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Case Report

Study on the distribution characteristics of affected myocardium in non-compaction of left ventricular myocardium

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Abstract: Objectives: This study aims to investigate the distribution characteristics of the diseased area in non-compaction of left ventricular myocardium. Methods: In combination with the standardized myocardial segmentation of the American Heart Association, color Doppler ultrasound was used to analyze the occurrence of lesions in each segment of left ventricular walls in 21 patients with non-compaction of left ventricular myocardium. Results: The distribution characteristics in the lesions area in non-compaction of left ventricular myocardium were as follows: lesion rate in the apical tip was the highest (100%), followed by the lower and side walls of the apical segment, and the mid-cavity segments. Conclusions: Standardized myocardial segmentation is of great significance for the diagnosis of noncompaction of ventricular myocardium (NVM). Apical tip involvement is one of the sensitive and important bases of the ultrasonic diagnosis of this disease.

Keywords: Myocardial diseases, noncompaction of ventricular myocardium, standardized myocardial segmentation, ultrasonic cardiogram, apex segment

Introduction

Noncompaction of ventricular myocardium (NVM) is a congenital cardiomyopathy that was first reported by Chin *et al.* in 1990 [1]. In 1995, the working group of the World Health Organization and the International Society and Federation of Cardiology (WHO/ISFC) classified this disease as an "unclassified cardiomyopathy". In the past, this disease was considered rare. With the gradual increase of the understanding of this disease and the continuous development of echocardiography equipment and technology, the number of reports on this disease has continuously increased [2]. In 2006, the American Heart Association (AHA) formally assigned this condition to the independent type of primary cardiomyopathy [3]. Due to lack of specific symptoms and signs in NVM patients, NVM is often easily misdiagnosed as dilated cardiomyopathy (DCM), coronary heart disease (CHD), or rheumatic heart disease (RHD) in clinical practice. Ultrasound cardiograms and clinical data of NVM patients, who were diagnosed in recent years, were reviewed. Furthermore, the distribution characteristics of the diseased area were analyzed by applying standard myocardial segmentation, which is the latest recommendation of AHA [4], to improve the diagnosis of this disease.

Materials and methods

Subjects

Data of 21 NVM patients diagnosed in our hospital from August 2000 to 2015 were included into this study. Among these patients, 15 patients were male and six patients were female; and age of these patients ranged within 2-73 years old. Furthermore, among these patients, 11 patients went to see a doctor due to heart palpitations and chest tightness, nine patients went to see a doctor due to murmurs in cardiac auscultation, and one patient went to see a doctor due to a sudden syncope. Among

the 21 patients who mostly failed to obtain a clear diagnosis before admission, only three patients were transferred to our hospital due to the reason of "suspected NVM". The total rate of missed diagnosis and misdiagnosis in the initial diagnosis was 85.7%. Among these patients, nine patients were misdiagnosed as DCM?, two patients were misdiagnosed as RHD?, six patients were misdiagnosed as ischemic cardiomyopathy, and one patient was misdiagnosed as simple congenital ventricular septal defect. All patients had precordial murmurs, in which 16 patients were level II/6-III/6 and five cases were level IV/6. Based on the New York Heart Association (NYHA) classification for cardiac function, 12 patients were grades I-II, and nine patients were grades III-IV. All patients underwent echocardiography and electrocardiogram examination after being admitted to the hospital, in which 19 patients underwent heart X-ray examinations and eight patients underwent cardiac catheterization with coronary angiography examination.

Methods

A Philips IE33 and a Philips Sonos 5500 color Doppler ultrasound machine were used with a transthoracic cardiac probe. Patients laid in the 45° left-side-up decubitusposition or the supine position. Conventional echocardiography was used to observe two-dimensional morphologies in patients such as ventricular wall thickness, shape, the non-compact area and ventricular wall motion, and hemodynamic changes such as heart valve ejection and backflow, as well as blood flow fullness in ventricular cavity. Diseased ventricular cavity size, ejection fraction, and valvular reflux area were measured; and the thickness ratio of the non-compact ventricular myocardium to compact ventricular myocardium in the end systolic phase was calculated. Pulmonary artery systolic pressure was estimated *via* the tricuspid regurgitation approach.

Criteria for myocardial segmentation and ultrasound diagnosis

The distribution of the myocardial involvement site was analyzed by the 17-segment model of the standardized myocardial segmentation of the AHA in 2002. Ultrasonic diagnosis was based on the latest revision of the standard proposed by Jenni [5], as follows. (1) The lesion area of the ventricular wall was a double-layer structure, the thinner outer layer comprised of a compact myocardium, and the thicker inner layer comprised of a non-compact myocardium. Deep recesses could be found in the middle of the non-compact myocardium. (2) The ratio of the thickness of the non-compact myocardium to the thickness of the compact myocardium in the end systolic phase was > 2.0. (3) Color Doppler ultrasound revealed the existence of blood flow connecting the deep recesses and ventricular cavity.

Results

Electrocardiogram, cardiac X-ray film and imaging examination

All patients had abnormal electrocardiogram results, in which there were eight cases of atrial fibrillation, two cases of atrial flutter, one case of paroxysmal ventricular tachycardia, one case of complete left bundle branch block, two cases of incomplete left bundle branch block, one case of first-degree atrioventricular block, one case of type-I second-degree atrioventricular block, and two cases of type-A pre-excitation syndrome. In the electrocardiograms of 20 cases, left ventricular hypertrophy and left deviation of the electrical axis were found; and heart X-ray examination exhibited an increased cardiac shadow. Electrocardiograms of five patients exhibited T-wave inversion and ST segment depression, while electrocardiograms of three patients revealed an abnormal Q wave. After cardiac catheterization with coronary angiography screening, myocardial ischemic change was excluded in these eight patients.

Echocardiography examination

In all 21 patients, 17 patients were detected with isolated NVM by transthoracic echocardiography. Both left and right ventricular involvements were found in three patients, while non-compaction of left ventricular myocardium with a ventricular septal defect near the apex was found in one patient. Echocardiography changes in patients appeared as follows. (1) Ventricular cavity enlargement: all 21 patients exhibited left ventricular enlargement, with an average size of 59 ± 10 mm; and the one patient with right ventricular involvement developed right ventricular enlargement in the apical site, with a size of approximately 32 mm. (2)

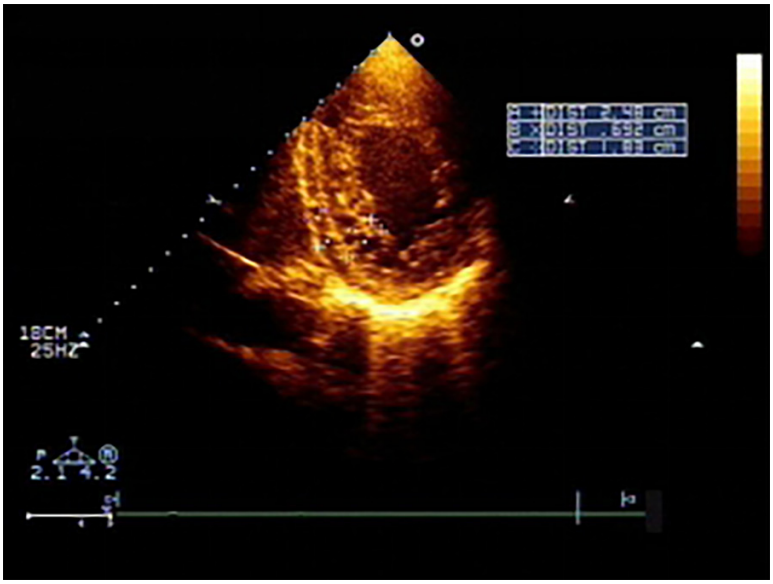

Figure 1. The ratio of the thickness of the non-compact. myocardium to the thickness of the compact myocardium in the end systolic phase is > 2.0.

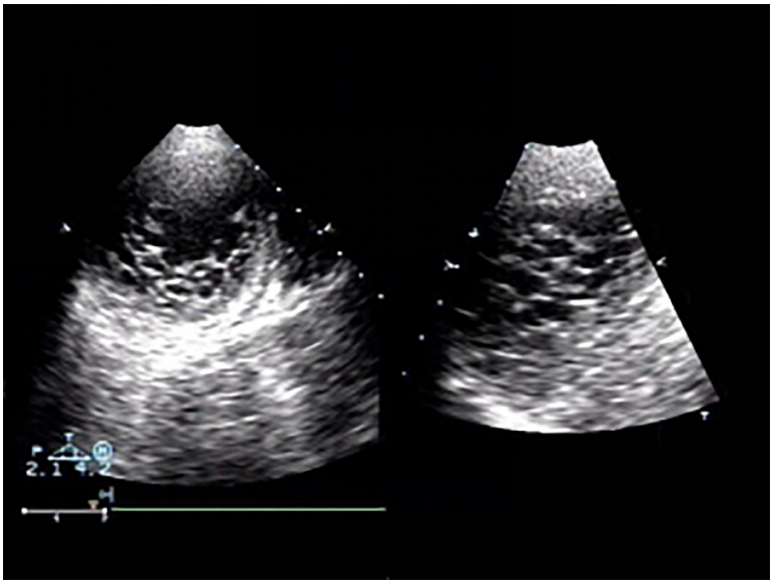

Figure 2. Non-compact myocardia in the inner layer of the ventricular wall of the lesion area present a large number of strong echoes of interlaced strip-shaped or fence-shaped trabeculae, and non-compact trabeculae in the top apex segment present a net-like shape.

The ventricular wall of the affected segments thickened and exhibited a double-layer structure. The non-compact myocardium in the inner layer was thicker, while the compact myocardium in the outer layer was thinner. The ratio of the thickness of the non-compact myocardium to the thickness of the compact myocardium in the end systolic phase was > 2.0 (approximately 4.2 ± 0.9), as shown in **Figure 1**. (3) The ratio of compact myocardium thickness in the lesion area to the left ventricular anterior wall thickness in the basal segment decreased, with an average of 0.37 ± 0.16. (4) Non-compact myocardia present a large number of echoes of interlaced strip-shaped or fence-shaped trabeculae, and the free-end had no chordae tendineae and was connected to the papillary muscle. In the trabeculae, miliary or narrow anechoic recesses were found, which were connected to the ventricular cavity. The cross-section of non-compact myocardium in the apical tip exhibited grid changes, as shown in **Figure 2**. (5) Color Doppler demonstrated that the blood flow in the left ventricular cavity run in and out of the recesses, along with the cardiac cycle. Blood flow in the recesses was dark. The trabecular area exhibited a blood filling defect, as shown in **Figure 3**. (6) The motion curve of affected ventricular walls in M type echocardiogram was composed of multiple parallel lines, and the motion amplitude and ventricular systolic thickening rate decreased. (7) Ejection fraction of affected ventricles reduced: left ventricular ejection fraction was approximately 35 ± 9%, in 21 affected left ventricles and 31% in one affected right ventricle. (8) Heart valvular regurgitation: 18 patients had bicuspid valve regurgitation, and the area was approximately 6.7 ± 2.1 cm^2; nine patients had aortic valve regurgitation, and the area was approximately 5.8 ± 1.7 cm^2; 11 patients had tricuspid regurgitation, and the area was approximately 4.9 ± 2.3 cm^2; 15 patients had pulmonary valve regurgitation, and the area was approximately 3.1 ± 1.0 cm^2.

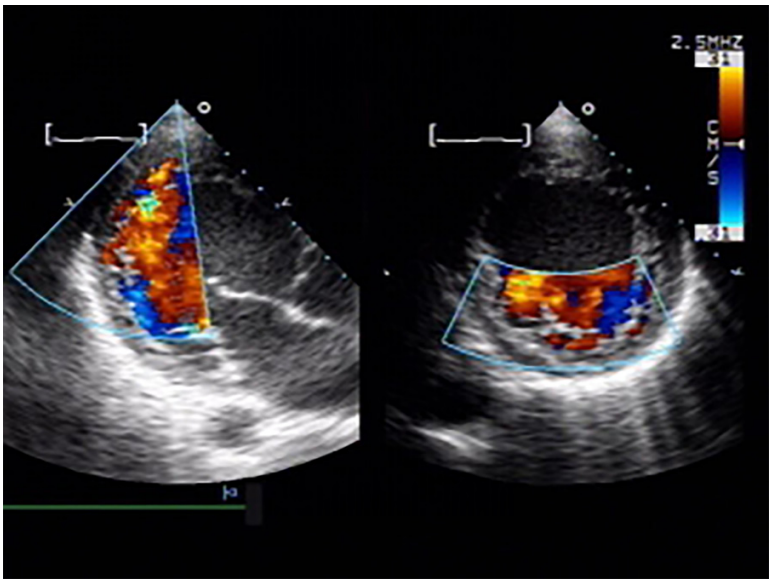

Figure 3. Recesses in the non-compact trabeculae exhibit blood flow connecting with the ventricular cavity.

Table 1. Affected situations of left ventricular segments in 21 patients

Segments of left ventricular myocardium		Affected cases	Rate (%)
The apical tip	-	21	100
The apical segment	Inferior wall	18	85.7
	Side wall	16	76.2
	Interventricular septum	9	42.9
	Anterior wall	8	38.1
The mid-cavity segments	Inferior wall	16	76.2
	Inferolateral wall	10	47.6
	Anterolateral wall	1	4.7
	Inferior septum	3	14.3
	Anterior septum	0	0
	Anterior wall	0	0
Basal segment	Inferior wall	2	9.5
	Inferolateral wall	1	4.7
	Anterolateral wall	0	0
	Inferior septum	0	0
	Anterior septum	0	0
	Anterior wall	0	0

(9) Pulmonary hypertension: Pulmonary artery systolic pressure was estimated *via* the tricuspid regurgitation approach. Results revealed that five of 21 patients developed increased pulmonary artery systolic pressure, with an average of approximately 49 ± 13 mmHg.

According to the 17-segment model of the standardized myocardial segmentation proposed by AHA, distribution characteristics of the diseased left ventricular segments in patients with non-compaction of left ventricular myocardium were as follows: the lesion rate in the apical tip was the highest (100%), followed by the lower and side walls of the apical segment, and the mid-cavity segments. Left ventricular walls of the basal anterior segment in all patients were not affected, as shown in **Table 1**.

Discussion

NVM is caused by intrauterine arrest of the myocardial compaction process in the beginning of fetal development. Under this condition, the trabeculae grows exceedingly bulky, trabecular recesses continue to exist, leads to a decrease in compact myocardium in the corresponding region, and the muscular layer of the ventricular walls maintain a loose state [6]. This disease gives priority to invasion to the left ventricular myocardium, and invasion to the right ventricle may also occur [7]. It may be distributed, and can manifest as the autosomal dominant inheritance or familial incidence of X chromosome-related diseases. The relationship of its pathogenesis to the mutations of G4.5, α-dystrobrevin and FK binding protein 12 remains controversial, which is associated with human muscular dystrophy [8, 9]. Although AHA defined NVM as an independent cardiomyopathy, some studies have considered this disease as a different manifestation of hypertrophic cardiomyopathy, based on the same cardiomyopathy spectrum; in which NVM has the same pathogenetic factors with its constant combined diseases such as coronary artery fistula, bicuspid aortic valve abnormalities and ventricular septal defect, patent ductus arteriosus, and other congenital heart defects [10, 11]. Some studies have reported that this disease has a certain association with bronchiectasis, polycystic kidney, and congeni-

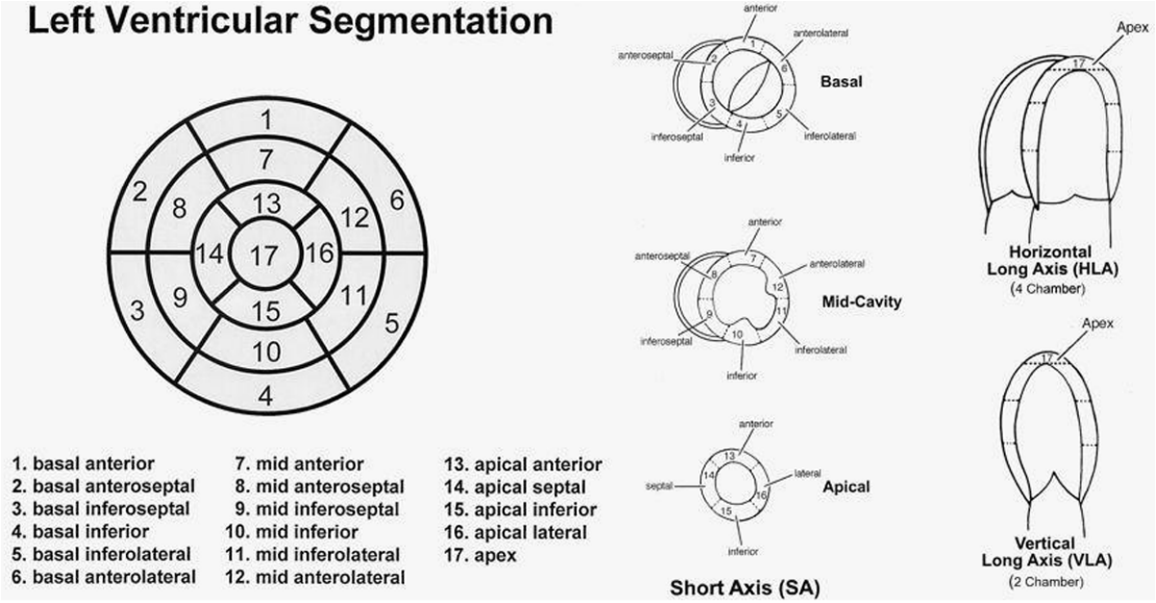

Figure 4. The 17-segment model of standardized myocardial segmentation proposed by the American Heart Association.

tal dwarf-dementia syndrome (also called Noonan syndrome). Hence, it has been considered that NVM may only be a manifestation of several different diseases [12-15].

The incidence of this disease is higher in male patients than in female patients. Furthermore, both infant and young children, as well as adults, can develop this disease. Its clinical symptoms are atypical, which include three types of clinical manifestations: arrhythmia, cardiac insufficiency and cardioembolism. Early stage patients exhibit no obvious symptoms, develop chronic heart failure along with its progression, and finally die due to heart failure or fatal arrhythmia. In recent years, the incidence of asymptomatic NVM in the crowd of young people continues to increase. This is combined with the high incidence of fatal arrhythmia, heart failure and thrombotic events. Furthermore, the accurate diagnosis and treatment scheme of this disease have also gained more clinical attention [16-18]. Due to its nonspecific clinical characteristics and laboratory examination results, as well as insufficiencies in imaging observations on the left ventricular apex, it appears to be far more severe than that reported in literature; that is, this disease is misdiagnosed as DCM [19]. Imaging findings can accurately reflect characteristic morphological changes in diseased myocardia, which has become the important diagnostic basis of NVM [20]; while echocardiography has been considered to be the preferred method for confirming NVM [21].

The previously existing 16-segment model of myocardial segmentation ignores the left ventricular apical myocardium beneath the end of the cavity, leading to inadequate observations on the apical myocardial structure by echocardiography. Furthermore, it is not convenient to compare its results with results obtained from myocardial radionuclide imaging, cardiac MRI and myocardial contrast techniques. Compared with the previous 16-segment model of myocardial segmentation, the 17-segment model of myocardial segmentation established by the heart segmentation and image registration writing group of the AHA is more suitable for its comparative study with different myocardial imaging. This segmentation first divides the apical myocardium at the apical cap without the cardiac cavity in left ventricular end as an independent segment, and defines it as the apex segment, as shown in **Figure 4**. Since the order of myocardial compaction is from the right ventricle to the left ventricle, from epicardium to endocardium, and from the base to the apex, the affected sites of non-compaction of myocardium are mostly located at the left ventricle and is closer to the apex, when lesions

are more severe [22]. Therefore, the apex segment should be the most vulnerable site to NVM, with the most significant pathological changes. In this study, all 21 patients had affected ventricular walls in the apex segment, prompting that the involvement of this segment is the most sensitive and important diagnostic basis for this disease by ultrasonic diagnosis. In addition, since the left ventricular wall of the basal anterior segment is less affected, it can be used as an evaluation reference of the lesion degree of the affected segment. The ratio of the compact myocardium thickness in the lesion area to the left ventricular wall thickness in the basal segment can reflect the extent of decrease of the compact myocardium. In addition to the ratio of non-compact myocardial thickness to compact myocardial thickness in the lesion area, these parameters have a certain reference value in the quantitative diagnosis of NVM.

Combined with literature, the author summarizes the main points of echocardiography in the diagnosis of NVM as follows. (1) Ventricular walls in the diseased area present a double-layer structure; in which the outer layer is thin and compact, the inner layer is thick but loose, and deep recesses could be found in the non-compact myocardium. Color Doppler ultrasound revealed that there was blood flow connecting the deep recesses and ventricular cavity. (2) The myocardia in top apex segment all present non-compact changes; and its pathological changes are the most significant, followed by the lower and side walls of the apical segment, and the mid-cavity segments. (3) The ratio of the thickness of the non-compact myocardium to the thickness of the compact myocardium in the end systolic phase was > 2.0. The ratio of compact myocardium thickness in the diseased area to the left ventricular wall thickness in the basal anterior segment decreases. (4) The affected ventricular cavity enlarges, or presents a segmental local expansion. (5) Motion intensity of the ventricular wall in the lesion area decreases [23].

In conclusion, we believe that NVM has characteristic sonographic findings, and the distribution characteristic of the affected myocardia is clear. The involvement of the top apex segment is one of the necessary conditions for the diagnosis of this disease.

Disclosure of conflict of interest

None.

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