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Review Article (Pages: 11719-11725)

Right Ventricular Non-Compaction Cardiomyopathy in Children: Brief Review Literature

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Abstract

Right ventricular non-compaction cardiomyopathy (RVNC) is a genetic heterogeneous cardiomyopathy. Despite the increasing number of RVNC cases, the classification and natural history of this disorder are not completely clear. Also, because the pathogenic non-compaction cannot be easily differentiated from normal trabeculations, it is usually hard to accurately measure the prevalence of RV involvement. In this review, we searched main databases including Medline, Web of Science, EMBASE, and Scopus. In addition, the Google Scholar was searched until December 2019. Owing to the disagreements over RVNC classification and lack of diagnostic tests, there is no reliable and accurate statistical data about the prevalence of RVNC in newborn and children populations. Hypothetically, it is propounded that the disorder is being over-diagnosed as the number of RVNC cases reported during recent years has significantly increased.

Key Words: Children, Heart Ventricular, Right Ventricular Hypertrabeculation/Noncompact.

*Please cite this article as: Ghandi Y, Mehrabi S. Right Ventricular Non-Compaction Cardiomyopathy in Children: Brief Review Literature. Int J Pediatr 2020; 8(7): 11719-725. DOI: **10.22038/ijp.2020.45397.3725**

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Received date: Mar.21, 2020; Accepted date: Jun.12, 2020

1- INTRODUCTION

Despite advances in left ventricular non-complication (LVNC), to date, there is not a complete review article in Right ventricular non-compaction cardiomyopathy (RVNC). The RVNC is an uncommon cardiomyopathy that may cause symptoms of variable severity, clinical manifestation, and complications. To prevent adverse outcomes, it is vital to appropriately recognize and manage this RVNC cardiomyopathy. Our study aimed to evaluate definition, incidence, risk factors, and clinical manifestations, heart failure, life-threatening arrhythmias, and embolic events, diagnosis, management, electrocardiography, echocardiographic factors and therapeutic options in RVNC patients.

Definition

At present, there is some agreement about what constitutes LVNC and the echocardiographic criteria have been provided for the diagnosis, while there are not any certain echocardiographic criteria for RVNC (1). There are particular criteria for the LVNC diagnosis. For instance, Jenni et al. (2001), defined the diagnostic criteria which comprised 2 layers of myocardium including a compacted layer (C), and a thicker non-compacted (NC) one with endomyocardial recesses: the ratio of NC/C > 2 measured at end-systole (1). LVNC was also described by Chin et al. (2) as a ratio of C/ (NC + C) <0.5 at end-diastole. Moreover, this disorder is defined by Stöllberger and Finsterer as four or more trabeculations on the LV wall, located apically to the papillary muscles (3). However, there is not an accurate definition for RVNC; some authors have proposed applying the LVNC criteria for the definition of RVNC (4). In a study from Burke et al., a histological scale was considered for the diagnosis of RVNC which defined the disorder as the transmural thickness of the non-compacted RV more than 75 % (5). It is also suggested that RVNC might be related to the RV dilation (6). In this regard, Yun et al. examined three patients with dilated RV and only one of them had a normal-volume RV. Based on their study, dilation of the RV could help to diagnose RVNC (7).

2- MATERIALS AND METHODS

All main databases including Medline (via PubMed), Web of Science, EMBASE, and Scopus were searched until December 2019. Then, the Google Scholar was searched by two authors (YG and SM). Following keywords were searched single and combined "Right Ventricular Non-compaction Cardiomyopathy OR RVNC" AND "Children OR Child". Results of search were entered to EndNote software and duplicate references were removed. The studies were selected according to inclusion criteria and based on PICOS (Population: children with heart disease, Intervention: any heart evaluation, Comparison: heart function, Outcome: RVNC, and Study: any type of study). Finally, two authors (YG and SM) reviewed title and abstract of 1,156 articles independently and the most relevant articles were selected. In addition, two authors conducted extraction of data independently. Disagreement was solved by discussion.

3- RESULTS

3-1. Right Ventricular Myocardial Development/Trabeculation

Non-compaction cardiomyopathy is a rare genetic disorder. It is morphologically specified by deep trabeculations and intertrabecular recesses which make the appearance of myocardium "spongiform" (8, 9). Non-compaction cardiomyopathy usually occurs due to the morphogenesis of endomycardium, which results in the failure of trabecular compaction during myocardial development (10). According

to the recent scientific data, any disturbance that affects normal myocardial compaction during gestation week's five to eight would cause non-compaction (11). The pathogenesis of hypertrabeculation/non-compaction (HT/NC) is still unclear; however, it is proposed that hypertrabeculation would be a compensatory mechanism to increase the surface of the endocardium and cardiac output in chambers with reduced contractility or chambers with volume overload (12). Another suggested mechanism for hypertrabeculation is the myocardium transformation to a meshform of trabeculae which is the result of gap junction's malfunction and decreased adhesion of cardiac myocytes. Similar mechanisms can be found in the spongy icefish cardiovascular system; pseudohypertrophy of myocardium for example, and the ability of pumping larger stroke volumes in low-pressure conditions.

3-2. Genetic Causes and Chromosomal Conditions Associated with RVNC

Congenital ventricular non-compaction is very rare and the prevalence of this disorder is 0.01% in adults and 0.14% in children that varies between 0.06% and 0.24% in the general population. Although the hereditary pattern of non-compaction cardiomyopathies has been considered as a male predominance, it has not yet been confirmed in recent studies. The right ventricle is usually involved and the septum can be affected as well. Prashanth Panduranga and Rajarao (2018), described a young patient with typical and clinical phenotypes of Williams's syndrome and the evidence of right ventricular non-compaction. This report proposed a question of whether Williams syndrome and ventricular non-compaction are genetically linked together, which needs further confirmatory studies (12). Owing to the complete AV block in this patient and his death after the surgery, it may indicate that isolated right ventricular HT/NC is arrhythmogenic and consequently, immediate interventions, the implantation of Implantable Cardioverter-Defibrillator (ICDs) are needed to prevent arrhythmias and Sudden Cardiac Death (SCD) (12).

3-3. Clinical Presentation

While it is rare that HT/NC involves just the RV and there are limited case reports in this regard, there are a variety of presentations for myocardial HT/NC from no symptoms to cardiac failure, systemic thromboembolism, dysrhythmias, and SCD. Non-compaction cardiomyopathy would be clinically presented with cardiac failure, stroke, and arrhythmia in pediatrics; however, it can be an incidental finding in the patients with no symptoms (8).

3-4. Prenatal Diagnosis

The diagnosis of IVNC during the prenatal period is difficult but possible. It may cause different complications and ultimately, neonatal death. It is better to consider IVNC for the fetuses with increased first-trimester nuchal translucency. Moreover, familial occurrence should be considered if ventricular NC is diagnosed during this period. Both echocardiography and color Doppler sonography help to diagnose Isolated Ventricular Non Compaction (IVNC) during the prenatal period as they can show the flow from the ventricles to the intertrabecular recesses (13). In a study by Tian et al. (2015), an abnormal dilated RV and an increase in the ventricle's wall without obstruction were detected. Besides, deep recesses and trabeculations were observed in the apex, base of the free wall, and the center of the inter-ventricular septum. Color Doppler ultrasonography is an effective way to observe the flow between the recesses and diagnose RVNC (14).

3-5. Non-cardiac Manifestations of RVNC

Zhi-Qiang et al (2015), reported a patient with cerebral infarction and right ventricular HT/NC (15). However, the neurovascular complications, especially cerebral infarction in RVHT have not been discovered completely, possible clinical neurovascular presentations in Right Ventricular Hypertension (RVHT) have to be noted. The mechanisms of these complications in RVHT would be associated with thrombi in the intertrabecular space. There are particular reasons for the formation of thrombi such as trabeculae ventricle, depressed systolic function, and atrial fibrillation. Therefore, it seems that prophylactic anticoagulation would be helpful in RVHT and systolic dysfunction, particularly for the prevention of pulmonary emboli.

3-6. Electrocardiogram Findings

Both atrial and ventricular arrhythmias are prevalent in IVNC. Subendocardial ischemia might ultimately lead to arrhythmias as it can cause localized necrosis and endocardial fibroelastosis. In a study by Ying et al., it was assumed that implantation of a biventricular pacemaker could help to decrease the risk of SCD and other complications in a patient with IRVNC. The patient had a regular junctional rhythm with absent P wave and his 24-Holter monitoring follow-up showed atrial standstill (15). Aggarwal et al. (2016), also reported a case of IRVNC whose electrocardiogram showed ST elevation in the Right Pericardial Leads (V1-V3) (16). Several mechanisms have been proposed for ventricular arrhythmias because of HT/NC; micro and macro re-entry for instance, which usually occur due to localized necrosis and fibrosis caused by sub-endocardial ischemia and microcirculatory dysfunction. Another mechanism is the presence of an abnormality in the conducting fiber of Purkinje. It seems that mortality and major complications are more significant in case of either sustained or non-sustained ventricular tachycardia (17, 18). Bekheit et al. (2018), reported ventricular tachyarrhythmia and SCD in 3 patients with IRVNC. It suggests that RVNC would be arrhythmogenic, and has a high mortality rate (17).

3-7. Echocardiographic Assessment of RVNC

RVNC is very rare, and since the RV apex is intensely trabeculated, it is not easy to differentiate normal patterns from pathologic ones. Echocardiography is the first-line diagnostic tool for RVNC, but other imaging techniques such as cardiac magnetic resonance imaging (MRI) would be useful as they helps to confirm the diagnosis and find potential complications. The presence of trabecular meshwork in particular areas and the dilation of the RV are also related to the diagnosis of RVNC (6).

3-8. CT and Cardiac Magnetic Resonance Imaging in RVNC

Cardiac MRI is a noninvasive alternative to assess patients with isolated non-compaction ventricular myopathy (INVM). It is less operator-dependent compared with traditional methods such as echocardiography. Meanwhile, the contrast between myocardium and blood is higher in cardiac MRI and consequently, the abnormal trabeculations can be easily found (18). Contrast-enhanced CT can show INVM and evaluate the arteries to recognize anomalies or stenosis, while cardiac MRI and echocardiography are not able to do this evaluation (7, 19). Prominent trabeculations, deep intertrabecular recesses and an increase in the non-compacted/compacted myocardium layers (NC/C ratio) in diastole are some of the changes that would be characteristic for IVNM in cardiac MRI (7). Owing to the lack of

certain diagnostic criteria for RVNC and since different degrees of RV trabeculations can be normally observed in the heart, the true diagnosis of RVNC may be difficult. When trabeculations increase in the RV and deep recesses can be seen through the RV wall, the RV is probably involved (5, 19).

3-9. RVNC and Congenital Heart Disease

Myocardial non-compaction is an embryonic endomyocardial morphogenesis disorder that is frequently associated with congenital cardiac abnormalities. It mostly affects the ventricles and may occur isolated in the RV or be associated with LV involvement. Today, myocardial HT/RVNC is being diagnosed more and more due to the awareness on this disorder and the more useful diagnostic tools such as echocardiography and cardiac MRI. Myocardial HT/NC is sometimes associated with other congenital diseases, namely neuro-muscular disorders, Ebstein anomaly, Barth syndrome, and tetralogy of Fallot. Isolated right ventricular non-compaction is, however, very rare in newborn (20).

Different congenital cardiac malformations including atrial and ventricular septal defects, aortic stenosis, and aortic coarctation can be responsible for non-compaction cardiomyopathy. However, these malformations are not commonly present in the isolated form of RVNC (8, 21, 22). RVNC is usually seen in association with the left ventricle involvement rather than the isolated form. Gardner et al. (2017), reported three neonates with RVNC associated with hypoplastic left heart syndrome (HLHS) who underwent a Norwood operation. One of them experienced pseudoaneurysm after pericardiocentesis that could be related to the RVNC. The second patient had to be treated with digoxin due to the elevated serum brain natriuretic peptide after the operation; and the third patient, with nearly normal RV function, required medical management for pericardial effusion. It seems that RVNC with HLHC could have serious complications after the operation (23).

3-10. RVNC and Pulmonary Embolic Events

Even though IRVNC is uncommon in clinics, it is better to consider this disorder in the patients with PE, especially those without notable risk factors or with normal results in lower extremity deep venous system examination (24). Since IRVNC-induced right ventricular thrombosis can lead to chronic recurrent PE or even life-threatening large PE, the possibility of IRVNC in the patients with PE should always be considered.

3-11. Medical Management

Unfortunately, not many studies have been performed on medical therapy in patients with RVNC. It seems that, instead of the main disorder, its clinical manifestations and complications, such as heart failure and arrhythmia, are usually treated. Since the right tuberculation cannot be corrected after birth, it is required to diagnose the disorder during the prenatal period and treat the condition if it is possible.

3-12. Prognosis

Since there are not enough follow up studies on patients with IRVNC, there are no specific prognostic criteria for this disorder. Nevertheless, heart failure, arrhythmia, and coexisting cardiovascular malformations and extracardiac complications can increase morbidity, mortality, and even death in these patients. In this regard, Bekheit et al. proposed that IRVNC would be significantly arrhythmogenic and linked to the higher mortality rate as this disorder was found on the echocardiography of 3 patients with ventricular tachyarrhythmia and sudden cardiac death (17).

4- CONCLUSION

Recently, more findings about etiology, genetics, diagnosis, complications, and outcome of right ventricular non-compaction have been discovered. It is important to consider other presentations such as right heart failure, RV originated arrhythmia, pulmonary embolic event, and coexisting cardiovascular malformations for this type of cardiomyopathy. Although no accurate diagnostic criteria have been proposed for RVNC, it seems that echocardiography and cardiac MRI are significantly helpful in its diagnosis. Understanding of the process in this disorder is limited and needs further investigation, with focus on the treatment and prognosis to follow up these patients efficiently.

5- CONFLICT OF INTEREST: None.

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