of developing significant lesion in patients with raised cTnI. Majority (77%) of the patients who developed significant coronary artery stenosis had raised cTnI compared to 23% of the patients who did not develop significant stenosis ($p < 0.001$). The chance of having significant lesion in patients with raised cTnI was 9.09 times higher than that in patients with normal or low cTnI (Table 8).

Table 6: Comparison of type of lesions between groups

Type of lesion*	Group		p-value
	Group-I (*n* = 47)	Group-II (*n* = 34)	
Type A	4(8.5)	7(20)	0.117
Type B	14(30)	1(3)	<0.005
Type C	22(47)	5(14)	<0.005

Data were analyzed using Chi-square (χ^2) test.

Table 7: Comparison of collateral circulation between groups

Collateral circulation#	Group		p-value
	Group-I (*n* = 47)	Group-II (*n* = 34)	
Present	19(40.5)	3(8.8)	<0.002
Absent	28(59.5)	31(91.7)	

Data were analyzed using Chi-square (χ^2) test.

Table 8: Risk of developing significant lesion in patients with raised cTnI

Significant lesion#	Group		Odds ratio*
	Developed (*n* = 45)	Not developed (*n* = 36)	
Troponin-I (≥0.06)	36(76.59)	11(23.41)	9.09
Troponin-II (< 0.06)	9(26.47)	25(73.53)	

*Risk of developing significant lesion was estimated using odds ratio.

DISCUSSION

Since the extent of myocardial injury is an important determinant of the risk of death, it is necessary to identify serum markers to predict prognosis, in order to initiate appropriate medical treatment and/or invasive procedures in these patients. The presence of high normal cTnI in serum is a significant prognostic indicator in patients with unstable angina. Its independent prognostic potential persists even after adjustment for independent baseline variables known to be significantly associated with an increased risk of cardiac events. The use of cTnI in the triage of patients with unstable coronary disease may identify those at greater risk for adverse cardiac events.[21]

The present study aimed at determining the role of cTnI in assessing the extent of myocardial injury in patients with unstable angina. Patients were divided into high normal and low normal groups based on cTnI values. Angiographic severity was assessed in terms of significant stenosis, number of vessel involvement, type and site of lesion in major coronary arteries as well as presence of collaterals.

Our study reported that majority of the patients in the high-normal group exhibited significant lesion in LAD, RCA, and LCX than that in the low normal group ($p < 0.001$). DVDs and TVDs were frequently encountered in the former group than those in the latter group ($p < 0.001$). Proximal lesion demonstrated their significant presence in the high normal group than that in the low normal group ($p < 0.001$) with Type-B and Type-C lesions common in the former group. In a study majority of the patients with elevated cTn-I had significant CAD, had more Type-C lesions, double, and triple vessel disease and left main coronary artery involvement with higher mean percentage of stenosis than those in Group-II thereby favoring the findings of the present study.[18] A previous study showed that patients with increased levels of cTn-I and normal creatine kinase levels had a higher prevalence of coronary artery stenosis >50% compared to patients who had normal values of both markers (80% vs. 27%; $p = 0.001$),[22] but similar to patients who had an elevation of both markers (87% vs. 80%; p = NS).

A recent study showed that a majority of patients with elevated cTn-I in the presence of normal creatine kinase levels have significant CAD. Almost half of these patients had significant CAD of at least 2 vessels and 18% had 3-vessel disease.[20] These results are consistent with findings of the present study.

In patients who were enrolled in the PURSUIT trial and who underwent in-hospital angiography, 88% had significant CAD (any stenosis >50%), 6% had mild CAD (any stenosis ≤50%), and 6% had no stenosis identified, which correlates with our data.[23]

However, cTn-I as a predictor of angiographic picture of the coronary arteries in patients with unstable coronary disease, has certain limitations. Although the overall prevalence of false-positive serum in the general population is low, it may be increased in patients with conditions other than acute coronary syndromes, such as sepsis, septic shock, myocarditis, heart failure, cardiac arrhythmias, renal failure, pulmonary embolism, and cerebrovascular accidents.[24]

These findings show that high-normal troponin-I level is not a spurious finding, but may actually be a marker of advanced CAD. The severity of CAD has shown in previous studies to correlate with prognosis of patients and until now our knowledge of the quantitative coronary angiographic characteristics of patients with increased cTn-I but normal creatine kinase levels has been limited.

Cardiac-specific troponins are gaining acceptance as the primary biochemical cardiac marker in patients with unstable angina. They have greater diagnostic sensitivity due to their ability to identify patients with lesser amounts of myocardial damage. Elevated levels of cTn-I convey prognostic information beyond that supplied by the clinical characteristics of the patient or the ECG at presentation. Furthermore, among patients without ST-segment elevation and normal CK-MB levels, borderline raised cTn-I concentrations identify those at increased risk of death and are thought to represent microinfarctions that result from microemboli from an unstable plaque.[25,13]

Thus the introduction of cTn-I into daily routine practice allows for highly accurate, sensitive, and specific determination of myocardial injury in patients with chest pain. Any increase in these markers implies extent of myocardial injury and an adverse outcome for these patients, with increased risk of death.[13]

CONCLUSION

In the light of the findings of the present study and discussion thereof it can be concluded that majority of the patients of unstable angina with high normal cTn-I possess significant stenosis in the coronary arteries than the patients with low-normal cTn-I value. Double vessel and triple vessel

disease are frequently common in the high-normal cTn-I level than that in the low-normal cTn-I level. A proximal lesion (which usually carries a worse prognosis) is frequently present in the high-normal cTn-I level than that in the low-normal cTn-I level with predominantly Type-B and Type-C lesions. Borderline elevated cTn-I level conveys prognostic information beyond that supplied by the clinical characteristics of the patient or the ECG at presentation.

REFERENCES

1. National Center for Health Statistics: Vital and Health Statistics: Detailed Diagnosis and Procedures for Patients Discharged from Short Stay Hospitals. US Department of Health and Human Services, Public Health Service, Series 13; No. 90, Hyattsville, Md, 1987.
2. Julian DG. The natural history of unstable angina. In: Hugenholtz PG, Goldman BS, editors. Unstable angina: current concepts and management. Stuttgart: Schattauer; 1985. pp. 65–70.
3. Falk E. Why do plaques rupture? Circulation. 1992;86 Suppl 6:S30–S42.
4. Malik A, Islam MN, Zafar A, Khan AK, Ramizuddin M. Clinical patterns of ischemic heart diseases and its association with some known risk factors. Bangladesh Heart J. 1987;2:1–9.
5. Fuster V, Badimon L, Badimon J, Chesebro The pathogenesis of coronary artery disease and the acute coronary syndromes (first of two parts). N Engl J Med. 1992;326:242–50.
6. Butman S, Olson H, Butman L. Early exercise testing after stabilization of unstable angina: correlation with coronary angiographic findings and subsequent cardiac events. Am Heart J. 1986;111:11–18.
7. Conti CR. Risk stratification in unstable angina: how to select patients who need emergency revascularization. J Card Surg. 1993;8:391–5.
8. Davies MJ, Thomas AC, Knapman PA, Hangartner JR. Intramyocardial platelet aggregation in patients with unstable angina suffering sudden ischemic cardiac death. Circulation 1986;73:418–42.
9. Moise A, Theroux P, Taeymans Y, Descoings B, Lesperance J, Waters DD, Pelletier GB, Bourassa M. Unstable angina and progression of coronary atherosclerosis. N Engl JMed. 1983;309:685–9.
10. Ambrose JA, Winters SL, Arora RR, Eng A, Ricco A, Gorlin R, Fuster V. Angiographic evolution of coronary artery morphology in unstable angina. J Am Coll Cardiol. 1986;7:472–8.
11. Capone G, Wolf N, Meyer B, Meister S. Frequency of intracoronary filling defects by angiography in angina pectoris at rest. Am J Cardiol. 1985;56:l403–6.
12. Lindahl B, Andren B, Ohlsson J, Venge P, Wallentin L. Noninvasive risk stratification in unstable coronary artery disease: exercise test and biochemical markers. FRISC Study Group. Am J Cardiol. 1997;80:40E–44E.
13. Antman EM, Tanasijevic MJ, Thompson B, Schactman M, McCabe CH, Cannon CP, Fischer GA, Fung AY, Thompson C, Wybenga D, Braunwald E. Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. N Engl J Med. 1996;335:1342–49.
14. Panteghini M, Cuccia C, Pagani F, Turla C, Bonetti G, Bonini E. Coronary angiographic findings in patients with clinical unstable angina according to cardiac troponin I and T concentrations in serum. 2002;126: 448–51.
15. Jurlander B, Farhi ER, Banas JJ Jr, Keany CM, Balu D, Grande D, Ellis AK. Coronary angiographic findings and troponin T in patients with unstable angina pectoris. Am J Cardiol. 2000;85:810–14.
16. Benamer H, Steg PG, Benessiano J, Vicaut E, Gaultier CJ, Aubry P, Boudvillain O, Sarfati L, Brochet E, Feldman LJ, Himbert D. Elevated Cardiac troponin I predicts a high-risk angiographic anatomy of the culprit lesion in unstable angina. Am Heart J. 1999; 137(5): 815–20.
17. Heeschen C, Goldmann BU, Langenbrink L, Matschuck G, Hamm CW. Evaluation of a rapid whole blood ELISA for qualification of troponin I in patients with acute chest pain. Clin Chem. 1999;45(10):1789–96.
18. Janorkar S, Koning R, Eltchaninoff H, Andres H, Lavoinne A, Cribier A. Relation between serum cardiac troponin I values and severity of clinical electrocardiographic and quantitative angiographic features in unstable angina. Indian Heart J. 1999;51(1):31–34.
19. Gruberg L, Sudarsky D, Kerner A, Hammerman H, Kapeliovich M, Beyar R. Troponin-positive, CK-MB-negative acute myocardial infarction: clinical, electrocardiographic and angiographic characteristics. J Invasive Cardiol. 2008;20(3): 125–28.

continued...

REFERENCES

20. Pham MX, Whooley MA, Evans GT, Liu C, Emadi H, Tong W, Murphy MC, Fleischmann KE. Prognostic value of low-level cardiac troponin-I elevations in patients without definite acute coronary syndromes, Am Heart J. 2004;148:739–42.
21. Tanasijevic MJ, Cannon CP, Antman EM. The role of cardiac troponin-I (cTnI) in risk stratification of patients with unstable coronary artery disease. Clin Cardiol. 1999;22(1):13–16.
22. Almeda FQ, Calvin JE, Parrillo JE, Sun FG, Barron JT. Prevalence of angiographically significant stenosis in patients with chest pain and an elevated troponin I level and normal creatine kinase and creatine kinase-MB levels. Am J Cardiol. 2001;87:1286–89.
23. *Roe MT*, *Harrington* RA, *Prosper* OM, Pieper KS, Bhatt DL, Lincoff AM, Simoons ML. For the platelet glycoprotein IIb/IIIa in unstable angina clinical and therapeutic profile of patients presenting with acute coronary syndromes who do not have significant coronary artery disease. Circulation. 2000;102:1101–106.
24. Ammann P, Pfisterer M, Fehr T, Rickli H. Raised cardiac troponins B Med J. 2004;328:1028–29.
25. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, Jones RH, Keveiakes D, Kupersmith J, Levin TN, Pepine CJ. ACC/AHA guidelines for the management of patients with unstable angina and non–ST-segment elevation myocardial infarction. Circulation. 2000;102(10):1193–209.