



Left ventricular noncompaction: clinical-echocardiographic study

Kliničko i ehokardiografsko ispitivanje bolesnika sa nedovoljno formiranim miokardom leve komore

Aleksandra Nikolić^{*†}, Ljiljana Jovović[†], Slobodan Tomić[†], Milan Vuković[†]

^{*}Faculty of Medicine, University of Belgrade, Belgrade, Serbia; [†]Institute for Cardiovascular Disease “Dedinje”, Belgrade, Serbia

Abstract

Background/Aim. Left ventricular noncompaction (LVNC) is a disorder in endomyocardial morphogenesis, seen either isolated (in the absence of other cardiac anomalies) or in association with congenital heart disease and some neuromuscular diseases. Intrauterine arrest of the compaction of myocardial fibers is postulated to be the reason of LVNC. Recognition of this condition is extremely important due to its high mortality and morbidity that lead to progressive heart failure, ventricular arrhythmias and thromboembolic events. The aim of this study was to determine the prevalence and clinical presentation of LVNC among consecutive outpatients according to clinical and echocardiographic findings. **Method.** A total of 3,854 consecutive patients examined at the Institute for Cardiovascular Diseases within a period January 2006 – January 2007 were included in the study. All the patients underwent echocardiographic examination using the same equipment (Vivid 7, GE Medical System). Echocardiographic parameters and clinical presentation in patients with echocardiographic criteria for LVNC were analyzed. **Results.** Analyzing 3,854 consecutive outpatients, using two-dimensional Color Doppler echocardiography from January 2006 to January 2007, 12 patients met the criteria for LVNC. Seven of them were male. The mean age at diagnosis was 45 ± 15 years. Analyzing clinical manifestation of LVNC it was found that seven patients had signs of heart failure, six had arrhythmias with no embolic events. **Conclusion.** Our results suggest that the real prevalence of LVNC may be higher than expected. New studies have to be done to solve this problem.

Key words:

heart defects, congenital; ventricular dysfunction; echocardiography; diagnosis; prevalence.

Apstrakt

Uvod/Cilj. Nedovoljno formiran miokard leve komore (*left ventricular noncompaction* – LVNC) je poremećaj endomiokardijalne morfogeneze koji se viđa izolovan (u odsustvu drugih srčanih anomalija) ili udružen sa kongenitalnim srčanim oboljenjem i nekim neuromuskularnim bolestima. Smatra se da je intrauterini zastoj u formiranju miokardnih vlakana razlog za LVNC. Zbog visokog mortaliteta i morbiditeta koji vodi ka progresivnoj srčanoj slabosti, ventrikularnim aritmijama i tromboembolijskim događajima, prepoznavanje ovog stanja je veoma važno. Cilj rada bio je da se utvrde prevalencija i klinička prezentacija LVNC kod ehokardiografski pregledanih bolesnika. **Metode.** Ovom prospektivnom studijom obuhvaćeno je 3 854 bolesnika, koji su sukcesivno pregledani u Institutu za kardiovaskularne bolesti „Dedinje” tokom jedne godine (januar 2006–januar 2007). Pregled je vršen dvodimenzionalnim kolor dopler ultrazvučnim aparatom (*Vivid 7, GE Medical system*). Analizirani su ehokardiografski parametri i kliničke karakteristike bolesnika kojima je ehokardiografskim pregledom ustanovljen LVNC. **Rezultati.** Analizom podataka o 3 854 uzastopno pregledana bolesnika od januara 2006. do januara 2007. godine, utvrđeno je da je 12 bolesnika ispunjavalo kriterijume za LVNC. Prosečno životno doba bolesnika bilo je 45 ± 15 godina; sedam bolesnika bilo je muškog pola. Znake srčane slabosti imalo je sedam bolesnika, šest bolesnika je imalo aritmije, a tromboembolijski događaji nisu registrovani. **Zaključak.** Rezultati našeg ispitivanja ukazuju na to da prevalencija LVNC može biti viša od očekivane. Potrebne su nove studije o LVNC koje će rešiti taj problem.

Ključne reči:

srce, kongenitalne mane; disfunkcija leve komore; ehokardiografija; dijagnoza; prevalenca.

Introduction

Noncompaction of the left ventricle (LVNC) was an unclassified cardiac abnormality until the year 2006 when

according to the new Contemporary Definitions and Classification of the Cardiomyopathies it was classified as primary cardiomyopathy with genetic cause leading to an arrest in intrauterine endomyocardial morphogenesis¹⁻³. It is thought

that pathogenesis of this cardiomyopathy is unknown, but two hypotheses have been proposed: congenital and acquired. The first one was performed due to the arrest of an in-uterine compaction of the myocardial fibers in the absence of any other structural heart diseases. The mechanism of the second hypothesis was less convincing than the first one and it was described as based on higher hemodynamics demands in some situations (left ventricular pressure or volume overload), which could change endomyocardium⁴. However, arguments supporting the genetic cause of LVNC frequently include association of LVNC with congenital cardiac abnormalities (mutations in α -dystrobrevin gene and transcription factor NKX2.5), familiar occurrences of this disease, mitochondrial mutations and X-linked inheritance and other genetics disorders (Barth syndrome in neonates)^{1,2}.

Validation of the well-known disorder was the first case of this abnormality, which was described in 1932 in the newborn with aortic atresia and coronary-ventricular fistula⁵. Since then, we were able to find publications where myocardium was described as a "spongy myocardium" in animal and human beings^{6,7}. There are two forms of this abnormality: an isolated and nonisolated where the difference depends on the presence of other cardiac abnormalities⁸. The first case, without any other morphogenetic cardiac abnormality, was described in 1984 in a form of the persistence of isolated myocardial sinusoids⁹.

Noncompaction of the left ventricular myocardium is an uncommon finding and remains frequently overlooked even by experienced echocardiographers. The natural history of LVNC is largely unresolved but includes left ventricular systolic dysfunction and heart failure (in some cases heart transplantation), diverse forms of remodeling, arrhythmias, sudden death, and thromboembolic events. There are studies showing that patients with LVNC would not have poor prognosis if we detected them and started with the treatment earlier^{9,10}.

The aim of this study was to determine the frequency and the clinical presentation of LVNC among consecutive outpatients in the one-year period, according to clinical and echocardiographic findings, and to find out if there are any similarities among them.

Methods

We performed transthoracic echocardiography and other necessary exams to all consecutive outpatients who came to our Institute from January 2006 to January 2007. After initial clinical assessment (detailed medical history using standard questionnaires, physical exam), all the outpatients were classified according to the probability of having coronary artery disease, valvular heart disease, cardiomyopathies or electrophysiological abnormalities. These patients were sent to our echocardiography laboratory for further evaluation of their condition. The echocardiography exam was performed by a Vivid 7, GE Medical System. In this study four physicians (who applied echocardiography routinely in our Institution) were involved. Echocardiographic diagnostic criteria include: the noncompacted endo-

cardial layer, which is thicker than the compacted epicardial layer (ratio of noncompacted/compacted ≥ 2) and consists of: prominent and excessive trabeculations (more than three), and deep recesses filled with blood from the ventricular cavity visualized on color doppler imaging¹⁻⁸. A complete two-dimensional and Doppler echocardiography examination was performed in all patients according to the recommendations of the American Society of Echocardiography⁹. Left ventricular ejection fraction was calculated using the biplane area length method. The left ventricular wall was divided into 17 segments to describe the location of the noncompacted segments: the whole apex was one segment, apical segments (included apical thirds) of the anterior, septal, lateral, inferior walls and basal or middle parts of the anterior, anteroseptal, anterolateral, inferior, inferoseptal, inferolateral walls. Diastolic function was measured in the left ventricular inflow pattern at the tip of the mitral valve leaflets. Diastolic function was graded as follows: normal, abnormal relaxation, pseudonormal or restrictive pattern.

Results

Within a year, from January 2006 to January 2007, we performed 3,854 consecutive outpatient studies by 2D echocardiography. LVNC criteria were determined in 12 patients (0.31%). Seven of them were men. The mean age of the patients at diagnosis was 45 ± 15 years (Table 1). The transthoracic echocardiographic parameters pointed out border line enlargement of the left side cavities and in the half of the patients, ejection fraction were impaired (Table 1).

Table 1
Clinical and LV echocardiographic (ECG) characteristics of 12 patients with left ventricular noncompaction (LVNC)

Clinical and LV ECG characteristics	Values
Age (year), $\bar{x} \pm SD$	45 ± 15
Men, n (%)	7 (58%)
Angina pectoris/infarction, n (%)	3 (25)
Familial occurrence of LVNC	no presence
Functional class I/II, n (%)	5 (42)
Functional class III/IV, n (%)	7 (58)
EDD (mm), $\bar{x} \pm SD$	56 ± 6
ESD (mm), $\bar{x} \pm SD$	40 ± 8
Left atrium (mm), $\bar{x} \pm SD$	40 ± 16
Mitral regurgitation (mild/severe), n (%)	5 (42)
Ejection fraction normal, n (%)	3 (25)
Impaired ejection fraction ($< 30\%$), n (%)	6 (50)
Impaired relaxation of LV, n (%)	7 (58)
Restrictive pattern of LV, n (%)	2 (28)

EDD – end-diastolic dimension; ESD – end-systolic dimension;
LV – left ventricle

The previous exams were initially performed in other regional hospitals or private cardiology practice. In our study the true diagnosis of this abnormality was determined on the first visit, but only in three patients. On the other hand, there were 75% of those who were with at least one or two previously determined diagnoses, which were not related to LVNC. One of these three patients, which were mentioned previously with the exact initial diagnosis, had symptoms

and it was predominantly palpitation and chest discomfort on effort. We performed a 24-hour Holter monitoring, which showed nonsustained ventricular tachycardia. 2D echocardiographic exam showed normal left cavity dimensions, mitral valve prolapse with moderate to severe mitral regurgitation and normal ejection fraction. The second patient, from the same group, was the oldest patient (69 year old) who had some lung problems probably caused by tuberculosis (not definitely diagnosed) and normal left cavity size with non-compaction segments and impaired systolic function (ejection fraction 40%) (Figure 1A). The third patient did not

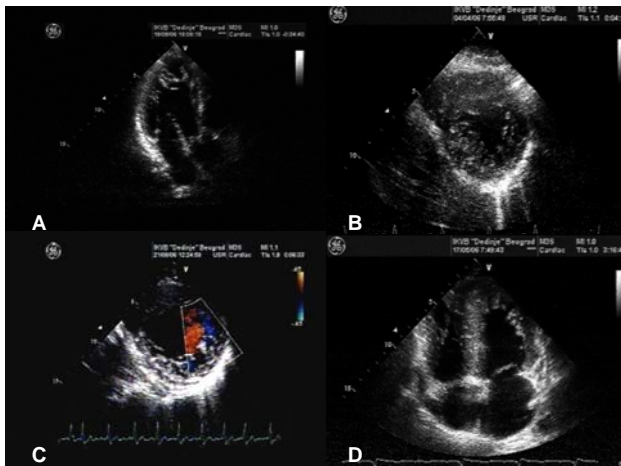


Fig. 1 – A) A 70-year-old patient with normal left ventricle cavity size and impaired ejection fraction: 3-chamber view shows deep recesses in the apical third of posterior wall; B) Routine echocardiography exam in a 37-year-old patient before operative treatment of breast tumor (parasternal short axis view shows hypertrabeculation in basal segments of inferior, posterior and lateral walls of the left ventricle); C) Parasternal short axis view shows meshwork in the middle ventricle segments of inferior, posterior and lateral walls in a 36-year-old patient with mitral valve prolapse, normal systolic function and a nonsustained ventricular tachycardia; D) Four-chamber view clearly shows deep recesses with intertrabecular spaces in the apex and in the lateral wall in a 28-year-old female on whom ablation of atrial fibrillation was performed

have systolic dysfunction or any other heart problems (valve disease, arrhythmias, etc.) except moderate effort on exercise (Figure 1B). In the group of patients who were first misinterpreted, the diagnosis was based on the clinical exams, symptoms, signs of various morphological (structural) abnormalities based on echocardiography exams or electrophysiological disturbances. Accordingly, two patients with

severe mitral valve regurgitation were sent to our Institution to be followed up to the time of operation. The first one of these patients had dilatation of mitral annulus caused by cardiomyopathy of “unknown” cause with impaired systolic function (ejection fraction 30%). The next patient had prolapse of the anterior mitral leaflet with enlarged left ventricle dimensions and still not impaired systolic function (Figure 1C). These two patients had atrial fibrillation at the beginning.

According to the guidelines for valvular heart disease, 3 patients in these two groups (true diagnosis or misdiagnosis) were operated (they were implanted artificial mechanical prosthesis in mitral position). In operated patients, before valve replacement, coronarography was done and found non-significant stenosis in coronary arteries. Eleven month after operation, due to cardiac arrest caused by sustained ventricular tachycardia and successful cardiopulmonary resuscitation, cardioverter defibrillators (ICD) were implanted in the first patient. A year and a half after the operation, nonsustained ventricular tachycardia was registered in the second patient and it was decided that after amiodarone loading he would be included in electrophysiological study. The third patient had nonsustained ventricular tachycardia before and after the operation (first true diagnosis group). In the group of the next five patients with the signs of heart failure, (the New York Heart Association NYHA) III or IV, 2 patients felt better thanks to drugs (NYHA II) and 3 patients had some of electrophysiological interventions (2 pacemakers, 1 of them was ICD and 1 ablation), resulting in improvement in functional classes (Figure 1D). One of the last 2 patients had myocardial infarction with occlusion of the right coronary artery and nonsignificant stenosis in other coronary arteries and the second patient had systolic and diastolic dysfunction without symptoms.

Analyzing clinical manifestation of LVNC, it was found that 8 patients had signs of heart failure (67%), 7 (58%) arrhythmias (Table 2), 11 ECG abnormality (91%) with no embolic complication.

The most frequent distribution of noncompaction segments, as already known, were in the apex and in the apical and middle parts of septum, lateral and posterior walls (Figure 2).

We did not find familiar occurrence of LVNC at our patients group, according to their anamnesis, because of frequent refusal of their relatives to allow us to determine the status of their present condition, as well. In only 6 cases, we succeeded to make echocardiography in the first relatives, who agreed to be checked up, and these exams were within normal range.

Table 2
Electrocardiographic (ECG) abnormalities in 12 patients with left ventricular noncompaction

ECG abnormalities	Number of patients
Chronic atrial fibrillation	4
Ventricular tachycardia	3
Left bundle branch block	3
Premature ventricular contraction	3
High grade atrioventricular (AV) block	1

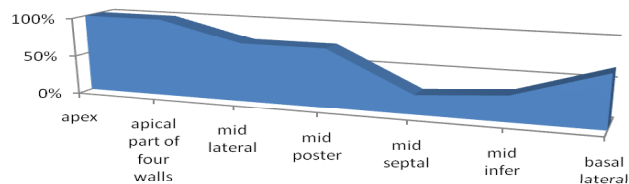


Fig. 2 – Distribution of noncompaction segments of the left ventricular myocardium in our study

Discussion

Although LVNC is a recently recognized congenital cardiomyopathy, there are publications which instruct us to make better diagnosis of this disorder in our daily, routine practice^{11, 12}. The prevalence of LVNC has been reported to be from 0.05% to 0.24% in the largest adult series and 0.14% in the largest pediatric series, but according to our results (0.31%) the real prevalence is thought to be higher^{13, 14}. No data are available on the prevalence of LVNC from autopsy series¹⁵. The real prevalence of LVNC and determination of this value in specific groups (health population, hospital population, patients with cardiomyopathies, etc) is not really known. In population there is a lack of interest for determination of their present health condition during the time when they are without any symptoms. The diagnosis of LVNC could be made with two-dimensional Doppler echocardiography, cardiac magnetic resonance imaging, cardiac computed tomography, left ventricular angiography, after cardiac transplantation or autopsy¹⁶. Echocardiography is the most available technique for diagnosing and following-up of patients with LVNC¹⁷⁻¹⁹. Older echocardiographic machines and still “new” entities would cause a risk in sense of misinterpretations or misdiagnosis. During primary echocardiographic investigations, LVNC was diagnosed in approximately less than 50% of patients¹⁷, though this percentage in our study was much higher (75%). The most frequently misinterpreted were apical or localized hypertrophic cardiomyopathy, dilated cardiomyopathy, endocardial fibroelastosis, endomyocardial fibrosis, restrictive cardiomyopathy, myocarditis, left ventricular masses or thrombus and some other myocardial or pericardial disease. The misinterpretations in our study group included apical hypertrophic cardiomyopathy (n = 1), dilated cardiomyopathies (n = 7) and as the new and distinctive – patients with primary mitral valve pathology (n = 3). The reason we substantially report LVNC when the ventricular dilatation occurs is the low possibility to visualize deep hypertrabeculation in hypertrophied myocardium with poor function.

The false diagnose of LVNC, might include false tendons, aberrant bands, thrombus which are frequently seen or obliterate processes of the left ventricle cavity, intramyocardial hematomas, cardiac metastases and intramyocardial abscesses which are very rare^{12, 14, 16, 17}. We should be aware that an overlap exists between different cardiac abnormalities, which might be mixed up or associated with the LVNC¹².

If we look for available data for prognosis in this group, we will see that the first studies²⁰⁻²² reported high morbidity and mortality rate because physicians did not recognize this pathology and according to that, they made the diagnosis relatively late. The longest follow-up period of patients with LVNC was 24 years and it demonstrated that some patients could have a favorable prognosis¹⁵. If we have to evaluate status of these patients at the time of diagnoses and during following-up period, we would see that there were some contrarities. The latest studies, which included a great number of patients, suggesting that noncompaction alone does not seem to be a risk factor for malignant supraventricular or ventricular arrhythmias. At the beginning, in our group of patients, 58% had a kind of arrhythmias and not all of these patients had systolic dysfunction. We would like to suggest that at the first visit it has to be predominantly evaluation of the patients with arrhythmias or ECG abnormalities (apart from the presence of systolic dysfunction or not) and the patients with valvular heart disease, not just aortic stenosis which has been already published, when patients with mitral insufficiency (caused by mitral valve prolapse) have to be focused on, before occurring of systolic dysfunction or dilatation^{11, 23, 24}. New medical treatment options could change life risk by treating arrhythmias, as well as to lead to the improvements in drugs selection and possibility to have new and accessible procedures that could change both length and quality of life. The pitfalls in the diagnosis of LVNC are still present and it could challenge physicians to put effort in new etiology investigations and on better diagnostics imaging techniques^{11, 12}.

Conclusion

Although many cardiologists have focused on LVNC, there is no genuine data about prevalence of this abnormality. This study points out different initial signs and symptoms and very widely variation of treatment possibilities. New studies in this field are necessary to make this problem easier for understanding and to provide a required information to physicians who perform echocardiography for better diagnostics of this disease in the future, because it is very important to start treating these patients in their oligosymptomatic or asymptomatic period.

REFERENCES

1. Maron BJ, Towbin JA, Thiene G, Antzelevitch C, Corrado D, Arnett D, et al. Contemporary definitions and classification of the cardiomyopathies: an American Heart Association Scientific Statement from the Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functional Genomics and Translational Biology Interdisciplinary Working Groups; and Council on Epidemiology and Prevention. *Circulation* 2006; 113(14): 1807–16.
2. Elliott P, Andersson B, Arbustini E, Bilinska Z, Cecchi F, Charron P, et al. Classification of the cardiomyopathies: a position statement from the European Society Of Cardiology Working

- Group on Myocardial and Pericardial Diseases. *Eur Heart J* 2008; 29(2): 270–6.
3. Richardson P, McKenna W, Bristow M, Maisch B, Mautner B, O'Connell J, et al. Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of cardiomyopathies. *Circulation* 1996; 93(5): 841–2.
 4. Stöllberger C, Finsterer J. Left ventricular hypertrabeculation/noncompaction. *J Am Soc Echocardiogr* 2004; 17(1): 91–100.
 5. Bellet S, Gouley BA. Congenital heart disease with multiple cardiac anomalies: report of a case showing aortic atresia, fibrous scar in myocardium and embryonal sinusoidal remains. *Am J Med Sci* 1932; 183: 458–65.
 6. Burchell HB. Large vascular sinuses in the myocardium of dog. *Anat Rec* 1939; 23: 732–4.
 7. Jenni R, Oechslin E, Schneider J, Attenhofer Jost C, Kaufmann PA. Echocardiographic and pathoanatomical characteristics of isolated left ventricular non-compaction: a step towards classification as a distinct cardiomyopathy. *Heart* 2001; 86(6): 666–71.
 8. Engberding R, Bender F. Identification of a rare congenital anomaly of the myocardium by two-dimensional echocardiography: persistence of isolated myocardial sinusoids. *Am J Cardiol* 1984; 53(11): 1733–4.
 9. Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof E, Fleischmann KE, et al. ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Developed in Collaboration With the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology and Society for Vascular Surgery. *Circulation* 2007; 116(17): 1971–96.
 10. Murphy RT, Thaman R, Blanes JG, Ward D, Sevdalis E, Papra E, et al. Natural history and familial characteristics of isolated left ventricular non-compaction. *Eur Heart J* 2005; 26(2): 187–92.
 11. Nikolić A, Jovović L. Myocardial noncompaction—a rarity or something else. *Vojnosanit Pregl* 2007; 64(3): 211–7. (Serbian)
 12. Stöllberger C, Finsterer J. Pitfalls in the diagnosis of left ventricular hypertrabeculation/non-compaction. *Postgrad Med J* 2006; 82(972): 679–83.
 13. Lofiego C, Biagini E, Ferlito M, Pasquale F, Rocchi G, Perugini E, et al. Paradoxical contributions of non-compacted and compacted segments to global left ventricular dysfunction in isolated left ventricular noncompaction. *Am J Cardiol* 2006; 97(5): 738–41.
 14. Stöllberger C, Finsterer J, Blazek G. Isolated left ventricular abnormal trabeculation: follow-up and association with neuromuscular disorders. *Can J Cardiol* 2001; 17(2): 163–8.
 15. Boyd MT, Seward JB, Tajik AJ, Edwards WD. Frequency and location of prominent left ventricular trabeculations at autopsy in 474 normal human hearts: implications for evaluation of mural thrombi by two-dimensional echocardiography. *J Am Coll Cardiol* 1987; 9(2): 323–6.
 16. Salemi VM, Rochitte CE, Lemos P, Benvenuti LA, Pita CG, Mady C. Long-term survival of a patient with isolated noncompaction of the ventricular myocardium. *J Am Soc Echocardiogr* 2006; 19(3): 354.e1–354.e3.
 17. Frischknecht BS, Attenhofer Jost CH, Oechslin EN, Seifert B, Hoigné P, Roos M, et al. Validation of noncompaction criteria in dilated cardiomyopathy, and valvular and hypertensive heart disease. *J Am Soc Echocardiogr* 2005; 18(8): 865–72.
 18. Kelley-Hedgpeth A, Towbin JA, Maron MS. Images in cardiovascular medicine. Overlapping phenotypes: left ventricular non-compaction and hypertrophic cardiomyopathy. *Circulation* 2009; 119(23): e588–9.
 19. Thuny F, Jacquier A, Jop B, Giorgi R, Gaubert JY, Bartoli JM, et al. Assessment of left ventricular non-compaction in adults: side-by-side comparison of cardiac magnetic resonance imaging with echocardiography. *Arch Cardiovasc Dis* 2010; 103(3): 150–9.
 20. Chin TK, Perloff JK, Williams RG, Jue K, Mohrmann R. Isolated noncompaction of left ventricular myocardium. A study of eight cases. *Circulation* 1990; 82(2): 507–13.
 21. Ritter M, Oechslin E, Sütsch G, Attenhofer C, Schneider J, Jenni R. Isolated noncompaction of the myocardium in adults. *Mayo Clin Proc* 1997; 72(1): 26–31.
 22. Ichida F, Hamamichi Y, Miyawaki T, Ono Y, Kamiya T, Akagi T, et al. Clinical features of isolated noncompaction of the ventricular myocardium: long-term clinical course, hemodynamic properties, and genetic background. *J Am Coll Cardiol* 1999; 34(1): 233–40.
 23. Captur G, Nihoyannopoulos P. Left ventricular non-compaction: genetic heterogeneity, diagnosis and clinical course. *Int J Cardiol* 2010; 140(2): 145–53.
 24. George KM, Badhwar V. Sustainable myocardial recovery after mitral reconstruction for left ventricular noncompaction. *Ann Thorac Surg* 2010; 89(4): 1283–4.

Received on March 16, 2010.

Accepted on October 11, 2010.