Guiding the Management of Ventricular Arrhythmias in Patients With Left Ventricular Noncompaction Cardiomyopathy: A Knowledge Gap

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Left ventricular noncompaction (LVNC) is a cardiomyopathy that occurs due to an arrest of myocardial maturation during embryogenesis. The diagnostic echocardiographic features in individuals with LVNC include a thick, bilayered myocardium, prominent ventricular trabeculations, and deep intertrabecular recesses. Clinical features associated with LVNC vary in asymptomatic and symptomatic patients, and include the potential for heart failure, conduction defects (eg, left bundle branch block), supraventricular and ventricular arrhythmias, thromboembolic events, and sudden cardiac death. The authors report five cases that emphasize asymptomatic and apparently benign symptoms in patients with LVNC; despite normal physical examination and 12-lead electrocardiogram results, all of these cases unveiled potentially serious clinical consequences. These cases highlight the concern that LVNC patients with mild to moderate left ventricular systolic dysfunction, particularly in the presence of ventricular arrhythmias or a family history of sudden cardiac death, may need consideration for an implantable cardioverter defibrillator (ICD). All potential benefits of an ICD need to be balanced by the risk of device infection, lead and device malfunction, and potential for inappropriate shocks.

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KEY WORDS

Left ventricular noncompaction • Ventricular tachycardia • Heart failure • Sudden cardiac death • Echocardiography • Noncompacted myocardium • Exercise testing • Rhythm disturbance surveillance

Echocardiography and magnetic resonance imaging (MRI) technology have allowed new insights into the recognition and understanding of the cardiomyopathy left ventricular noncompaction (LVNC). LVNC has unique morphologic features that are most logically linked to a suppression of myocardial maturation during embryogenesis.[1,2]

The classic echocardiographic features in individuals affected by LVNC include a thick, bilayered (compacted and noncompacted) myocardium, prominent ventricular trabeculations, and deep intertrabecular recesses.[3] Echocardiographic criteria include an apical short-axis image revealing a noncompacted/compacted (NC/C) myocardium ratio $>$ 2 at end-diastole.[4,5]

Clinical features affect both symptomatic and asymptomatic patients; the latter have the potential for progressive deterioration of cardiac function. Major complications associated with LVNC include heart failure, arrhythmias, thromboembolic events, and sudden cardiac death (SCD).[6] The recognition of LVNC with echocardiography should prompt careful cardiovascular evaluation to assess systolic and diastolic heart function, rhythm disturbances, and potential for thromboembolism.

There is currently a lack of data and a gap in knowledge regarding implantable cardioverter defibrillators (ICDs) in patients with LVNC. There is also a known association of ventricular arrhythmias with LVNC; the incidence of ventricular arrhythmias is variable, ranging from 6% to 62% in the literature.[7,8] The relationship between impaired left ventricular (LV) systolic function and ventricular arrhythmias is well established. There is a lack of evidence-based data regarding normal LV systolic function or mild to moderate LV systolic dysfunction in patients with LVNC and risk for ventricular arrhythmias with adverse clinical consequence.

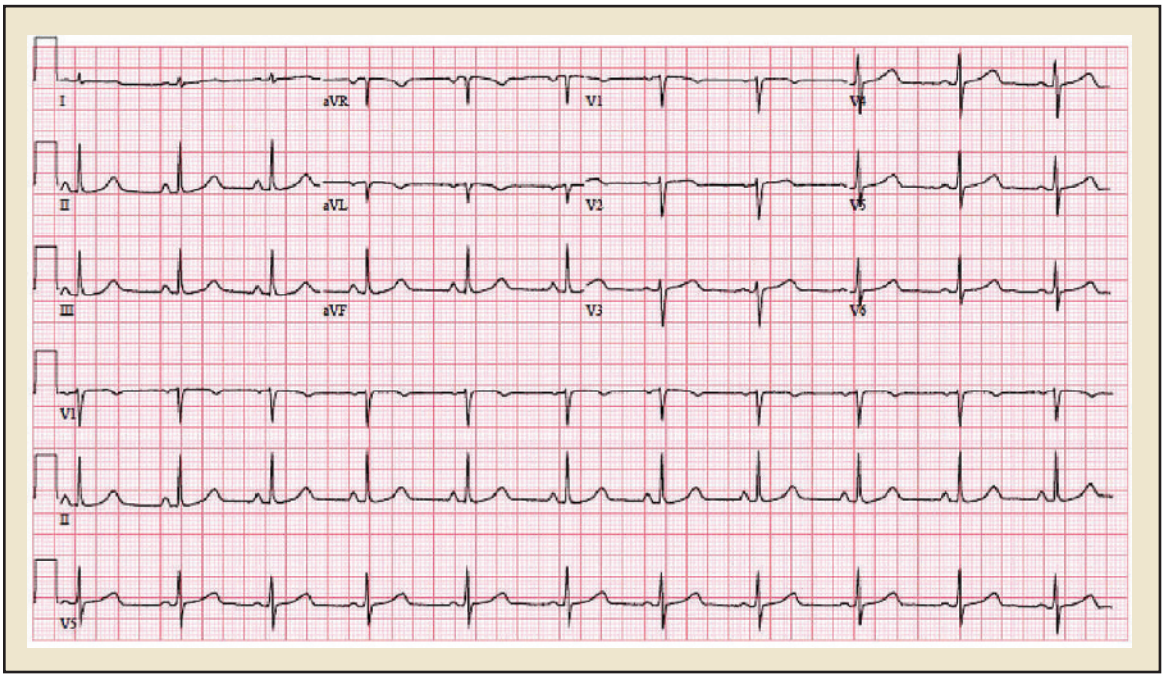
We present five cases that emphasize that asymptomatic patients and patients with symptoms of palpitations, lightheadedness, LVNC, and normal physical examination and 12-lead electrocardiogram (ECG) results can be at risk for serious ventricular arrhythmias. These cases highlight the concern that LVNC patients with mild to moderate LV systolic dysfunction, particularly in the presence of ventricular arrhythmias and/or a family history of SCD, may need further diagnostic evaluation and consideration of an ICD. LVNC with mild to moderate LV systolic dysfunction appears to have the potential to cause lethal ventricular rhythm disturbance and SCD, as evidenced by these cases.

Case Reports

Case 1

A 48-year-old woman had a 12-month history of recurrent palpitations and episodes of lightheadedness for which she kept the car window open to maintain consciousness while driving. She had no history of hypertension, diabetes, smoking, or illicit drug use. The patient had no family history of heart disease, including no history of cardiomyopathy, rhythm disturbance, SCD, or premature cardiac death. The patient's physical examination and 12-lead ECG results were normal (Figure 1).

Figure 1. Normal 12-lead electrocardiogram.



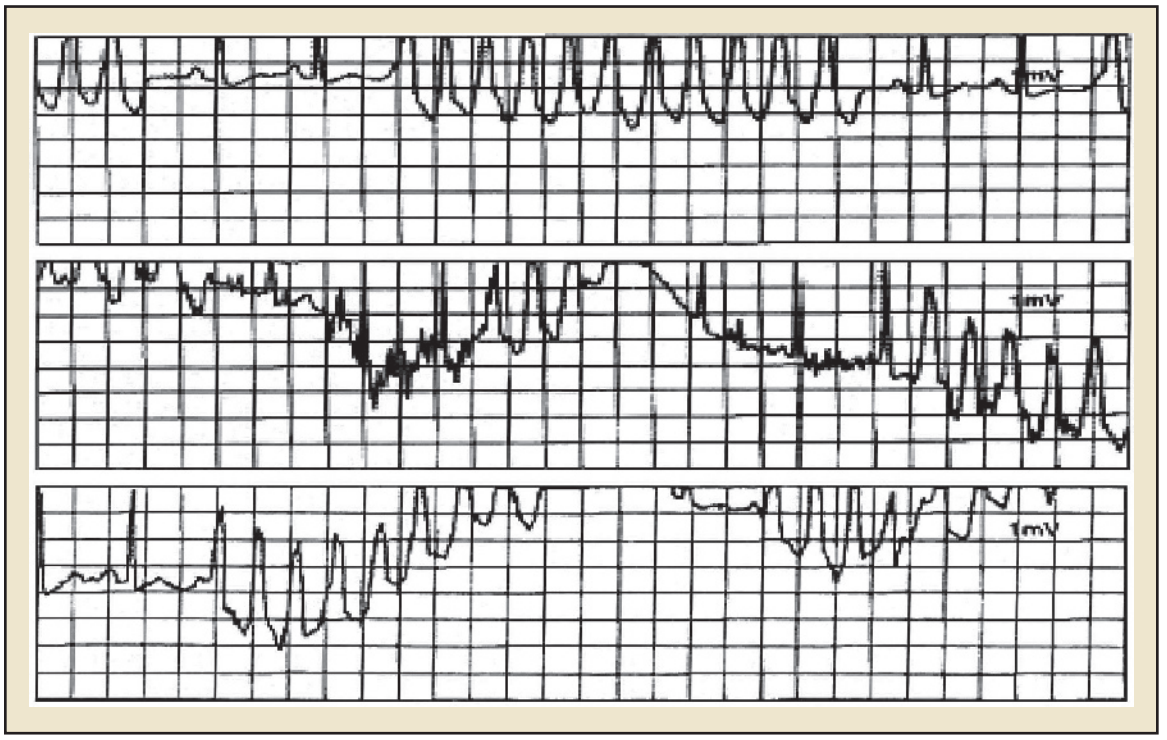


Figure 2. Monitoring strips revealing monomorphic ventricular tachycardia.

Following an episode of lightheadedness and palpitations, ECG event monitoring identified monomorphic ventricular tachycardia (VT; Figure 2). The patient was hospitalized, and cardiac catheterization was performed to rule out coronary artery disease. Catheterization revealed normal coronary arteries, and the left ventriculogram revealed depressed LV systolic function. An echocardiogram revealed normal LV dimensions, wall thickness, and diastolic parameters. The calculated ejection fraction (EF) on echocardiography was 45%. The LV apex was abnormal with noncompacted myocardium on the inferior, apical, and lateral walls of the left ventricle. The apical short-axis view in end-diastole revealed an NC/C myocardial ratio of 2.7, which is consistent with LVNC (Figure 3).[5] Diastolic function and pulmonary artery pressure were normal. An electrophysiology (EP) study revealed normal baseline conduction intervals and inducible nonsustained monomorphic VT. No inducible supraventricular tachycardia or sustained VT was identified.

A cardiac MRI revealed normal LV dimensions and mildly reduced EF (53%). Apical findings were consistent with LVNC. Delayed gadolinium enhancement revealed no evidence of fibrosis. Results of genetic testing for catecholaminergic polymorphic ventricular tachycardia were negative. Genetic testing for LVNC was not performed.

The patient's history of syncope in the setting of spontaneous monomorphic VT, depressed LV systolic function, and echocardiographic and MRI findings of LVNC put her at risk for SCD. Therefore, an ICD was implanted after a careful risk-to-benefit analysis was reviewed with the patient. The patient was placed on a comprehensive medical therapy program for heart failure with a β-blocker and an angiotensin-converting enzyme inhibitor. Follow-up evaluation at 6 months revealed the patient had experienced one successful defibrillation of polymorphic VT, and 12-month evaluation revealed two additional successful defibrillations of polymorphic VT (Table 1).

Case 2

A 58-year-old man presented with cardiac arrest and was defibrillated to sinus rhythm. The patient had no prior symptoms or history of syncopal episodes. There was no family history of cardiac disease or sudden or premature death. Results of the patient's physical examination were normal. The 12-lead ECG revealed sinus rhythm with left bundle branch block (LBBB). Cardiac catheterization revealed normal coronary arteries.

An echocardiogram confirmed normal LV size with depressed systolic function (EF 47%). Short-axis apical imaging revealed inferior, lateral, and apical noncompacted myocardium with an end-diastolic NC/C ratio of 2.9, consistent with LVNC. Echocardiography/Doppler diastolic function revealed increased left atrial volume (40 mL/m^2) and abnormal E/A ratio (0.7). The e′, E/e′, and deceleration time were normal.

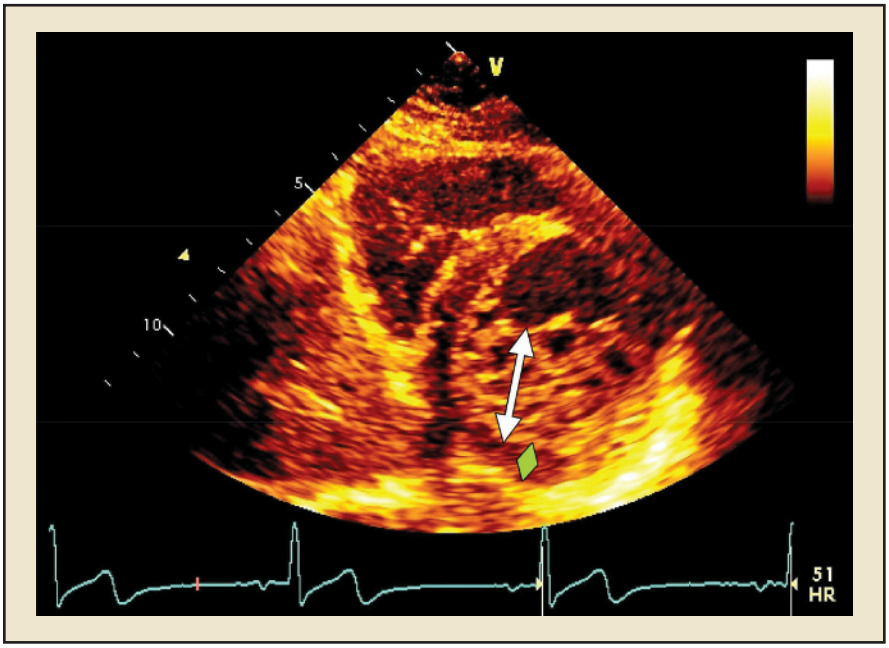


Figure 3. Apical parasternal short-axis echocardiographic view demonstrating noncompacted (NC) myocardium (*white arrow*) and compacted (C) myocardium (*green diamond*) at end-diastole with an NC/C ratio > 2, consistent with left ventricular noncompaction.

Pulmonary artery systolic pressure (PASP) was 35 mm Hg.

The patient received an ICD because of the aborted episode of sudden death. The patient's medications included sotalol, 80 mg twice daily, atorvastatin, 20 mg/d, and lisinopril, 10 mg twice daily. ICD interrogation revealed recurrent episodes of nonsustained VT lasting up to 3 seconds (Table 1).

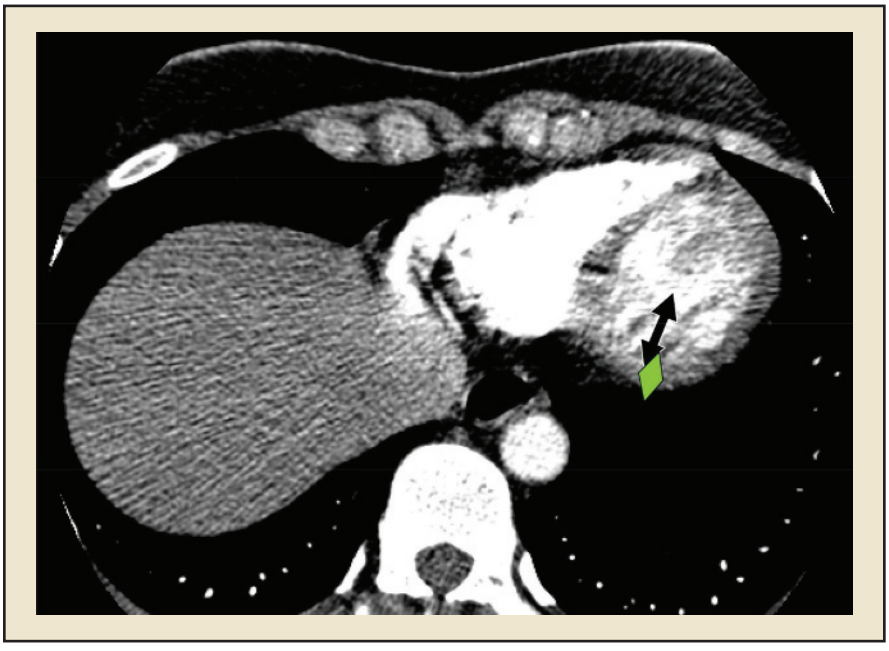
Case 3

A 42-year-old woman with a family history of SCD presented for cardiac evaluation and opinion regarding idiopathic cardiomyopathy. Prior cardiac computed tomography (CT) raised the question of amyloid heart disease. The patient's father and brother both died suddenly at age 42. The deceased brother's echocardiogram was reviewed and met the criteria for LVNC (apical short-axis end-diastolic frame revealed an NC/C ratio > 2). The father's records were not available. The deceased brother's two children, ages 13 and 15 years, were screened and each had echocardiographic evidence of LVNC with normal systolic and diastolic function, and normal strain, twist, and torsion. A second brother, aged 41 years, was evaluated with screening echocardiography and found to have LVNC with depressed systolic function. His calculated EF was 30%. Cardiac MRI revealed delayed gadolinium enhancement (fibrosis). He received an automatic ICD, and the 6-month follow-up revealed three successful defibrillations of monomorphic VT.

The index patient had no symptoms with regular exercise, including aerobics classes and long-distance bike riding. Results of her physical examination, including a detailed cardiac examination, were normal. The 12-lead ECG revealed normal sinus rhythm with low voltage in the precordial and limb leads. Echocardiography revealed normal LV dimension with an EF of 35% and evidence of apical noncompaction. Diastolic function and PASP were both normal.

The cardiac CT was reviewed and felt to demonstrate LVNC, which was verified by echocardiography. The CT revealed normal LV chamber dimension and EF of 40%. There was evidence of apical noncompaction (Figure 4). Stress testing revealed a flat blood pressure response (100/60 mm Hg to 110/60 mm Hg); with exercise,

Figure 4. Cardiac computed tomography of the left ventricle revealing noncompacted myocardium (*black arrow*) and compacted myocardium (*green diamond*) suggestive of left ventricular noncompaction.



the LV dilated and LV contractility decreased. There was a 5-beat wide complex tachycardia at peak exercise. Ambulatory blood pressure monitoring and rhythm monitoring revealed normal blood pressure results and recurrent episodes of 5 to 12 beats of nonsustained wide complex tachycardia. The heart rate during tachycardia was 120 beats/min.

A comprehensive discussion of the patient's risks—integrating her strong family history, echocardiography results, stress testing data, and ambulatory rhythm results—led to the placement of an ICD. The patient was treated with metoprolol, 50 mg/d, and lisinopril, 10 mg/d. Follow-up over the next 12 months revealed that the patient continued to function well, and interrogation of the ICD has revealed no complex rhythm disturbance (Table 1).

Case 4

A 59-year-old man presented for a cardiology opinion about his abnormal ECG results, which showed broad LBBB with prolonged atrioventricular delay (400 ms). The patient was being assessed as part of a marine medical examination for fitness to drive a passenger ferry and the abnormal ECG result was detected on screening. The patient denied any symptoms or significant medical history. He described normal exercise tolerance in the absence of chest pain or shortness of breath, and no presyncopal or syncopal episodes. He reported no significant family history of cardiac symptoms or premature or sudden death. Cardiac physical examination revealed a soft systolic murmur at the lower left sternal edge, which did not radiate and did not augment or diminish with the Valsalva maneuver.

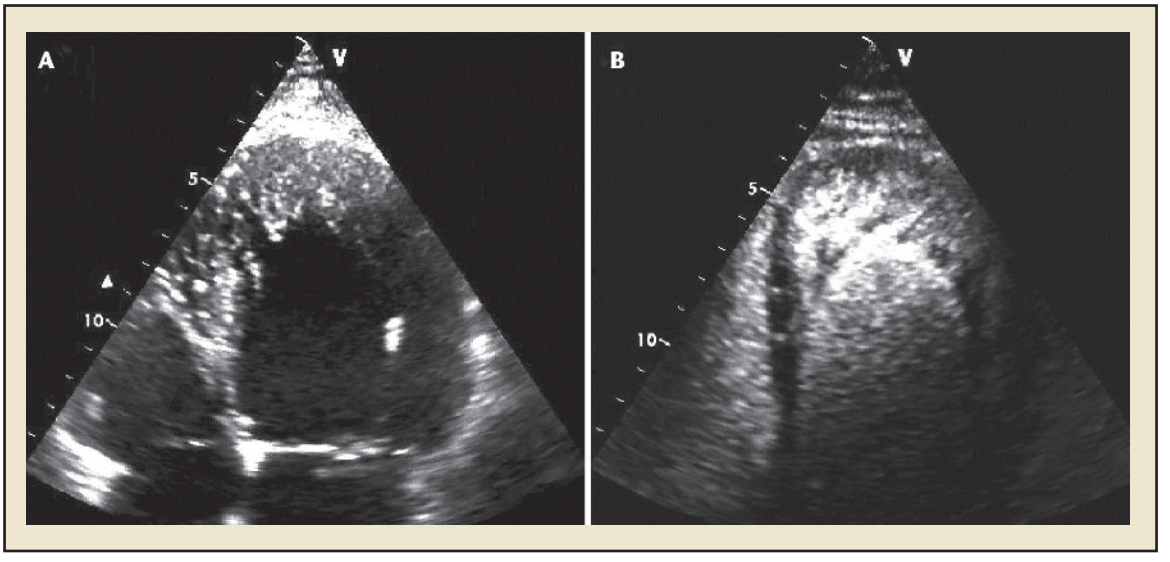
Transthoracic echocardiogram raised the suspicion of a diagnosis of LVNC. The LV systolic function was mildly depressed with an EF of 50%. Multivariate diastolic function was analyzed and revealed grade 2/4 diastolic dysfunction (e′ = 5 cm/s). PASP was normal.

The patient exercised 9 minutes on a standard Bruce protocol echocardiographic stress test. Despite feeling asymptomatic with a normal hemodynamic response, he had new-onset atrial fibrillation and multifocal, nonsustained VT at peak exercise and during recovery. His myocardial contractile reserve was globally reduced, with an EF of 40% at peak exercise while in atrial fibrillation.

He was admitted to the hospital for further surveillance and investigation. Contrast transthoracic echocardiogram confirmed the presence of deep myocardial recesses, which were less clear on routine two-dimensional imaging (Figure 5). Cardiac catheterization revealed normal coronary arteries. Monitoring revealed episodes of asymptomatic sustained VT (up to 32 s), and an ICD for primary prevention of SCD was considered and subsequently implanted. MRI imaging confirmed the diagnosis of LVNC. LV ejection fraction (LVEF) was calculated at 50%. Delayed gadolinium enhancement did not reveal myocardial fibrosis (Figure 6). The patient was anticoagulated for prophylaxis of thromboembolic event risk with dabigatran, and started on sotalol and a statin drug. He was subsequently cardioverted from atrial fibrillation to sinus rhythm.

His marine license for driving a passenger ferry was not granted on the grounds of the diagnosis and potential complications. ICD monitoring over the next 12 months revealed two shocks for VT.

Figure 5. Apical four-chamber image of the left ventricle with increased apical trabeculations in a patient with left ventricular noncompaction **(A)**. In the same patient, contrast enhancement of the left ventricle with evidence of apical trabeculations and intertrabecular recesses **(B)**.



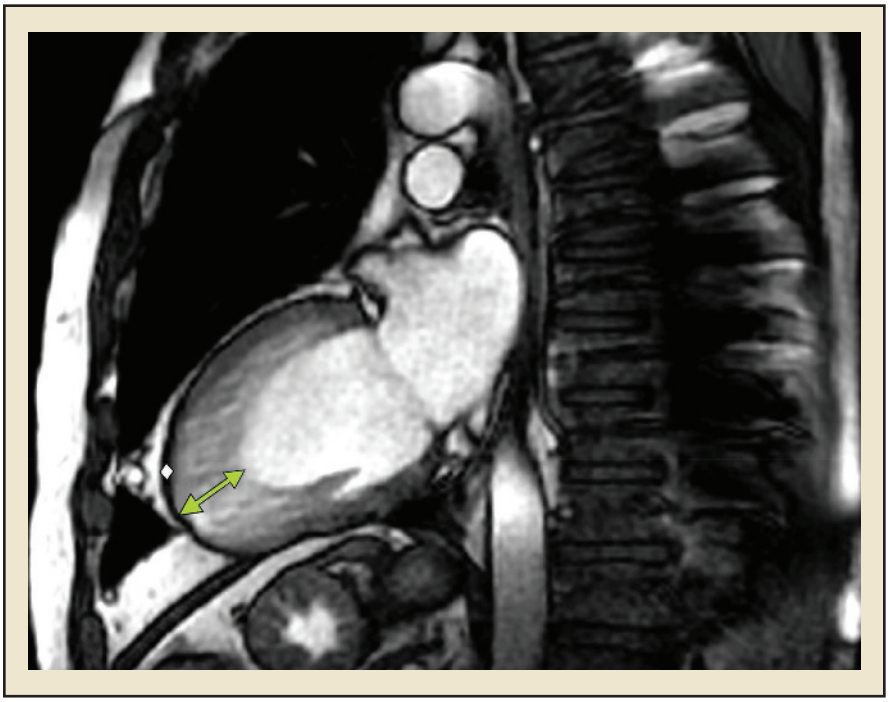


Figure 6. Cardiac magnetic resonance image in a patient with left ventricular noncompaction showing evidence of a noncompacted (*green arrow*) to compacted (*white diamond*) myocardium ratio > 2 at end-diastole.

Case 5

A 45-year-old woman presented for further evaluation of nonischemic cardiomyopathy with a history of symptomatic VT for which she had ablation and an automatic ICD implanted. She presented with episodes of fast heart rates and exertion-related dyspnea. Family history highlighted the premature sudden death of her brother, who had been awaiting cardiac transplantation for an indeterminate cardiomyopathy. Autopsy had not been performed.

Physical examination revealed mild hypertensive blood pressure (140/85 mm Hg), a heart rate of 75 beats/min, a fourth heart sound, and otherwise normal cardiovascular findings. The ECG revealed a paced atrial rhythm with LBBB pattern.

Echocardiogram revealed normal LV size and depressed LV systolic function (calculated EF 47%). Left atrial volume was 32 mL/m^2. Diastolic analysis revealed an E/A ratio of 2 with a normal deceleration time, depressed e′, and elevated LV filling pressure. PASP was normal. The morphology of the apex revealed an NC/C myocardial ratio of 3.1, consistent with LVNC (Figure 7).

Recent automatic ICD interrogation revealed sustained VT that was defibrillated to normal sinus rhythm on two occasions. The EP service added flecainide, 100 mg twice daily, to carvedilol, 25 mg twice daily, and irbesartan, 75 mg twice daily. Echocardiography screening of her children did not identify LVNC.

Discussion

These five cases emphasize the knowledge gap and lack of evidence-based data guiding implantation of ICD in patients with LVNC. Ventricular and supraventricular tachycardia can readily be induced in the EP laboratory in patients with LVNC, whereas the inducibility of a sustained monomorphic VT is low.[9] Patients with a history of sustained VT or an enlarged left atrium have a more unstable course and prognosis.[10]

An important observation in these five cases is that malignant

Figure 7. Apical short-axis view of the left ventricle with classic compacted (*green diamond*) and noncompacted (*blue arrow*) myocardium in a patient with left ventricular noncompaction.

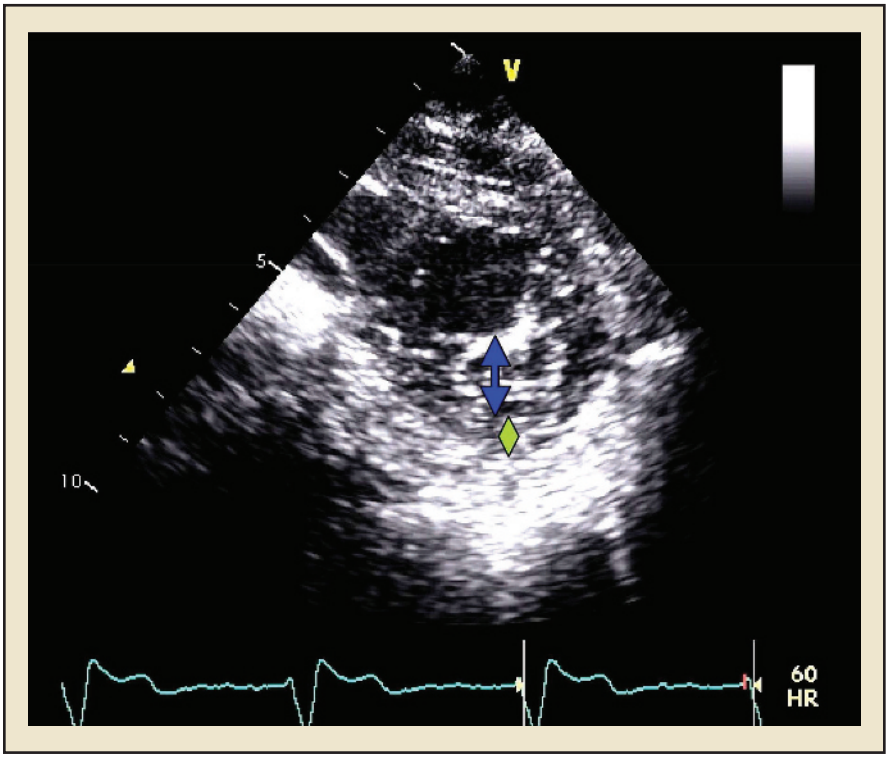


TABLE 1

Summary of Cases With Left Ventricular Noncompaction Cardiomyopathy, Mild to Moderate Left Ventricular Systolic Dysfunction, and Ventricular Arrhythmias

Case No.	Sex/Age	Symptoms	Personal/ Family History	ECG	Identified Rhythms	CAD	Imaging	Stress Test	EP Study	ICD
1	F/48	Palpitations, lightheadedness	0	NSR	Monomorphic VT	0	Echo: 45% EF MRI: 53% EF DGE: -	0	Monomorphic/ polymorphic VT	+
2	M/58	0	0	LBBB	VT/VF, aborted SCD	0	Echo: 47% EF	0	0	+
3	F/42	0	+[a]	NSR	0	0	Echo: 35% EF	5-beat WCT at peak exercise	0	+
4	M/59	0	0	LBBB	NSVT, AF	0	Echo: 50% EF MRI: 52% EF DGE: -	AF, NSVT	0	+
5	F/45	0	+[b]	LBBB	SVT and VT	0	Echo: 47% EF	0	0	+

[a]Brother and father deceased at age 42 years; brother diagnosed with left ventricular noncompaction.

[b]Personal history included ischemic cardiomyopathy, (status post) ablation and ICD, awaiting transplant for cardiomyopathy; brother deceased at age 40 years.

AF, atrial fibrillation; CAD, coronary artery disease; DGE, delayed gadolinium enhancement; ECG, electrocardiogram; Echo, echocardiography; EF, ejection fraction; EP, electrophysiology; ICD, implantable cardioverter defibrillator; LBBB, left bundle branch block; MRI, magnetic resonance imaging; NSR, normal sinus rhythm; NSVT, nonsustained ventricular tachycardia; SCD, sudden cardiac death; SVT, supraventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia; WCT, wide complex tachycardia.

ventricular arrhythmias were present in a range of EFs that are usually not considered to be an indication for prophylactic ICD implantation. This raises the question of whether to consider ICD implantation in patients with LVNC and mild to moderate LV systolic dysfunction, particularly in the presence of ventricular arrhythmias and/or a family history of SCD.

Another knowledge deficit is how to risk stratify patients with LVNC for arrhythmia risk. One large center performed Holter monitoring on 15 patients with known LVNC, and VT (nonsustained and sustained) was identified in 4 patients (27%).[11] EP testing has a low likelihood of inducing sustained monomorphic VT.[9] Presently, there are no guidelines for risk stratification of arrhythmia risk in patients with LVNC.

We know that patients with LVNC who have sustained VT or VF need an ICD implant for prevention of SCD. With regard to ICD implantation, patients with LVNC and impaired systolic function (LVEF < 35%) are treated similarly to patients with dilated cardiomyopathy. Evidence is lacking with regard to how to manage LVNC patients outside these two clinical scenarios. Three of the five cases we describe in this review represent anecdotal examples that led to ICD implantation in the absence of evidence-based medicine. It is important to reinforce that all the potential benefits of an ICD need to be tempered by the risk of device infection, lead and device failure, and inappropriate shocks. In Cases 1 and 3, clinical decision making determined ICD implantation after weighing risks and benefits. These cases reify the concern that LVNC is a heterogeneous cardiomyopathy with the potential for serious clinical consequence in the presence of mild to moderate LV systolic dysfunction. The two cases in which MRI was performed revealed no evidence of fibrosis.

We know that patients with LVNC who have sustained VT or VF need an ICD implant for prevention of SCD.

This case series identifies a need to overcome our knowledge gap by developing registries to evaluate all manifestations of LVNC across age, sex, medical history, symptoms, EF, stress testing, and EP testing in order to help develop evidence-based guidelines for the management of LVNC patients with mild to moderate LV systolic dysfunction.

Current Limitations

LVNC is frequently not identified in echocardiography laboratories across the United States. There is an incomplete understanding of the potential risks associated with this heterogeneous cardiomyopathy. The potential for lethal rhythm disturbances has not been

MAIN POINTS

- Left ventricular noncompaction (LVNC) is a cardiomyopathy that occurs due to an arrest of myocardial maturation during embryogenesis. Clinical features include the potential for heart failure, conduction defects (eg, left bundle branch block), supraventricular and ventricular arrhythmias, thromboembolic events, and sudden cardiac death.
- Echocardiography is essential to establishing the diagnosis of LVNC. After diagnosis, patients require comprehensive cardiovascular evaluation because of the potential for life-threatening arrhythmias. This also allows for a more in-depth understanding of the arrhythmia mechanisms and potential medical, device, and ablation therapies.
- The genetic potential and heterogeneous nature of LVNC should lead to an echocardiographic evaluation of all first-degree relatives.
- LVNC patients with mild to moderate left ventricular systolic dysfunction, particularly in the presence of ventricular arrhythmias or a family history of sudden cardiac death, should be considered for an implantable cardioverter defibrillator.
- LVNC is frequently not identified in echocardiography laboratories across the United States and there is an incomplete understanding of its associated risks. Presently, clinicians lack guidelines on the management of ventricular arrhythmias in LVNC patients with mild and moderate LV systolic dysfunction; there is a need for registries to evaluate all the manifestations of LVNC so preventive strategies can be developed.

identified in the medical literature in the subset of LVNC patients with normal LV systolic function or mild to moderate dysfunction. There are no registries established that would help further study of this complex cardiomyopathy and its clinical consequences.

Conclusions

These cases reify the importance of careful clinical evaluation and multimodality imaging in patients with LVNC who are asymptomatic and those presenting with symptomatic arrhythmias. EP consultation is an essential component of the comprehensive evaluation because of the potential for life-threatening arrhythmias when the diagnosis of LVNC is established. This allows for a more in-depth understanding of the arrhythmia mechanisms and potential medical, device, and ablation therapies. The genetic potential and heterogeneous nature of LVNC should lead to an echocardiographic evaluation in all first-degree relatives, as demonstrated in Case 3.

LVNC is a heterogeneous cardiomyopathy with the potential for serious clinical consequences, including arrhythmias and SCD. Echocardiography is essential to establishing the diagnosis. Once the diagnosis is established, comprehensive cardiovascular evaluation is required. There is a need for registries to evaluate all the manifestations of LVNC so preventive strategies can be developed. Presently, clinicians lack guidelines on the management of ventricular arrhythmias in LVNC patients with mild and moderate LV systolic dysfunction. ■

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