ORIGINAL MANUSCRIPT

Left Ventricular Noncompaction in Adulthood: Heart Failure Clinic Experience

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Abstract

Background: Left ventricular noncompaction (LVNC) is a distinct type of cardiomyopathy that presents several specific characteristics. The natural course of this condition is not totally known.
Objectives: To define the clinical characteristics, complications and survival of patients with LVNC assisted in heart failure (HF) healthcare service.
Methods: Retrospective study that included patients with LVNC treated in a HF healthcare service from Hospital São João, in Porto, Portugal, from January 2006 to February 2014. Demographic data, symptoms of heart failure and ejection fraction at the beginning of treatment, the course of LVNC (changes in functional class), side effects and survival were recorded from medical records.
Results: The study included 10 patients, 6 males, with a median of 63 years of age. Nine had symptoms of HF and started taking medication to modify prognosis. Everyone had left ventricular ejection fraction <45%. One patient did not start oral anticoagulation; 7 had some degree of recovery symptoms of HF; 3 were hospitalized with heart failure exacerbations; 1 had cardioembolic stroke; and 1 patient underwent heart transplant.
Conclusions: Patients with LVNC had similar comorbidities as the general population of their age group, except the apparent increase in the prevalence of AF. These patients responded well to therapy for IC with some clinical benefit. There were few complications, most remained clinically stable, without any hospitalization and low mortality rate. However, it is a small group of patients with short follow-up time.

Keywords: Heart failure, systolic; Heart failure; Isolated noncompaction of the ventricular myocardium

Introduction

Left ventricular noncompaction (LVNC) is a distinct type of non-classified cardiomyopathy[1-3] that features a number of specific echocardiographic features, such as thickening of both myocardial layers with prominent trabeculations[4]. It may occur in isolation or associated with several heart defects or neuromuscular diseases[5]. Normal myocardial compaction usually starts in the embryonic period (between six and eight weeks), continuing during the fetal period, between 12 and 18 weeks of gestation, developing from the epicardium to the endocardium and from the base to the apex of the heart[2]. Chin et al.[6] postulated that the interruption of the normal process of myocardial compaction during endomyocardial morphogenesis would be the pathophysiological basis of LVNC[6]. However, the possibility of the existence of acquired forms of LVNC[1] has been recently proposed.

The prevalence of this disease is still unknown, but it appears to be increasing, probably due to the advancement of echocardiography methods and devices and the growing interest of the health professionals in this pathology[7]. The prevalence of isolated LVNC was 3.0% in a clinical study conducted in a heart failure healthcare service[8].

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ABBREVIATIONS AND ACRONYMS

- *ACEI – angiotensin-converting enzyme inhibitor*
- *AF – atrial fibrillation*
- *BNP – brain natriuretic peptide*
- *HF – heart failure*
- *LVEF – left ventricular ejection fraction*
- *LVNC – left ventricular noncompaction*
- *NMR – nuclear magnetic resonance*
- *NYHA – New York Heart Association*

It is still not fully understood the fact that there is a wide spectrum of manifestations of the disease, with distinct phenotypic and clinical expressions[2]. There is great diversity of clinical presentations, from asymptomatic patients who are diagnosed through routine echocardiogram to those with heart failure or sudden death. Prognosis is also variable, being the most frequent complications ventricular arrhythmias and cardioembolic events[7].

Randomized clinical trials or specific guidelines on LVEF are not found. Treatment is based on symptomatic control and therapy directed to ventricular dysfunction. Usually, patients with ventricular dysfunction are treated with HF prognosis modifying drugs. There are, however, few reports of recovery of left ventricular function[1]. When there is HF with decreased left ventricular ejection fraction (LVEF), prophylaxis of cardioembolic events with oral anticoagulants is recommended[9]. In terminal HF, heart transplant must be considered[1,2].

This study aimed to define the clinical features, complications and survival of a group of patients with LVNC assisted in HF outpatient care.

Methods

Retrospective study included adult patients diagnosed with LVNC admitted for HF consultation from January 2006 to February 2014 in Hospital Central, a reference for the northern region of Portugal.

The study included patients with HF, especially with LVEF in any functional class of the New York Heart Association (NYHA). There were no exclusion criteria.

To diagnose LVNC, echocardiography was used, using the criteria of Jenni et al[4]: ratio between the uncompacted and the compacted area at the end of ventricular systole > 2. When there were doubts about the echocardiographic diagnosis, this was confirmed by nuclear magnetic resonance (NMR) heart, using the criteria of Petersen et al[10]: ratio mentioned above > 2.3 in telediastole.

All initial echocardiograms were revised by the same expert in order to validate the LVNC diagnosis. Other echocardiographic data were obtained: number and location of uncompacted segments. The basal, mid and apical segments were divided according to the model of 16 myocardial segments through short-axis projections[11]; and LVEF. All patients underwent echocardiography at diagnosis and other diagnostic tests (cardiac catheterization or Holter monitoring) were carried out as recommended by the assistant doctor.

Demographic data, symptoms, initial LVEF, the course of LVNC (through changes in functional NYHA class), adverse events and survival were collected from patient records in a retrospective way, and analyzed using descriptive statistical methods. The Statistical Package for the Social Sciences version 21.0 (SPSS Inc., Chicago, IL) was used.

This study was approved by the Research Ethics Committee at Hospital São João Research under no. 72/15. The Ethics Commission did not require Informed Consent due to the retrospective and descriptive nature of the study.

Results

Ten patients with a median follow-up time of 18 months (3-96 months) were included in the study. All were Caucasian, 6 men, with a median age at diagnosis of 63 years (41-80 years). Nine patients were referred for consultation due to symptoms of HF, especially dyspnea, fatigue and edema of the lower limbs; 1 patient after being evaluated for respiratory infection; 1 patient had family history of dilated cardiomyopathy, 1 had one relative with family history of sudden cardiac death and 1 had one child with aorta coarctation. One patient had dysmorphic face with no specific syndrome diagnosed.

Five patients had a history of hypertension, 5 had dyslipidemia and 4 had diabetes (1 patient had type 1 diabetes and the other patients had type 2 diabetes). Only 1 patient had a history of acute myocardial infarction and 3 had permanent atrial fibrillation (AF) (Table 1).

Table 1
Clinical characteristics of the patients studied

	Age	Sex	Symptoms on diagnosis	NYHA Class	Follow-up (months)	Family history heart disease	Comorbidities
1	61	M	Dyspnea + coughing + fever	II	18	Yes	Coronary disease, dyslipidemia, AF
2	65	M	Dyspnea + edema	II	21	No	None
3	69	F	Dyspnea	IV	24	No	Hypertension, type 2 diabetes
4	65	F	Dyspnea + edema	II	3	Yes	Hypertension, diabetes, dyslipidemia
5	41	M	Dyspnea	II	18	No	Hypertension
6	80	M	Dyspnea + edema + pleural effusion	III	12	No	Hypertension, dyslipidemia
7	55	F	Dyspnea + edema	II	7	Yes	None
8	51	M	Dyspnea	II	48	Yes	None
9	70	M	Dyspnea + pulmonary embolism	II	12	No	AF
10	51	F	Dyspnea + edema	III	96	No	Hypertension, dyslipidemia, AF, pulmonary disease

M – male; F – female; AF – atrial fibrillation; NYHA – New York Heart Association

Seven patients presented abnormalities on echocardiography. The most common patterns were AF (n=3) and ventricular conduction abnormalities (2 had left bundle branch block and 1 had left anterior fascicular block).

During the initial evaluation, 8 patients underwent cardiac catheterization, and 2 patients had significant coronary artery disease (three-vessel disease). Two patients had cardiac NMR to confirm the diagnosis of LVNC (Table 2).

All patients had echocardiographic diagnostic criteria of LVNC and had involvement of apical segments of the myocardium, 9 had left medio ventricular involvement and only 3 had noncompaction at the base (Figure 1). All patients had decreased LVEF, with median value of 19% (10-31%), and 5 had a high E/e' ratio suggesting increased ventricular filling pressures. One patient had patent foramen ovale and the other had intraventricular thrombus (Table 3).

Table 2
Initial diagnostic evaluation of the patients studied

	ECG	Catheterization	Holter	Electrophysiological study	NMR
1	Atrial fibrillation, QS inferior wall	Yes – three-vessel disease	No	No	No
2	Left axis diversion	Yes – no coronary artery disease	No	No	No
3	Left bundle branch block	Yes – no coronary artery disease	Yes – ventricular extrasystoles	No	No
4	Left bundle branch block	Yes – three-vessel disease	Yes – ventricular extrasystoles	No	Yes – with criteria
5	Left ventricular hypertrophy criterion	Yes – no coronary artery disease	No	No	No
6	Normal	Yes – no coronary artery disease	No	No	No
7	Normal	Yes – no coronary artery disease	No	No	No
8	Normal	Yes – no coronary artery disease	No	No	Yes – with criteria
9	Atrial fibrillation	No	Yes – ventricular extrasystoles	No	No
10	Atrial fibrillation	No	No	No	No

ECG – electrocardiography; NMR – nuclear magnetic resonance

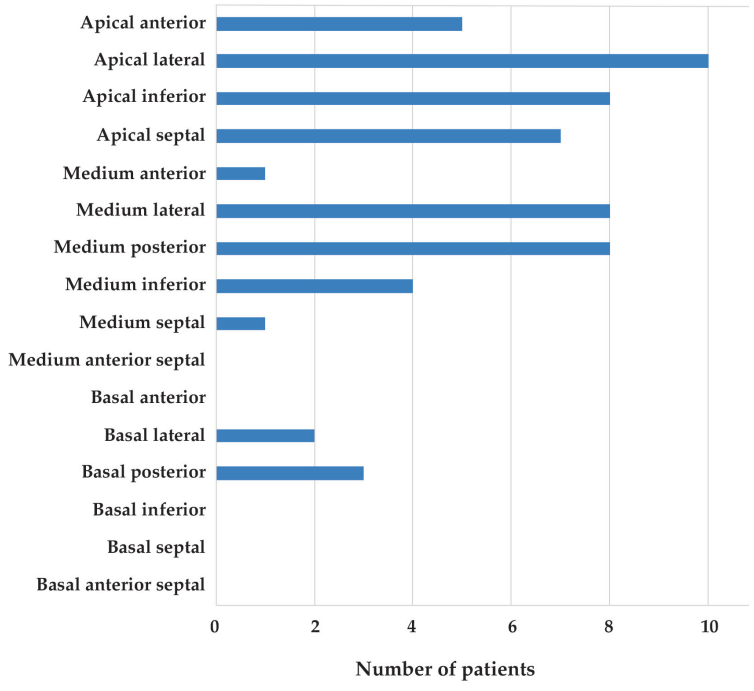

Figure 1
Distribution of non-compacted left ventricular areas

Table 3
Initial echocardiography evaluation of the patients studied

	Left ventricular ejection fraction (%)	Right ventricular ejection fraction	Pulmonary artery pressure (mmHg)	Left ventricular filling pressures (ratio E/e')	Others
1	18	Reduced	41	16	-
2	22	Normal	51	25	-
3	22	Reduced	70	< 8	-
4	12	Reduced	64	< 8	-
5	38	Normal	25	< 8	-
6	11	Normal	31	13	Patent foramen ovale
7	24	Reduced	67	37	Intraventricular thrombus
8	10	Reduced	60	< 8	-
9	18	Reduced	32	21	-
10	20	Normal	23	8	-

At diagnosis, 7 patients were in NYHA class II, with median BNP value of 1415 ng/L (281-3818 ng/L). Nine patients started HF prognosis modifying medication 8 with angiotensin-converting enzyme inhibitors (ACEI), 7 with beta blockers, 5 with spironolactone and 1 with ivabradine. In only 1 patient, it was possible to optimize the HF therapy. The main impediment to non-optimization was the presence of symptomatic hypotension (Table 4). Only one patient did not start oral anticoagulation due to its high hemorrhagic risk measured by high HASBLED classification[12].

During follow-up, it was found that 5 patients showed improvement of HF symptoms, moving to NYHA class I. Three patients remained in the same NYHA class (2 in class II and 1 in Class IV) and 2 presented worsening of HF complaints: one went from class I to class II and one from class II to NYHA class III. Seven patients had their initial BNP value decreased, 5 of which to a BNP value of < 100 ng/L. One patient had BNP increased from 281 ng/L to 664 ng/L. Three patients required hospitalization due to acute exacerbations of HF: 2 due to infectious pulmonary complications, and 1 due to progression of HF. One patient had cardioembolic stroke and another one underwent heart transplantation.

Table 4
Medication for HF. Functional and analytical evolution

	ACEI	Betablocker	Ivabradine	Spironolactone	Reason for the non therapeutic optimization	NYHA class after optimization	Oral anticoagulant	Initial BNP (ng/L)	BNP after optimization (ng/L)	Hosp	Reason for HF decompensation	Clinical evolution
1	Lisinopril 5 mg q24h	Carvedilol 6.25 mg q12h	No	12.5 mg q24h	Hypotension + AF	I	Yes	281	664	1	Respiratory infection	No complications. Still under follow-up
2	Lisinopril 2.5 mg q24h	No	7.5 mg q12h	12.5 mg q24h	Hypotension	II	Yes	1507	36	0	No decompensation	No complications. Still under follow-up
3	No	No	No	12.5 mg q24h	Hypotension + bradycardia	IV	Yes	No information	1894	1	Disease progression	No complications. Still under follow-up
4	Lisinopril 20 mg q24h	Carvedilol 25 mg q12h	No	No	Under optimization	I	Yes	2246	629	0	No decompensation	No complications. Still under follow-up
5	Lisinopril 10 mg q24h	Nebivolol 7.5 mg q24h	No	No	Hypotension	II	Yes	500	33	0	No decompensation	No complications. Still under follow-up
6	Lisinopril 5 mg q24h	Carvedilol 3.125 mg q12h	No	25 mg q24h	Hypotension	I	No	2822	77	0	No decompensation	No complications. Still under follow-up
7	Lisinopril 5 mg q24h	Bisoprolol 5 mg q24h	No	12.5 mg q24h	Hypotension	I	Yes	674	67	0	No decompensation	Cardioembolic stroke
8	No	No	No	No	No information	III	Yes	No information	5000	5	Respiratory infection + disease progression	Heart transplant → death from infection
9	Lisinopril 20 mg q24h	Bisoprolol 7.5 mg q24h	No	No	No information	I	Yes	3818	344	0	No decompensation	No complications. Still under follow-up
10	Lisinopril 10 mg q24h	Carvedilol 12.5 mg q12h	No	No	No information	II	Yes	1324	17	0	No decompensation	No complications. Still under follow-up

Optim. – optimization; BNP – brain natriuretic peptide; ACEI – angiotensin-converting enzyme inhibitor; NYHA – New York Heart Association; HF – heart failure; Hosp – number of hospitalizations; AF – atrial fibrillation; q12h – one tablet every 12 hours; q24h – one tablet every 24 hours

Discussion

In the cohort studied, most were male, which is consistent with other series published[7]. The median age at diagnosis was 63, representing a higher age compared with other series[7]. This can be explained by the fact that any of the patients studied have been referenced by the Pediatric Department. The youngest patient was 41 on diagnosis, which increased the median age of the sample.

The patients had the expected comorbidities in people of the same age, especially arterial hypertension and dyslipidemia. However, the prevalence of AF seems to be higher than in patients of the same age and without LVNC[13], which is consistent with data from other series published[1,5]. This may be related to cardiac structural changes in LVNC, contributing to an increase in ventricular filling pressures, dilating the left atrium and predisposing to the onset of AF.

LVNC also predisposes to alteration of intraventricular electrical transmission pathways, which may explain the fact that most of the patients studied present some kind of anomaly on electrocardiography, especially FA and bundle branch blocks. These data are consistent with data published from another series of patients with LVNC from a Portuguese hospital[14].

Eight patients underwent catheterization to assess the presence of coronary atherosclerosis: 2 had abnormal examination, and 1 patient had complications of coronary artery disease, with previous history of acute myocardial infarction. This patient had probably LVNC along with metabolic syndrome complicated with coronary artery disease, inducing multifactorial HF. Most of the patients studied had normal coronary angiography and, despite the existence of other cardiovascular risk factors, it appears that the main etiological factor for HF would be the existence of LVNC.

In this series, only 2 patients had to undergo cardiac NMR to confirm the diagnosis. Since all were Caucasian, NMR was only useful to confirm the diagnosis of LVNC when the initial echocardiography remained inconclusive.

All patients had decreased LVEF and have been treated according to the latest guidelines for HF[15]. Eight of them were being treated with ACEI and 7 with betablockers, but the full therapeutic optimization was difficult, especially because of symptomatic hypotension. Still, most patients showed improvement in NYHA functional class (n=5) and reduced initial BNP value (n=7). Only 3 patients required hospitalization during follow-up. Respiratory infections were the main factor for decompensation. These results are consistent with other previously published series[16]. Patients with HF decompensation were those that worst tolerated therapy optimization, which may represent greater susceptible to other events that worsen the symptoms of HF.

Only one patient was not treated with oral anticoagulants due to high risk of bleeding (HASBLED classification > 4). The fact that most patients studied are hypocoagulated may explain the low rate of embolic complications, which is consistent with data from other series[16]. Only one patient underwent heart transplantation for refractory heart failure and died as a result of post-transplant infection. It should be noted that most of the patients have a short follow-up time. The sample is too small to withdraw conclusions regarding the use of heart transplantation in these situations.

This study has several methodological limitations, including a selection bias, which is due to the following: all patients studied were adults, because the Hospital has a Cardiology Department following up adult patients with congenital cardiomyopathies, which may explain the high age this series; the HF outpatient care especially follows up patients with reduced LVEF and this is probably one of the reasons why all patients have HF with left ventricular dysfunction.

Conclusion

Patients with LVNC had similar comorbidities as the general population of their age group, except for the apparent increase in the prevalence of AF. These patients responded well to therapy for HF with some clinical benefit. There were few complications, most of them remained clinically stable, without any hospitalization and low mortality rate. The results of this series seem to corroborate the hypothesis that patients with LVNC may have a better prognosis than that previously reported. However, it is a small group of patients with a short follow-up time.

Potential Conflicts of Interest

This study has no relevant conflicts of interest.

Sources of Funding

This study had no external funding sources.

Academic Association

This study is not associated with any graduate programs.

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