

ORIGINAL ARTICLE

Ventricular Function

Noninvasive and Invasive Evaluation of Noncompaction Cardiomyopathy

Jeroen J. Bax,* Douwe E. Atsma, Hildo J. Lamb, Sidney A. Rebergen, Marianne Bootsma, Paul J. Voogd, Soeresh Somer, Martin J. Schalij, Albert de Roos, and Ernst E. van der Wall

Department of Cardiology and Radiology, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands

ABSTRACT

Noncompaction cardiomyopathy is a recently described rare congenital cardiomyopathy; patients can be asymptomatic or develop diastolic and/or systolic left ventricular dysfunction with heart failure, systemic emboli or ventricular arrhythmias. Long-term prognosis is poor. Currently, diagnosis is based on findings on 2D echocardiography; in the current case report we demonstrate the use of MRI to diagnose noncompaction cardiomyopathy.

Key Words: *Noncompaction; Cardiomyopathy*

Noncompaction of the myocardium is a rare congenital cardiomyopathy caused by an arrest in endomyocardial morphogenesis. It was originally reported in infants,^[1,2] but recently, various reports have demonstrated its prevalence in adults.^[3–5] Patients may be asymptomatic or demonstrate diastolic/systolic left ventricular (LV) dysfunction with heart failure, systemic emboli or ventricular arrhythmias.^[3–5] The disorder is diagnosed by 2D transthoracic echocardiography, showing large prominent trabeculations and deep intertrabecular recesses,

particularly pronounced in the LV apex and lateral wall.^[3–7] In this report, we describe the diagnostic evaluation of a patient with isolated noncompaction cardiomyopathy using noninvasive and invasive testing.

CASE REPORT

A 37-year-old man was hospitalized for evaluation of acute occlusion of the right ciliary artery. Family history

*Corresponding author. Fax: +31-71-5266809; E-mail: jbx@knoware.nl

revealed one case of sudden cardiac death (father, age 45 years), and the patient's history revealed two episodes of syncope during exercise within the last 2 years.

Blood pressure was normal (110/70 mmHg), heart-rate 90 bpm. Cardiac auscultation demonstrated a loud S4 with mild mitral regurgitation. The ECG showed LV hypertrophy. Holter monitoring showed frequent premature supraventricular and ventricular contractions and one episode of nonsustained ventricular tachycardia. Chest radiography was normal. All laboratory tests were normal, except high cholesterol levels (total 7.17 mmol L^{-1} , HDL 1.35 mmol L^{-1} , low density lipoprotein (LDL) 5.4 mmol L^{-1} , triglycerides 0.78 mmol L^{-1}).

Transthoracic 2D echocardiography (Vingmed System FiVe, Horten, Norway) demonstrated an enlarged left atrium (transverse diameter 47 mm), with normal LV dimensions (LV end-diastolic diameter 51 mm, LV end-systolic diameter 34 mm) with preserved systolic function (fractional shortening 35%), without regional wall motion abnormalities. Diastolic function was abnormal, as evidenced by the impaired relaxation (Table 1). Pulse Doppler recordings of the mitral valve showed a decreased E wave, reduced E/A ratio and a prolonged isovolumetric relaxation time. Pulmonary venous flow revealed a normal S wave with a decreased D wave and a deep A wave reversal. Doppler myocardial imaging at the level of the mitral valve annulus showed a reduced E wave (0.05 m/sec) with an increased A wave (0.10 m/sec).

The LV demonstrated the typical prominent trabeculations, located in the LV apex and extending to the lateral wall, with deep intertrabecular recesses (Figs. 1 and 2). The deep intertrabecular recesses communicated with the LV cavity as evidenced by color flow imaging.

Table 1

Assessment of Diastolic Function Using Transmitral Pulse Doppler Recordings and Pulmonary Venous Flow

| | Normal | Patient |
|------------------|---------------|---------|
| LV inflow | | |
| E wave (cm/sec) | 72 ± 14 | 47 |
| A wave (cm/sec) | 40 ± 10 | 33 |
| E/A ratio | 1.9 ± 0.6 | 1.4 |
| DT (msec) | 179 ± 20 | 186 |
| IVRT (msec) | 76 ± 11 | 117 |
| Pulmonary vein | | |
| Peak S (cm/sec) | 48 ± 9 | 44 |
| Peak D (cm/sec) | 50 ± 10 | 21 |
| Peak AR (cm/sec) | 19 ± 4 | 38 |

Normal values based on Ref. [10].

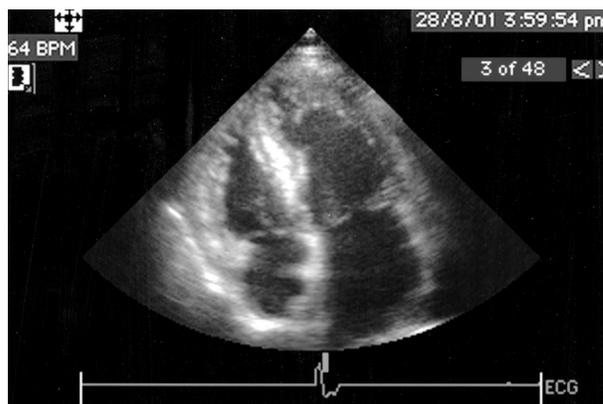


Figure 1. Apical 4-chamber view, showing the typical prominent trabeculations, located in the LV apex and extending to the lateral wall, with deep intertrabecular recesses. Moreover, the thin epicardial layer and the thick spongy endocardial layer can be differentiated.

The basal septum did not show trabecularizations but was hypertrophic (19 mm), without a gradient in the LV outflow tract. The right ventricle also showed trabecularizations, although not as prominent as in the LV. A clear delineation between the thin compacted epicardial layer and the thick, "spongy" noncompacted endocardial layer was present. No thrombus was observed in the recesses of the LV. To further exclude the presence of a LV thrombus, intravenous contrast was administered (Levovist, Schering SA, Berlin, Germany) which

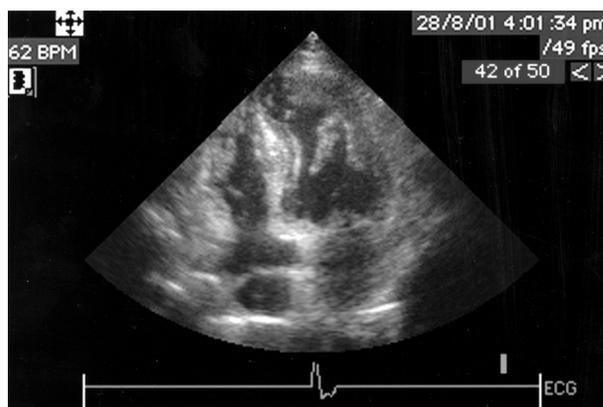


Figure 2. Apical 4-chamber view, showing the typical prominent trabeculations, located in the LV apex and extending to the lateral wall, with deep intertrabecular recesses. Moreover, the thin epicardial layer and the thick spongy endocardial layer can be differentiated.

allowed opacification of the LV cavity and superior delineation of the endocardial borders.

All valves were normal, a mild degree of functional mitral and tricuspid regurgitation (pressure 30 mmHg) was present.

A transesophageal echocardiogram confirmed all findings and demonstrated a thrombus in the left atrial appendage.

Cardiac catheterization (left- and right-sided) revealed normal coronary arteries, increased LV end-diastolic pressure (35 mmHg), elevated Wedge pressure (20 mmHg) with increased *v* waves (30 mmHg). Right ventricular and atrial pressures were also elevated (40 and 10 mmHg, respectively). Mean pulmonary artery pressure was 30 mmHg.

The LV angiogram showed preserved systolic function (LV ejection fraction 55%, LV end-diastolic volume 99 mL, end-systolic volume 45 mL). No gradient could be measured in the LV outflow tract (at rest, during pacing or during infusion of isoprenaline).

Magnetic resonance imaging (MRI) was performed with a 1.5 Tesla ACS-NT15 (Philips Medical Systems, Best, The Netherlands) using prospective ECG triggering. A stack of short axis images consisting of 10–12 slices with a thickness of 8 mm and an intersection gap of 1–2 mm (depending on the heart size) was acquired using breath-

hold balanced fast field echo (FFE) imaging and black blood imaging. The MRI showed a clear difference between the thinner, denser outer wall (compacted myocardium) with the spongy noncompacted inner zone (Fig. 3). The noncompacted endocardial layer had a thickness of 12 mm and the compacted epicardial layer was 3 mm. Moreover, black blood images demonstrated the trabecularization of the LV apex, with blood flowing in the recesses (Fig. 4).

Thus, all findings resulted in the diagnosis of noncompaction cardiomyopathy. This patient had preserved systolic function, but abnormal diastolic function (impaired relaxation, elevated LV end-diastolic pressure). No thrombus was observed in the recesses of the LV, but the left atrial appendage contained a thrombus. Finally, Holter monitoring demonstrated frequent premature ventricular contractions and one episode of nonsustained VT.

DISCUSSION

Recently, a few case reports and one long-term follow-up study have been published on the diagnosis of noncompaction cardiomyopathy.^{13–51} Noncompaction of the LV myocardium is the result of an arrest in endomyocardial morphogenesis; it can also occur in the



Figure 3. Magnetic resonance imaging: short-axis slice showing the spongy noncompacted myocardium in the anterior/apical region.



Figure 4. Magnetic resonance imaging: black blood image (short-axis slice) showing the blood in between the trabecularizations in the anterior/apical region.

right ventricle. Thus, a thin, compacted epicardial layer and a thick spongy, heavily trabecularized endomyocardial layer, with deep intertrabecular recesses can be observed (Fig. 1).^[3-5] These abnormalities are most pronounced in the LV apex and lateral wall,^[6,7] as was the case in the current patient.

The disease was originally reported in infants.^[1,2] Most frequently it is isolated, but a combination with Becker's muscular dystrophy has been reported, and nonspecific dysmorphic facial features have been observed.^[8]

Recent data have been reported on the prevalence of the disease in adults. Oechslin et al.^[4] have reported a series of 34 adults with noncompaction cardiomyopathy; these individuals were selected from all patients referred to the echocardiography department in 14 years (0.014% of all patients referred). Both sporadic and familial forms have been described; in the 34 patients described by Oechslin et al.,^[4] 18% of the patients had a familial form.

Patients can be asymptomatic or have symptoms of (1) heart failure, related to altered diastolic/systolic LV function, (2) systemic embolization, related to LV thrombi, and/or (3) ventricular arrhythmias. The current patient did not complain of chest pain or dyspnea, but presented with systemic embolism and syncope. Extensive echocardiographic examination demonstrated noncompaction cardiomyopathy accompanied by diastolic dysfunction, thrombus in the left atrial appendage, and ventricular arrhythmias on Holter monitoring. Of the 34 patients reported by Oechslin et al.,^[4] 35% had symptoms of severe heart failure (NYHA class III/IV), thromboembolic events occurred in 24%, syncope in 18%, and ventricular tachycardia in 41%.

The disorder is diagnosed by 2D transthoracic echocardiography, showing large prominent trabeculations and deep intertrabecular recesses, as observed in the current patient. Besides the trabecularizations/recesses, the two layered wall structure (thin compacted epicardium and thick, noncompacted endocardium) is essential for the correct diagnosis. An end-systolic thickness ratio of the noncompacted vs. compacted layers equal or more than two is considered diagnostic for noncompaction cardiomyopathy,^[3-5] as was the case in the current patient. Moreover, Ritter and colleagues have demonstrated that the echocardiographic findings correlated well with necropsy findings.^[9] Transesophageal echocardiography may be superior to transthoracic echocardiography for assessment of noncompaction cardiomyopathy.^[5] Besides echocardiography, MRI can also be very useful in diagnosing this disorder. In particular, since the diagnosis is based on morphological criteria, MRI may become the technique for diagnosing noncompaction cardiomyopathy.

Also, the differentiation between the endo- and epicardial layers may be more easy with MRI.

Importantly, the prognosis of patients with noncompaction cardiomyopathy is poor; Oechslin et al.^[4] showed during a follow-up period of 44 ± 39 months a mortality rate of 35%. Cardiac death was related to heart failure in 33% and sudden in 50%. An additional 12% of the patients underwent heart transplantation.

Thus, therapy should be directed at the prevention/management of heart failure, ventricular arrhythmias and prevention of thromboembolic events. In the current patient, medication consisted of statins, angiotensin converting enzyme (ACE) inhibition, oral anticoagulants, and beta blockade. Electrophysiologic testing will be performed and implantation of an internal cardio-defibrillator (ICD) will be discussed.

REFERENCES

1. Chin, T.K.; Perloff, J.K.; Williams, R.G.; Jue, K.; Mohrmann, R. Isolated Noncompaction of the Left Ventricular Myocardium. *Circulation* **1990**, *82*, 507-513.
2. Ichida, F.; Hamamichi, Y.; Miyawaki, T.; Ono, Y.; Kamiya, T.; Akagi, T.; Hamada, H.; Hirose, O.; Isobe, T.; Yamada, K.; Kurotobi, S.; Mito, H.; Miyake, T.; Murakami, Y.; Nishi, T.; Shinohara, M.; Seguchi, M.; Tashiro, S.; Tomimatsu, H. Clinical Features of Isolated Noncompaction of the Ventricular Myocardium. Long-Term Clinical Course, Hemodynamic Properties, and Genetic Background. *J. Am. Coll. Cardiol.* **1999**, *34*, 233-240.
3. Agmon, Y.; Connolly, H.M.; Olson, L.J.; Khandheria, B.K.; Seward, J.B. Noncompaction of the Ventricular Myocardium. *J. Am. Soc. Echocardiogr.* **1999**, *12*, 859-863.
4. Oechslin, E.N.; Attenhofer Jost, C.H.; Rojas, J.R.; Kauffmann, P.A.; Jenni, R. Long-Term Follow-Up of 34 Patients with Isolated Left Ventricular Noncompaction: A Distinct Cardiomyopathy with Poor Prognosis. *J. Am. Coll. Cardiol.* **2000**, *36*, 493-500.
5. Maltagliati, A.; Pepi, M. Isolated Noncompaction of the Myocardium: Multiplane Transesophageal Echocardiography Diagnosis in an Adult. *J. Am. Soc. Echocardiogr.* **2000**, *13*, 1047-1049.
6. Jenni, R.; Oechslin, E.; Schneider, J.; Jost, C.A.; Kaufmann, P.A. Echocardiographic and Pathoanatomic Characteristics of Isolated Non-compaction: A Step Towards Classification as a Distinct Cardiomyopathy. *Heart* **2001**, *86*, 666-671.
7. Varnava, A.M. Isolated Left Ventricular Non-compaction: A Distinct Cardiomyopathy? *Heart* **2001**, *86*, 599-600.

8. Ichida, F.; Hamamichi, Y.; Miyawaki, T.; Ono, Y.; Kamiya, T.; Akagi, T.; Hamada, H.; Hirose, O.; Isobe, T.; Yamada, K.; Kurotobi, S.; Mito, H.; Miyake, T.; Murakami, Y.; Nishi, T.; Shinohara, M.; Seguchi, M.; Tashiro, S.; Tomimatsu, H. Clinical Features of Isolated Noncompaction of the Left Ventricular Myocardium. Long-Term Clinical Course, Hemodynamic Properties, and Genetic Background. *J. Am. Coll. Cardiol.* **1999**, *34*, 233–240.
9. Ritter, M.; Oechslin, E.; Sutsch, G.; Attenhofer, C.; Schneider, J.; Jenni, R. Isolated Noncompaction of the Myocardium in Adults. *Mayo Clin. Proc.* **1997**, *72*, 26–31.
10. Klein, A.L.; Cohen, G.I. Doppler Echocardiographic Assessment of Constrictive Pericarditis, Cardiac Amyloidosis and Cardiac Tamponade. *Clevel. Clin. J. Med.* **1992**, *59*, 281.

Received January 4, 2002

Accepted April 24, 2002