

Noncompaction of Ventricular Myocardium: A Study of Twelve Patients

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We report 12 patients with ventricular noncompaction who were echocardiographically identified at our institution since 1991.

The mean age at presentation was 3.5 years. Five patients had isolated noncompaction. Three of them had subnormal left ventricular systolic function at presentation. Noncompaction was associated with complex congenital heart defect in 3 patients. Four patients had simple congenital heart defects: pulmonary stenosis, coarctation of aorta with aberrant origin of right subclavian artery, ventricular septal defect, and partial anomalous pulmonary venous

return. The observed rhythm abnormalities were Wolff-Parkinson-White syndrome and paroxysmal supraventricular tachycardia, bigemini ventricular extrasystoles, and left bundle branch block. A transvenous pacemaker was implanted in a patient because of complete heart block.

Noncompaction of the ventricular myocardium is rare. Our patients clearly represent the clinical and morphological spectrum of this disorder. Distinct morphological features can be diagnosed on 2-dimensional echocardiography. (J Am Soc Echocardiogr 2002;15:1523-8.)

Noncompaction of the ventricular myocardium is a recently described anomaly. It is a result of an arrest in myocardial morphogenesis and is characterized by prominent and excessive trabeculations in a ventricular wall segment, with deep intertrabecular spaces perfused from the ventricular cavity.¹ It has been described in association with other congenital heart defects such as severe obstruction of right or left ventricular outflow tracts and anomalous origin of the left coronary artery from the pulmonary trunk.² It can also exist as an isolated lesion.²⁻⁵ We describe the entity of ventricular noncompaction and present a series of patients in a childhood population with this rare disorder.

MATERIALS AND METHODS

The study comprises 12 patients (11 male/1 female) referred to the Hacettepe University Pediatric Cardiology Department since 1991. The mean age at diagnosis was 3.5 years (range: 1 day-11 years). The data includes personal and family history; physical examination; 12-lead electrocardiogram (ECG); chest radiograph; and M-mode, 2-dimensional, and Doppler echocardiographic examinations. The echocardiograms were recorded with Sono-

layer SSH 160 A (Toshiba, Tokyo, Japan) and Vingmed 2000, System 5 Performance (General Electric, Oslo, Norway) by the same echocardiographer. This echocardiographer performed a total of 20,341 echocardiograms since 1991 for various indications. A diagnosis of noncompaction of ventricular myocardium was on the basis of the presence of numerous, excessively prominent trabeculations associated with deep intertrabecular spaces. To quantify the extension of trabecular meshwork, the thickness of ventricular wall and X-to-Y ratios were measured as reported by Chin et al,⁵ where X represents total free-wall thickness to the peak of trabeculation and Y represents the distance between epicardial surface and trough of the recess. The ratio of noncompacted zone to compacted zone being ≥ 2 was considered diagnostic (Figure 1). Table also gives the X/Y ratios of individual patients. Coexisting cardiac anomalies were also recorded. The left ventricular end diastolic diameter, ejection fraction (EF) and fractional shortening (FS) were measured by M-mode echocardiography. The measurements were done in parasternal long-axis view, just beneath the mitral valve and at the level of papillary muscle. The inner wall of the left ventricle was traced as the trough of the recess in systole and diastole.

RESULTS

Clinical Information

Since 1991, 12 cases of left ventricular noncompaction were identified in our institution (Table).

Isolated left ventricular myocardial noncompaction. Five patients had isolated noncompaction of the left ventricular myocardium (patients 4, 5, 6, 8,

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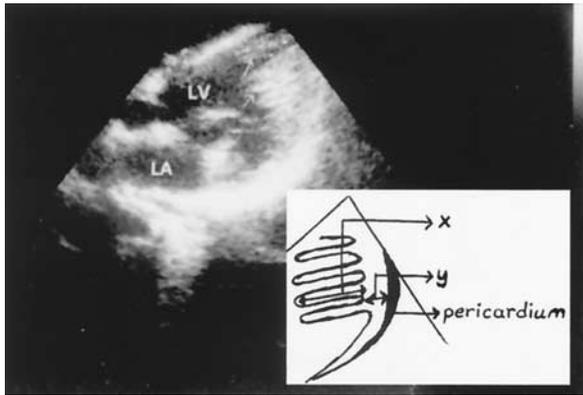


Figure 1 Two-dimensional echocardiographic representation of noncompacted ventricle. Apical 2-chamber view shows prominent and excessive trabeculations in left ventricle (LV) wall from patient 3. *Schematic drawing* demonstrates the measurement of total free-wall thickness to peak of trabeculation (X) and distance between epicardial surface and trough of recess (Y). LA, left atrium.

and 11). Patient 6 had chronic renal failure. He was normotensive and had normal left ventricular systolic function. Patient 4 was referred to our center because of hypertrophic cardiomyopathy. Patients 8 and 11 were referred because of dilated cardiomyopathy and were on anticongestive therapy. These patients had subnormal left ventricular systolic function. Patient 11 also had complete atrioventricular block at presentation. Patient 5 presented with syncope and normal left ventricular systolic function. He had ventricular extrasystoles and was thoroughly investigated for arrhythmia. The clinical information about patients 4, 5, and 11 are also given in the "Rhythm Abnormalities" section.

Rhythm abnormalities. Patient 4 (Figure 2) had Wolff-Parkinson-White (WPW) syndrome and paroxysmal supraventricular tachycardia. He had depressed left ventricular function (EF, 56.1%; FS, 28.3%). This patient had hypertrophic cardiomyopathy misdiagnosed at another institution. He is treated with sotalol hydrochloride to prevent recurrent supraventricular tachycardia and had been symptom free for the last 2 years.

Patient 5 (Figure 3) presented with recurrent syncope related to exercise. The ECG revealed uniform bigemini ventricular extrasystoles, and the corrected QT interval was 423 milliseconds. On echocardiography he had noncompaction of the left ventricle with normal systolic function. The neurologic examination, including electroencephalogram, 24-hour ambulatory ECG, and exercise test with modified Bruce protocol, produced normal findings. Ventricular tachycardia was not induced with a programmed ventricular stimulation during the electrophysiologic study. After 2 years of follow-up, no ventricular tachycardia attacks were observed, but the patient had weaker left ventricular systolic func-

tion (EF, 54%; FS, 26%). This patient is now under anticongestive therapy.

Patient 8 had left bundle branch block (LBBB) on the surface ECG, and depressed left ventricular systolic function (EF, 52.6%; FS, 20.8%) on echocardiogram. Holter recordings did not reveal any sign of atrioventricular block or other dysrhythmia.

A transvenous pacemaker was implanted in patient 11 because of complete atrioventricular block. Significant improvement in left ventricular systolic function was not observed after the pacemaker implantation and this patient is still receiving anticongestive therapy.

Other cardiac anomalies. Patient 1 has complex congenital heart disease consistent with dextrocardia, heterotaxy syndrome, and ventricular inversion. Initially the morphological left ventricle was interpreted as the right ventricle because of the prominent trabeculations associated with the noncompaction. He also had isolated multifocal premature ventricular beats, but ventricular tachycardia was not observed in Holter records.

The complex cardiac anatomy of patient 9 was diagnosed prenatally in the thirty-second week of gestation. The fetus had left atrial isomerism, hypoplastic right ventricle, single ventricle with the left ventricular morphology giving rise to D-malposed great arteries, and pulmonary stenosis. Noncompaction of the single left ventricle was revealed postnatally. See Table for details of patient 10 with associated complex cardiac disease.

Patient 3 had partial anomalous pulmonary venous return (left pulmonary vein draining into innominate vein) associated with noncompaction. He was diagnosed at 4 years of age and was operated on for partial anomalous pulmonary venous return. Depressed left ventricular systolic function became apparent after 6 years of follow-up. See Table for clinical findings of patients 2, 7, and 12.

At follow-up (mean 2.58 years), patients 1, 3, 9, 10, and 12 were operated on for their associated cardiac anomalies. Balloon valvuloplasty was performed for pulmonary stenosis in patient 7. Patients 4, 5, 8, and 11 were receiving anticongestive therapy for heart failure, whereas patients 2 and 6 were still asymptomatic. The morphological appearance of the noncompacted myocardium persisted in all of the patients, and prominent deterioration of the ventricular systolic function was seen in patients 3 and 5.

DISCUSSION

This rare congenital anomaly usually involves the left ventricle, although the right ventricle and the interventricular septum can also be affected. It may occur with or without additional heart malforma-

Table Clinical manifestations of the patients

Patient	Age	Sex	Clinical presentation	Associated cardiac defect	Rhythm abnormalities	EF/FS	X/Y	Outcome	Follow-up
1	6 mo	M	Congenital heart defect	Dextrocardia, heterotaxy syndrome, hypoplastic right ventricle, ventricular inversion	VES	62/32	2.8	BT shunt at 6 months of age. Treated for bacterial endocarditis 5 months postoperatively.	10 y
2	4 mo	M	Congenital heart defect	VSD (spontaneously closed)	None	61/31	2.5	Asymptomatic	10 y
3	4 y	M	Congenital heart defect	PAPVR	None	70/38 (initial) 54/28 (follow-up)	2.7	Correction of PAPVR. Anti-CHF treatment for depressed left ventricle function	6 y
4	5 y	M	CHF	None	WPW, SVT	56/28	4.2	Anti-CHF treatment+sotalol hydrochloride	2 y
5	14 y	M	Syncope	None	VES	76/44 (initial) 54/26 (follow-up)	2.6	Anti-CHF treatment	2 y
6	4 y	M	Pneumothorax	None	None	67/36	2.7	Asymptomatic	6 mo
7	1 y	M	Congenital heart defect	PS	None	70/39	2.9	Balloon valvuloplasty. Residual gradient: 28 mm Hg. Asymptomatic	6 mo
8	2 y	M	CHF	None	LBBB	52/21	2.4	Anti-CHF treatment	4 mo
9	32nd* week of gestation	F	Congenital heart defect (prenatal diagnosis)	Left atrial isomerism, DOLV, hypoplastic right ventricle, D-malposition of great arteries, PS	None	67/35	2.6	BT-shunt	2 mo
10	11 mo	M	Congenital heart defect	DORV, VSD (multiple), ASD, D-malposition of great arteries, straddling tricuspid valve	None	69/31	3.0	Pulmonary band	2 mo
11	10 y	M	CHF	None	Complete heart block	40/21	3.1	Anti-CHF treatment+PM	2 mo
12	3 mo	M	Congenital heart defect	Coarctation of aorta, aberrant origin of right subclavian artery	None	25/10	2.8	Operated ON for coarctation of aorta at 1 month	1 mo

ASD, Atrial septal defect; BT, Blalock-Taussig; CHF, congestive heart failure; DOLV, double outlet left ventricle; DORV, double outlet right ventricle; EF, ejection fraction; FS, fractional shortening; LBBB, left bundle branch block; PAPVR, partial anomalous pulmonary venous return; PM, pacemaker; PS, pulmonary stenosis; SVT, supraventricular tachycardia; VES, ventricular extrasystole; VSD, ventricular septal defect; WPW, Wolff-Parkinson-White syndrome; X, measure of free-wall thickness to peak of trabeculation; Y, distance between epicardial surface a trough of recess.

*Non-compaction diagnosed postnatally.

tion.⁶ Noncompacted myocardium has been categorized as “unclassified cardiomyopathy” by the World Health Organization in the recently published report on definition and classification of cardiomyopathies.⁷ Ventricular noncompaction can be easily diagnosed by echocardiography if the echocardiographer is familiar with this congenital disorder and if clear-cut diagnostic criteria are used.⁸ Echocardiographic pattern allows correct diagnosis and is in

excellent agreement with the necropsy findings.⁹ However, prominent left ventricular trabeculations can be found in up to 68% of healthy hearts and can be observed in hypertrophic hearts secondary to dilated, valvular, or hypertensive cardiomyopathy.^{8,10} Thus, the differentiation between normal variants and the noncompacted ventricle may be difficult. The crucial diagnostic characteristic of noncompaction is the 2-layered myocardial wall



Figure 2 Noncompacted myocardium of patient 4 in parasternal long-axis (*upper frame*) and 2-chamber at diastole (*lower frame*) views. *LV*, left ventricle; *Ao*, aorta.



Figure 3 Apical views of patient 5. *LV*, left ventricle; *LA*, left atrium; *RA*, right atrium; *RV*, right ventricle; *M*, mitral valve.

consisting of a thin epicardial compacted zone and extremely thickened endocardial noncompacted zone. Usually a ratio of noncompacted/compacted zone ≥ 2 is diagnostic for ventricular noncompaction. Furthermore, the trabeculations in patients with noncompaction are frequently apical, inferior, and lateral, whereas the normal trabeculations frequently course from the free wall to the ventricular septum.^{5,8} All these diagnostic criteria are strictly followed up for all of our patients.

Ventricular noncompaction is usually associated with other congenital cardiac malformations, including anomalous origin of the left coronary artery from the pulmonary trunk,^{2,11} and obstruction to right or left ventricular outflow.^{2,11-14} Seven patients in our study (patients 1, 2, 3, 7, 9, 10, and 12) had congenital heart defects associated with ventricular noncompaction. Among them, patients 1, 9, and 10 had common pathologies of hypoplastic right ventricle. Although the patients with ventricular hypoplasia may have abnormal myocardium, the unaffected ventricle in these patients is usually morphologically and physiologically normal.¹⁵ Among our patients with hypoplastic right ventricle or physiologic single ventricle, only the mentioned patients (patients 1, 9, and 10) had X/Y ratios ≥ 2 , which was diagnostic of ventricular noncompaction. Because we do not have a population of patients with hypoplastic right heart syndrome to

compare these measurements, only the X/Y ratios were considered in the diagnosis of noncompaction.

Isolated left ventricular noncompaction is even more rare.^{2-5,14} Five patients in our study (patients 4, 5, 6, 8, and 11) had isolated left ventricular noncompaction. Three types of cardiac risks have been described in patients with isolated left ventricular noncompaction: 1) depressed left ventricular systolic function, 2) endocardial clot with systemic embolization, and 3) ventricular arrhythmias.^{2,5} Depressed left ventricular systolic function was observed in patients 4, 8, and 11, whereas patients 5 and 6 had normal systolic function at presentation. At follow-up, the left ventricular systolic function was decreased in patient 5. Patient 2 (with spontaneously closed ventricular septal defect) also had normal systolic function. In patients 3 and 12, where the noncompacted ventricle was associated with other cardiac anomalies, the left ventricular systolic function was also subnormal. Depressed left ventricular function may be absent at the time of presentation and may become clinically overt later in childhood (as in our patient 3) or by adolescence. The cause of progressive myocardial failure has not been yet elucidated. The noncompacted left ventricle is perfused normally by left coronary artery, however, the intramural perfusion, especially subendocardial, may be adversely affected by the prominent trabeculations and deep intertrabecular recesses. The

epicardial coronary arteries do not continue to the deep recesses, which are communicating with the left ventricular cavity. Thickened endocardium and prominent trabeculae may be the cause of ischemia.^{5,8} Endomyocardial biopsies of patients with isolated left ventricular noncompaction have shown interstitial fibrosis, endomyocardial thickening, and subendocardial fibroelastosis.¹⁴

The morphology of the noncompacted ventricular myocardium is not arrhythmogenic by itself, however, progressive ischemia and subsequent scar tissue may be an arrhythmogenic substrate for ventricular arrhythmias.^{3,8} Furthermore, the zones of thin ventricular wall in the troughs of the intertrabecular recesses are reminiscent of the morphology of the right ventricle in arrhythmogenic right ventricular dysplasia. An analogy to arrhythmogenic right ventricular dysplasia is appealing, but hypothetical.⁵ Ventricular arrhythmias were documented in patient 5, who had isolated left ventricular noncompaction and in patient 1 who had complex cardiac anomaly. However, further rhythm studies (including electrophysiologic study in patient 5) did not reveal ventricular tachycardia in either of these patients.

The ECG of the previously reported patients showed first-degree heart block, abnormal P waves, intraventricular conduction defects, ventricular tachycardia, and paroxysmal supraventricular tachycardia with WPW syndrome.^{4,14} Patient 4 had supraventricular tachycardia attacks as a result of WPW syndrome; patient 8 had LBBB. In the largest multicentered study from Japan,¹⁴ pediatric LBBB and ventricular tachycardia were reported more rare in children than that described in adults, whereas WPW syndrome had relatively high incidence. Robida and Hajar⁴ have observed the development of LBBB during the follow-up of a patient who initially presented with normal ECG, and correlated the late occurrence of this entity by progressive development of endocardial fibroelastosis. The WPW syndrome is thought to arise from failed regression of developmental embryologic atrioventricular anatomical and electrical continuity attributable to abnormal embryologic persistence of atrioventricular muscular continuity, which can accompany the failing regression of noncompacted myocardium.^{14,16} Patient 11 had complete heart block. We are not aware of congenital heart block previously reported with noncompacted ventricular myocardium. Although we are not sure this association is attributable to the myocardial abnormality, complete heart block may be an associated feature of noncompacted myocardium.

No systemic embolic events or ventricular thrombi were observed in our patients. This finding is similar to that described by Ichida et al¹⁴ in Japanese children.

Familial occurrence has also been observed among patients with ventricular noncompaction.^{5,8,14,17,18} Nevertheless, the families of our patients were not routinely screened for this anomaly, therefore, genetic inheritance or familial occurrence can not be addressed in this study.

True prevalence of this disorder in an unselected group is not known. Our population is far from clarifying this matter because it only consists of patients referred to a tertiary care center. Among 20,341 transthoracic echocardiographic studies performed at our hospital between 1991 and 2001, 12 cases of ventricular noncompaction were identified in pediatric patients, therefore, the frequency of detection of noncompacted ventricle at echocardiography seems to be 6/10,000 in our institution.

CONCLUSION

Noncompaction of the ventricular myocardium is a rare congenital malformation with variable clinical manifestations and natural history. Our patients perfectly represent the clinical and morphological spectrum of this disorder. Distinct morphological features can be diagnosed on 2-dimensional echocardiography. The cardiologist should be aware of various rhythm abnormalities in these patients. WPW syndrome, supraventricular tachycardia, LBBB, and complete atrioventricular block may be associated with noncompaction other than the previously reported ventricular arrhythmias or ventricular tachycardias. Because of the risk of familial occurrence, first-degree relatives should be examined by echocardiography to screen asymptomatic patients. This will also enable early diagnosis and possibly preventive treatment of typical complications.

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