



Left ventricular noncompaction in a patient presenting with a left ventricular failure

Nekompaktna leva komora kao uzrok srčane slabosti

Andelka Ristić-Andelkov^{*†}, Danijela Vraneš^{*†}, Zorica Mladenović^{*‡},
Siniša Rusović^{*§}, Nenad Ratković^{*†}, Snježana Vukotić^{*†}, Lidija Torbica^{*†},
Veljko Milić^{*†}, Tanja Mišić^{||}, Mirjana Ristić^{||}, Branislav Baškot^{**}, Milena Pandrc^{||}

University of Defence, ^{*}Faculty of Medicine of the Military Medical Academy, Belgrade, Serbia; [†]Military Medical Academy, [‡]Clinic for Emergency and Internal Medicine, [‡]Clinic for Cardiology, [§]Institute for Radiology, Belgrade, Serbia; ^{||}Internal Medicine Practice „Nada-a“, Belgrade, Serbia; ^{||}Military Medical Center „Slavija“, Belgrade, Serbia; ^{**}Specialistic Nuclear Medicine Practice „Dr Baškot“

Abstract

Introduction. Left ventricular noncompaction (LVNC) is a congenital disorder characterised by prominent trabeculations in the left ventricular myocardium. This heart condition very often goes completely undetected, or is mistaken for hypertrophic cardiomyopathy or coronary disease. **Case report.** A middle-aged female with a positive family history of coronary disease was admitted with chest pain, electrocardiography (ECG) changes in the area of the inferolateral wall and elevation in cardiac specific enzymes. Initially, she was suspected of having acute coronary syndrome. However, in the left ventricular apex, especially alongside the lateral and inferior walls, cardiac ultrasound visualised hypertrabeculation with multiple trabeculae projecting inside the left ventricular cavity. A short-axis view of the heart above the papillary muscles revealed the presence of two layers of the myocardium: a compacted homogeneous layer adjacent to the epicardium and a spongy layer with trabeculae and sinusoids under the endocardium. The thickness ratio between the two layers was 2.2:1. The same abnormalities were corroborated by multislice computed tomography (MSCT) of the heart. **Conclusion.** Left ventricular noncompaction is a rare, usually hereditary cardiomyopathy, which should be considered as a possibility in patients with myocardial hypertrophy. It is very often mistaken for coronary disease owing to ECG changes and elevated cardiac specific enzymes associated with myocardial hypertrophy and heart failure.

Key words:

ventricular dysfunction, left; heart failure; isolated noncompaction of the ventricular myocardium; coronary vasospasm; echocardiography; tomography; diagnosis, differential.

Apstrakt

Uvod. Nekompaktna leva komora (NKLK) je urođena bolest koju karakteriše izrazita trabekularizacija miokarda leve komore. Vrlo često se promene na srcu potpuno previde ili se zamene za hipertrofiju miokarda ili koronarnu bolest. **Prikaz bolesnika.** Bolesnica srednjih godina, sa porodičnim opterećenjem za koronarnu bolest, primljena je zbog bolova u grudima, promena u elektrokardiogramu (EKG-u) u zoni inferolateralnog zida i porasta kardiospecifičnih enzima. U prvom trenutku posumnjalo se na akutni koronarni sindrom. Međutim, na ultrazvučnom pregledu srca, u vrhu leve komore, posebno duž lateralnog i donjeg zida, viđena je hipertrabekularizacija sa brojnim resicama koje su prominirale u šupljinu leve komore. Poprečni presek srca iznad papilarnih mišića ukazao je na postojanje dva sloja miokarda: uz epikard je bio prisutan kompaktni i homogeni sloj, a ispod endokarda rastresiti sloj sa trabekulama i sinusoidima. Odnos debljine ova dva sloja iznosio je 2,2:1. Iste promene potvrđene su na multislajskoj kompjuterizovanoj tomografiji (MSCT) srca. **Zaključak.** Nekompaktna leva komora je retka, najčešće nasledna kardiomiopatija, na koju treba misliti kod bolesnika sa hipertrofijom miokarda. Vrlo često se zamenjuje za koronarnu bolest zbog promena u EKG-u i porasta kardiospecifičnih enzima koji su posledica hipertrofije miokarda i srčane slabosti.

Ključne reči:

srce, disfunkcije leve komore; srce, insuficijencija; miokard, komorni, izolovana nonkompakcija; aa. coronariae, spazam; ehokardiografija; tomografija; dijagnoza, diferencijalna.

Introduction

Left ventricular noncompaction (LVNC) is a congenital disorder characterised by prominent trabeculations in the left ventricular myocardium. The disease is believed to appear during intrauterine development as a result of arrested morphogenesis of a compacted myocardium, the consequence of which is the formation of an excessively thick myocardium consisting of two layers: a thinner homogeneous layer under the epicardium and a prominently spongy and non-compacted layer with multiple trabeculations and recesses under the endocardium^{1,2}. It can develop either as an isolated disorder, or in association with congenital anomalies of the left or right ventricular outflow tract³. Actual prevalence of this disease is still unknown. However, in patients with heart failure, it appears in approximately 3–4% of the cases⁴.

Case report

A 50-year-old female patient was admitted to our institution with signs of acute coronary syndrome. On the day of admittance, she felt pain in the left side of her chest and her left shoulder, accompanied by shortness of breath, coughing and diaphoresis. For the past month she had been experiencing extreme fatigue, even after slight exertion. The patient saw a physician at the primary health centre and was found to have high arterial pressure (160/100 mmHg), while electrocardiogram (ECG) showed negative T waves in leads D₂, D₃, aVF, V₃-V₆. Urgent blood tests revealed elevation in cardiac specific enzymes: troponin I 0.44 ng/mL (< 0.14). Dual antiplatelet therapy was prescribed: aspirin 300 mg and clopidogrel 300 mg and the patient was referred to hospital for treatment with suspicion of non-ST elevation myocardial infarction.

Anamnesis revealed that the patient had suffered from left-sided sciatica for two weeks, that she used non-steroidal antirheumatics, muscle relaxants and corticosteroids. Five years earlier, she had deep venous thrombosis of both lower limbs and had used anticoagulation therapy for 6 months. She cited that 10 years earlier she had underwent hysterectomy and cholecystectomy; she had had two childbirths and several miscarriages. The patient is a non-smoker, normotensive and has a family history of coronary artery disease.

Upon hospitalisation, her respiratory sounds were normal, with inspiratory crackles basally. Heart activity was rhythmic, the sounds distinct, with no murmurs, frequency (f) 88/min, blood pressure – 130/75 mmHg.

The ECG registered sinus rhythm, a normogram, a 1 mm downsloping ST segment depression with negative T waves in D₂, D₃, aVF, V₃-V₆ (Figure 1). Chest radiography revealed interstitial and perivascular edema basally, with hilar enlargement.

Blood test results were: erythrocyte sedimentation rate (ESR) – 7 mm/h, C-reactive protein (CRP) – 3.5 mg/mL, blood count: white blood cells (WBC) – 12.0 10⁹/L dominated by granulocytes (10.7%), haemoglobin (Hgb) – 154 g/L, red blood cells (RBC) – 4.92 10¹²/L, Platelets (Pt) – 330 10⁹/L. The test showed increased concentration of enzymes associated with myocardial necrosis: creatine kinase (CK) – 485 U/L (< 200), CK_{MB} – 35 ng/mL (< 25), troponin I – 0.44 ng/mL (< 0.14), aspartate aminotransferases (AST) – 50 U/L, alanine transaminase (ALT) – 83 U/L, LDH – 269 U/L, as well as elevated levels of the brain natriuretic protein (BNP) – 361 pg/mL (< 256). Other blood and urine test values were in their normal reference ranges, except for an increased concentration of amyloids 16.5 pmol/L (< 6.8), while serum and urine protein electrophoresis and immunoelectrophoresis were normal.

Echocardiography showed: left atrium was dilated – 4.7 cm. The size of the left ventricle was in normal reference values: end systolic diameter (ESD) – 3.23 cm, endodiastolic diameter (EDD) – 4.73 cm. Concentric left ventricular hypertrophy was registered, with ventricular walls of 1.5 cm and a highly hyperechoic myocardium. Myocardial contractility was preserved, the ejection fraction (EF) was 58.2% according to the Teichholz formula and 56% calculated by Simpson's rule, Fractional shortening (FS) was 29.8%. Left ventricular mass was increased – 293 g or 161 gm² (Cube). In the left ventricular apex, especially alongside the lateral and inferior walls, ultrasound revealed hypertrabeculation with multiple trabeculae projecting inside the left ventricular cav-

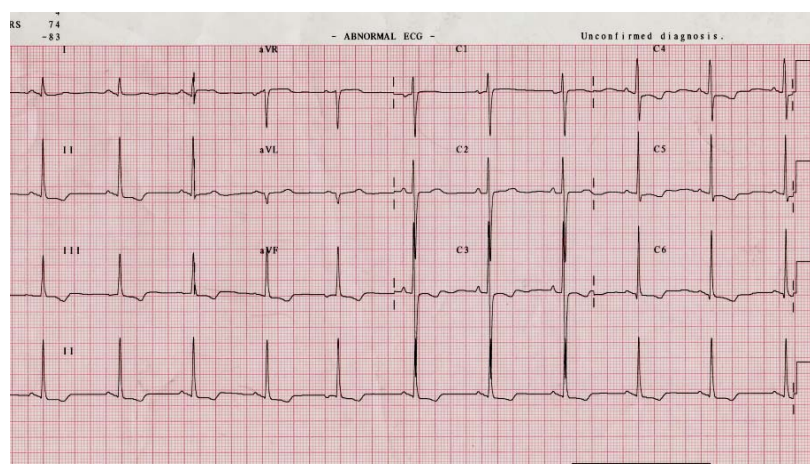


Fig. 1 – Electrocardiography showing ST segment depression of 1 mm with negative T waves in the leads D₂, D₃, aVF, V₃-V₆.

ity. Colour Doppler echocardiography showed that blood filled intertrabecular recesses in the lateral wall and the left ventricular apex (Figure 2).

A short-axis view of the heart above the papillary muscles revealed the presence of two layers of the myocardium: a compacted homogeneous layer adjacent to the epicardium and a spongy layer with trabeculae and sinusoids under the endocardium. The thickness ratio between the two layers was 2.2:1 (Figure 3).

The type of blood flow registered above the mitral valve was typical of impaired relaxation, with the E/A ratio of 0.6 and mitral regurgitation grade 1+. The size of the right ventricle was within the upper reference limit (2.8 cm), with tricuspid regurgitation grade 1+. The systolic pressure in the right ventricle was increased – 48 mmHg. A pericardial effusion of 0.4 cm was detected around the entire heart.

Holter monitoring registered a sinus rhythm, with a short episode of absolute arrhythmia, which lasted for 6 seconds at the frequency of 153/min. There were 163 atrial extrasystoles, which were isolated, rarely paired, as well as 4 single ventricular extrasystoles.

On the multislice computed tomography (MSCT) of the heart with angiography: blood vessel imaging showed normal results (Figure 4).

Since magnetic resonance imaging of the heart was not available in our institution, we conducted an MSCT test, which included multiple long- and short-axis slices that revealed concentric myocardial hypertrophy with prominent trabeculations and deep recesses above the papillary muscles, especially in the area of the apex and the anterolateral wall (Figure 5).

On the basis of the anamnesis, the clinical picture and the undertaken examinations, we concluded that the patient suffered from noncompaction cardiomyopathy presenting as heart failure (New York Heart Association – NYHA II/III). The initial diagnosis of acute coronary syndrome was abandoned. Laboratory analyses registered only slight elevations of cardiac-specific enzymes, which were explained by myocardial hypertrophy and heart failure, considering that coronary blood vessels were unobstructed. Owing to suspected transient ischaemic attack, we performed an MSCT of the endocranium, which returned



Fig. 2 – Echocardiography and multislice computed tomography of the heart – apical 4-chamber view showing prominent trabeculations of the left ventricular apex and lateral wall, with colour Doppler evidence of deep intertrabecular recesses filled with blood.

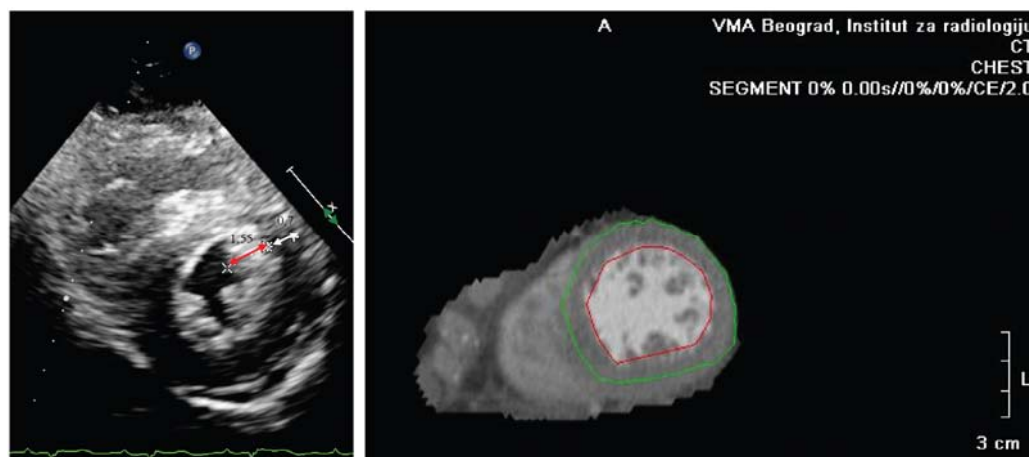


Fig. 3 – Echocardiography: short-axis view of the left ventricle at end systole, and multislice computed tomography of the heart: the left ventricular myocardium consists of 2 layers – the thick non-compacted layer and the thin compacted layer, their thickness ratio being 2.2:1.

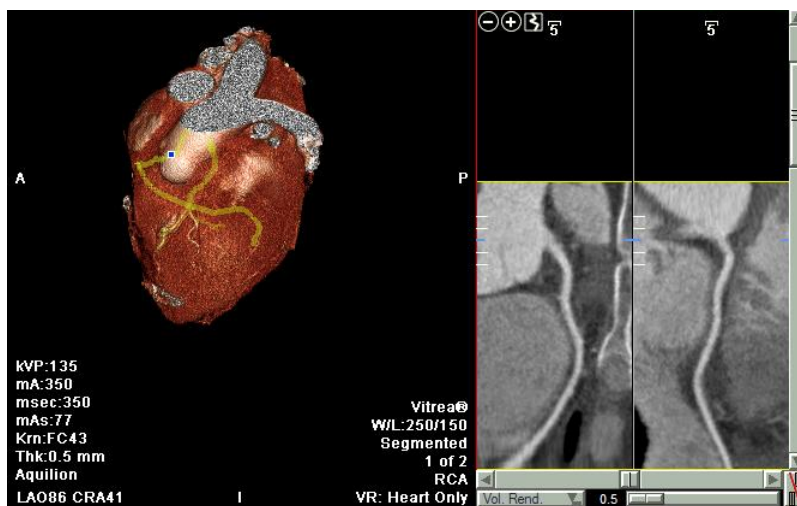


Fig. 4 – Multislice computed tomography coronarography: all coronary blood vessels are free of plaque and show no signs of stenosis.

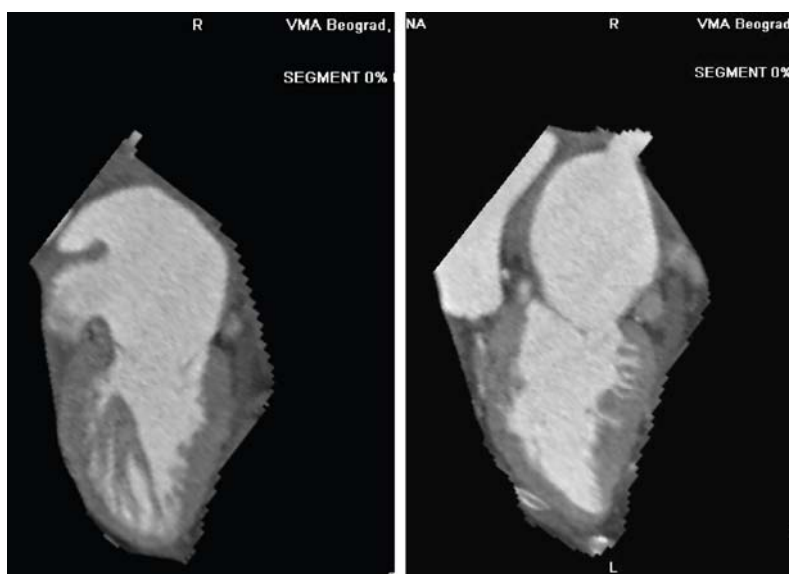


Fig. 5 – Multislice computed tomography of the heart with left ventricular noncompaction. Multiple trabeculations and recesses between them are visible apically, on lateral and inferior walls.

normal results. The patient was initially treated with dual antiplatelet therapy until the coronarography examination, and then an oral anticoagulant was introduced in the therapy, in addition to cardiotonics and diuretics, due to verified paroxysmal atrial fibrillation.

Discussion

Left ventricular noncompaction is a congenital disorder characterised by prominent trabeculations in the left ventricular myocardium^{1,2}. The European Society of Cardiology (Working Group on Myocardial and Pericardial Diseases) included this defect in the group of unclassified cardiomyopathies, along with Takotsubo cardiomyopathy, whereas the American Heart Association classifies it as a primary congenital cardiomyopathy^{5,6}.

The disorder appears in isolated form, but it may also be inherited, usually through autosomal dominant inheritance. In many families, the disorder is found in the gene re-

sponsible for the synthesis of beta-myoglobin heavy chains. Furthermore, in some cases the mutation is found in the genes G4.5, P121L, E101K, which are responsible for the synthesis of cytoskeletal proteins: beta-myosin, alpha-actin and troponin^{7,8}.

Noncompaction of the left ventricular myocardium is sometimes seen as part of congenital anomalies of the left or right ventricular outflow tract, such as: pulmonary artery atresia, bicuspid aortic valve, congenitally corrected transposition and Ebstein's anomaly. Moreover, this disorder is occasionally detected in conjunction with ventricular septal defect (VSD), or in association with neuromuscular diseases³.

The disease is believed to appear during intrauterine development as a result of arrested morphogenesis of a compacted myocardium. Namely, the heart muscle is markedly heterogeneous during the embryonic stage, with many sinusoid blood vessels interwoven with myofibril bundles, which provide blood supply to the myocardium. Towards the end of the intrauterine development, the myofibrils are condensed

and the left ventricular myocardium becomes compacted. As a result of disrupted embryonic development, the myocardium becomes excessively thick and consists of two layers: a homogeneous layer, located under the epicardium, and a distinctly spongy and non-compacted layer, located under the endocardium, characterised by multiple trabeculations and recesses. The intertrabecular recesses open into the left ventricular cavity and are filled with blood, with no communication with epicardial blood vessels^{9,10}.

Actual prevalence of this disease is still unknown. However, in patients with heart failure, it appears in approx. 3–4% of the cases¹¹.

Some patients are asymptomatic and their diagnosis is established fortuitously, usually based on echocardiography. Other patients develop three types of symptoms: heart failure, atrial and ventricular arrhythmias, thromboembolic complications.

The disorder usually manifests itself as heart failure in 79% of cases (dyspnoea, fatigue after slight exertion, cough and swelling). Chronic atrial fibrillation is the most common type of arrhythmia, while other registered abnormalities include left or right bundle branch block, fascicular block or ventricular tachycardia. In the left ventricular cavity, thrombi often form between trabeculae, which leads to thromboembolic complications. The clinical presentation usually appears in adults, but it is not rare to see children or even infants suffering from heart failure resulting from left ventricular noncompaction⁴.

Electrocardiogram (ECG) reveals left ventricular hypertrophy, as well as various rhythm and conduction disturbances¹².

Echocardiography is the method of choice in diagnosing LVNC. Other applicable methods include magnetic resonance imaging, multi-slice scanner, left ventricular ventriculography and genetic testing.

In 2001, Jenni et al.¹³ proposed 3 criteria for echocardiographic diagnosis of this disorder: considerable thickening of the left ventricular wall, which consists of two layers – thinner compacted layer underneath the epicardium, and thickened layer under the endocardium, with multiple trabeculae and deep recesses. The ratio of non-compacted to compacted myocardium is higher than 2:1 at end systole, at parasternal short-axis view; deep intertrabecular recesses, in which blood flow is visible in colour Doppler echocardiography; pronounced meshwork of trabeculae in the left ventricular apical area and the mid segments of the inferior and lateral walls.

For LVNC diagnosis to be established, all three of the above criteria need to be fulfilled. In addition to these manifestations, there is also the hypokinesia of the affected left ventricular segments¹³.

Stöllberger et al.¹⁴ proposed somewhat different criteria that involve hypertrabeculation: the presence of more than three trabeculations at the left ventricular apex, above the papillary muscles, all of which are visible in a single image plane, and intertrabecular spaces are perfused with blood from the left ventricular cavity, which is visible in colour Doppler imaging.

Aside from these, other manifestations that may be detected include diffusely reduced left ventricular systolic function, diastolic dysfunction, thrombi in the left ventricular cavity and structural anomalies of the papillary muscle, which is also trabeculated.

In terms of the differential diagnosis, one of the considerations is dilated cardiomyopathy, which occasionally also exhibits two myocardial layers, one of which is non-compacted. The ratio between the two layers is also higher than 2:1; however, the main difference is that dilated cardiomyopathy is characterised by myocardial wall thinning. The differential diagnosis should also take into consideration apical hypertrophic cardiomyopathy, various forms of infiltrative cardiomyopathies, heart anomalies associated with arterial hypertension, as well as the hypereosinophilic syndrome¹⁵.

Magnetic resonance imaging and the MSCT scanner produce a somewhat different image to that of echocardiography. Trabeculations and recesses are detected much more frequently, even in healthy people, especially in patients who suffer from any type of myocardial hypertrophy, and they are located at the left ventricular apex, anterior or lateral walls. The only difference is that the ratio of non-compacted to compacted myocardium is greater than 2.3:1 in diastole, visible in three cross-section views; hence, this is the basic criterion for diagnosing LVNC using magnetic resonance imaging^{16,17}.

Treatment is symptomatic and involves the therapy of heart failure and rhythm disorders. Focus should be on anticoagulation therapy, which is compulsory for patients with $EF < 40\%$ and/or absolute arrhythmia. In the final stage, heart transplantation or implantation of a cardioverter-defibrillator are recommended^{18–24}.

Until recently, LVNC was associated with poor prognosis and it was believed that most patients died as a result of complications. A long-term follow-up of 34 patients with an average age of 42 years, published in 2000, showed that heart failure manifested in 53%, ventricular rhythm disorders in 44% (cardioverter-defibrillators were implanted in 12% of them), while thromboembolic complications occurred in 24% of the patients. Over the follow-up period of 44 months, one third of the patients died – half of them by sudden death, whereas 12% underwent heart transplantation. They were all patients with serious health problems²⁰.

Following the publication of this study, physicians started paying more attention to similar patients who had much milder clinical presentation, or were entirely asymptomatic and identified by chance. In 2005, Murphy et al.²¹ presented a study in which 45 patients of an average age of 37 years were followed up over an average period of 4 years. Survival rate was 97%, while thromboembolic events occurred in only 2 patients. Lofiego et al.⁴ divided 65 patients with LVNC into two groups: symptomatic patients (48) had poor prognosis – 31% of them died or underwent heart transplantation over the average follow-up period of 46 months. Asymptomatic patients, who were usually family members of the affected patients, had no complications^{22,23}.

Conclusion

Left ventricular noncompaction is a rare, usually hereditary cardiomyopathy, which should be considered as a possibility in patients with myocardial hypertrophy. It is very often mistaken for coronary disease owing to ECG changes

and elevated cardiac-specific enzymes associated with myocardial hypertrophy and heart failure. The disorder is usually detected fortuitously and patients with LVNC have a normal life expectancy, while about a third of them present with symptoms of heart failure, arrhythmias or thromboembolic events, with a very poor prognosis.

R E F E R E N C E S

- 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.
- Weiford BC, Subbarao VD, Mulhern KM. Noncompaction of the ventricular myocardium. *Circulation* 2004; 109(24): 2965–71.
- Attenhofer Jost CH, Connolly HM, O'Leary PW, Warnes CA, Tajik AJ, Seward JB. Left heart lesions in patients with Ebstein anomaly. *Mayo Clin Proc* 2005; 80(3): 361–8.
- Lofiego C, Biagini E, Pasquale F, Ferlito M, Rocchi G, Perugini E, et al. Wide spectrum of presentation and variable outcomes of isolated left ventricular non-compaction. *Heart* 2007; 93(1): 65–71.
- 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.
- 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.
- Hoedemaekers YM, Caliskan K, Majoor-Krakauer D, van de Laar I, Michels M, Witsenburg M, et al. Cardiac beta-myosin heavy chain defects in two families with non-compaction cardiomyopathy: linking non-compaction to hypertrophic, restrictive, and dilated cardiomyopathies. *Eur Heart J* 2007; 28(22): 2732–7.
- Ichida F, Tsubata S, Bowles KR, Haneda N, Uese K, Miyawaki T, et al. Novel gene mutations in patients with left ventricular non-compaction or Barth syndrome. *Circulation* 2001; 103(9): 1256–63.
- Ichida F. Left ventricular noncompaction. *Circ J* 2009; 73(1): 19–26.
- Pantazis AA, Elliott PM. Left ventricular noncompaction. *Curr Opin Cardiol* 2009; 24(3): 209–13.
- Pignatelli RH, McMahon CJ, Dreyer WJ, Denfield SW, Price J, Belmont JW, et al. Clinical characterization of left ventricular non-compaction in children: a relatively common form of cardiomyopathy. *Circulation* 2003; 108(21): 2672–8.
- Lin YN, Wang YQ, Yu Y, Cao Q, Wang F, Chen SY. Left ventricular noncompaction cardiomyopathy: a case report and literature review. *Int J Clin Exp Med* 2014; 7(12): 5130–3.
- 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.
- Stöllberger C, Kopsa W, Tscherny R, Finsterer J. Diagnosing left ventricular noncompaction by echocardiography and cardiac magnetic resonance imaging and its dependency on neuromuscular disorders. *Clin Cardiol* 2008; 31(8): 383–7.
- Rosa LV, Salemi VM, Alexandre LM, Mady C. Noncompaction cardiomyopathy: a current view. *Arq Bras Cardiol* 2011; 97(1): e13–9. (English, Portuguese, Spanish)
- Petersen SE, Selwanayagam JB, Wiesmann F, Robson MD, Francis JM, Anderson RH, et al. Left ventricular non-compaction: insights from cardiovascular magnetic resonance imaging. *J Am Coll Cardiol* 2005; 46(1): 101–5.
- Jaquier A, Thuny F, Jop B, Giorgi R, Cohen F, Gaubert JY, et al. Measurement of trabeculated left ventricular mass using cardiac magnetic resonance imaging in the diagnosis of left ventricular non-compaction. *Eur Heart J* 2010; 31(9): 1098–104.
- Kovacevic-Preradovic T, Jenni R, Oechslin EN, Noll G, Seifert B, Attenhofer Jost CH. Isolated left ventricular noncompaction as a cause for heart failure and heart transplantation: a single center experience. *Cardiology* 2009; 112(2): 158–64.
- Stamou SC, Lefrak EA, Athari FC, Burton NA, Massimiano PS. Heart transplantation in a patient with isolated noncompaction of the left ventricular myocardium. *Ann Thorac Surg* 2004; 77(5): 1806–8.
- Oechslin EN, Attenhofer Jost CH, Rojas JR, Kaufmann PA, Jenni R. Long-term follow-up of 34 adults with isolated left ventricular noncompaction: a distinct cardiomyopathy with poor prognosis. *J Am Coll Cardiol* 2000; 36(2): 493–500.
- 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.
- Greutmann M, Mab ML, Silversides CK, Klaassen S, Attenhofer Jost CH, Jenni R, et al. Predictors of adverse outcome in adolescents and adults with isolated left ventricular noncompaction. *Am J Cardiol* 2012; 109(2): 276–81.
- Bhatia NL, Tajik AJ, Wilansky S, Steidley DE, Mookadam F. Isolated noncompaction of the left ventricular myocardium in adults: a systematic overview. *J Card Fail* 2011; 17(9): 771–8.
- Udeoji DU, Philip KJ, Morrissey RP, Phan A, Schwarz ER. Left ventricular noncompaction cardiomyopathy: updated review. *Ther Adv Cardiovasc Dis* 2013; 7(5): 260–73.

Received on January 24, 2016.

Revised on August 8, 2016.

Accepted on August 26, 2016.

Online First November, 2016.