Arrhythmias in Left Ventricular Noncompaction

Christina Y. Miyake, MD, MS, Jeffrey J. Kim, MD*

KEYWORDS

• Cardiomyopathy • Arrhythmias • Left ventricular noncompaction • Heart failure
• Electrocardiogram • Sudden death • Ventricular tachycardia • Atrial fibrillation

KEY POINTS

- Left ventricular noncompaction (LVNC) is associated with heart failure, arrhythmias, thromboembolic events, and sudden death.
- Arrhythmias are common and may have prognostic significance in LVNC; the risk of sudden death seems to be associated with left ventricular (LV) size, systolic function, and presence of arrhythmias.
- Arrhythmias are not restricted to noncompacted myocardium and include atrial fibrillation (AF) (adults), atrioventricular (AV) accessory pathways/Wolff-Parkinson-White (WPW) syndrome (children), and ventricular tachycardia (VT).
- Management strategies include antiarrhythmic medications, ablation, and implantable cardioverter-defibrillator (ICD) implantation.

INTRODUCTION

Since initial pathologic descriptions in the 1920s, LVNC has been identified in association with a variety of congenital heart malformations or metabolic syndromes.[1–4] More recently, it has become recognized in its isolated form as a distinct form of cardiomyopathy.[5–11] LVNC is thought to be caused by the intrauterine arrest of the normal compaction process of myocardial fibers and meshwork in the ventricular endocardium,[5,12] although recent debate regarding later development of trabeculations has arisen.[13] Clinically, it is characterized by the presence of deep intertrabecular recesses in hypertrophied segments of the LV myocardium (**Fig. 1**). Suggested diagnostic criteria are summarized in **Table 1**. Although it was initially thought to be an exceedingly rare disorder, it has recently become clear that LVNC is much more prevalent than previously recognized. Current studies in children and young adults estimate that LVNC accounts for approximately 9% of newly diagnosed cardiomyopathies.[7,14] The prevalence of LVNC in adult screening echocardiograms is reported to be approximately 0.05%.[8]

The clinical manifestations of LVNC are highly variable, ranging from asymptomatic to progressive heart failure and recurrent or life-threatening arrhythmias. Therefore, great interest has developed in characterizing the natural history of this disease and its associated arrhythmias, in order to help guide the counseling and management of this heterogeneous patient population. Both

The authors have nothing to disclose.
Section of Pediatric Cardiology, Department of Pediatrics, Baylor College of Medicine, Texas Children's Hospital, 6621 Fannin Street, Houston, TX 77030, USA
* Corresponding author. Section of Pediatric Cardiology, Texas Children's Hospital, 6621 Fannin Street, MC# 19345-C, Houston, TX 77030.
E-mail address: jjkim@texaschildrens.org

Card Electrophysiol Clin ■ (2015) ■–■
http://dx.doi.org/10.1016/j.ccep.2015.03.007
1877-9182/15/$ – see front matter

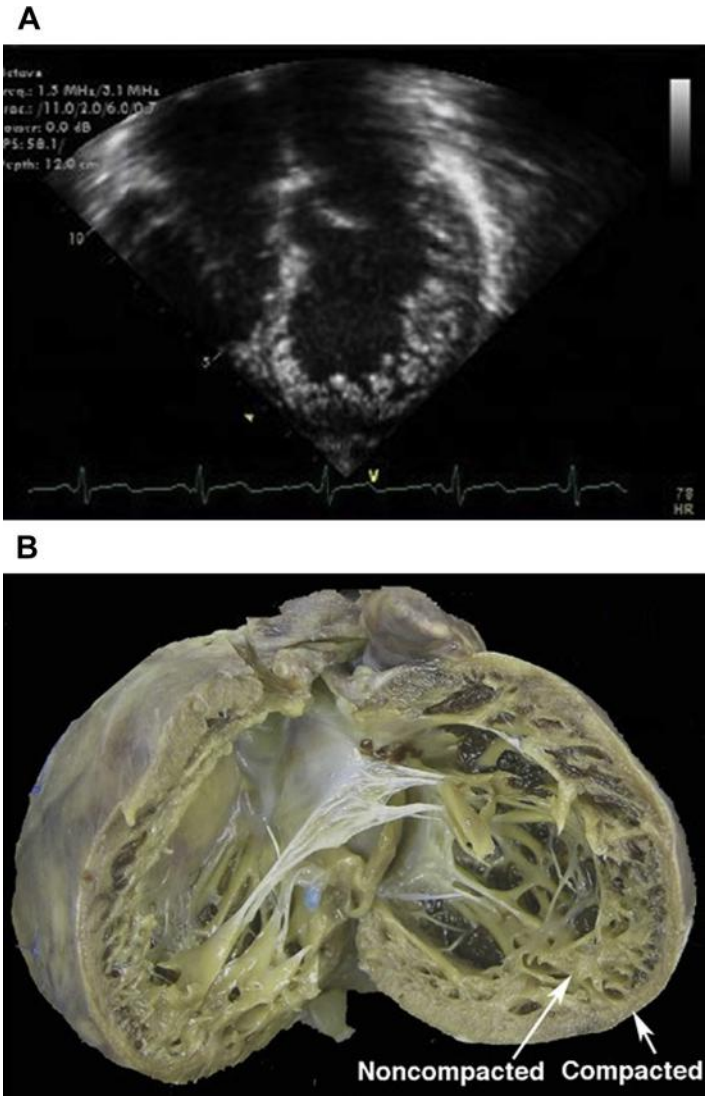

Fig. 1. (*A*) Echocardiographic still frame of LVNC. Noncompacted to compacted ratio of 2.3:1. (*B*) Pathologic specimen of LVNC. (*Courtesy of* Norman Silverman, MD, Palo Alto, CA.)

ventricular and supraventricular arrhythmias are now well described as prominent clinical components of LVNC.[15] Throughout the spectrum of age, they have been associated with prognosis and outcome, and thus, clinical management of these arrhythmias is an important part of patient care.[16–18] This review aims to describe the findings in literature related to arrhythmias in LVNC, allowing us to better define the presentation, history, significance, and management of rhythm abnormalities in this relatively newly defined patient population.

GENETICS

LVNC is associated with both sporadic and familial cases, with an estimated familial recurrence rate of 23% to 33%.[16,19–22] Inheritance most commonly follows an autosomal dominant or X-linked pattern, although autosomal recessive and mitochondrial inheritance have also been observed.[23,24] As is seen with many inherited cardiac diseases, variable penetrance and phenotypic variability result in lack of clear genotype-phenotype correlation, even among family members carrying the same mutation. Although multiple genes have now been identified (**Table 2**), these mutations have not been shown to affect risk assessment, and therefore at this time there is no role for genetic testing to guide clinical management.[22–38] LVNC has been observed in case reports of patients with gene mutations involving cardiac arrhythmia syndromes including CPVT (RYR2) and long QT (KCNH2/KCNQ1)[35,36] and may be affected by SCN5a variants.[38]

Table 1
Proposed diagnostic criteria for LVNC

Echocardiography	
Chin et al[5] • Parasternal short axis, measurements at end diastole	• Two-layered structure of myocardium • Determine X to Y ratio ($\leq$0.5) • X = distance between epicardial surface and trough of intertrabecular recess • Y = distance between epicardial surface and peak of trabeculation
Jenni et al[10] • Short axis, measured at end systole	• Two-layered myocardium • Noncompacted to compacted ratio >2.0 • Color Doppler of LV deep intertrabecular recesses filled with blood • Absence of coexisting cardiac anomalies
Stöllberger et al[15,21] • Apical 4-chamber view, angle views to obtain the technically best picture for differentiation between false chords/aberrant bands and trabeculations	• >3 trabeculations protruding from LV wall, located apically to papillary muscles and visible in 1 image plane • Trabeculations with the same echogenicity as the myocardium and synchronous movement with ventricular contractions • Perfusion of intertrabecular spaces from LV cavity • Ratio of noncompacted to compacted >2 at end diastole (added subsequently)
van Dalen et al[74]	• Consider speckle tracking to determine LV ventricular twist
Cardiac MRI	
Petersen et al[26] • Measured at end diastole	• Ratio between noncompacted to compacted >2.3
Jacquier[27] • Measured at end diastole	• Trabeculated LV mass >20% of global LV mass

Adapted from Oechslin E, Jenni R. Left ventricular non-compaction revisited: a distinct phenotype with genetic heterogeneity? Eur Heart J 2011;32:1446–56.

ELECTROCARDIOGRAPHIC FINDINGS

Electrocardiographic (ECG) abnormalities are a hallmark of many cardiomyopathies. Early findings in recent studies suggest that LVNC may be similar in this regard. An evaluation by Steffel and colleagues[39] found that only 13% of adults with diagnosed LVNC had normal results of ECGs at presentation.[39] The most common findings were intraventricular conduction delay such as left bundle branch block, voltage signs of hypertrophy, and repolarization abnormalities (**Table 3**). Over 70% of the individuals were noted to have pathologic repolarization with over 50% having prolongation in their QT intervals. No ECG findings were thought to be specific for LVNC, although conduction delay and prolongation of the QTc were associated with reduced systolic function and voltage findings of LV hypertrophy were associated with systemic embolic events ($P<.05$). Alternatively, those with normal results of ECGs at presentation were more likely to have better left ventricular ejection fractions (LVEF).

A subsequent study using a prospective noncompaction cardiomyopathy registry found early repolarization to be highly prevalent on ECG in 39% of this cohort. Early repolarization was noted to be more common in those presenting with VT/ventricular fibrillation (VF) (75%) as opposed to those without VT/VF (31%) ($P = .02$). Long-term outcome for VT/VF also seemed to be worse in those with early repolarization ($P = .05$).[40] Mechanistically, it was proposed that increased trabeculation with deep intramyocardial invagination, carrying the Purkinje system deeper into the myocardium, resulted in both delayed depolarization and inhomogeneous repolarization.

WPW syndrome has also been reported in association with LVNC since early descriptions.[6] Although precise estimates in adults are not delineated, it seems that WPW is more commonly seen in children, ranging from 8% to 14%.[6,16] As expected, this can be associated with the

Table 2
Genes associated with LVNC

Gene	Protein
ACTC1	α-Actinin-2
ACTN2	α-Cardiac actin
DTNA	α-Dystrobrevin
DYS/nZASP	Dystrophin
GLA	α-Galactosidase
LDB3	LIM-domain binding 3
LMNA	Lamin A/C
MYBPC3	Myosin-binding protein C
MYH7	β-Myosin heavy chain 7
TAZ	Tafazzin
TNNT2	Cardiac troponin T, type 2
TPM1	α-Tropomyosin
TNNI3	Cardiac troponin I

Data from Refs.[22–38]

development of future episodes of supraventricular arrhythmias. It is hypothesized that in these patients, primitive AV connections persist because of the generalized arrest in cardiac development, resulting in direct continuity between the atrial and ventricular myocardium across the annulus fibrosus.

Table 3
Baseline ECG findings at initial diagnosis in patients with LVNC

ECG Findings	Adults (n = 78)	Children (n = 242)
Normal result of ECG	10 (13%)	32 (13%)
Right bundle branch block	2 (3%)	10 (4%)
Left bundle branch block	15 (19%)	1 (<1%)
WPW	2 (3%)	20 (8%)
Left axis deviation	-	21 (9%)
LV hypertrophy	30 (38%)	87 (36%)
RV hypertrophy	5 (6%)	13 (5%)
P mitrale	20 (26%)	17 (7%)
P pulmonale	12 (15%)	28 (12%)
First-degree AV block	12 (15%)	2 (1%)
Complete AV block	2 (3%)	2 (1%)
ST-segment changes	48 (61%)	82 (34%)
T-wave inversion	32 (41%)	78 (32%)
QTc prolongation	40 (52%)	22 (9%)

Data from Steffel J, Kobza R, Oechslin E, et al. Electrocardiographic characteristics at initial diagnosis in patients with isolated left ventricular noncompaction. Am J Cardiol 2009;104:984–9; and Brescia ST, Rossano JW, Pignatelli R, et al. Mortality and sudden death in pediatric left ventricular noncompaction in a tertiary referral center. Circulation 2013;127:2202–8.

With regard to children with LVNC, similar to adults, ECG abnormalities should be considered the norm. A study by Brescia and colleagues[16] found that only 13% of children had normal results of ECGs at presentation, with the majority having significant abnormalities. The most common finding in children was voltage criteria for ventricular hypertrophy, some with extreme QRS voltage similar to that seen in Pompe disease. Other common findings included repolarization abnormalities, atrial enlargement, axis deviation, and WPW syndrome (see **Table 3**). Children were less likely to have conduction abnormalities than adults, such as bundle branch block or AV block. Again, no findings were specific to LVNC; however, T-wave inversion and ST-segment changes were associated with increased mortality ($P \leq .05$).

These early descriptions highlight the fact that ECG abnormalities are indeed commonplace in LVNC and may be associated with mechanisms for arrhythmogenesis. Use of electrocardiography in this cohort may therefore be important because it may harbor both diagnostic and prognostic potential. Whether these ECG findings have more prominent implications in patient outcomes warrant further prospective investigation.

VENTRICULAR ARRHYTHMIAS

Early descriptions of LVNC point to 3 major clinical manifestations of the disease, including heart failure, embolic events, and arrhythmias.[5,8] Although a variety of arrhythmias have subsequently been identified in association with LVNC, ventricular tachyarrhythmias have been considered the hallmark. Recent larger series have found VT in as many as 47% of affected individuals (**Table 4**), with sudden cardiac death (SCD) accounting for a significant portion of the mortality.[5,8,17,40,41] There has been wide variability, however, with some studies suggesting a much lower prevalence of ventricular arrhythmias.[42] A recent systematic overview of literature by Bhatia and colleagues,[43] including over 200 adults, found the prevalence of VT (both sustained and nonsustained) to be 38%. This finding was thought to merit special attention because SCD accounted for greater than 55% of all LVNC-related mortality in their analysis. In children, the reported prevalence of ventricular arrhythmias has varied widely, ranging from 0% to 40%.[5,6,16] The most recent description by Brescia and colleagues[16] reported an incidence of VT in 17% of children, with most developing during the course of follow-up. Owing to these

Table 4
Prevalence of arrhythmias and mortality in LVNC

	Chin et al[5]	Ichida et al[6]	Brescia et al[16]	Ritter et al[8]	Oechslin et al[17]	Murphy et al[20]	Stöllberger & Finsterer[40]	Aras et al[21]
Patients (n)	8	27	242	17	34	45	62	67
Median age (y)	7	5	7 (mean)	45	42	37 (mean)	50 (mean)	41
Median follow-up (y)	—	6	4	2.5 (mean)	3 (mean)	2.7	—	2.5
ECG abnormalities (%)	88	88	87	88	94	91	92	88
VT (%)	38	0	17	47	41	20	18	36
AF (%)	—	—	1	29	26	7	5	12
Atrial flutter (%)	0	0	2	—	—	—	—	0
Atrial tachycardia (%)	0	0	6	—	—	—	3	0
Supraventricular tachycardia (%)	13	7	8	—	—	—	0	0
Mortality (%)	38	7	13	47	35	2	—	15
Sudden death (%)	13	0	6	18	18	2	—	9

The symbol "—" denotes unreported.

findings, several investigators recommend routine monitoring for arrhythmias with regimented follow-up, as well as aggressive management including antiarrhythmic therapy and consideration for implantation of cardioverter-defibrillators.

Although the primary form of ventricular arrhythmia reported in studies remains sustained or nonsustained monomorphic VT, specific morphologic descriptions have not been carried out and series to date have emphasized the broad spectrum of presentation. Indeed, case reports have found a variety of ventricular arrhythmias in association with LVNC, including bundle branch reentry, right ventricular outflow tract (RVOT) origin, apparent idiopathic VT, left bundle branch and right bundle branch morphologies, fascicular VT, bidirectional VT, polymorphic VT, and VF.[44–48] Despite overarching lack of specificity, on case-by-case bases, morphologic assessment may be helpful in determining possible therapeutic approaches as discussed below. In addition, the arrhythmias may be a diagnostic trigger where LVNC was not considered before, pointing to the need for a high index of suspicion.

The precise mechanism for ventricular arrhythmias in patients with LVNC is not delineated. However, it is postulated that developmental arrest of conduction and the presence of intratrabecular crypts may create pathways for reentrant circuits. In addition, relatively decreased perfusion and ischemia-related fibrosis at subendocardial noncompacted regions can cause electrical inhomogeneity and microreentry resulting in ventricular arrhythmias.[45,49] Histologic examination has demonstrated evidence of increased subendocardial fibrosis within areas of noncompacted myocardium supporting this theory.[5] The presence of late potentials or prolonged QT dispersion has also been described, which may play a role in the substrate for ventricular arrhythmias and sudden death.

The prognostic implications of ventricular arrhythmias in LVNC are being evaluated. Although results are limited to date, the presence of ventricular arrhythmias seems to be associated with an increased risk of death or transplantation. A recent study of 65 adults found a history of sustained VT (>30 seconds) to be an independent risk factor for cardiovascular death or heart transplantation based on multivariate analysis, with a hazard ratio (HR) of 10.1 ($P = .004$).[19] In children, the presence of VT was similarly found to be a risk factor for death or transplantation with an HR of 4.0 ($P = .001$).[16] Further study is warranted, but early data suggest, as might be expected, that ventricular arrhythmias may be a harbinger of poor prognosis.

SUPRAVENTRICULAR ARRHYTHMIAS

Recent reports suggest that supraventricular arrhythmias are also implicated in the natural history of LVNC. In adults, this seems to be primarily manifested by AF. Studies by Weiford and colleagues[18] and Ritter and colleagues[8] describe a prevalence of AF in their cohorts of as high as 29% (see **Table 4**). Other evaluations, however, found a slightly lower prevalence of AF in LVNC, ranging from 5% to 26%.[20,21,50] The mechanistic role of LVNC in the development of AF remains unclear; it may be related to atrial dilation secondary to cardiac dysfunction and relative AV valve regurgitation or primary myocardial involvement because of underlying myopathy and affected ion channels. When patients with LVNC and AF were investigated by cardiac MRI, however, no areas of fibrosis in the atria were reported.[51]

Prognostically, in patients with LVNC, the presence of AF was associated with increased symptoms of heart failure, higher New York Heart Association (NYHA) class, and worse systolic function ($P<.01$). In addition, based on log rank testing, patients with AF had higher mortality rates than patients without AF ($P = .012$).[50] In one study, multivariate analysis found AF to be an independent predictor of mortality in LVNC with an HR of 3.3, causing the investigators to question whether more aggressive AF therapy would potentially improve prognosis.[52]

In children, the mechanisms for supraventricular arrhythmias seem to be more related to AV reentrant tachycardia or focal atrial tachycardia than primary intra-atrial pathology. Pediatric studies to date show a low prevalence of AF or atrial flutter, but describe a 7% to 13% prevalence of supraventricular tachycardia (SVT) (see **Table 4**). Recent assessment by Brescia and colleagues[16] found macroreentrant SVT in 8% and focal atrial tachycardia in 6% of their cohort. This higher incidence of SVT in children may be related to the relatively common association with WPW, as mentioned previously. Although the presence of any arrhythmia in children with LVNC seems to increase the risk of cardiac death (HR, 2.8; $P = .002$),[16] it is thought that ventricular arrhythmias remain the predominant player and it is unclear what prognostic contribution supraventricular arrhythmias might have.

SUDDEN DEATH

In current reports, rates of sudden death have varied significantly, ranging from 0% to 18%, possibly because of differences in selection of patient population (isolated vs nonisolated LVNC) and length of follow-up.[5,6,8,16,17,19–21,52] In the

largest pediatric study of isolated LVNC to date, the risk of sudden death was reported to be 6%.[16] In the scheme of all-cause mortality, sudden death may account for up to 50% of deaths, suggesting the possible importance of primary or secondary prevention schemes.[5,8,16,17,19,21] Unfortunately, definitive risks of sudden death have not been well defined as of yet. However, several factors including age at presentation and presence of cardiac and extracardiac manifestations have been suggested to contribute to the overall risk profile. In particular, decreased LV systolic function, abnormal LV dimensions, and the presence of ventricular arrhythmias seem to contribute to sudden death rates.[16,17,19,21]

In pediatric patients, dysmorphic features (in particular a prominent forehead, low-set ears, strabismus, micrognathia) and the presence of AV bypass tracts have also been associated with increased risk of ventricular arrhythmias and sudden death.[5,53–55] An electrophysiology (EP) study, risk assessment, and ablation procedure should therefore be considered in the presence of WPW. In addition, an ICD may be considered in certain subsets of patients as described below.[5,53–55]

RISK ASSESSMENT

The ability to identify predictors of outcome is important in the effective and optimal management of all patients with cardiomyopathy. Unfortunately, determining risk factors for mortality or sudden death in LVNC has been complicated by several factors including: (1) phenotypic heterogeneity of disease, (2) varying diagnostic criteria, and (3) lack of randomized controlled studies. Thus, definitive risk factors remain lacking. Nonetheless, as mentioned above, increased mortality does seem to be associated with increased LV size, decreased LV systolic function, and the presence of ventricular arrhythmias.[16,17,19,21] In addition, symptomatic heart failure (ie, NYHA class III/IV) and AF in adults and repolarization abnormalities (ST changes and T-wave inversion) in pediatric patients may also be harbingers of poor outcome.[16,17,19,21,52] As such, periodic echocardiography and ambulatory monitoring for arrhythmias at regular intervals is recommended, likely at minimum on an annual basis.[16] Age has not been implicated as a risk factor unless presentation occurs at less than 1 year of age.[16,17,21] Gender, location, and degree of noncompaction also do not seem to be risk factors. Risk factors suggested in the literature are demonstrated in **Box 1**.

Data regarding the utility of programmed electrical stimulation (PES) in LVNC is limited, and there are no guidelines or recommendations regarding its use. In the largest adult study to date, Steffel and colleagues[56] demonstrated inducible ventricular arrhythmias in 9 of 24 patients (38%) referred for PES. Among 7 patients with inducible VT who underwent ICD implantation, 3 received appropriate device therapy during a follow-up period of 30 ± 19 months. Among 13 patients without inducible VT, symptomatic tachyarrhythmias were not seen in follow-up. Nevertheless, there have been several case reports of patients with documented atrial and ventricular tachyarrhythmias (including polymorphic VT) and even sudden death that did not have inducible arrhythmias at the EP study, suggesting that the negative predictive value may be inadequate.[48,57,58] Thus, the usefulness of PES for risk stratification in this population remains to be determined.[56]

Characterization of myocardial fibrosis by cardiac MRI has been prognostic in some forms of cardiomyopathy; however, in LVNC, late gadolinium enhancement has a heterogeneous distribution and has neither been shown to be of prognostic value in patients with arrhythmias nor been shown to correlate with mortality.[59]

Box 1
Risk factors for increased mortality in LVNC

Risk factors for mortality (death, OHT)

All patients

- Increased LV dimensions
- Decreased LV systolic function
- NYHA class III/IV
- Ventricular arrhythmias
- AF

Pediatric patients

- Age at presentation less than 1 year
- ECG changes (ST changes or T-wave inversions)
- Dysmorphic facies (prominent forehead, strabismus, low-set ears, micrognathia, high arched palate)

THERAPEUTIC APPROACHES

Proposed therapeutic strategies for arrhythmias in LVNC are summarized in **Table 5**.

Supraventricular Arrhythmias

In adult patients, treatment of AF should be based on published guidelines. Owing to the increased risk of embolic events in this patient population, aggressive anticoagulation strategies may be

Table 5
Proposed diagnostic evaluation and therapeutic strategies for LVNC

Diagnostic evaluation	
Echocardiogram	• See Table 1 for criteria
Cardiac MRI	• Ratio of noncompacted to compacted >2.3 • Trabeculated mass >20% global mass
Neurologic examination	
Family screening (first degree)	• Echocardiogram and/or genetic testing
Genetic testing	
Electrophysiology study	• Symptomatic arrhythmias or unexplained syncope
Therapeutic strategies	
If normal LV size and function and without arrhythmias	• Children: yearly echocardiogram and Holter • Adults: every 2 y
Heart failure	• Follow standard guidelines
Anticoagulation	• Consider aspirin if LVEF $\geq$40% and <55% • If LVEF <40% or history of AF, goal INR 2–3
Supraventricular arrhythmias	• Standard treatment of AF • Risk stratification of WPW syndrome and ablation in symptomatic (and/or asymptomatic) WPW syndrome • Consider Holter q 6 mo
Ventricular arrhythmias	• Antiarrhythmic medications (β-blockers, sotalol, amiodarone) • Consider PES and/or ablation • Consider ICD if history of aborted arrest, refractory to medications or ablation • Consider Holter q 6 mo
ICD	• Secondary prevention and/or primary prevention based on current published guidelines
Biventricular resynchronization	• LVEF <35% with dyssynchrony

Abbreviation: INR, international normalized ratio.

warranted. Case reports of successful ablation with pulmonary vein isolation, in AF with rapid ventricular response, have been described.[60] Pediatric patients with reentrant SVT due to AV bypass tracts (WPW and concealed) can also be managed with antiarrhythmic medications or ablation. Patients with WPW may warrant risk stratification with an EP study given the risks of rapid antegrade conduction and sudden death. Also, because of possible associations with dyssynchrony from anomalous AV excitation and progressive cardiac dysfunction, WPW in the presence of LVNC may merit more assertive approaches to ablation. Reentrant SVT due to accessory bypass tracts as well as focal atrial tachycardia have been successfully ablated in LVNC.[16,21]

Ventricular Arrhythmias

There have been no controlled studies to determine efficacy of antiarrhythmic treatment of ventricular tachyarrhythmias in LVNC. β-Blockade as a single agent for nonsustained VT has been used; however, most reports suggest that combination therapy or more potent antiarrhythmics may be necessary, with amiodarone being the most frequently used medication among adults and in those with severely depressed function. Amiodarone seems to have good efficacy in this scenario; however, incomplete control has also been described.[61,62] Monomorphic ventricular arrhythmias, particularly those that are sustained, have been successfully mapped and ablated using radiofrequency energy in patients with LVNC.[16,45,62] Arrhythmogenic substrate (most often microreentrant or focal) can be located within the noncompacted endocardium, noncompacted myocardium, or compacted epicardium. VT ablation, therefore, although typically amenable to endocardial approach, may require epicardial ablation in certain cases.[63,64]

Implantable Cardioverter-Defibrillator

Patients with a history of aborted cardiac arrest, ventricular arrhythmias refractory to antiarrhythmic therapy or not amenable to ablation, may benefit from ICD implantation. There are no

specific guidelines for primary prevention ICD implantation in patients with LVNC; however, extrapolation from current guidelines based on underlying substrate (hypertrophic or dilated) may be effective to some degree until more definitive data are available.[65,66] As such, it may be reasonable to use documented risk factors for HCM (hypertrophic cardiomyopathy) in patients with LVNC and a hypertrophic phenotype or corollary ejection fractions and cardiac dimensions believed to be risk factors in DCM for patients with a dilated phenotype. Small studies have demonstrated appropriate shocks in both secondary and primary prevention, suggesting the potential utility of ICDs in this cohort. In nearly all reported cases, ICDs have been shown to be an effective treatment strategy,[16,19,65,67,68] with only 1 reported case of a patient death due to recalcitrant VT despite an ICD.[17] Conversely, inappropriate shock rates in this population have been reported to be 13% to 20%.[65,66] Therefore, because of the high prevalence of supraventricular arrhythmias in this cohort of patients, dual-chamber devices with enhanced detection and discrimination algorithms should be considered.

Sympathetic Denervation

Information and long-term follow-up of left cardiac sympathetic denervation in patients with LVNC is lacking. Based on short-term follow-up of 2 patients with LVNC, sympathetic denervation may be an adjunct therapy if there are poorly controlled ventricular arrhythmias; however, further studies are needed.[69]

Bradyarrhythmias

Although less common, patients with LVNC have been reported to demonstrate a wide variety of bradyarrhythmias including sinus bradycardia and varying degrees of AV block including complete heart block.[21,61,70] Pacemakers have been implanted successfully with good results.[5,19,21,61]

Biventricular Resynchronization Therapy

Data regarding the use of biventricular pacing and cardiac resynchronization therapy (CRT) in patients with LVNC are limited. In adult patients in whom a biventricular pacemaker or ICD was implanted based on existing heart failure guidelines, improvement in LVEF, LV end diastolic volume, and functional capacity has been reported.[71–73] However, response is not uniform, and to date there are no data to differentiate responders from nonresponders. Data regarding CRT in the pediatric LVNC population are not available.

SUMMARY

LVNC is a newly recognized form of cardiomyopathy that has been associated with heart failure, arrhythmias, thromboembolic events, and sudden death. Both ventricular and supraventricular arrhythmias are now well described as prominent clinical components of LVNC. Arrhythmias are not restricted to noncompacted myocardium and can include AF (adults), AV accessory pathways/WPW and SVT (children), and VT. Throughout the spectrum of age, these arrhythmias have been associated with prognosis and outcome, and their clinical management is therefore an important aspect of patient care. The risk of sudden death seems to be associated with ventricular dilation, systolic dysfunction, and the presence of arrhythmias. Proposed management strategies shown to have efficacy include antiarrhythmic therapy, ablation techniques, and ICD implantation.

REFERENCES

1. Betrián Blasco P, Gallardo Agromayor E. Ebstein's anomaly and left ventricular noncompaction association. Int J Cardiol 2007;119:264–5.
2. Feldt RH, Rahimtoola SH, Davis GD, et al. Anomalous ventricular myocardial patterns in a child with complex congenital heart disease. Am J Cardiol 1969;23:732–4.
3. Freedom RM, Patel RG, Bloom KR, et al. Congenital absence of the pulmonary valve associated with imperforate membrane type of tricuspid atresia, right ventricular tensor apparatus and intact ventricular septum: a curious developmental complex. Eur J Cardiol 1979;10:171–96.
4. Ichida F, Tsubata S, Bowles KR, et al. Novel gene mutations in patients with left ventricular noncompaction or Barth syndrome. Circulation 2001;103:1256–63.
5. Chin TK, Perloff JK, Williams RG, et al. Isolated noncompaction of left ventricular myocardium. A study of eight cases. Circulation 1990;82:507–13.
6. Ichida F, Hamamichi Y, Miyawaki T, et al. Clinical features of isolated noncompaction of the ventricular myocardium: long-term clinical course, hemodynamic properties, and genetic background. J Am Coll Cardiol 1999;34:233–40.
7. Pignatelli RH, McMahon CJ, Dreyer WJ, et al. Clinical characterization of left ventricular noncompaction in children: a relatively common form of cardiomyopathy. Circulation 2003;108:2672–8.
8. Ritter M, Oechslin E, Sütsch G, et al. Isolated noncompaction of the myocardium in adults. Mayo Clin Proc 1997;72:26–31.
9. Wald R, Veldtman G, Golding F, et al. Determinants of outcome in isolated ventricular noncompaction in childhood. Am J Cardiol 2004;94:1581–4.

10. Jenni R, Rojas J, Oechslin E. Isolated noncompaction of the myocardium. N Engl J Med 1999;340:966–7.
11. Hook S, Ratliff NB, Rosenkranz E, et al. Isolated noncompaction of the ventricular myocardium. Pediatr Cardiol 1996;17:43–5.
12. Pepper MS. Transforming growth factor-beta: vasculogenesis, angiogenesis, and vessel wall integrity. Cytokine Growth Factor Rev 1997;8:21–43.
13. Oechslin E, Jenni R. Left ventricular non-compaction revisited: a distinct phenotype with genetic heterogeneity? Eur Heart J 2011;32:1446–56.
14. Nugent AW, Daubeney PE, Chondros P, et al. National Australian Childhood Cardiomyopathy Study. Clinical features and outcomes of childhood hypertrophic cardiomyopathy: results from a national population-based study. Circulation 2005;112:1332–8.
15. Steffel J, Duru F. Rhythm disorders in isolated left ventricular noncompaction. Ann Med 2012;44:101–8.
16. Brescia ST, Rossano JW, Pignatelli R, et al. Mortality and sudden death in pediatric left ventricular noncompaction in a tertiary referral center. Circulation 2013;127:2202–8.
17. Oechslin EN, Attenhofer Jost CH, Rojas JR, et al. Long-term follow-up of 34 adults with isolated left ventricular noncompaction: a distinct cardiomyopathy with poor prognosis. J Am Coll Cardiol 2000;36:493–500.
18. Weiford BC, Subbarao VD, Mulhern KM. Noncompaction of the ventricular myocardium. Circulation 2004;109:2965–71.
19. Lofiego C, Biagini E, Pasquale F, et al. Wide spectrum of presentation and variable outcomes of isolated left ventricular non-compaction. Heart 2007;93:65–71.
20. Murphy RT, Thaman R, Blanes JG, et al. Natural history and familial characteristics of isolated left ventricular non-compaction. Eur Heart J 2005;26:187–92.
21. Aras D, Tufekcioglu O, Ergun K, et al. Clinical features of isolated ventricular noncompaction in adults long-term clinical course, echocardiographic properties, and predictors of left ventricular failure. J Card Fail 2006;12:726–33.
22. Gimeno JR, Lacunza J, García-Alberola A, et al. Penetrance and risk profile in inherited cardiac diseases studied in a dedicated screening clinic. Am J Cardiol 2009;104:406–10.
23. Digilio MC, Marino B, Bevilacqua M, et al. Genetic heterogeneity of isolated noncompaction of the left ventricular myocardium. Am J Med Genet 1999;85:90–1.
24. Towbin JA. Left ventricular noncompaction: a new form of heart failure. Heart Fail Clin 2010;6:453–69, viii.
25. Sasse-Klaassen S, Gerull B, Oechslin E, et al. Isolated noncompaction of the left ventricular myocardium in the adult is an autosomal dominant disorder in the majority of patients. Am J Med Genet A 2003;119A:162–7.
26. Towbin JA. Inherited cardiomyopathies. Circ J 2014;78:2347–56.
27. Wessels MW, Herkert JC, Frohn-Mulder IM, et al. Compound heterozygous or homozygous truncating MYBPC3 mutations cause lethal cardiomyopathy with features of noncompaction and septal defects. Eur J Hum Genet 2014. [Epub ahead of print].
28. Bagnall RD, Molloy LK, Kalman JM, et al. Exome sequencing identifies a mutation in the ACTN2 gene in a family with idiopathic ventricular fibrillation, left ventricular noncompaction, and sudden death. BMC Med Genet 2014;15:99.
29. Klaassen S, Probst S, Oechslin E, et al. Mutations in sarcomere protein genes in left ventricular noncompaction. Circulation 2008;117:2893–901.
30. Probst S, Oechslin E, Schuler P, et al. Sarcomere gene mutations in isolated left ventricular noncompaction cardiomyopathy do not predict clinical phenotype. Circ Cardiovasc Genet 2011;4:367–74.
31. Luedde M, Ehlermann P, Weichenhan D, et al. Severe familial left ventricular non-compaction cardiomyopathy due to a novel troponin T (TNNT2) mutation. Cardiovasc Res 2010;86:452–60.
32. Chang B, Nishizawa T, Furutani M, et al. Noncompaction study collaborators. Identification of a novel TPM1 mutation in a family with left ventricular noncompaction and sudden death. Mol Genet Metab 2011;102:200–6.
33. Teekakirikul P, Kelly MA, Rehm HL, et al. Inherited cardiomyopathies: molecular genetics and clinical genetic testing in the postgenomic era. J Mol Diagn 2013;15:158–70.
34. Shieh JT. Implications of genetic testing in noncompaction/hypertrabeculation. Am J Med Genet C Semin Med Genet 2013;163C:206–11.
35. Szentpáli Z, Szili-Torok T, Caliskan K. Primary electrical disorder or primary cardiomyopathy? A case with a unique association of noncompaction cardiomyopathy and cathecolaminergic polymorphic ventricular tachycardia caused by ryanodine receptor mutation. Circulation 2013;127:1165–6.
36. Nakashima K, Kusakawa I, Yamamoto T, et al. A left ventricular noncompaction in a patient with long QT syndrome caused by a KCNQ1 mutation: a case report. Heart Vessels 2013;28:126–9.
37. Ogawa K, Nakamura Y, Terano K, et al. Isolated noncompaction of the ventricular myocardium associated with long QT syndrome: a report of 2 cases. Circ J 2009;73:2169–72.
38. Shan L, Makita N, Xing Y, et al. SCN5A variants in Japanese patients with left ventricular noncompaction and arrhythmia. Mol Genet Metab 2008;93:468–74.

39. Steffel J, Kobza R, Oechslin E, et al. Electrocardiographic characteristics at initial diagnosis in patients with isolated left ventricular noncompaction. Am J Cardiol 2009;104:984–9.
40. Stöllberger C, Finsterer J. Arrhythmias and left ventricular hypertrabeculation/noncompaction. Curr Pharm Des 2010;16:2880–94.
41. Rigopoulos A, Rizos IK, Aggeli C, et al. Isolated left ventricular noncompaction: an unclassified cardiomyopathy with severe prognosis in adults. Cardiology 2002;98:25–32.
42. Fazio G, Corrado G, Zachara E, et al. Ventricular tachycardia in non-compaction of left ventricle: is this a frequent complication? Pacing Clin Electrophysiol 2007;30:544–6.
43. Bhatia NL, Tajik AJ, Wilansky S, et al. Isolated noncompaction of the left ventricular myocardium in adults: a systematic overview. J Card Fail 2011;17:771–8.
44. Güvenç TS, Ilhan E, Alper AT, et al. Exercise-induced right ventricular outflow tract tachycardia in a patient with isolated left ventricular noncompaction. ISRN Cardiol 2011;2011:729040–4.
45. Derval N, Jais P, O'Neill MD, et al. Apparent idiopathic ventricular tachycardia associated with isolated ventricular noncompaction. Heart Rhythm 2009;6:385–8.
46. Barra S, Moreno N, Providência R, et al. Incessant slow bundle branch reentrant ventricular tachycardia in a young patient with left ventricular noncompaction. Rev Port Cardiol 2013;32:523–9.
47. Santoro F, Manuppelli V, Brunetti ND. Multiple morphology ventricular tachycardia in noncompaction cardiomyopathy: multi-modal imaging. Europace 2013;15:304.
48. Serés L, Lopez J, Larrousse E, et al. Isolated noncompaction left ventricular myocardium and polymorphic ventricular tachycardia. Clin Cardiol 2003;26:46–8.
49. Junga G, Kneifel S, Smekal Von A, et al. Myocardial ischaemia in children with isolated ventricular noncompaction. Eur Heart J 1999;20:910–6.
50. Stöllberger C, Blazek G, Winkler-Dworak M, et al. Atrial fibrillation in left ventricular noncompaction with and without neuromuscular disorders is associated with a poor prognosis. Int J Cardiol 2009;133:41–5.
51. Ivan D, Flamm SD, Abrams J, et al. Isolated ventricular non-compaction in adults with idiopathic cardiomyopathy: cardiac magnetic resonance and pathologic characterization of the anomaly. J Heart Lung Transplant 2005;24:781–6.
52. Stöllberger C, Blazek G, Wegner C, et al. Heart failure, atrial fibrillation and neuromuscular disorders influence mortality in left ventricular hypertrabeculation/noncompaction. Cardiology 2011;119:176–82.
53. Yasukawa K, Terai M, Honda A, et al. Isolated noncompaction of ventricular myocardium associated with fatal ventricular fibrillation. Pediatr Cardiol 2001;22:512–4.
54. Fichet J, Legras A, Bernard A, et al. Aborted sudden cardiac death revealing isolated noncompaction of the left ventricle in a patient with Wolff-Parkinson-White syndrome. Pacing Clin Electrophysiol 2007;30:444–7.
55. Nihei K, Shinomiya N, Kabayama H, et al. Wolff-Parkinson-White (WPW) syndrome in isolated noncompaction of the ventricular myocardium (INVM). Circ J 2004;68:82–4.
56. Steffel J, Kobza R, Namdar M, et al. Electrophysiological findings in patients with isolated left ventricular non-compaction. Europace 2009;11:1193–200.
57. Seethala S, Knollman F, McNamara D, et al. Exercise-induced atrial and ventricular tachycardias in a patient with left ventricular noncompaction and normal ejection fraction. Pacing Clin Electrophysiol 2011;34:e94–7.
58. Coppola G, Guttilla D, Corrado E, et al. ICD implantation in noncompaction of the left ventricular myocardium: a case report. Pacing Clin Electrophysiol 2009;32:1092–5.
59. Nucifora G, Aquaro GD, Pingitore A, et al. Myocardial fibrosis in isolated left ventricular noncompaction and its relation to disease severity. Eur J Heart Fail 2011;13(2):170–6.
60. Kato Y, Horigome H, Takahashi-Igari M, et al. Isolation of pulmonary vein and superior vena cava for paroxysmal atrial fibrillation in a young adult with left ventricular non-compaction. Europace 2010;12:1040–1.
61. Celiker A, Ozkutlu S, Dilber E, et al. Rhythm abnormalities in children with isolated ventricular noncompaction. Pacing Clin Electrophysiol 2005;28:1198–202.
62. Fiala M, Januska J, Bulková V, et al. Septal ventricular tachycardia with alternating LBBB-RBBB morphology in isolated ventricular noncompaction. J Cardiovasc Electrophysiol 2010;21:704–7.
63. Lim HE, Pak HN, Shim WJ, et al. Epicardial ablation of ventricular tachycardia associated with isolated ventricular noncompaction. Pacing Clin Electrophysiol 2006;29:797–9.
64. Chinushi M, Iijima K, Furushima H, et al. Suppression of storms of ventricular tachycardia by epicardial ablation of isolated delayed potential in noncompaction cardiomyopathy. Pacing Clin Electrophysiol 2013;36:e115–9.
65. Kobza R, Steffel J, Erne P, et al. Implantable cardioverter-defibrillator and cardiac resynchronization therapy in patients with left ventricular noncompaction. Heart Rhythm 2010;7:1545–9.
66. Caliskan K, Szili-Torok T, Theuns DA, et al. Indications and outcome of implantable cardioverter-defibrillators

for primary and secondary prophylaxis in patients with noncompaction cardiomyopathy. J Cardiovasc Electrophysiol 2011;22:898–904.
67. Amadieu R, Acar P, Séguéla PE. Implantable cardioverter defibrillator in a young child with left ventricular noncompaction. Arch Cardiovasc Dis 2011;104:417–8.
68. Celiker A, Kafali G, Doğan R. Cardioverter defibrillator implantation in a child with isolated noncompaction of the ventricular myocardium and ventricular fibrillation. Pacing Clin Electrophysiol 2004;27:104–8.
69. Coleman MA, Bos JM, Johnson JN, et al. Videoscopic left cardiac sympathetic denervation for patients with recurrent ventricular fibrillation/malignant ventricular arrhythmia syndromes besides congenital long-QT syndrome. Circ Arrhythm Electrophysiol 2012;5:782–8.
70. Nascimento BR, Vidigal DF, De Carvalho Bicalho Carneiro R, et al. Complete atrioventricular block as the first manifestation of noncompaction of the ventricular myocardium. Pacing Clin Electrophysiol 2013;36:e107–10.
71. Okubo K, Sato Y, Matsumoto N, et al. Cardiac resynchronization and cardioverter defibrillation therapy in a patient with isolated noncompaction of the ventricular myocardium. Int J Cardiol 2009;136:e66–8.
72. Kobza R, Jenni R, Erne P, et al. Implantable cardioverter-defibrillators in patients with left ventricular noncompaction. Pacing Clin Electrophysiol 2008;31:461–7.
73. Kubota S, Nogami A, Sugiyasu A, et al. Cardiac resynchronization therapy in a patient with isolated noncompaction of the left ventricle and a narrow QRS complex. Heart Rhythm 2006;3:619–20.
74. van Dalen BM, Caliskan K, Soliman OI, et al. Left ventricular solid body rotation in non-compaction cardiomyopathy: a potential new objective and quantitative functional diagnostic criterion? Eur J Heart Fail 2008;10:1088–93.