Original Article

Clinical and Echocardiography Features of Diagnosed in Adulthood Isolated Left Ventricular Noncompaction: A Case Series Study

CME Credits

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Abstract

Background: Left ventricular noncompaction cardiomyopathy (LVNC) is a primary genetic cardiomyopathy with morphologically unique characteristics, including loose "spongy" meshwork. Subjects carrying these disorders were typically presented with triad of heart failure, cardiac arrhythmias, and consequences of mural thrombi formation. The clinical and echocardiographic features regarding LVNC, however, are not widely known. **Methods:** A retrospective survey involving 11 patients who fulfilled echocardiographic criteria for LVNC defined by Jenni *et al*. was conducted at MacKay Memorial Hospital from January 2009 to March 2017. Parameters assessed by echocardiography and clinical data were further analyzed. **Results:** Significantly depressed left ventricular systolic function assessed by echocardiography was noticed in a majority of our adult study cases. **Conclusion:** Considering the fatal complications LVNC may lead to, it is essential for clinical cardiologists to early identify suspicious individuals, and the establishment of definitive criteria and early treatment is essential.

Keywords: Cardiomyopathy, echocardiography, heart failure, isolated left ventricular noncompaction

Introduction

Left ventricular noncompaction cardiomyopathy (LVNC) is a rare congenital disorder involving the arrest of myocardial compaction during the phase of fetal development. LVNC is typically featured by thickened and prominent trabeculations of myocardium, which is structurally comprised by a thin compacted layer and a noncompacted layer with deep intertrabecular recesses that communicate between ventricular cavity, forming a unique morphological trait as a distinct disease entity. LVNC can be familial, and several genes have been found to be related to the development of LVNC.[1] As primarily genetic cardiomyopathy with heterogeneous traits, its diagnosis may be as early as in childhood in which population the outcomes may be better[1] or is associated with other coexisted congenital heart diseases. The term isolated left ventricular noncompaction (iLVNC) describes a specific clinical entity of isolated persistence of "sinusoids" and "spongy" form of myocardium without other concomitant structural anomalies.

While a series of research proposed that participants with iLVNC may experience poor prognosis with high clinical morbidity and mortality including heart failure, ventricular arrhythmia and thromboembolic events,[2] early recognition of such disease entity, and possible therapeutic management may be helpful and evolving. Thus, high clinical index of suspicion for this disease is necessary, especially in patients with early-onset heart failure when diagnosed in early adult life. Echocardiography is the key tool for diagnosis, while three-dimensional echocardiography and cardiac magnetic

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resonance (CMR) have been reported to be helpful to identify LVNC.[3] Herein, we reported clinical characters and echocardiographic features in 11 adult patients with iLVNC.

Patients and Methods

A retrospective survey was conducted at MacKay Memorial Hospital, currently a tertiary medical center located in Northern Taiwan, Taipei, during the observational study interval from January 2009 to March 2017. The study population comprised 11 adults diagnosed with fulfilled criteria of IVNC during the study observation period in their adult life. The definition employed in this study was based on echocardiographic criteria proposed by Jenni *et al*.:[4] in the absence of co-existing congenital cardiac abnormality, the ratio of noncompacted myocardial layer to compacted layer at the end of systole is over 2, in addition to the blood in intertrabecular communicating with intraventricular cavity to be shown on color Doppler imaging.

The echocardiography equipment used in this study was the GE system (Vivid i, Vingmed, Horten, Norway) equipped with 2–4-MHz transducer. Standard echocardiography imaging protocol included M-mode based measurement of LA diameter, LV end-diastolic and systolic diameter, wall thickness, and LV mass calculation (the American Society of Echocardiography criteria). Clinical data, including age distribution, gender, clinical symptoms, electrocardiograms (ECGs) findings, and echocardiography parameters were collected (IRB number: 17MMHIS145).

Results

Clinical data

The clinical information and echocardiographic parameters are summarized in Table 1 and Table 2. The age of study population mainly ranges from 40 to 60 years old (82%), and over 36% (4 out of 11) are in the New York Heart Association function Class III and higher. Eight reported patients (73%) were appearing symptoms of acute decompensated heart failure (exertional dyspnea) when being diagnosed with noncompaction cardiomyopathy. One patient (9%) presented with atypical chest tightness while the rest 2 (18%) were accidentally findings without specific cardiovascular-related symptoms. Except for two cases (case 4 and case 7) whose ECGs were normal, the remaining 9 cases' ECGs demonstrated abnormal findings: 2 cases (18%) showed sinus tachycardia; atrial fibrillation accounted for 2 study patients (18%); 2 cases (18%) had left bundle branch block; ST-T segment change was noticed in 3 cases; and premature ventricular contraction (PVC) was manifest in one case. Among the 11 study cases, 8 (73%) have undergone continuous ambulatory electrocardiography, all demonstrated PVC with one (9%) had recorded nonsustained ventricular tachycardia.

Echocardiographic data

The echocardiography demonstrated a dilated left ventricular internal diameter at end diastole in the majority of cases (all range: 52–73 mm), accompanied by impaired systolic function in terms of ejection fraction (all range: 16.1%–52.1%, 91% <50%) with only one patient within normal range. Among them, 5 patients (45%) were noticed to present with enlarged left atrium (range: 19–40 mm). Thickened interventricular septum (all range: 7–11 mm) and posterior wall (all range: 9–11 mm) were manifested in 55% ($n = 6$) and 64% ($n = 7$) of patients, respectively. Impaired diastolic dysfunction developed among all study patients with over a half (55%) who had Grade III or more severe diastolic dysfunctions and all cases presented with markedly lower myocardial relaxation velocity e'_{septal} (normal range: 6.1–11.4 cm/s)[5] and substantially elevated LV filling E/e'_{septum} (normal range: 5.5–14.3).[5] No ventricular thrombus was detected by transthoracic echocardiography in all cases. Of note, we observed a slightly higher prevalence of significant (defined as moderate-to-severe degree) valvular disorders (mainly aortic regurgitation), and higher averaged estimated systolic pulmonary artery pressure

Table 1: Baseline characteristics of 11 study participants in current case series

Case	Age of clinical diagnosis	Gender	NYHA class	Clinical presentations	ECG	Holter ECG	Chest plain film	Additional findings
1	49	Male	4	DOE	ST-T change		Cardiomegaly	
2	62	Male	3	DOE	AF	PVC	Cardiomegaly	
3	49	Male	3	DOE	ST-T change	PVC, VT	Cardiomegaly	
4	50	Male	2	DOE	NSR	PVC	Cardiomegaly	
5	58	Male	2	DOE	LBBB	PVC	Cardiomegaly	
6	59	Male	1		PVC	PVC	Cardiomegaly	
7	40	Female	2	DOE	NSR	-	Cardiomegaly	
8	66	Male	1		LBBB	PVC	Cardiomegaly	Penetrative atherosclerotic ulcers (thoracic aorta)
9	73	Male	2	Chest tightness	AF with RVR		Cardiomegaly	
10	25	Female	2	DOE Orthopnea	Sinus tachycardia	PVC		
11	46	Female	3	DOE	Sinus tachycardia ST-T change	PVC	Cardiomegaly	

DOE: Dyspnea on exertion, AF: Atrial fibrillation, RVR: Rapid ventricular response, PVC: Premature ventricular contraction, NSR: Normal sinus rhythm, LBBB: Left bundle branch block, ECG: Electrocardiograms, VT: Ventricular tachycardia, NYHA: New York Heart Association

(mean 44.9 mmHg), possibly reflecting chronicity of elevated LA pressure.

Discussion

The clinical manifestations of isolated left ventricular noncompaction

According to our data, although LVNC seems to be male predominant, there is a trend that female patients tend to become symptomatic in younger age. Patients with LVNC can have a variety of clinical manifestations. At the time of diagnosis, the majority of cases (73%) presented with overt symptoms of acute decompensated heart failure, while atypical or silent presentation also existed in our study. Meanwhile, 36% of study patients had heart failure of function Class III and Class IV. Our results are consistent with a 34-case research conducted by Oechslin *et al*.[2] with 27 patients (79%) presenting dyspnea and 12 (35%) in the New York Heart Association (NYHA) function Class III and worse. ECG findings are mostly abnormal with frequency of 73% in our cases, a bit lower than other similar study ranging from 88% to 94% to be found with abnormal ECG. Clinical characteristics of adult patients with LVNC from our data and another three studies are presented in Table 3. There were no specific ECG findings associated with LVNC except for PVC in the current case series, which appeared in all continuous ambulatory electrocardiography results.

Diagnostic imaging for isolated left ventricular noncompaction

The echocardiography findings were characterized by dilated diastolic diameter of LV, reduced ejection fraction, and diastolic dysfunction. Compromised LV systolic function appeared in all our study cases as initial presentation with 73% developed overt heart failure. With similar age group, a retrospective study involving 62 patients diagnosed with LVNC conducted by Stöllberger *et al*.[7] demonstrated similar results with 73% of study cases having congestive heart failure. Compared to the relatively lower proportion of heart failure in pediatric group, these results indicate a progressive nature and impact of LVNC on cardiac function: with morphological presentation of LVNC at birth, manifested as systolic and diastolic dysfunctions with increasing age, and eventually heart failure as a more prevalent phenotype in adult life.[8]

Table 2: Echocardiography features of 11 study participants in current case series

Case	LVIDd (mm)	Ejection fraction (%)	Left atrial size (mm)	Interventricular septum (mm)	Thickness of posterior wall (mm)	Left ventricular thrombi	LV e'$_{septal}$ (cm/s)	E/e'$_{septum}$ ratio by TDI	sPAP (mmHg)	Additional findings
1	58	45.1	38	16	14	-	6.2	17.3	60	TR, pleural effusion
2	53	19.9	25	15	13.5	-	3.52	20.5	44	AR
3	59	16.1	36	8.6	9.7	-	4.78	16.8	35	RVE
4	63	24.8	51	13	11	-	3.47	28.6	54	MR, TR, RVE
5	73	25.7	34	7	13.5	-	2.17	35.2	40	AR, QRS complex widening
6	56	34.9	46	8.5	7.3	-	7.54	12.3	54	MR, TR, RVE, PVC
7	53	52.1	44	15	13	-	3.7	16.7	48	AR
8	56	40.6	26	16	16	-	2.51	19.5	32	LBBB
9	59	27.6	40	13.5	14	-	3.9	20.1	40	N/A
10	52	29.8	45	11	11	-	6.85	14.3	45	MR
11	60	30.4	42	10	14	-	4.68	22.9	42	MR

LV: Left ventricular, LVIDd: Left ventricular internal diameter, TDI: Tissue Doppler imaging, sPAP: Systolic pulmonary arterial pressure, TR: Tricuspid regurgitation, AR: Aortic regurgitation, MR: Mitral regurgitation, RVE: Right ventricular enlargement, LBBB: Left bundle branch block, PVC: Premature ventricular contraction, N/A: Not available

Table 3: Adult patients with left ventricular noncompaction cardiomyopathy

	Ritter *et al*.[6]	Oechslin *et al*.[2]	Stöllberger *et al*.[7]	Present study (Huang *et al*.)
Patients (*n*)	17	34	62	11
Males (%)	82	74	70	73
Mean age at diagnosis	45	40	50	52
Age range (year)	18-71	16-71	18-75	25-73
Abnormal ECG (%)	88	94	92	73
Bundle branch block (%)	47	56	26	18
VT (%)	47	41	18	9
AF (%)	29	26	5	18
Left ventricular systolic dysfunction (%)	76	82	58	100
Congestive heart failure (%)	53	68	73	73

AF: Atrial fibrillation, VT: Ventricular tachycardia, ECGs: Electrocardiograms

Despite the fact that the gold standard for diagnostic criteria has not been established, echocardiography still plays a major role in diagnosis for LVNC. Several echocardiographic criteria have been proposed [Table 4]. In general, it requires two modes of echocardiographic images to make the diagnosis: two-dimensional echocardiography to detect the morphologic characteristics of "spongy", and prominent "non-compacted" myocardium [Figure 1], and color Doppler to prove the connection between ventricular cavity and deep recesses [Figure 2]. However, there are various limitations regarding morphological interpretation using echocardiography, including improper visualization of apex, which is where the most prominent trabecula are, and more importantly, difficulty in differentiating "hypertrabeculation" from trabeculae of aberrant bands, false tendons, abnormal insertion of papillary muscles, given their phenotypic overlapping. Therefore, supplemental use of cardiac MRI for those suspected diagnoses made by echocardiography is occasionally recommended.[10] The criteria for diagnosis by CMR are shown in table [Table 5]. Furthermore, despite the advanced quality of echocardiography equipment with more clear and better visualization of ventricular trabecula than before, the differentiation between normal and pathologic hypertrabeculation remain technically difficult. The current diagnostic criteria, no matter made by echocardiography or CMR, are simply morphological descriptions without functional assessment, making establishment of the diagnosis more uncertain and challenging, leading to potential misdiagnosis.[13] Thus, installation of an integrated clinical criterion for diagnosis is a critical mission in the future.

Clinical outcomes of isolated left ventricular noncompaction

The major complications of advanced LVNC include heart failure, ventricular arrhythmias and thromboembolic events. The mortality ranges from 7% to 47% among various research,[8] which overall, was shown without significantly different compared with nonischemic dilated cardiomyopathy.[14] Previous studies have discovered that, in adult group, poor prognosis is associated with more enlarged diastolic diameter of LV, decreased global ventricular ejection fraction, advanced heart failure (NYHA III–IV) at initial presentation, existence of persistent/permanent atrial fibrillation, and bundle branch block.[2] In spite of that, the consensus regarding the timing of the initiation of primary prevention (e.g., implantable cardioverter–defibrillator implantation) or assessment for transplant has yet to be determined.[1] In our current series, all our patients who undergone continuous ambulatory electrocardiography examination appeared to have PVCs, while none of them had previous ventricular arrhythmia history. It has been known that LVNC is associated with increasing incidence of ventricular arrhythmia and resulting sudden death; thus, annual check of atrial and ventricular arrhythmias by continuous ambulatory electrocardiography is essential.[1]

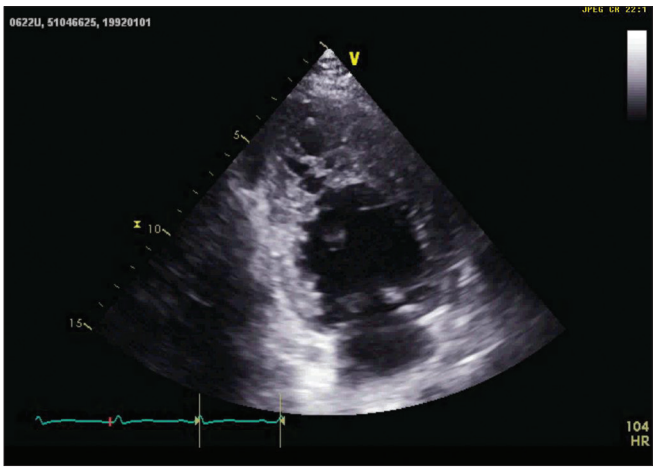


Figure 1: Echocardiography of a patient with isolated left ventricular noncompaction illustrating prominent trabeculations of myocardium involving apical and mid ventricular region on apical two chamber view

Table 4: Diagnostic criteria by echocardiography

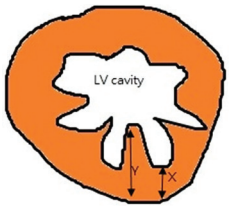
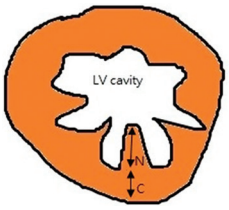
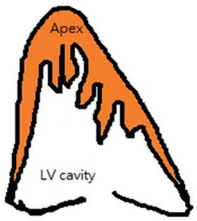
Chin *et al*.[9] A ratio of X/Y ≤0.5 defines LVNC, where X: Distance from epicardial surface to the trabecular recess Y: Distance from epicardial surface to the peak of trabeculation Applied to the trabeculae at the left ventricular apex on subxiphoid or apical four-chamber views at end-diastole	
Jenni *et al*.[4] (1) Thicken myocardium comprised by two layers, a thin compacted layer and a thick noncompacted layer; a ratio of N/C >2 at end-systole defines LVNC, where N: Noncompacted layer C: Compacted layer (2) Absence of coexisting cardiac structural abnormalities (3) Prominent trabeculae are mostly located on apex or midventricular segments of the inferior and lateral wall (4) Color Doppler confirms intraventricular blood supplies recesses	
Stöllberger *et al*.[7] (1) More than three trabeculations protruding from the wall of left ventricular, to papillary muscles at the apex, visualized in one image plane (2) Intertrabecular spaces, perfused from the ventricular cavity, viewed by color Doppler imaging	

Table 5: Diagnostic criteria by cardiac magnetic resonance

Petersen *et al*.[11]
A ratio of noncompacted myocardium to compacted myocardium >2.3 during the diastole defines LVNC
Jacquier *et al*.[12]
A trabeculated left ventricular mass >20% of total mass

LVNC: Left ventricular noncompaction cardiomyopathy

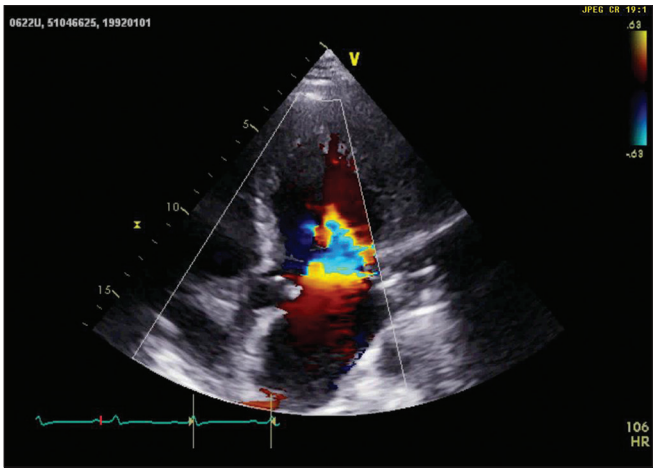


Figure 2: Color Doppler demonstrating blood flow directly connecting ventricular cavity and deep recesses in a patient with isolated left ventricular noncompaction

The application of anti-arrhythmia agents and prevention devises regarding lethal arrhythmias based on international guidelines is advised.

Systemic embolic events developed in around a quarter to one-third patients with LVNC.[8] It is believed to be related to reduced systolic function of LV and the thrombogenic feature of deep intertrabecular recesses. Whether anticoagulants should be administered to every LVNC patients is, however, still debated.[1] Our patients have not yet been found with any thromboembolic complications during follow-up period, and only 2 patients, who concurrently have persistent or permanent atrial fibrillation, are undergoing anticoagulation therapy. A long-term follow-up is needed to disclose the necessity of anticoagulation therapy.

Conclusion

LVNC is a distinct cardiomyopathy related to heart failure, ventricular arrhythmia, and thromboembolic events. Although various diagnostic tools, including echocardiography, three-dimensional echo, and CMR, have been utilized to identify LVNC, the definitive diagnostic criteria have yet to established. With poor prognosis, it is essential for clinical cardiologist to early detect this disease.

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Conflicts of interest

There are no conflicts of interest.

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