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Received 28 April 2018
Available online 28 June 2018

https://doi.org/10.1016/j.jjcc.2018.05.016

Left ventricular noncompaction cardiomyopathy: Recent update on genetics, usefulness of biomarkers, and speckle imaging

We appreciate Dr Bandyopadhyay's letter concerning our article [1] on isolated left ventricular noncompaction cardiomyopathy (LVNC) in adults. LVNC refers to a myocardial phenotype with excessive trabeculations of the LV myocardium and severe thickening of the endocardial noncompacted layer compared with the epicardial compacted layer. LVNC is the morphological expression of an underlying cardiomyopathy (primary or secondary), and debate continues over whether LVNC is a distinct cardiomyopathy/trait or the myocardial phenotype of a different underlying disease. Indeed, LVNC is listed as a genetic cardiomyopathy by the American Heart Association, whereas it is classified as an unclassified cardiomyopathy by the World Health Organization and European Society of Cardiology.

Owing to the use of high quality cardiovascular (CV) imaging modalities and low threshold for screening patients with nonspecific symptoms for underlying cardiac disease, an increasing number of subjects meet the diagnostic criteria of LVNC. It is challenging to distinguish patients with the myocardial phenotype of LVNC, who have an underlying cardiomyopathy, from healthy individuals with excessive trabeculations as a normal variant. The lack of universally accepted diagnostic criteria sometimes leads to over-diagnosis of LVNC in subjects with physiologic, reversible remodeling of the LV myocardium with excessive trabeculations such as pregnant women and athletes. Kohli et al. reported that 30 patients (15%) fulfilled Jenni's echocardiographic criteria for LVNC out of 199 patients with LV systolic dysfunction in a single center [2]. Similarly, we reported 23 patients (7.7%) who fulfilled Jenni's echocardiographic criteria for LVNC among 300 consecutive adult patients with LV systolic dysfunction. We found that LV trabeculations of 9 patients (39%) visibly reduced in association with improvement of LV contractility after optimal heart failure therapy [3]. These observations suggest that it is possible to misclassify a transient deformation of the myocardium with excessive trabeculations as LVNC using the current morphological criteria alone.

As you mentioned that we do not have robust data regarding risk stratification and prognostication for LVNC, identifying higher risk patients for future CV events and who need regular follow-up is critical. Therefore, genetic assessment, along with biomarkers and new CV imaging modalities, may improve diagnostic accuracy. Van Waning et al. highlighted the knowledge gap in the mechanisms of LVNC with its marked genetic heterogeneity and sarcomere gene mutations shared with other myocardial disorders [4]. There were significantly more genetic mutations in children (45%) than in adults (30%), and LV systolic dysfunction was a risk factor for CV events in carriers of a mutation. They emphasized the importance of routine genetic testing to establish a genotype–phenotype correlation. We conducted a nationwide survey and retrospectively evaluated adult patients with morphologic LVNC including congenital, acquired, or significant valvular heart disease, neuro-muscular disease, or secondary cardiomyopathy in Japan (unpublished data). A total of 310 patients (232 male, 74.8%) were registered from 60 institutions in Japan. The median age and LV ejection fraction were 55 years and 35.0%, respectively. Half of the patients (148 cases, 47.7%) had underlying cardiac diseases (dilated cardiomyopathy, 23.2%; adult congenital heart diseases, 5.2%; valvular heart diseases, 4.5%; hypertrophic cardiomyopathy, 4.2%) and only 7 patients (2.5%) had a family history of LVNC. We evaluated 272 patients, who were followed-up for more than 30 days for the incidence of CV events, including all-cause death, hospitalization for worsening heart failure, ventricular arrhythmia, and systemic thromboembolism. Over a 3.6-year median follow-up period, all-cause death ($n = 22$, 8.1%), CV death ($n = 16$, 5.9%), hospitalization for heart failure ($n = 59$, 21.7%), ventricular arrhythmia ($n = 28$, 10.3%), and systemic thromboembolism ($n = 7$, 2.6%) were observed. There was no difference in the incidence of CV events between patients with underlying cardiac diseases ($n = 134$) and those without (i.e. isolated LVNC) ($n = 138$) (CV events rate at 5 years: 30.3% vs. 31.1%, $p = 0.58$). We found that hospitalization for heart failure was the most common cause of CV events and such events did not appear to be influenced by the etiology of CV diseases in this patient population.

LVNC is increasingly being diagnosed in clinical practice, although there are still many unanswered clinical questions with regard to this condition. An international registry including a larger number of subjects with excessive trabeculations with a prospective follow-up and a multidisciplinary, international collaboration of clinicians, pathologists, geneticists, imaging specialists, and epidemiologists may aid in resolving several questions [5]. This larger study should be considered to elucidate the real prevalence assessment of LVNC, clarify the useful prognostic factors for patient management, and determine appropriate therapeutic interventions for these patients.

Funding sources

This work was supported by Health and Labour Sciences Research Grant.

Conflict of interest

The authors declare that there is no conflict of interest.

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Received 31 May 2018
Available online 30 June 2018

https://doi.org/10.1016/j.jjcc.2018.06.001