Texas Heart Institute Journal

Case Series

Continuous Arrhythmia Monitoring in Pediatric and Adult Patients With Left Ventricular Noncompaction

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Patients with left ventricular noncompaction (LVNC) are at risk of clinically significant arrhythmias and sudden death. We evaluated whether implantable loop recorders could detect significant arrhythmias that might be missed in these patients during annual Holter monitoring.

Selected pediatric and adult patients with LVNC who consented to implantable loop recorder placement were monitored for 3 years (study duration, 10 April 2014–9 December 2019). Fourteen subjects were included (age range, 6.5–36.4 yr; 8 males). Of 13 patients who remained after one device extrusion, one underwent implantable cardioverter-defibrillator placement. Four patients (31%) had significant arrhythmias: atrial tachycardia (n=2), nonsustained ventricular tachycardia (n=1), and atrial fibrillation (n=1). All 4 events were clinically asymptomatic and not associated with left ventricular ejection fraction. In addition, a high frequency of benign arrhythmic patterns was detected.

Implantable loop recorders enable continuous, long-term detection of important subclinical arrhythmias in selected patients who have LVNC. These devices may prove to be most valuable in patients who have LVNC and moderate or greater ventricular dysfunction.
(Tex Heart Inst J 2022;49(2):e207497)

Citation:
Jefferies JL, Spar DS, Chaouki AS, Khoury PR, Casson P, Czosek RJ. Continuous arrhythmia monitoring in pediatric and adult patients with left ventricular noncompaction. Tex Heart Inst J 2022;49(2):e207497. doi: 10.14503/THIJ-20-7497

Key words:
Arrhythmias, cardiac/diagnosis/prevention & control/therapy; cardiomyopathies/pathology; electrocardiography, ambulatory; electrophysiologic techniques, cardiac/methods; heart function tests; isolated noncompaction of the ventricular myocardium/complications; monitoring, physiologic/methods; risk assessment/methods

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Left ventricular noncompaction (LVNC), a primary myocardial disease with no sex or age predilection, is increasingly diagnosed in asymptomatic patients as well in those with associated heart failure.[1] It occurs in isolation or in association with other cardiomyopathies and is characterized by dilated, hypertrophic, restrictive, or mixed dilated-hypertrophic type.[2] Left ventricular noncompaction is associated with increased morbidity and mortality, particularly in the presence of myocardial dysfunction or arrhythmias.[3-5] Specifically, ventricular arrhythmias in patients with LVNC have been associated with an elevated risk of poor outcome,[6] including sudden cardiac death (SCD) or the need for cardiac transplantation.[4] To date, no recommendations have been proposed in terms of the best and most cost-effective means of arrhythmia screening.[3-7] Typically, arrhythmias in this population are detected once yearly with use of 24-hour Holter monitoring; however, no active monitoring occurs otherwise. We decided to study whether implantable loop recorders (ILRs) would effectively identify high-risk patients who have underlying subclinical arrhythmias, and whether ILR use would optimize long-term patient care by enabling consideration of implantable cardioverter-defibrillator (ICD) placement, electrophysiologic studies, or antiarrhythmic therapy.

Patients and Methods

This descriptive, single-center case series study (duration, 10 April 2014–9 December 2019) was approved by the institutional review board of Cincinnati Children's Hospital Medical Center.

Patients included in our study had a confirmed diagnosis of LVNC in accordance with accepted echocardiographic or cardiac magnetic resonance (CMR) criteria. All had undergone routine Holter monitoring every 6 to 12 months in our cardiology clinic. Written informed consent for Reveal LINQ (Medtronic) ILR placement and prospective collection of transmission data was obtained for each patient.

We excluded patients who had histories of arrhythmia determined by means of abnormal Holter, electrocardiographic (ECG), event monitoring, or exercise test results, or if they had clinical symptoms concerning for arrhythmia. We defined depressed systolic function as an LV ejection fraction (LVEF) <55%, in accordance with American Society of Echocardiography guidelines. Baseline patient data included demographic details, cardiac history, and current medications. Baseline results from CMR, ECG, echocardiography, and exercise tests were obtained as part of routine care before ILR placement.

Cardiac genetic test results were obtained in accordance with routine practice and for familial cascade screening. We defined a pathogenic mutation as a sufficiently evident disease-causing DNA alteration, and a variant of unknown significance (VUS) as a DNA alteration with limited or conflicting evidence as to pathogenicity.

The ILR settings were programmed for detection as follows: atrial tachycardia (AT) and atrial fibrillation (AF), on; tachycardia, >207 beats/min for 5 beats; bradycardia, <30 beats/min for 4 beats; and asystole, <20 beats/min. In addition to routine data collection every 3 months, data were collected off-cycle for patient-activated transmissions and device-activated transmissions caused by automatically detected episodes. We defined significant findings as AT, AF, atrial flutter, supraventricular tachycardia, sustained ventricular tachycardia, and nonsustained ventricular tachycardia (NSVT). For all arrhythmia types, we defined sustained arrhythmia as lasting ≥30 seconds, and nonsustained as lasting >3 beats but <30 seconds. Every 6 to 12 months after ILR placement, patients underwent routine clinical examination, transthoracic echocardiography, and ECG. Additional visits were scheduled on the basis of ILR findings or reported symptoms. Consequent changes to patient care included medication initiation or adjustment, and new recommendations for ICD or pacemaker placement.

The patient population was small, so we performed no statistical comparisons. Quantitative data are presented as median and interquartile range; and qualitative data, as number and percentage.

Results

Fourteen patients (age range, 6.5–36.5 yr; 8 males) from 13 families were enrolled (Table I). Five (36%) had LV systolic dysfunction. Seven patients (50%) were taking angiotensin-converting enzyme inhibitors. Of 9 patients (64%) who underwent genetic testing, 2 (22%) had a pathogenic mutation, and 3 (33%) had a VUS.

TABLE I. Baseline Characteristics of Each Patient and Change in Care During Treatment

Pt. No.	Age (yr), Sex	LVEF at ILR Placement (%)	ACEI	Diuretic	β-Blocker	Aspirin	Significant ILR Finding	Change in Care
1	33.9, M	40	Yes	No	Yes	Yes	NSVT	ICD placed at 480 d
2	6.5, M	25	Yes	Yes	Yes	Yes	None	Extruded device removed at 122 d
3	36.4, F	61	No	Yes	Yes	No	None	None
4	16.1, F	55	No	No	No	No	AT	None
5	10.3, F	56	No	No	No	No	None	None
6	7.9, F	58	Yes	No	Yes	Yes	AF	Oral anticoagulation
7	17.2, M	55	No	No	Yes	Yes	None	None
8	16.2, M	53	Yes	No	Yes	No	AT	Medication change and compliance
9	17.9, M	56	Yes	No	Yes	Yes	None	None
10	12.6, M	55	No	No	No	No	None	None
11	16.8, F	46	Yes	No	No	No	None	None
12	17.1, M	44	Yes	No	Yes	No	None	None
13	13.2, M	69	No	No	No	No	None	None
14	22.9, F	60	No	No	Yes	Yes	None	None

ACEI = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; AT = atrial tachycardia; F = female; ICD = implantable cardioverter-defibrillator; ILR = implantable loop recorder; LVEF = left ventricular ejection fraction; M = male; NSVT = nonsustained ventricular tachycardia; Pt. = patient

Three families declined testing; in the remaining 2, other family members with LVNC had negative genetic results.

In the youngest patient, device extrusion of unknown cause was noted 122 days after implantation, and the ILR was not replaced.[8] Of the remaining 13 patients, 12 (92%) completed 3 years of ILR monitoring, and one had the ILR replaced with an ICD 480 days after ILR placement.

Four patients (31%) had significant arrhythmias: 2 teenagers had AT, an adult had NSVT, and a child had AF. All were clinically asymptomatic. One patient with AT had frequent episodes of atrial ectopy consisting of atrial couplets and a single instance of nonsustained AT episodes lasting 3 to 4 beats; the second patient had a self-terminating episode of sustained AT (duration, 56 sec; rate, 215 beats/min). The patient with ventricular ectopy had 3 asymptomatic episodes of NSVT (Fig. 1), one lasting for 6 beats and 2 lasting for 19 beats each (maximum rate, 207 beats/min).

Three of these 4 patients underwent changes in care. The adult had an ICD placed and had no ventricular arrhythmias for 15 months thereafter, the child was prescribed oral anticoagulation, and one teenager who had not taken prescribed antiarrhythmic medication for several weeks was restarted on a higher dose with compliance monitoring. The other teenager needed no intervention and had no further notable arrhythmias.

Our important findings were all documented during the first 12 months after ILR placement in the 13 patients who completed ILR monitoring (Table II). The mean time to ILR-detected events was 286 ± 29 days (Fig. 2).

Of 297 device transmissions, 233 events (78%) were recorded routinely. In 111 transmissions (37%), an

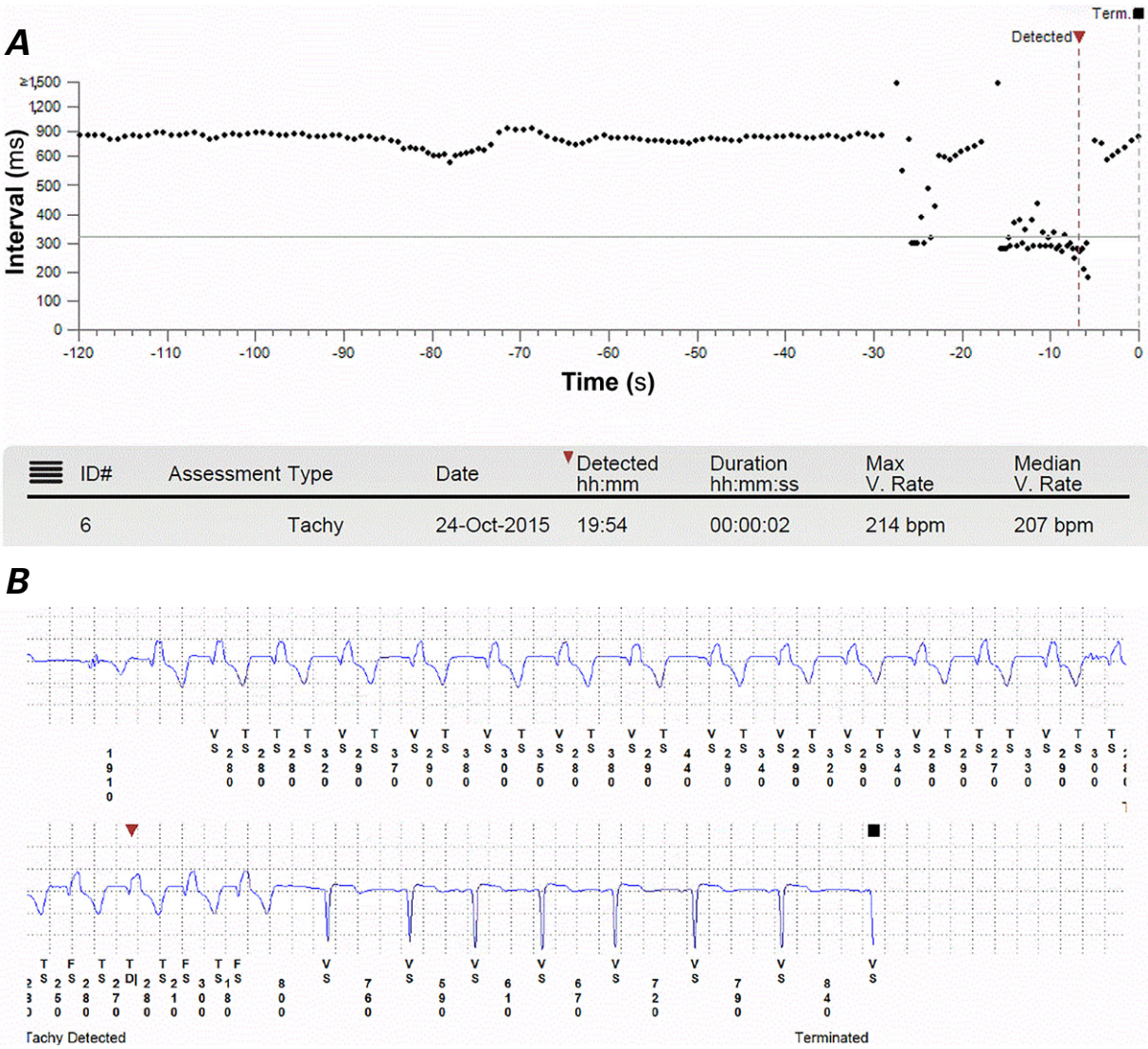

Fig. 1 *Patient 6.* ***A****) Loop recorder histogram shows asymptomatic ventricular arrhythmia.* ***B****) Loop recorder electrograms show an episode of nonsustained ventricular tachycardia.*

bpm = beats per minute; Tachy = tachycardia; Term. = termination; V. = ventricular

TABLE II. Demographic Data and Clinical Findings

Variable	All Patients (N=13)*	Significant ILR Finding (n=4)	No Significant ILR Finding (n=9)
Patient Demographics			
Age (yr)	168 (13.1–17.9)	17.1 (13.2–17.9)	16.2 (12–25.1)
Female	6 (46)	2 (50)	4 (44)
Race**			
Black	2 (15)	0	2 (22)
White	11 (85)	4 (100)	7 (78)
Medication use	10 (77)	3 (75)	7 (78)
Baseline Data			
Echocardiographic			
LVEF (%)	55 (50–57)	54 (47–57)	56 (51–58)
LV septal thickness (mm)	7.3 (5.7–7.9)	6.7 (5.2–7.9)	7.3 (6.2–7.9)
LV diastolic dimension (cm)	5.0 (4.4–5.6)	5.0 (4.1–5.9)	5.0 (4.6–5.6)
Electrocardiographic			
Heart rate (beats/min)	63 (55–68)	65 (57–68)	63 (55–68)
PR interval (ms)	136 (127–149)	135 (127–139)	141 (127–160)
QRS duration (ms)	96 (89–98)	94 (89–101)	96 (88–98)
QTc interval (ms)	411 (400–432)	423 (411–458)	404 (394–428)
12-Month Follow-Up Data			
Echocardiographic			
LVEF (%)	57 (50–59)	50 (40–54)	59 (55–60)
LV septal thickness (mm)	7.7 (7.3–8.4)	7.3 (6.3–9.9)	7.7 (7.3–8.4)
LV diastolic dimension (cm)	5.1 (4.4–5.8)	5.6 (4.2–6.1)	5.1 (4.4–5.9)
Electrocardiographic			
Heart rate (beats/min)	63 (55–71)	70 (60–71)	61 (55–71)
PR interval (ms)	138 (128–154)	138 (124–144)	138 (128–162)
QRS duration (ms)	96 (88–102)	100 (86–102)	92 (90–102)
QTc (ms)	418 (394–435)	432 (432–462)	399 (394–424)

ILR = implantable loop recorder; LV = left ventricular; LVEF = left ventricular ejection fraction; QTc = corrected QT interval

*Data for the patient with early device extrusion are not included.

**Of 2 patients who were of Hispanic ethnicity, one had a significant ILR finding.

Data are presented as median and interquartile range or as number and percentage.

arrhythmia was noted, most often isolated premature atrial contractions (PACs) (Table III). Of the 64 nonroutine transmissions, 3 (5%) were triggered by symptomatic patients, 2 consequent to palpitations and 1 to syncope. The transmissions resulting in changes to patient care were automatically triggered and not associated with symptoms.

Discussion

Most patients with LVNC tend to do well clinically and remain free of significant arrhythmias; however, some are at risk of malignant arrhythmias and SCD.[1] Our continuous ILR monitoring revealed a relatively high frequency of benign patterns, such as PACs and premature ventricular contractions (PVCs), along with the malignant patterns.

In our 13 pediatric and adult patients with LVNC, 4 previously asymptomatic patients with no arrhythmia history (31%) had clinically relevant arrhythmic events during continuous ILR monitoring, and 3 of the 4 underwent changes in care. Ventricular arrhythmias have been detected in patients with LVNC (up to a 17% prevalence), as has an association between SCD and arrhythmias, particularly ventricular.[5,6] Early detection may aid early intervention. Although atrial arrhythmias

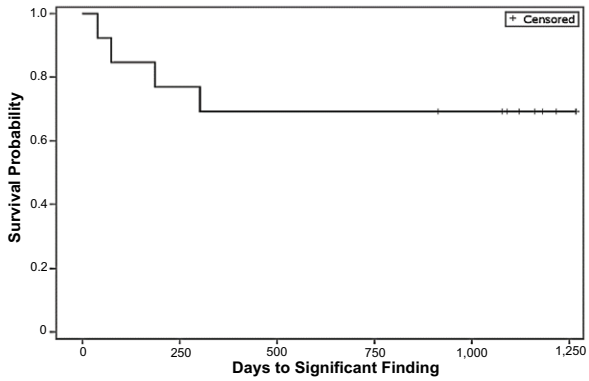

Fig. 2 *Graph of loop recorder data in patients with left ventricular noncompaction shows freedom from significant arrhythmia.*

TABLE III. Findings in 297 Implantable Loop Recorder Transmissions

Finding*	Value
Premature atrial contractions	63 (21)
Atrial tachycardia	6 (2)
Atrial fibrillation	1 (0.3)
Premature ventricular contractions	27 (9)
Nonsustained ventricular tachycardia	1 (0.3)
Bradycardia	2 (0.7)
Other	11 (4)

*Of 297 device transmissions, 111 (37%) revealed an arrhythmia.

Data are presented as number and percentage.

have not been directly associated with SCD, patients with a hypertrabeculated LV have a higher risk of clots and stroke.[9] Of note, our identifying AF in a patient <10 years old prompted anticoagulation therapy. Atrial fibrillation, atypical in a child, may not often be considered as a diagnosis in pediatric cardiology clinics. In that AF increases risks of cryptogenic stroke in adults, our finding may expand insights into thromboembolic mechanisms in children who have LVNC.[10]

Ventricular events are typically associated with poor systolic dysfunction, such as the NSVT in our patient whose LVEF was 40%. In contrast, half of our clinically important findings were in patients who had normal ventricular function, warranting further study in larger populations.

Although ILRs detect various arrhythmic events, the clinical implications of the findings are undetermined; for example, the patient upgraded to an ICD had no device interventions for malignant arrhythmia thereafter. Clinical significance is particularly important, because ILRs cost more than Holter monitoring. In addition, ILR transmissions increase the processing time spent by providers and the uncertainty experienced by families while arrhythmias (often ultimately benign) are analyzed. Similar to data from intermittent Holter monitoring, our patients' ILRs transmitted numerous PACs and PVCs, generally benign patterns that nevertheless warrant reports and analysis.[11] More than one-third of our patients had transmissions of benign arrhythmias. Regardless, findings of frequent PVCs may indicate necessary therapy.[12] Furthermore, few data exist to define risk factors for morbidity and death in patients with LVNC, and ILR findings may further inform long-term management of the LVNC phenotype.[13,14]

None of our patients' significant arrhythmias was associated with symptoms. This factor is important in the clinical management of cardiomyopathy. If arrhythmia detection over time relies purely on symptoms and annual Holter results, the opportunity for meaningful intervention may be limited. Similarly, the one syncopal episode in our study was not associated with clinical arrhythmia, and this knowledge obviated the need to consider primary prevention.

The long-term benefit of interventions for asymptomatic arrhythmias in the LVNC population is uncertain. Given considerations of cost and outcome improvement, the best use of ILR monitoring may be in patients who are at greatest risk of malignant outcomes. The most benefit might be seen in patients with LVNC and at least moderate systolic dysfunction, ventricular dilation, high-risk age factors, associated genetic factors, and relevant family medical histories.[9] Given our relatively frequent arrhythmia findings, a larger patient population should be randomized to ILR or intermittent Holter monitoring.

Study Limitations

This study was limited by small cohort size, wide age range, and no control arm to determine whether interventions changed patient outcomes. Furthermore, ILRs provide less detailed arrhythmia data than do 24-hour Holter monitors—the latter capture data for each heartbeat, whereas ILRs record data only on the basis of device settings or a patient-activated symptomatic episode. An ILR does not provide counts for PACs or PVCs, arrhythmias which may or may not be of clinical interest. The impact of these differences could not be determined.

Conclusion

In comparison with annual Holter monitoring, ILRs enable the continuous detection of subclinical but potentially important arrhythmias in selected patients with LVNC. By detecting arrhythmias that may prompt changes in care, ILRs may be valuable in the long-term monitoring of patients who have LVNC and

moderate or severe ventricular dysfunction. Larger prospective studies are warranted.

Acknowledgment

We thank the Heart Institute Research Core, Cincinnati Children's Hospital, for providing research infrastructure support for this trial.

Published: 8 April 2022

Conflict of interest disclosure: This study was supported by grant funding from Medtronic.

References

1. Towbin JA, Lorts A, Jefferies JL. Left ventricular noncompaction cardiomyopathy. Lancet 2015;386(9995):813-25.
2. Jefferies JL, Wilkinson JD, Sleeper LA, Colan SD, Lu M, Pahl E, et al. Cardiomyopathy phenotypes and outcomes for children with left ventricular myocardial noncompaction: results from the Pediatric Cardiomyopathy Registry. J Card Fail 2015;21(11):877-84.
3. Celiker A, Ozkutlu S, Dilber E, Karagoz T. Rhythm abnormalities in children with isolated ventricular noncompaction. Pacing Clin Electrophysiol 2005;28(11):1198-202.
4. Miyake CY, Kim JJ. Arrhythmias in left ventricular noncompaction. Card Electrophysiol Clin 2015;7(2):319-30.
5. Brescia ST, Rossano JW, Pignatelli R, Jefferies JL, Price JF, Decker JA, et al. Mortality and sudden death in pediatric left ventricular noncompaction in a tertiary referral center. Circulation 2013;127(22):2202-8.
6. Greutmann M, Mah ML, Silversides CK, Klaassen S, Attenhofer Jost CH, Jenni R, Oechslin EN. Predictors of adverse outcome in adolescents and adults with isolated left ventricular noncompaction. Am J Cardiol 2012;109(2):276-81.
7. Stollberger C, Keller H, Steger C, Finsterer J. Implantable loop-recorders in myopathic and non-myopathic patients with left ventricular hypertrabeculation/noncompaction. Int J Cardiol 2013;163(2):146-8.
8. Chaouki AS, Czosek RJ, Spar DS. Missing LINQ: extrusion of a new-generation implantable loop recorder in a child. Cardiol Young 2016;26(7):1445-7.
9. Aung N, Doimo S, Ricci F, Sanghvi MM, Pedrosa C, Woodbridge SP, et al. Prognostic significance of left ventricular noncompaction: systematic review and meta-analysis of observational studies. Circ Cardiovasc Imaging 2020;13(1):e009712.
10. Sanna T, Diener HC, Passman RS, Di Lazzaro V, Bernstein RA, Morillo CA, et al. Cryptogenic stroke and underlying atrial fibrillation. N Engl J Med 2014;370(26):2478-86.
11. Czosek RJ, Spar DS, Khoury PR, Anderson JB, Wilmot I, Knilans TK, et al. Outcomes, arrhythmic burden and ambulatory monitoring of pediatric patients with left ventricular non-compaction and preserved left ventricular function. Am J Cardiol 2015;115(7):962-6.
12. Muser D, Liang JJ, Witschey WR, Pathak RK, Castro S, Magnani S, et al. Ventricular arrhythmias associated with left ventricular noncompaction: electrophysiologic characteristics, mapping, and ablation. Heart Rhythm 2017;14(2):166-75.
13. Jenni R, Oechslin E, Schneider J, Attenhofer Jost C, Kaufmann PA. Echocardiographic and pathoanatomical characteristics of isolated left ventricular non-compaction: a step towards classification as a distinct cardiomyopathy. Heart 2001;86(6):666-71.
14. Petersen SE, Selvanayagam JB, Wiesmann F, Robson MD, Francis JM, Anderson RH, et al. Left ventricular non-compaction: insights from cardiovascular magnetic resonance imaging. J Am Coll Cardiol 2005;46(1):101-5.