THE NEW ARMENIAN MEDICAL JOURNAL
Vol.10 (2016), No 2, p.20-26

CASE REPORT AND LITERATURE REVIEW

RIGHT VENTRICULAR NONCOMPACTION

LARICCHIA A.[1], SPOLADORE R.[1], MARANTA F.[1], FRAGASSO G.[1]*, MARGONATO A.[2]

[1] Clinical Cardiology Unit, San Raffaele University Hospital, Milan, Italy
[2] Vita-Salute San Raffaele University, Milan, Italy

Received 29/07/2015; accepted for printing 24/03/2016

ABSTRACT

Left ventricular noncompaction is a rare genetic cardiomyopathy characterized by non-compacted endocardial and compacted epicardial layers with a ratio >2. This condition presents an extremely high morphological variability and it is not yet defined as either a distinct cardiomyopathy or a morphologic trait shared by different cardiomyopathies. The left ventricle is the most commonly involved structure, but in rare cases, it may include only the right ventricle. Clinical presentation of this disease is variable and may be manifested at any age but in symptomatic patients has unfavorable prognosis.

Electrocardiography findings are non-specific and include left ventricular hypertrophy, repolarization changes, inverted T waves, ST-segment changes, intraventricular conduction abnormalities, and atrioventricular blocks. Arrhythmias are common, including ventricular tachyarrhythmias, atrial fibrillation, and paroxysmal supraventricular tachycardia.

Cardiac magnetic resonance imaging plays an essential role in the assessment of myocardial fibrosis and final diagnosis.

Asymptomatic patients can be followed by clinical monitoring, whereas for symptomatic patients therapy is aimed to treat previously mentioned triads of symptoms.

Heart failure symptoms treatment is carried out by the general guidelines on heart failure and includes the use of mechanical devices such as cardioverter defibrillator implantation and cardiac resynchronization therapy in primary prevention. When heart failure is refractory to medical and device therapy, heart transplantation should be considered.

In patients with non compaction cardiomyopathy with implanted defibrillator either in primary or secondary prevention for sudden cardiac death, there was an appropriate shock in 25% and 50% of cases respectively, in a follow-up time of 3 years.

KEYWORDS: *left ventricular noncompaction, cardiomyopathy, echocardiography, cardiac magnetic resonance imaging.*

CASE REPORT

A man aged 18-years with dizziness and palpitation was referred to the Department of Cardiology. Inversion of T waves and clipping were revealed in the first three precordial leads on ECG during ventricular repolarization only in lead V2 (Fig. 1).

Echo images showed a rare case of isolated right ventricular noncompaction with mild dilation of the hypertrabeculated right ventricle and without left ventricle involvement (Fig. 2).

Cardiac magnetic resonance short axis views (Fig. 3A, B) and long axis views (Fig. 3C) confirmed the presence of right ventricular noncompaction. Late gadolinium analysis (Fig. 4A, B) excluded the presence of myocardial fibrosis and/or fat tissue in both ventricles.

Considering ECG, echocardiography and cardiac magnetic resonance abnormalities it was de-

ADDRESS FOR CORRESPONDENCE:
San Raffaele University Hospital
Via Olgettina 60, Milan 20132, Italy
Tel.: (00390226437366)
Fax: (00390226437359)
Email: gabriele.fragasso@hsr.it

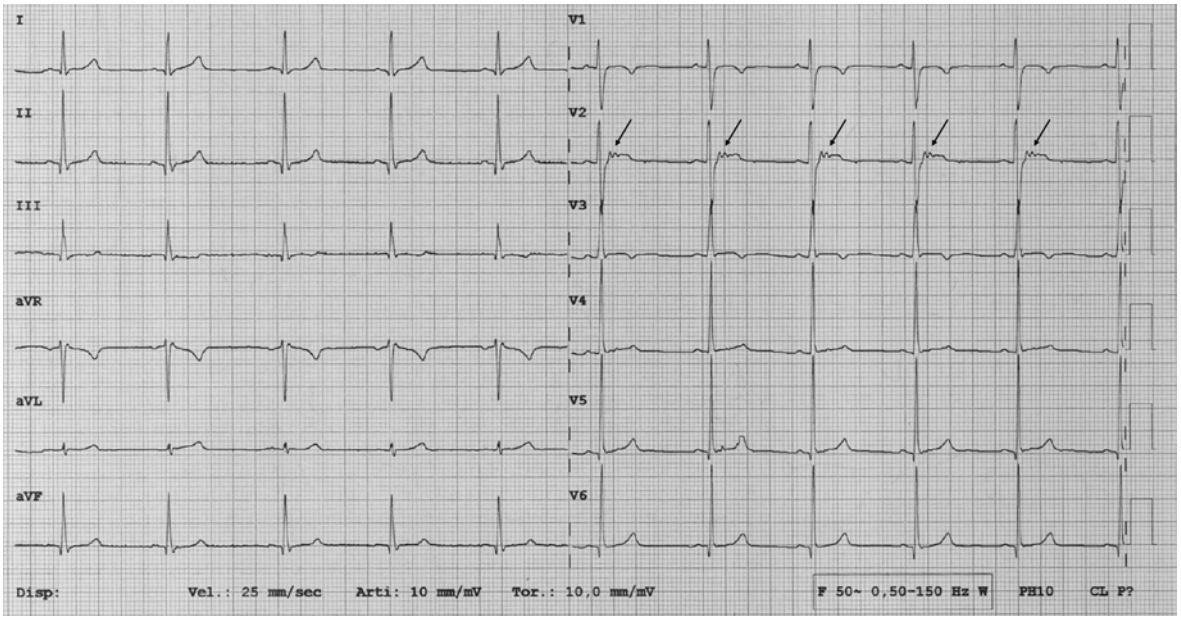

Figure 1. *ECG tracing revealing inversion of T waves in the first three precordial leads and a recess during ventricular repolarization in lead V2*

cided to perform an endocavitary electrophysiological study that induced a sustained ventricular tachycardia, with complicated cardiac arrest, successfully treated with direct current shock. The patient was then implanted with cardioverter defibrillator. This is a rare description of isolated non-compaction of the right myocardium in an adult subject. Besides the right localization of the non-compaction, this case should be considered unique for the peculiar association of the V2 lead on ECG (such as a sort of epsilon wave) and hypertrabeculated right ventricle, in the absence of ventricular fibrosis and/or fat tissue.

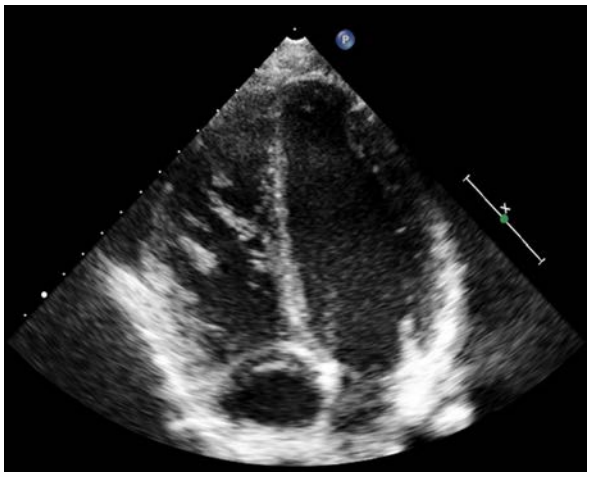

Figure 2. *Echo images showing isolated right ventricular non-compaction, without left ventricle involvement*

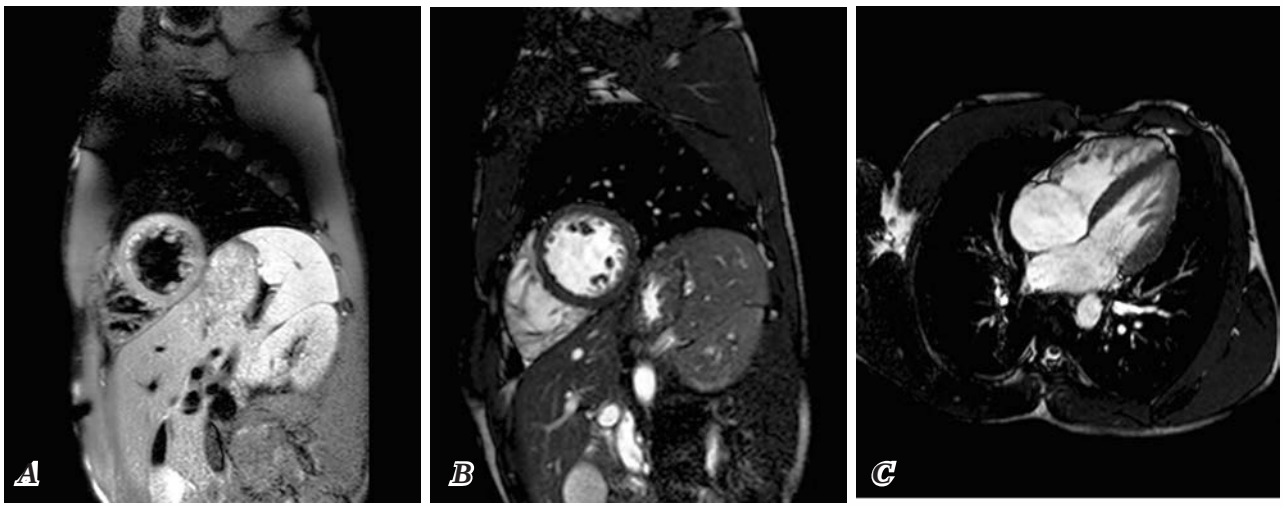

Figure 3. *Cardiac magnetic resonance of short axis views (A and B) and long axis view (C) confirming right ventricular non-compaction*

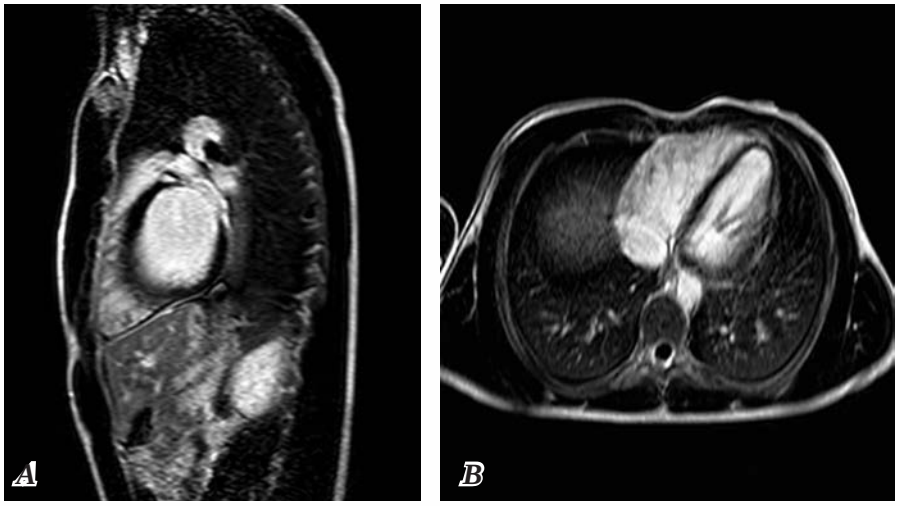

Figure 4. *Short axis (A) and four chambers (B), late-gadolinium analysis views excluding the presence of myocardial fibrosis and/or fat tissue in both ventricles*

INTRODUCTION

Left ventricular noncompaction is a rare genetic cardiomyopathy characterized by non-compacted endocardial and compacted epicardial layers in the myocardial wall connected with trabecular recesses [*Oechslin E, Jenni R, 2011*].

This pathology affect both children and adults, and can be sporadic or genetical, autosomal dominant, X-linked or mitochondrial in origin. There is not a major genetic cause, as a significant genetic heterogeneity has been noted, together with a poor correlation between genotype and phenotypic expression [*Oechslin E, Jenni R, 2011*]. Moreover, there is a huge overlap among cardiomyopathy genes. In fact, major gene mutations associated with ventricular noncompaction are shared with other cardiac disorders.

It should be mentioned that among sporadic cases, apart from genetic ones, some others can be acquired, as observed in pregnancy, in highly trained athletes and in patients with sickle cell anemia [*Gati S et al., Mar 2013; Gati S et al., Sep 2013; Gati S et al., 2014*]. In these cases the results of phenotypes with increased mechanical load may disappear as the primary mechanism dissipates.

The disease more often involves the left ventricle, but in some cases both ventricles are involved, and more uncommonly, the right ventricle.

Finally, even if the cases of isolated ventricular noncompaction exist, many of them are found in the context of other cardiomyopathies, congenital heart abnormalities or multisystem syndromes such as neuromuscular disorders [*Stöllberger C et al., 2002*].

In this context, left ventricular noncompaction is formally classified by the American Heart Association as a distinct cardiomyopathy, while the European Society of Cardiology defines it as an unclassified cardiomyopathy [*Maron B et al., 2006; Elliott P et al., 2008*].

It is difficult to establish the real prevalence of the disease for all the above mentioned reasons.

Among children with primary cardiomyopathies, left ventricular noncompaction is thought to be the third most common type after dilated cardiomyopathy and hypertrophic cardiomyopathy, with prevalence of about 9% [*Andrews R et al., 2008*].

In the adult population, from the registries of referral institutions, the prevalence is between 0.05% and 0.26% in asymptomatic patients and up to 4% in heart failure patients, based on echocardiographic examinations [*Aras D et al., 2006; Sandhu R et al., 2008*].

PATHOGENESIS

During embryogenesis the heart initially has a “spongy” appearance; it consists of a meshwork of muscle fibers and trabeculations separated by some recesses known as sinusoids. These recesses communicate with the ventricular cavity to receive blood supply. Between 5-8 weeks of gestation, when coronary arteries develop, the process of

"compaction" from myocardial fibers starts and proceeds from the epicardium to the endocardium and from the base to the apex of the heart [*Sedmera D et al., 2000*].

Ventricular noncompaction results from intrauterine arrest of this process; signaling pathways are compromised throughout the myocardium, which leads to persistent ventricular trabeculation [*Towbin J et al., 2015*].

There could also be an association with the absence of well-formed papillary muscles, as assessed by autopsy studies [*Burke A et al., 2005*].

Clinical presentation

Clinical presentation is very variable and can occur at any age. Many patients are asymptomatic, so that the diagnosis of ventricular noncompaction is incidental or more commonly made during screening of asymptomatic family members of affected patients. In these cases the course of the disease is generally stable over years.

Conversely, among symptomatic patients the course of the disease may be more unstable and has an unfavorable prognosis [*Murphy R et al., 2005*]. The most common presentation is heart failure, followed by the other two typical manifestations, arrhythmias (both bradyarrhythmias and tachyarrhythmias) and embolic events [*Stöllberger C et al., 2011; Steffel J, Duru F, 2012*]. Subendocardial or transmural perfusion deficits and reduced coronary flow reserve can play a certain role in ventricular diastolic and/or systolic dysfunction and altered myocardial metabolism with possible occurrence of malignant arrhythmias, despite normal epicardial coronary arteries [*Spoladore R et al., 2014*].

The mean time from symptoms onset to diagnosis is still 3.5 years, because the disease is often underdiagnosed.

Diagnosis

There is not a consensus on absolute diagnostic criteria.

Electrocardiography findings are non-specific and include left ventricular hypertrophy, repolarization changes, inverted T waves, ST-segment changes, intraventricular conduction abnormalities, and atrioventricular blocks. Arrhythmias are common, including ventricular tachyarrhythmias, atrial fibrillation, and paroxysmal supraventricular tachycardia.

Echocardiography remains an easily accessible and useful tool. A typical finding is the segmental thickening of ventricular wall that is composed of two layers, a thin compacted epicardial one, and a thickened endocardial one with prominent trabeculations and deep recesses. Ratio of noncompacted to compacted layer is >2 as measured at end-systole in the parasternal short-axis view (Fig. 5) [*Jenni R et al., 2001*]. Color Doppler helps identifying the deep, perfused intertrabecular recesses

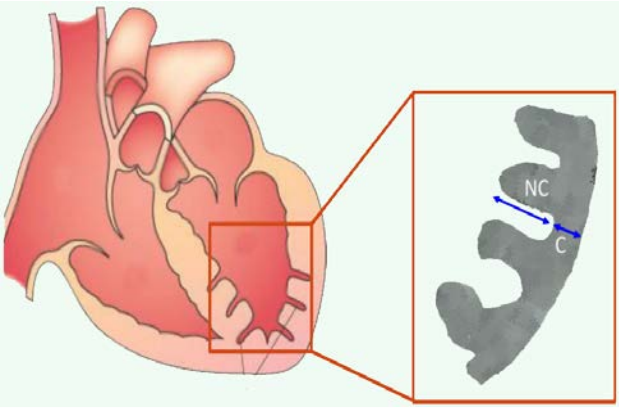

Figure 5. *Ratio of non-compacted to compacted, adapted from Ikeda U and co-authors*

[*Ikeda U et al., 2015*].

The typical anatomic distribution of myocardial noncompaction is preferably apical, followed by mid-ventricular (on lateral and inferior walls, typically sparing the septum) and then basal segments. Notably the number of segments involved is strongly associated to the development and severity of systolic dysfunction [*Punn R, Silverman N, 2010*].

By improvement of imaging modalities, cardiac magnetic resonance provides a detailed view of cardiac morphology and helps visualizing the apex. Diagnostic findings include: a non-compacted left ventricular myocardial mass >20% from total mass and a non-compacted/compacted myocardium ratio >2.3 in at least 1 segment [*Jacquier A et al., 2010; Petersen S et al., 2005*].

It should be noted, that the measurement of cardiac magnetic resonance studies were performed during diastole, whereas the echocardiographic criteria were determined during systole.

Cardiac magnetic resonance is essential in order to assess the presence and extension of myocardial

fibrosis by the delayed gadolinium enhancement analysis with important prognostic information [*Dodd J et al., 2007; Nucifora G et al., 2011*].

Finally, computed tomography is not usually recommended for the diagnosis of ventricular non-compaction, however it can provide information about coronary arteries and it may be useful when magnetic resonance imaging is contraindicated or difficult to perform, even if there are not specific diagnostic criteria [*Sidhu M et al., 2014*].

Current management and treatment options

Asymptomatic patients can be followed by clinical monitoring, whereas for symptomatic patients therapy is aimed to treat previously mentioned triads of symptoms.

Heart failure symptoms treatment is carried out by the general guidelines on heart failure and includes the use of mechanical devices such as cardioverter defibrillator implantation and cardiac resynchronization therapy in primary prevention. When heart failure is refractory to medical and device therapy, heart transplantation should be considered [*Kovacevic-Preradovic T et al., 2009*].

As the most dangerous manifestation of the disease is sudden death from ventricular tachyarrhythmia, regular Holter monitoring is mandatory [*Stanton C et al., 2009*].

The incidence of ventricular arrhythmias (sustained or not) on Holter monitoring is about 26% as a whole. In patients with NCC with implanted defibrillator either in primary or secondary prevention for sudden cardiac death, there was an appropriate shock in 25% and 50% of cases respectively, in a follow-up time of 3 years [*Spoladore R et al., 2014*]. Therefore, current trends support an early aggressive approach, despite the indications for cardioverter defibrillator implantation both in this population and in other patients with systolic heart failure [*Epstein A et al., 2008*].

Finally, as thromboembolic events are common complications with an incidence of about 5-38%, oral anticoagulants are indicated for NCC patients with reduced ejection fraction (<40%), history of previous thromboembolic complications and intracardiac thrombi [*Lofiego C et al., 2007*].

REFERENCES

1. *Andrews RE, Fenton MJ, Ridout DA, Burch M; British Congenital Cardiac Association.* New-onset heart failure due to heart muscle disease in childhood: a prospective study in the United Kingdom and Ireland. Circulation. 2008; 117(1): 79-84.
2. *Aras D, Tufekcioglu O, Ergun K, Ozeke O, Yildiz A., et al*. Clinical features of isolated ventricular noncompaction in adults long-term clinical course, echocardiographic properties, and predictors of left ventricular failure. J Card Fail. 2006; 12(9):726-733.
3. *Burke A, Mont E, Kutys R, Virmani R*. Left ventricular noncompaction: a pathological study of 14 cases. Hum Pathol. 2005; 36(4): 403-411.
4. *Chiribiri A, Leuzzi S, Salvetti I, Patané S, Bonamini R, Trevi GP, Gaita F, Cesarani F.* Isolated noncompaction of the right ventricular myocardium in the adulthood? Int J Cardiol. 2009; 134(1): e17-19.
5. *Dodd JD, Holmvang G, Hoffmann U, Ferencik M, Abbara S, Brady TJ, Cury RC*. Quantification of left ventricular noncompaction and trabecular delayed hyperenhancement with cardiac MRI: correlation with clinical severity. AJR Am J Roentgenol. 2007; 189(4): 974-980.
6. *Elliott P, Andersson B, Arbustini E, Bilinska Z, Cecchi F., 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): 270-276.
7. *Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA 3rd, Freedman RA., et al.* ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices) developed in collab-

oration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. J Am Coll Cardiol. 2008; 51(21): e1-62.

8. *Fazio G, Lunetta M, Grassedonio E, Gullotti A, Ferro G, Bacarella D, Lo Re G, Novo G, Massimo M, Maresi E, Novo S.* Noncompaction of the right ventricle. Pediatr Cardiol. 2010; 31(4): 576-578.
9. *Gati S, Chandra N, Bennett RL, Reed M, Kervio G., et al*. Increased left ventricular trabeculation in highly trained athletes: do we need more stringent criteria for the diagnosis of left ventricular non-compaction in athletes? Heart. Mar, 2013; 99(6): 401-408.
10. *Gati S, Papadakis M, Papamichael ND, Zaidi A, Sheikh N., et al.* Reversible de novo left ventricular trabeculations in pregnant women: implications for the diagnosis of left ventricular noncompaction in low-risk populations. Circulation. 2014; 130(6): 475-83.
11. *Gati S, Papadakis M, Van Niekerk N, Reed M, Yeghen T, Sharma S*. Increased left ventricular trabeculation in individuals with sickle cell anaemia: physiology or pathology? Int J Cardiol. Sep, 2013; 168(2): 1658-1660.
12. *Ikeda U, Minamisawa M, Koyama J.* Isolated left ventricular non-compaction cardiomyopathy in adults. J Cardiol. 2015; 65(2): 91-97.
13. *Jacquier A, Thuny F, Jop B, Giorgi R, Cohen F., 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): 1098-1104.
14. *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): 666-671.
15. *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):158-164.
16. *Lofiego C, Biagini E, Pasquale F, Ferlito M, Rocchi G., et al.* Wide spectrum of presentation and variable outcomes of isolated left ventricular non-compaction. Heart. 2007; 93(1): 65-71.
17. *Maron BJ, Towbin JA, Thiene G, Antzelevitch C, Corrado 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): 1807-1816.
18. *Murphy RT, Thaman R, Blanes JG, Ward D, Sevdalis E., et al*. Natural history and familial characteristics of isolated left ventricular noncompaction. Eur Heart J. 2005; 26(2):187-192.
19. *Nucifora G, Aquaro GD, Pingitore A, Masci PG, Lombardi M*. Myocardial fibrosis in isolated left ventricular non-compaction and its relation to disease severity. Eur J Heart Fail. 2011; 13(2): 170-176.
20. *Oechslin E, Jenni R*. Left ventricular non-compaction revisited: a distinct phenotype with genetic heterogeneity? Eur Heart J. 2011; 32(12): 1446-1456.
21. *Petersen SE, Selvanayagam JB, Wiesmann F, Robson MD, Francis JM., et al*. Left ventricular non-compaction: insights from cardiovascular magnetic resonance imaging. J Am Coll Cardiol. 2005; 46(1): 101-105.
22. *Punn R, Silverman NH.* Cardiac segmental analysis in left ventricular noncompaction: experience in a pediatric population. J Am Soc Echocardiogr. 2010; 23(1): 46-53.
23. *Ranganathan A, Ganesan G, Sangareddi V, Pillai AP, Ramasamy A.* Isolated noncompaction of right ventricle--a case report. Echocardiography. 2012; 29(7): E169-172.
24. *Sandhu R, Finkelhor RS, Gunawardena DR, Bahler RC.* Prevalence and characteristics of left ventricular noncompaction in a community hospital cohort of patients with systolic dysfunction. Echocardiography. 2008; 25(1): 8-12.

25. *Sedmera D, Pexieder T, Vuillemin M, Thompson RP, Anderson RH*. Developmental patterning of the myocardium. Anat Rec. 2000; 258(4): 319-337.

26. *Sert A, Aypar E, Aslan E, Odabas D*. Isolated right ventricular noncompaction in a newborn. Pediatr Cardiol. 2013; 34(8): 1896-1898.

27. *Sidhu MS, Uthamalingam S, Ahmed W, Engel LC, Vorasettakarnkij Y., et al*. Defining left ventricular noncompaction using cardiac computed tomography. J Thorac Imaging. 2014; 29(1): 60-66.

28. *Spoladore R, Fisicaro A, Faccini A, Camici PG*. Coronary microvascular dysfunction in primary cardiomyopaties. Heart. 2014; 100(10): 806-813.

29. *Stanton C, Bruce C, Connolly H, Brady P, Syed I., et al.* Isolated left ventricular noncompaction syndrome. Am J Cardiol. 2009; 104(8): 1135-1138.

30. *Steffel J, Duru F.* Rhythm disorders in isolated left ventricular noncompaction. Ann Med. 2012; 44(2): 101-108.

31. *Stöllberger C, Blazek G, Dobias C, Hanafin A, Wegner C, Finsterer J.* Frequency of stroke and embolism in left ventricular hypertrabeculation/noncompaction. Am J Cardiol. 2011; 108(7): 1021-1023.

32. *Stöllberger C, Finsterer J, Blazek G.* Left ventricular hypertrabeculation/noncompaction and association with additional cardiac abnormalities and neuromuscular disorders. Am J Cardiol. 2002; 90(8): 899-902.

33. *Tigen K, Karaahmet T, Gurel E, Cevik C, Basaran Y*. Biventricular noncompaction: a case report. Echocardiography. 2008; 25(9): 993-996.

34. *Towbin JA, Lorts A, Jefferies JL.* Left ventricular non-compaction cardiomyopathy. Lancet. 2015; 386(9995): 813-825.