Clinical Investigations

Clinical Outcomes in Patients With Isolated Left Ventricular Noncompaction and Heart Failure

FERANDE PETERS, MD,[1] BIJOY K. KHANDHERIA, MD,[2] FRANCOIS BOTHA, MD,[1] ELENA LIBHABER, PhD,[1] HIRAL MATIODA, BSc,[1] CLAUDIA DOS SANTOS, MSc,[1] SAMANTHA GOVENDER, BSc,[1] RUCHIKA MEEL, MD,[1] AND MOHAMMED R. ESSOP, MD[1]

Johannesburg, South Africa and Milwaukee, Wisconsin

ABSTRACT

Background: We prospectively evaluated long-term clinical outcomes of patients diagnosed with isolated left ventricular noncompaction (ILVNC) and heart failure from a sub-Saharan African population.

Methods and Results: Patients in this single-center study were followed at a tertiary care institution. Clinical follow-up was performed with the use of protocol-driven echocardiographic screening for ventricular thrombus every 4 months. Warfarin was maintained or initiated only if thrombus was detected with the use of echocardiography. Fifty-five patients were followed for 16.7 ± 5.9 (range 12−33) months. All individuals had left ventricular (LV) ejection fraction <50% (mean 29.6 ± 11.8%). Of the 55 patients, 7 (12.7%) died, and sudden cardiac death was the cause in 5 (71.4%). There were no differences in baseline clinical, echocardiographic, or electrocardiographic characteristics between survivors and nonsurvivors. Recurrent heart failure developed in 12 patients (21.8%); 1 patient developed a ventricular arrhythmia. No thromboembolic or major bleeding complications occurred in the 16 patients on warfarin; 1 episode of thromboembolism occurred in the 39 patients not on warfarin. Mean survival probability at 33 months was 0.64.

Conclusions: Sudden cardiac death was the most common cause of death in patients with ILVNC and heart failure. Recurrent heart failure occurred in 21.8% of patients. Development of LV thrombus and cardioembolism is uncommon in this population. (*J Cardiac Fail 2014;20:709−715*)

Key Words: Left ventricular noncompaction, heart failure, sudden cardiac death, echocardiography.

Isolated left ventricular (LV) noncompaction (ILVNC) cardiomyopathy is thought to occur because of failure of intrauterine myocardial compaction.[1−3] The clinical spectrum of this disorder is varied and ranges from incidental diagnosis of asymptomatic individuals to those presenting with heart failure, life-threatening ventricular arrhythmias, and cardioembolism.[4,5] Earlier reports have documented that patients with ILVNC who present with severe heart failure have a poor prognosis, with end-stage heart failure and malignant ventricular arrhythmias accounting for the high mortality rate.[4,6,7] Furthermore, cardioembolism causes significant morbidity, occurring in almost one-fourth of patients at follow-up.[4] The clinical characteristics of patients with ILVNC from a sub-Saharan African population have been published recently.[8] Heart failure was the most common clinical manifestation, occurring in 98% of patients.[8] The long-term outcomes of standard medical therapy in these patients, where access to device therapy for heart failure and cardiac transplantation is infrequently available, has not been documented. Furthermore, the routine use of oral anticoagulation as primary cardioembolism prophylaxis is often prohibitive because of socioeconomic and patient-related factors that prevent adequate monitoring. We sought to prospectively study

From the [1]Department of Cardiology, Chris Hani Baragwanath Hospital, University of the Witwatersrand, Johannesburg, South Africa and [2]Aurora Cardiovascular Services, Aurora Sinai/Aurora St Luke's Medical Centers, University of Wisconsin School of Medicine and Public Health, Milwaukee, Wisconsin.

Manuscript received December 6, 2013; revised manuscript received July 3, 2014; revised manuscript accepted July 16, 2014.

Reprint requests: Bijoy K. Khandheria, MD, Aurora Cardiovascular Services, 2801 W Kinnickinnic River Parkway, #840, Milwaukee, WI 53215. Tel: (414) 649-3909; Fax: (414) 649-3551. E-mail: publishing22@aurora.org

See page 714 for disclosure information.

1071-9164/$ - see front matter

http://dx.doi.org/10.1016/j.cardfail.2014.07.007

the long-term clinical outcomes of patients diagnosed with ILVNC and heart failure who were followed at a tertiary care institution.

Methods

This prospective single-center study was conducted at the Chris Hani Baragwanath Hospital cardiomyopathy clinic. A total of 67 individuals diagnosed with ILVNC were enrolled in the hospital's cardiomyopathy registry from July 2009 to September 2011. Informed consent was obtained from each patient. The Baragwanath cardiomyopathy registry was established in June 2009 after receiving approval from the University of the Witwatersrand Ethics Committee. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. From this cohort, 55 patients were included in analysis, with the remaining 12 patients excluded owing to their inability to be reliably followed owing to geographic factors. Other exclusion criteria were age <18 years, hypertension, previously documented coronary artery disease, organic valvular disease, any systemic illness (eg, human immunodeficiency virus), diabetes mellitus, thyroid disease, and any primary organ failure (eg, chronic renal failure).

Inclusion criteria were diagnosis of ILVNC based on strict echocardiographic criteria and documented heart failure based on the Framingham heart failure criteria that required admission to the hospital. Echocardiographic diagnosis of ILVNC was based on the following criteria:

1. The ratio of the noncompacted to compacted myocardial width had to be >2 when measured at end-systole.
2. Presence of >3 prominent trabeculations in the LV apex that did not originate from the septum.
3. Deep intertrabecular recesses that filled with blood from the ventricular cavity as visualized with the use of color Doppler ultrasonography.
4. No evidence of congenital or acquired heart disease.

Only subjects definitively satisfying all of these criteria were diagnosed with ILVNC. Requiring that all of these criteria be met for diagnosis is a documented method for accurately differentiating between normal subjects of African descent who could have variants of hypertrabeculation and those with true ILVNC.[8]

Clinical data included history, physical examination, electrocardiography, and baseline echocardiography, which was recorded either within 14 days after discharge for heart failure or at a time when the patient was deemed to be clinically out of acute heart failure and the required drug therapy was commenced. Echocardiography was performed with the use of a commercially available system (iE33 xMATRIX; Philips Healthcare, Best, The Netherlands) equipped with an S5-1 transducer (frequency transmitted 1.7 MHz, received 3.4 MHz), according to a standardized protocol. All data were transferred to an Xcelera workstation (Philips Healthcare) and analyzed offline.

Measurements relating to chamber size and function were performed in accordance with the American Society of Echocardiography 2006 chamber quantification guidelines and 2010 right heart assessment guidelines.[9,10] The severity of mitral and tricuspid regurgitation was analyzed in accordance with American Society of Echocardiography guidelines on native valvular regurgitation.[11] The location of noncompaction was described with the use of a 9-segment model proposed by Oechslin et al.[4]

Routine clinical assessment was performed on all patients at 4 monthly intervals to up-titrate medication according to routine clinical practice based on individual patient requirements and included a history interview and physical examination. At each scheduled visit, screening echocardiography in the short-axis and apical views was performed to check for the presence of thrombus within the left and right ventricles. The echocardiograms were read by the treating clinician and subsequently reviewed by a single experienced cardiologist (F.P.). Only definite cases of thrombus were documented. Equivocal cases were further investigated with the use of transesophageal echocardiography or, in 1 instance, computerized tomography to either confirm or refute diagnosis.

Clinical outcomes recorded included:

1. Death ascribed to either heart failure or sudden cardiac death, which was defined as occurring within 1 hour of onset of acute symptoms[12] in a patient who was clinically stable and well before the event.
2. Recurrent heart failure, if a previously stable patient developed new-onset or worsening heart failure based on the Framingham criteria for the diagnosis of heart failure requiring either admission to the hospital or escalation of diuretic therapy.
3. New-onset arrhythmias not ascribed to any drug, electrolyte, or new systemic disorder.
4. New episodes of thromboembolism.
5. Detection of LV or right ventricular (RV) thrombus with the use of echocardiography.

Statistical Analysis

Statistical analyses were performed with the use of the SAS statistical program (version 9.12; SAS Institute, Cary, North Carolina). Data are presented as mean $\pm$ SD for continuous variables with normal distribution and as median and interquartile range for nonnormal distribution. Categoric variables are presented as frequencies and percentages. Comparisons of means and proportions between groups at baseline were performed with the use of an independent t test and chi-square statistics or Fisher exact test, respectively. A Wilcoxon rank-sum test was used where continuous data were not normally distributed. Product-moment survival estimates for baseline to 33 months were calculated with the use of the Kaplan-Meier method. Statistical significance was defined as a 2-tailed P value of $<.05$.

Results

Baseline clinical and echocardiographic characteristics are reported in Table 1. The mean age of this cohort (n = 55) was 42.2 $\pm$ 11.5 years (range 21–66 years) with 34 (61.8%) female patients. No patient had concomitant clinical evidence of neurologic abnormality or facial dysmorphism. There were 22 patients (40.0%) who were in New York Heart Association (NYHA) functional class 1 after commencement of medical therapy for heart failure, with all patients in sinus rhythm and 9 patients having left bundle branch block at baseline. The LV ejection fraction was $<50\%$ in all individuals (mean LV ejection fraction 29.6 $\pm$ 11.8%). In 28 patients (50.9%) RV dysfunction was documented. Pulmonary hypertension was noted in 23 patients (41.8%). No