ORIGINAL ARTICLE

Myonecrosis in Aortic Valvular Heart Diseases

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Abstract:

This cross sectional study was done among 20 patients with aortic stenosis and 20 healthy controls to evaluate the association of cardiac specific troponin I (cTnI) and aortic valvular heart diseases. The study was conducted in outpatient department in National Institute of Cardiovascular Diseases (NICVD.) A structured questionnaire and checklist was used to collect data through face to face interview. Color doppler echocarchiography was done and 5 ml of venous sample was drawn from each subjects and laboratory estimation of cTnI was done. The cTnI in control group and aortic stenosis patients showed significant difference in mean (<0.001). cTnI level in aortic stenosis patients increases in the absence of heart failure indicating that it can expose the cardiomyocytes to injury prior to development of overt left ventricular dysfunction. So, serial monitoring of cTnI may help clinicians to give definitive treatment before development of complications.

]Introduction:

Valvular heart disease is a common cardiac condition in our country. The valvular heart disease which is faced in day to day hospital and private practice is due to chronic sequlae of rheumatic fever. In chronic rheumatic heart disease, mitral valve is affected in more than 90% of cases and aortic valve is the next most frequently affected valve.

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In aortic stenosis, there occurs obstruction to left ventricular (LV) outflow during systole. Pressure gradient across the aortic valve (pressure higher in left ventricle than aorta during systole) causes chronic left ventricular pressure overload and compensatory left ventricular hypertrophy. Increased wall thickness and decreased cavity size oppose the increased wall stress. The left ventricular hypertrophy initially leads to diastolic dysfunction and later systolic dysfunction. This diastolic abnormality results from a combination of impaired myocardial relaxation because of hypertrophied LV and increased myocardial stiffness because of structural alteration[1]. Because of severe LV hypertrophy blood flow is increased through coronaries but coronary blood flow per 100 gm of LV mass is reduced. Apart from this, reduced coronary perfusion pressure and

compression of coronary arteries by hypertrophied myocardium during systole further compromises coronary blood flow.

In the late state, left ventricular systolic function can be reduced, as a result of myocardial fibrosis. The sequence of cardiac decomposition begins with ventricular dilatation, which further raises wall stress, leading to increased left ventricular hypertrophy and probably reduced blood flow to the hypertrophied myocardium, in turn leading to ischaemia with reduced left ventricular ejection fraction. Furthermore, aortic stenosis is itself associated with 50% increased risk of cardiovascular mortality and myocardial infarction[2].

Left ventricular systolic dysfunction and heart failure predict poor prognosis including a less favorable outcome after valve replacement in aortic stenosis[3]. The onset of heart failure is preceded by structural and functional alterations in the heart muscle with degeneration and death of the cardiac myocyte. Disease of the heart valves may progress with time and selected patients require regular review, usually every one or two years, to ensure that deterioration is detected before complication such as heart failure ensues. Detection of ongoing myocardial injury before the outbreak of overt left ventricular dysfunction could help promote earlier surgery in patients without symptoms or with vague symptoms.

Troponin-I is a protein molecule that plays an essential role in the contraction of the striated muscle. cTnI has been established as a reliable and highly heart specific marker of myocyte injury. Its background concentration is normally undetectable or very low and it is therefore sensitive to even minor heart muscle damage. Measuring circulating cardiac Troponin-I would help to detect ongoing silent myocyte damage in aortic stenosis[4]. cTnI was elevated even in the absence of heart failure indicating that it can expose cardiomyocyte injury prior to the development of overt left ventricular dysfunction. Serial monitoring of cTnI during follow up of asymptomatic aortic stenosis patient will show whether cTnI can assist in the timing of therapeutic interventions.

The aim of the study was to explore the relationship of serum cTnI and aortic stenosis. In turn it will help in the detection of ongoing myocardial injury in aortic stenosis patient before the outbreak of overt left ventricular dysfunction, which will help to promote earlier surgery in patients without symptom or with vague symptom.

Materials and method:

Twenty patients (18 male and two female) in the age range of 5-60 years having aortic stenosis that was confirmed by echocardiography were selected. All the patients came to the out patient department of NICVD with symptoms such as palpitation, syncope, presyncope, and exertional dyspnoea. Another 20 control subjects (17 male and three female) within the same age range were selected randomly. A blood sample for determination of cTnI was obtained by vein puncture. Micro particle enzyme immune assay was done for the quantitative determination of cTnI.

Data are presented as mean and ± SD. Mann Whitney U test was done as the test for significance. A probability value of $p < 0.05$ was considered significant. All calculations were done with SPSS system 10.0.

Results:

cTnI level was within normal physiological limits in all the control subjects. The mean value was 0.02±0.00ng/ml. Among the patients of aortic stenosis cTnI was undetectable in four (20%) patients, in four (20%) patients there was detectable cTnI but it was within normal physiological limits, and another 12 (60%) patients had elevated levels of cTnI. The mean cTnI level in aortic stenosis patient was 0.67±0.1ng/ml. cTnI level among aortic stenosis patients and control subjects showed significant difference in mean (p<0.001).

Ejection fraction of more than 55% was considered normal. The ejection fraction of aortic stenosis patients and control subjects were 63±6.33% and 65.25±3.26% respectively, having no significant difference between the groups. This indicated that the aortic stenosis patients had yet not developed overt systolic heart failure.

Table I: Ejection fraction and cTnI in study subjects and controls

Parameters	Aortic stenosis patients	controls	p value
Ejection fraction (%)	63.10±6.33	65.25±3.26	<0.6
cTnI (ng/ml)	0.67±0.81	0.02±0.00	<0.001

Discussion:

It is evident from the findings of the present study that there is a significant higher level of serum cTnI in aortic stenosis patients with normal ejection fraction. It was found that 20% patients with aortic stenosis had undetectable Troponin-I, 20% had elevated Troponin-I but within physolosical limit and rest 60% had abnomally elevated Troponin-I values. But Kupari et al found circulating cTnI was detectable in more than 50% cases and abnormally elevated in more than 20% of cases. The survival rates of the patients with symptomatic aortic stenosis are nearly normal, until the symptoms of angina, syncope or heart failure develop. The presence of symptoms of heart failure in patients of aortic stenosis causes a bad prognosis within a short period of time (mean survival <2 years). In the current study it was found that cTnI was elevated in the absence of heart failure indicating that it can expose cardiomyocyte injury prior to the development of overt left ventricular dysfunction. So, serial monitoring of cTnI could help clinicians give definitive treatment before development of complications.

Cardiac Troponin-I have been established as a reliable and highly heart specific marker of myocyte injury. Its background concentration in the circulation is normally undetectable or very low (normal level is 0.00-0.05 ng/ml) and they are therefore sensitive to even minor heart muscle damage[5]. The triggers of myocyte death in aortic stenosis have not been detailed, however the possible pathophysiology is that in aortic stenosis there occur narrowivg of aortic valve which causes decreased blood flow from the left ventricle to the aorta. This increases workload of the left ventricle. This forces the left ventricle to squeeze harder, as a result the walls become thicker in time and left ventricular hypertrophy develops[6]. The hypertrophied left ventricular muscle mass elevates myocardial oxygen requirements. Even in the absence of obstructive coronary

artery disease there may be interference with coronary blood flow. This is because of the compression of the coronary arteries by the hypertrophied myocardium[7]. This in turn results in the relative ischemia of the left ventricular myocardium and consequently death of the cardiac myocytes ultimately leading to the development of depressed systolic function and heart failure[8]. The triggers of cardiomyocyte death in aortic stenosis have not been detailed but may include various combinations of increased mechanical stress, activation of neurohumoral mechanisms, myocardial ischaemia, oxidative stress and the effects of inflammatory cytokines. However, it is noted that circulating cTnI was undetectable in two of the patients with severe aortic stenosis. This suggests that myocyte injury can be intermittent and may therefore escape detection.

An important limitation of this work is that there was financial constrain in serial measurement of cTnI and left ventricular functions in the patients. Therefore, the true predictive value of circulating cTnI could not be studied. Only serial monitoring of cTnI during follow up of asymptomatic aortic stenosis would show whether cTnI can assist in the timing of therapeutic interventions.

From the present study findings it may be concluded that circulating cTnI concentrations are frequently detectable and elevated in patients with severe aortic stenosis even in the absence of heart failure. Circulating cTnI deserves a potential warning signal in patients with severe but still asymptomatic aortic stenosis.

References:

1. Bloomfield, Bradbury A, Cumming AD, Stewart LH. Cardiovascular disease. In: Boon NA, Colledge NR, Walker BR, Hunter JAA. Davidson's Principle and Practice of Medicine, 19th edition. Edinburgh: Churchill Livingstone Publication, 2005. pp- 458-461.
2. Hein S, Arnon E, Kostin S, et al. Progression from compensated hypertrophy to failure in the pressure overload human heart, structural deterioration and compensatory mechanism. Circulation 2003; 107: 984-91.
3. Kupari M, Erilsson S, Turlo H, et al. Leakage of cardiac troponin-I in aortic valve stenosis. J Int Med 2005; 258: 231-237.
4. Mayo Foundation. Effects of congenital aortic stenosis, 2005. Available from: http:/www.Mayoclinic.org/congenitalaortic stenosis jax/effects. html. (1/5/2006).
5. Otto CM, Lind BK, Kitzman DW, et al. Association of aortic valve stenosis with cardiovascular mortality and morbidity in the elederly. N Engl J Med 1999; 341: 142-7.
6. Hess OM, Villari B, Krayer Buetil HP. Diastolic dysfunction in aortic stenosis. Criculation 1993; 87: 73-76.
7. Park MH. Timely intervention of asymptomatic aortic stenosis. Postgrad Med 2001; 341: 110.
8. Reydberg E, Gudmundsson P, Kennedy L, Erdardt L, Willenheimer R. Left arterioventricular plane displacement but not left ventricular ejection fraction is influenced by the degree of aortic stenosis. Heart 2004; 90: 1151-1155.