Evolution of Electrocardiographic Abnormalities in Association with Neuromuscular Disorders and Survival in Left Ventricular Hypertrabeculation/Noncompaction

Claudia Stöllberger, M.D.,* Daniel Gerger, M.D.,* Peter Jirak,*
Christian Wegner, Ph.D.,† and Josef Finsterer, M.D., Ph.D.*

From the *Hospital Rudolf Foundation, Vienna, and †Vienna Institute of Demography of the Austrian Academy of Sciences, Vienna, Austria

Background: Left ventricular hypertrabeculation/noncompaction (LVHT) is frequently associated with neuromuscular disorders (NMDs) and electrocardiographic (ECG) abnormalities. The prognostic relevance of newly developed ECG abnormalities in LVHT and its dependency on NMD is largely unknown. Aim of the following retrospective cohort study in LVHT patients was thus to assess the development of new ECG abnormalities and its dependency on NMD and survival

Methods: Included were patients in whom (a) LVHT was diagnosed between 1995 and 2011, (b) baseline ECG recordings (bECG), and (c) follow-up ECG recordings (fECG) were available. Survival status was assessed in June 2013.

Results: Included were 105 patients (mean age 55 years, 36 females, 67 with NMD). The interval between bECG and fECG was 3.6 years. ECG abnormalities increased in 46%, were unchanged in 44% and decreased in 11%. Increase was associated with age (59 years vs 49 years, $P = 0.0169$), exertional dyspnea (79% vs 53%, $P = 0.013$), heart failure (81% vs 47%, $P = 0.0149$), a left ventricular end-diastolic diameter $>57\text{mm}$ (76% vs 43%, $P = 0.004$) and a left ventricular fractional shortening $<25\%$ (68% vs 42%, $P = 0.0429$). New ECG abnormalities were ST–T wave abnormalities ($n = 35$), left anterior hemiblock ($n = 6$) and Q waves ($n = 6$). During 71 months, 40 patients died. Multivariate analysis identified age, male gender, “constant” (in bECG as well as fECG) atrial fibrillation, disappearance of atrial fibrillation, development as well as disappearance of low voltage ECG, increase of QRS width, constant QRS width $>120\text{ ms}$ and constant tall QRS complexes as predictors for mortality.

Conclusions: LVHT-patients develop frequently new ECG abnormalities of prognostic relevance.
Ann Noninvasive Electrocardiol 2014;19(6):567–573

cardiomyopathy; noncompaction; ECG; mortality; neuromuscular disorder; survival; prognosis;
cardiac conduction

Left ventricular hypertrabeculation/noncompaction (LVHT) is characterized by trabeculations in the inner core of the myocardium and a thinner than usual external compact myocardial layer. LVHT is frequently associated with neuromuscular disorders (NMDs), if patients are systematically screened.¹ Electrocardiographic (ECG) abnormalities including arrhythmias are frequent in LVHT-patients and comprise intraventricular conduction

delay, voltage signs of left ventricular hypertrophy, repolarization abnormalities, and atrial fibrillation.^{2–4} Quantitative ECG measures (QEMs) of repolarization in LVHT were found to be associated with heart failure and left ventricular dilatation.⁵ The prognostic relevance of newly developed ECG abnormalities and changes of QEMs in LVHT and its dependency on NMD is largely unknown. Thus, aim of the following

Address for correspondence: Claudia Stöllberger, M.D., Steingasse 31/18, A-1030 Wien, Österreich. Fax: +43 1 71165 2209; E-mail: claudia.stoellberger@chello.at

No financial support, no grants.

retrospective cohort study in LVHT patients was to assess the development of new ECG abnormalities and changes of QEMs over time and its dependency on NMD and survival.

METHODS

Included were patients in whom (a) LVHT was diagnosed between 1995 and 2011, (b) baseline ECG recordings (bECG), and (c) follow-up ECG recordings (fECG) were available. Two-dimensional and Doppler echocardiographic criteria for the diagnosis of LVHT were: >3 trabeculations protruding from the left ventricular wall, apically to the papillary muscles, visible in one echocardiographic image plane at end-diastole; trabeculations form the noncompacted part of a two-layered myocardial structure, best visible at end-systole; intertrabecular spaces perfused from the ventricular cavity, as visualized on color Doppler imaging. Trabeculations were defined as structures moving synchronously with the ventricular contractions, distinct from ventricular bands, false tendons and prominent papillary muscles. The diagnostic criteria remained the same during the study period. The location of LVHT was assessed and categorized as apical if it involved the left ventricular apex and as anterior, lateral or posterior, if it involved the anterior, lateral or posterior parts of the left ventricular wall.

All patients underwent a baseline cardiologic examination at which they were asked for their medical history and cardiovascular symptoms. A clinical examination was carried out and a 12-lead ECG was registered. All patients were invited for a neurological investigation comprising the history and a clinical neurological examination, and further instrumental investigations if a NMD was suspected. A NMD was diagnosed if clinical or instrumental findings indicated the presence of a NMD. NMDs were assessed as "specific" if a diagnosis could be established. Cases in which no specific diagnosis could be established were assessed as "NMD of unknown etiology."

Cardiologic and neurologic follow-up were carried out either by the referring physicians or the treating hospitals. In June 2013, the patients or their treating physicians were contacted by telephone by one of the authors (CS). It was assessed if the patient was alive or not. In June 2013 fECGs were searched from the patients'

data set and from the computer information system.

Presence or absence of ECG abnormalities were assessed according to predefined criteria.⁶ The following QEMs were measured: PR interval, QRS duration, and duration of the QT interval. QTc intervals were calculated according to Bazett's formula in patients with a heart rate of 60–100/min. In patients below and above that rate, Fredericia's formula was applied. The fECGs were assessed by two investigators (DG, PJ) who were unaware of the clinical course of the patients.

Equality of survivor functions was tested using the log-rank test. The multivariate analysis was done by applying Cox proportional hazard regression. All statistical analyses were performed by using the statistical software package R Version 2.15.3.⁷

RESULTS

Baseline Findings

Between 1995 and June 2011, LVHT was diagnosed in 172 patients.¹ In 105 of these patients (36 females, age range 13 to 93 years, mean age 55 years) baseline as well as follow-up ECG recordings were available, and these patients were included in the present study. In the remaining 67 patients, no fECGs were available due to technical or organizational reasons. Seventy-seven of the included 105 patients (73%) were investigated neurologically. A specific NMD was diagnosed in 14 of these 77 patients (18%): Metabolic myopathy $n = 8$; Leber's hereditary optic neuropathy $n = 1$; myotonic dystrophy $n = 2$; Becker muscular dystrophy $n = 1$; postpoliomyelitis syndrome $n = 1$; and Duchenne muscular dystrophy $n = 1$. A NMD of unknown etiology was diagnosed in 53 patients (69%), and the neurological investigation was normal in 10 (13%) patients. Baseline clinical, neurological, ECG, and echocardiographic findings of the 105 included patients are listed in Table 1.

ECG Changes and Baseline Findings

The mean duration between bECG and fECG was 3.6 years, ranging from 0 to 156 months. No change between bECG and fECG was found in 46 patients (34%). In 48 patients (46%), the number of ECG abnormalities increased and in 11 patients (11%) it decreased (Table 2). An increase in the

Table 1. Baseline Findings of 105 Patients with Left Ventricular Hypertrabeculation/Noncompaction in Whom Baseline and Follow-Up ECGs Were Available for Analysis

Characteristics	All (n = 105)	Survived (n = 65)	Died (n = 40)
Age, years (mean, $\pm$ SD)	55.0 (17)	51.6 (16)	60.6 (17)***
Age >55 years, n (%)	49 (47)	25 (39)	24 (60)***
Duration of follow-up, years (mean, $\pm$ SD)	5.9 (4.3)	6.8 (4.5)	4.3 (3.6)
Female, n (%)	36 (34)	27 (42)	9 (23)
Neurologically normal, n (%)	10 (10)	10 (15)	0 (0)**
Specific NMD, n (%)	14 (13)	7 (11)	7 (18)
NMD of unknown etiology, n (%)	53 (51)	27 (42)	26 (65)*
Neurologically not investigated, n (%)	28 (27)	21 (32)	7 (18)
Exertional dyspnea, n (%)	73 (70)	39 (60)	34 (85)*
Angina pectoris, n (%)	27 (26)	19 (29)	8 (20)
Edema, n (%)	33 (31)	13 (20)	20 (50)***
Palpitations/vertigo/syncope, n (%)	24 (23)	20 (31)	4 (10)
Diabetes mellitus, n (%)	24 (23)	9 (14)	15 (38)**
Arterial hypertension, n (%)	40 (38)	25 (39)	15 (38)
Heart failure, n (%)	77 (73)	40 (62)	37 (93)**
NYHA I, n (%)	7 (7)	7 (11)	0 (0)*
NYHA II, n (%)	15 (14)	10 (15)	5 (13)
NYHA III, n (%)	33 (31)	12 (19)	21 (53)***
NYHA IV, n (%)	22 (21)	11 (17)	11 (28)
ECG			
Tall QRS complex, n (%)	35 (33)	20 (31)	15 (38)
Pathological Q waves, n (%)	8 (8)	6 (9)	2 (5)
ST/T wave abnormality, n (%)	46 (43)	29 (45)	17 (43)
Left bundle branch block, n (%)	21 (20)	9 (14)	12 (30)
Atrial fibrillation, n (%)	18 (17)	5 (8)	13 (33)***
Left anterior hemiblock, n (%)	8 (8)	6 (9)	2 (5)
Right bundle branch block, n (%)	5 (5)	4 (6)	1 (3)
PQ > 200 ms ^a , n (%)	11 (11)	9 (14)	2 (5)
QRS > 120 ms, n (%)	20 (19)	9 (14)	11 (28)
QTc > 440 ms, n (%)	40 (38)	26 (40)	14 (35)
Echocardiography			
LV end-diastolic diameter, mm (mean, $\pm$ SD)	62 (13)	60 (14)	64 (11)
LV fractional shortening, % (mean, $\pm$ SD)	23 (10)	25 (10)	20 (9)*
Interventricular septum, mm (mean, $\pm$ SD)	12 (3)	12 (3)	13 (3)
LV posterior wall, mm (mean, $\pm$ SD)	13 (4)	12 (3)	13 (4)
Valvular abnormalities, n (%)	67 (64)	40 (62)	27 (69)
LVHT location: Apex, n (%)	97 (92)	59 (91)	38 (95)
Anterior wall, n (%)	3 (3)	2 (3)	1 (3)
Posterior wall, n (%)	18 (18)	8 (12)	10 (25)*
Lateral wall, n (%)	56 (53)	32 (49)	24 (60)*
LVHT-affected walls, (mean, $\pm$ SD)	1.7 (1)	1.6 (1)	1.9 (1)***

^an = 81, since the ECGs of 24 patients with atrial fibrillation were excluded.

LV, left ventricular; LVHT, left ventricular hypertrabeculation/noncompaction; NMD, neuromuscular disorder.

*P < 0.050.

**P < 0.010.

***P < 0.001.

number of ECG abnormalities was associated with a higher age at bECG (59 years vs 49 years, $P = 0.0169$), presence of exertional dyspnea (79% vs 53%, $P = 0.013$), heart failure (81% vs 47%, $P = 0.0149$), a left ventricular end-diastolic diameter >57mm (76% vs 43%, $P = 0.004$) and a left

ventricular fractional shortening <25% (68% vs 42%, $P = 0.0429$).

The most frequent new ECG abnormalities in fECGs were ST-T wave abnormalities ($n = 35$) followed by left anterior hemiblock ($n = 6$) and Q waves ($n = 6$). The most frequent ECG

Table 2. Change of ECG-Abnormalities and Mortality

ECG abnormality	Change of ECG Abnormality	Survived (n = 65)	%	Died (n = 40)	%
Tall QRS complex	no → no	43	(66)	23	(58)
	no → yes	2	(3)	2	(5)
	yes → yes	18	(28)	14	(35)
	yes → no	2	(3)	1	(3)
	no → no	15	(23)	9	(23)
ST-T wave abnormalities	no → yes	21	(32)	14	(35)
	yes → yes	28	(43)	14	(35)
	yes → no	1	(2)	3	(8)
	no → no	54	(83)	25	(63)
Left bundle branch block	no → yes	2	(3)	3	(8)
	yes → yes	9	(14)	12	(30)
	yes → no	—	—	—	—
	no → no	54	(83)	37	(93)
Pathological Q waves	no → yes	5	(8)	1	(3)
	yes → yes	6	(9)	1	(3)
	yes → no	0	0	1	(3)
	no → no	58	(89)	24	(60)***
Atrial fibrillation	no → yes	2	(3)	3	(8)
	yes → yes	3	(5)	9	(23)***
	yes → no	2	(3)	4	(10)*
	no → no	55	(85)	36	(90)
Left anterior hemiblock	no → yes	4	(6)	2	(5)
	yes → yes	3	(5)	1	(3)
	yes → no	3	(5)	1	(3)
	no → no	61	(94)	37	(93)
Right bundle branch block	no → yes	0	0	2	(5)
	yes → yes	3	(5)	1	(3)
	yes → no	1	(2)	0	0
	no → no	61	(94)	35	(88)
Low voltage	no → yes	0	0	3	(8)***
	yes → yes	3	(5)	1	(3)
	yes → no	1	(2)	1	(3)
	no → no	58	(89)	36	(90)
Sinustachycardia	no → yes	1	(2)	3	(8)
	yes → yes	1	(2)	1	(3)
	yes → no	5	(8)	0	0
	No change	32	(49)	14	(35)
Number of ECG abnormalities	Increased	27	(42)	21	(53)
	Decreased	6	(9)	5	(13)
	<200 → <200 ms	47	(83)	19	(79)
	<200 → >200 ms	1	(2)	3	(13)**
PQ interval	>200 → >200 ms	5	(9)	0	0
	>200 → <200 ms	4	(7)	2	(8)
	<120 → <120 ms	55	(85)	25	(63)
	<120 → >120 ms	1	(2)	4	(10)*
QRS width	>120 → >120 ms	6	(9)	6	(15)
	>120 → <120 ms	3	(5)	5	(13)
	<440 → <440 ms	31	(48)	18	(46)
	<440 → >440 ms	8	(12)	7	(18)
QTc duration	>440 → >440 ms	13	(20)	6	(15)
	>440 → <440 ms	13	(20)	8	(21)

*P < 0.050.

**P < 0.010.

***P < 0.001.

abnormalities which disappeared on fECG were atrial fibrillation ($n = 6$) and sinustachycardia ($n = 5$).

New ST-T wave abnormalities were found in the fECGs of 35 patients and were associated with increased age (59 years vs 46 years, $P = 0.027$), exertional dyspnea (80% vs 46%, $P = 0.066$), a left ventricular end-diastolic diameter >57 mm (83% vs 38%, $P = 0.004$), a left ventricular fractional shortening $<25\%$ (74% vs 21%, $P = 0.000$) and presence of valvular abnormalities (77% vs 38%, $P = 0.018$).

New atrial fibrillation was found in five patients and was associated with increased age (70 years vs 52 years, $P = 0.067$).

Changes in the PQ interval were found in 10 patients: in 4 patients the interval increased to >200 ms and in 6 patients it normalized from >200 ms to <200 ms. An increase in the PQ interval was associated with more segments affected by LVHT (2.8 segments vs 1.5 with no increase, $P = 0.004$).

Changes of QRS-width were found in 13 patients: in 5 patients the width increased to >120 ms and in 8 patients it normalized from >120 ms to <120 ms. An increase in the QRS width was associated with diabetes mellitus (80% vs 20%, $P = 0.060$) and number of segments affected by LVHT (2.4 segments vs 1.6 with no increase, $P = 0.091$). A new left bundle branch block was found in five patients in the fECGs and was associated with the number of segments affected by LVHT (2.6 segments vs 1.6 segments, $P = 0.007$). A new left anterior hemiblock was found in six patients and was associated with specific NMD (67% vs 11%, $P = 0.022$).

Changes in the QTc were found in 36 patients: in 15 patients the QTc increased to >440 ms and in 21 patients it normalized from >440 ms to <440 ms. An increase in the QTc was associated with NMD of unknown etiology (87% vs 43%, $P = 0.020$) and more segments affected by LVHT (2.2 segments vs 1.4 with no increase, $P = 0.001$).

ECG-Changes and Mortality

During a mean follow-up period of 71 (± 52) months, 40 patients died. Causes of death were heart failure ($n = 11$), pneumonia ($n = 7$), malignancy ($n = 5$), sudden death ($n = 4$), stroke ($n = 3$), sepsis ($n = 2$), hepatic failure ($n = 3$), pulmonary embolism ($n = 3$), and renal failure ($n = 2$). A comparison between the baseline

findings of the surviving and the deceased patients is listed in Table 1. Regarding changes between bECG and fECG, the following parameters were associated with mortality (Table 2) atrial fibrillation ($P = 0.0255$), development of low voltage ($P = 0.0078$), increase of the PQ interval >200 ms ($P = 0.0006$) and of the QRS width >120 ms (0.0307). When including age, gender, atrial fibrillation, low voltage, and QRS width in a multivariate model, the following parameters were predictors for mortality: age at baseline ($P = 0.0004$), male gender ($P = 0.0375$), atrial fibrillation in bECG as well as fECG ($P = 0.0147$), and development of low voltage ($P = 0.0013$). When adding tall QRS complexes, ST-T wave abnormalities, pathological Q waves and left anterior hemiblock to the model, the following parameters were significant for mortality: age at baseline ($P = 0.0002$), male gender ($P = 0.0349$), atrial fibrillation in bECG as well as fECG ($P = 0.0263$), disappearance of atrial fibrillation in fECG ($P = 0.0188$), development of low voltage ($P = 0.0011$), disappearance of low voltage in fECG ($P = 0.0336$), increase of QRS width from <120 ms to >120 ms ($P = 0.0056$), QRS width >120 ms in bECG as well as fECG ($P = 0.0184$) and tall QRS complexes in bECG as well as fECG ($P = 0.0126$).

DISCUSSION

Our study shows that in 46% of the LVHT patients new ECG abnormalities develop during a follow-up of 3.6 years. The most frequent new ECG abnormalities in fECGs were ST-T wave abnormalities, followed by left anterior hemiblock and Q waves, however, these abnormalities were not associated with mortality. ECG abnormalities, associated with mortality by univariate analysis were atrial fibrillation, development of low voltage ECG, increase of the PQ interval >200 ms and of the QRS width >120 ms. By multivariate analysis, age at baseline, male gender, "constant" (in bECG as well as fECG) atrial fibrillation, disappearance of atrial fibrillation, development as well as disappearance of low voltage ECG, increase of QRS width, constant QRS width >120 ms and constant tall QRS complexes were predictors for mortality. Surprisingly, neither QT prolongation nor QRS duration were predictors for mortality in LVHT patients neither by univariate nor by multivariate analysis. Patients with or without NMDs differed

only slightly regarding the development of new ECG abnormalities.

This study confirms previous findings showing that atrial fibrillation in LVHT is a frequent finding in up to 26% of patients and associated with a poor prognosis.^{1–8} In other cohorts of LVHT, atrial fibrillation had a lower prevalence of 4%–12%, and was not associated with a poor prognosis.^{3–10} Interestingly, not only atrial fibrillation at baseline but also disappearance of atrial fibrillation in fECG was associated with mortality. This might indicate that paroxysmal as well as chronic atrial fibrillation in LVHT patients is an indicator for increased mortality.

An increase in the PQ interval during follow-up was associated with mortality whereas an increased PQ interval at baseline was not. Whether prolongation of the PQ interval >200 ms, (first-degree AV block), is more frequent in patients with LVHT than without is unknown. In children with LVHT, a first-degree AV block was found in 4/46 of the cases.¹¹ In adults, a first-degree AV block was reported in a 61-year-old male with heart failure and myotonic dystrophy type 2,¹² and in a 34-year-old male with heart failure.¹³ In a series of 78 adult LVHT patients first-degree AV block was found in 15% and was associated with left ventricular dysfunction, left atrial enlargement and QRS-complex width >120 ms.² In a follow-up study from the same cohort, PQ duration in the baseline ECG was an independent predictor of a poor prognosis.³ Whether first-degree AV block in the general population is a nonrelevant finding or an indicator for increased cardiovascular risk is assessed controversially in the epidemiologic literature.^{14,15}

An increase in the QRS-width >120 ms during follow-up was associated with mortality. Changes in the depth distribution and/or extent of the Purkinje ventricular conduction network in patients with LVHT may lead to altered intraventricular conduction. Furthermore, the underlying cardiomyopathy might be responsible for changes in intraventricular conduction or repolarization. In a previous analysis of our LVHT patients, left bundle branch block has been identified by univariate analysis among others as a predictor for mortality, however, on multivariate analysis, significant predictors for mortality were heart failure, atrial fibrillation, and presence of NMDs.⁴

Although prolongation of the QT interval is not an arrhythmia per se, patients with prolonged QT

intervals are at risk for syncope due to torsade-de-pointes tachycardia and sudden cardiac death due to ventricular fibrillation. The prevalence of QT prolongation was investigated only in a series of 78 LVHT patients. Fifty-two percent had a prolonged QT interval, which was the second frequent ECG abnormality.² Whereas in that study, prolonged QTc was a predictor for mortality this was not the case in our study, which may be explained by different patient characteristics.³ Additionally, the QT interval as well as the ST–T waves are volatile and influenced by many factors, like vegetative tone, medication, and electrolyte status. Thus, changes in the QT interval and of the ST–T wave morphology were the most frequent changes found between bECG and fECG in our study.

Although not all LVHT patients in our study had dilated left ventricles and systolic dysfunction, there are several similarities in clinical presentation, prognosis and therapy between LVHT and idiopathic dilated cardiomyopathy (IDC). Data about the prognostic relevance of ECG changes during follow-up are conflicting: In a cohort of 539 patients with IDC from Italy, new onset of atrial fibrillation during 90 months was an indicator of poor survival.¹⁶ On the contrary, in a study from Germany of 480 patients with IDC, neither new left bundle branch block nor new onset of atrial fibrillation nor new ST/T depression were predictors of poor outcome during 47 months.¹⁷ Most probably, differences in the patient population and in the therapy may explain these controversial results. Due to the limited data it remains unclear whether ECG changes in LVHT patients are prognostically more relevant than in patients with IDC.

Limitations of the study are the low number of patients which make also the interpretation of the multivariate analysis difficult. Further limitations are that the cardiac medication at the time of the ECG registration was not assessed, that no specific diagnosis of a NMD could be established in every patient and that we did not evaluate the fragmentation of the QRS complex, which has been recently identified as a prognostic indicator in patients with LVHT.¹⁸

CONCLUSION

From our findings we conclude that LVHT patients develop frequently new ECG abnormalities

which might be of prognostic relevance. If LVHT is diagnosed, yearly ECG follow-up investigations are recommended to look especially for atrial fibrillation, for an increase in the duration of the PQ interval or the QRS width and low voltage ECG.

REFERENCES

1. Stöllberger C, Blazek G, Wegner C, et al. Neurological comorbidity affects prognosis in left ventricular hypertrabeculation/noncompaction. *Heart Lung* 2012;41:594–598.
2. Steffel J, Kobza R, Oechslin E, et al. Electrocardiographic characteristics at initial diagnosis in patients with isolated left ventricular noncompaction. *Am J Cardiol* 2009;104:984–989.
3. Steffel J, Hürlimann D, Namdar M, et al. Long-term follow-up of patients with isolated left ventricular noncompaction. Role of electrocardiography in predicting poor outcome. *Circ J* 2011;75:1728–1734.
4. Stöllberger C, Blazek G, Wegner C, et al. Heart failure, atrial fibrillation and neuromuscular disorders influence mortality in left ventricular hypertrabeculation/noncompaction. *Cardiology* 2011;119:176–182.
5. Stöllberger C, Gerger D, Wegner C, et al. Quantitative electrocardiographic measures, neuromuscular disorders, and survival in left ventricular hypertrabeculation/noncompaction. *Ann Noninvasive Electrocardiol* 2013;18:251–255.
6. Finsterer J, Stöllberger C, Köcher K, et al. ECG abnormalities in myopathies, coronary heart disease and controls. *Herz* 1997;22:277–282.
7. R Development Core Team, 2009:R: A language and environment for statistical computing. IN: R Foundation for Statistical Computing, Vienna [online]. Available at: <http://www.R-project.org>.
8. 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.
9. 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;12:726–733.
10. 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.
11. Tsai SF, Ebenroth ES, Hurwitz RA, et al. Is left ventricular noncompaction in children truly an isolated lesion? *Pediatr Cardiol* 2009;30:597–602.
12. Wahbi K, Meune C, Bassez G, et al. Left ventricular non-compaction in a patient with myotonic dystrophy type 2. *Neuromusc Dis* 2008;18:331–333.
13. Saraiva LR, Parente GB, Loureiro R, et al. Progression of ventricular repolarization in left bundle branch block in non-compaction of the myocardium. *Arq Bras Cardiol* 2006;87:e217–e218.
14. Cheng S, Keyes MJ, Larson MG, et al. Long-term outcomes in individuals with prolonged PR interval or first-degree atrioventricular block. *JAMA* 2009;301:2571–2577.
15. Aro AL, Anttonen O, Kerola T, et al. Prognostic significance of prolonged PR interval in the general population. *Eur Heart J* 2014;35:123–129.
16. Aleksova A, Merlo M, Zecchin M, et al. Impact of atrial fibrillation on outcome of patients with idiopathic dilated cardiomyopathy: data from the Heart Muscle Disease Registry of Trieste. *Clin Med Res* 2010;8:142–149.
17. Grünig E, Benz A, Mereles D, et al. Prognostic value of serial cardiac assessment and familial screening in patients with dilated cardiomyopathy. *Eur J Heart Fail* 2003;5:55–62.
18. Ning XH, Tang M, Chen KP, et al. The prognostic significance of fragmented QRS in patients with left ventricular noncompaction cardiomyopathy. *Can J Cardiol* 2012;28:508–514.