Isolated left ventricular noncompaction (ILVNC) is a rare congenital cardiomyopathy characterized by prominent trabeculae, deep intertrabecular recesses, and thickened myocardium in 2 distinct layers (compacted and noncompacted). Clinical characteristics, outcomes, and appropriate therapies remain poorly defined. Data were collected on patients diagnosed with ILVNC by echocardiographic criteria at the Mayo Clinic from 2001 through 2006. These data were entered prospectively into a clinical database and retrospectively analyzed. All-cause mortality, stroke, and development of atrial fibrillation (AF) were compared to community and nonischemic dilated cardiomyopathic (DC) controls. Implantable cardioverter-defibrillator (ICD) therapies were examined. Thirty patients with confirmed ILVNC were included in analyses (mean age at diagnosis 39 ± 19.5 years, 60% men). Three patients with ILVNC died during follow-up (mean 2.5 ± 1.2 years) compared to 5 DC and 1 community controls. No mortality difference was observed among these groups (p = 0.42 and 0.054, respectively). No ILVNC deaths were observed in patients with normal LV ejection fraction. New-onset AF was diagnosed in 2 patients with ILVNC, and none was observed in DC controls. Stroke occurred in 2 DC controls and none was observed in patients with ILVNC. ICDs were implanted in 11 patients with ILVNC. No appropriate therapies were identified during follow-up, but 2 patients underwent inappropriate therapies related to AF. In conclusion, mortality in patients with ILVNC is similar to that in DC patients. Deaths were observed only in patients with decreased LV ejection fraction, suggesting that ICD therapy may be reserved for this subgroup. New-onset AF may lead to inappropriate ICD discharges. © 2009 Elsevier Inc. All rights reserved. (Am J Cardiol 2009;104:1135–1138)
Additional echocardiographic data obtained included number and location of noncompacted segments (basal, midventricular, and apical short axis projections were divided into a 12 segment model) and LV ejection fraction (EF).

The primary outcome was all-cause mortality. Secondary outcomes were stroke and onset of atrial fibrillation (AF) during follow-up. Two control groups were used. The first was an Olmsted County Epidemiology Project population matched for age, gender, and year of first enrollment or initial contact (i.e., controls were temporal contemporaries of cases). A second control group consisted of patients with nonischemic dilated cardiomyopathy, matched for age, gender, and LVEF.

Probability of death from any cause, development of AF, and stroke were estimated using the Kaplan-Meier method. These end points were compared between the study group and the control groups using log-rank tests. Potential risk factors for end points were evaluated using Cox proportional hazards models. The correlation among echocardiographic parameters was evaluated using Spearman correlation coefficients.

**Results**

The initial database search identified 130 patients; 72 were excluded (46 had coexisting congenital disorders, 21 were <16 years old, 4 refused participation, and 1 had...
Distributions of noncompacted myocardial segments are shown in Figure 3. The apical lateral segment was most frequently involved (97%), and the apex was more likely to be involved than the mid or the base. LVEF was decreased in 77% of patients, with an overall mean LVEF of 41% (range 17 to 62). No significant correlation was observed between the number of segments involved and LVEF (R = -0.24, p = 0.20). Number of segments affected did not predict clinical end points (p = 0.55 for composite of stroke, AF, and death).

Electrocardiograms were obtained in 27 of 30 patients, of which only 2 were interpreted as normal. Table 2 presents electrocardiographic parameters. Holter monitoring was performed in 15 patients. Ventricular tachycardia (sustained or nonsustained) was noted in 4 patients. Abnormal electrocardiogram, QRS duration >120 ms, and QT prolongation were not predictive of death, stroke, or AF in patients with ILVNC (p = 0.99, 0.16, and 0.14, respectively).

ICDs were implanted in 11 patients with ILVNC. Stated indications for implantation within the ILVNC group were nonischemic dilated cardiomyopathy in 4 patients, ventricular tachycardia in 3 patients, and noncompaction in 6 patients (≥1 indication was used per patient). Mean LVEF in the ILVNC group implanted with ICDs was 41 ± 15%. Two patients had LVEF >55%. No appropriate therapies were identified during follow-up. Inappropriate therapies were documented in 2 patients for atrial arrhythmias. One patient received 13 inappropriate shocks.

**Discussion**

Awareness of ILVNC has increased substantially in recent years and it has been recognized as an “unclassified” cardiomyopathy by the World Health Organization. Interest has focused mainly on the concern that incompletely formed endocardium with channels and trabeculae may provide substrate for thromboembolic events, and that these patients might be at risk for the development of malignant ventricular tachyarrhythmias and LV systolic dysfunction. ILVNC has been the subject of several small, retrospective studies, but overall clinical event rates remain ill-defined. We found that incidences of death, ventricular tachycardia, clinically significant heart failure, and thromboembolism were lower than previously reported. Although the outcome trend in patients with ILVNC appeared worse than in the general population, it was similar to that of DC controls. This suggests that it is the development of ventricular dysfunction, rather than presence of noncompacted myocardium, that poses mortality risk.

Diagnosis and clinical management of patients with ILVNC continue to be difficult and controversial. Morphologic findings of noncompacted myocardium are at times encountered during echocardiography in asymptomatic patients. These findings, although not meeting published or “strict” diagnostic criteria, may be reported as noncompaction, possibly leading to further investigations and/or consultations. Echocardiographic criteria require a 2:1 ratio of noncompacted to compacted myocardium, and operator-dependent factors may affect interpretation. The complexity of image interpretation is highlighted by the fact that, of 39 patients with a diagnosis of noncompaction on an echocar-
diagnostic report in our series, 9 did not meet the formal diagnostic criteria on independent assessment by 2 experienced echocardiographers. Other reasons for variability in echocardiographic findings may be the existence of a spectrum of disease and variability in the myocardial segments involved. Another possible explanation for variability in echocardiographic characteristics is that the disease may be progressive and findings of noncompaction may evolve over time; however, this seems less likely given the congenital nature of the lesion. The variability in published criteria for diagnosis, within the echocardiographic literature and the imaging literature as a whole, provides another challenge in diagnosis.11,12,16

Prognosis of patients with ILVNC varies greatly from study to study. Mortality during follow-up has ranged from 2% to 47%,7–10 systemic embolic events in 4% to 29%,7–10 and clinically significant heart failure in 24% to 53%.7–9 of patients. Ventricular tachyarrhythmias are reported in 20%10 and these favorable outcomes may reflect detection of overall, our results are similar to the findings of Murphy et al10 and although this is mostly nonsustained ventricular tachycardia. Prognosis in our study was substantially better than in previous reports. We report an overall mortality at 3 years of 15% with no patients developing systemic emboli or stroke. It is conceivable that this underestimates true mortality, given that this group was primarily a referral population evaluated at a tertiary care center. Importantly, the 2 patients who died during follow-up had LV dysfunction. We found ventricular tachycardia (nonsustained) in 25% of patients undergoing Holter monitoring. Overall, our results are similar to the findings of Murphy et al10 and these favorable outcomes may reflect detection of less severe disease due to improvements in recognition, imaging technology, and/or heart failure therapy in patients with severe disease. Our observation that mortality did not differ significantly between patients with ILVNC and control patients with nonischemic dilated cardiomyopathy suggests that the resultant LV dysfunction, rather than the noncompacted myocardium itself, is the primary source of morbidity and mortality.

Therapeutic considerations in patients with ILVNC remain controversial. Oral anticoagulation, heart failure therapy, and ICD use have been advocated. Although outcomes in this study do not support the routine use of ICDs or oral anticoagulation, patient care must be individualized and may involve these therapies. Notably, 2 patients with ILVNC developed AF during follow-up, suggesting an alternative mechanism for previously observed cardioembolic events. Patients with ILVNC are known to have diastolic dysfunction and impaired relaxation13 that in turn promotes atrial arrhythmias, suggesting a role for surveillance for atrial arrhythmias. This is further supported by a recent report describing impaired survival for patients with ILVNC and AF.17 In patients who receive ICDs, use of dual-chamber devices, aggressive use of detection enhancements, delayed detection to minimize inappropriate detection, and use of remote monitoring alerts may aid in the detection of AF and in the prevention of inappropriate ICD therapies.18

This study is limited by its small numbers, retrospective nature, and referral bias. Further, because follow-up was limited to 2.5 years, perhaps increased morbidity and mortality might be observed with longer follow-up. Given the well-established difficulty in making this diagnosis and be-

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