Left Ventricular Noncompaction Suggests Myopathy
To the Editor:
We read with interest the article on left ventricular noncompaction (LVNC) in children by Pignatelli et al., who found that LVNC has a good prognosis and that LV systolic function may undulate between deterioration and recovery. The report raises several concerns: Thirteen of the 36 patients (36%) were suspected of having mitochondrial myopathy (MM), although only 5 underwent muscle biopsy. Muscle biopsy is an absolute requisite for diagnosing MM. Essential also are biochemical and genetic investigations, but abnormal biochemical investigations were reported only in a single patient. “Mitochondrial structural abnormalities with inclusion bodies” on electron-microscopy are non-specific and are found as well in other neuromuscular disorders (NMD). LVNC has been repeatedly reported in MM under the terms LV hypertrabeculation and isolated LV trabeculations. The underlying cause of LVNC is heterogeneous. Besides Barth syndrome and dystrophinopathy, LVNC is associated with myotonic dystrophy type-1, M. Pompe, cypher gene mutations, Becker muscular dystrophy, myoadenylate deaminase deficiency, and other rare genetic disorders. Coenzyme Q10, thiamine, riboflavin, and carnitine are not established therapy for MM. Uncritical administration of an obscure “metabolic cocktail” may have side effects, particularly in a disorder whose pathogenesis is not fully understood, and may be expensive. No data are presented on creatine-kinase, electromyography, nerve conduction studies, and imaging investigations, which may be abnormal in NMD. As LVNC has been reported to occur familially and is frequently associated with NMD, relatives of the 36 children should also have undergone neurologic investigation. In patients with LVNC but without NMD, muscle biopsy will be normal; therefore, endomyocardial biopsy remains a diagnostic option in these cases.

What was the indication for echocardiography in 3 asymptomatic and 1 dysmorphic patient(s)? Was it possible to calculate the ejection fraction in all patients, despite the heavily trabeculated ventricles? Restrictive filling-pattern is characterized by increased, not decreased, E/A ratio. In adults, LVNC is predominantly located in the lateral and anterior wall and the apex, sparing the interventricular septum. Was this distribution also found in children? How do the authors explain undulation of the left ventricular function? Could this finding be due to effective cardiac therapy or interobserver-variability? Did the authors observe growth or regression of LVNC in any of the patients? In how many patients did cardiac magnetic resonance imaging confirm LVNC? Why was acetyl salicylic acid given? The statement that undulation of LV function is responsible for the occurrence of LVNC in adulthood is not substantiated by the data presented. Because NMD are found in 82% of adults with LVNC, children with LVNC also require thorough neurological investigation.

Josef Finsterer, MD, PhD
Neurological Department
Krankenanstalt Rudolfstiftung
Vienna, Austria
duarte@aonmail.at

Claudia Stöllberger, MD
Second Medical Department
Krankenanstalt Rudolfstiftung
Vienna, Austria

Gerhard Blazek, MD
Medical Department
Hausch Krankenhaus
Vienna, Austria


Response
We appreciate the comments of Finsterer et al regarding our article, which raise several salient points.

1. Regarding the suggestion that skeletal muscle biopsy is “an absolute requisite for diagnosing mitochondrial myopathy,” there is some truth to this comment. However, unlike their adult patients, our patients are extremely small (9 children less than 1 week of age, 17 children less than 1 year of age) and ill, making biopsy clinically problematic, inaccurate, and dangerous. In their own recent report, the majority of adult patients did not undergo biopsy.

2. The etiology of left ventricular noncompaction (LVNC) is clearly heterogeneous. We have identified mutations in G4.5, α-dystrobrevin, and ZASP and have shown metabolic and biochemical abnormalities in others. The metabolic cocktail of coenzyme Q10, riboflavin, carnitine, and thiamine has been used in large populations of children with mitochondrial dysfunction with good results in the United States, with low side-effect profile, cost, and clinical benefit.


4. Echocardiography was performed in the 3 asymptomatic patients because of disease in other organ systems and in 1 dysmorphic patient because of the high incidence of cardiac disease in these children.

5. We agree that it is difficult to accurately analyze ventricular volume of a “sponge-like” structure. Ichida et al reported evaluation of ventricular function using the Pombo method, but multiple artificial echo lines can be generated on the posterior wall by trabeculations, making the analysis unreliable. Use of shortening fraction may not be optimal because of wall motion abnormalities. In our experience, the biplane Simpson’s method produces less interobserver variation than the bullet method.

6. Several patients had a decrease in E/A ratio consistent with impaired left ventricular diastolic relaxation.

7. In our population, LVNC was predominantly located in the apex and lateral wall, as reported by Stöllberger et al. However, unlike in adults, the interventricular septum was involved in several patients, which has been previously reported.

8. We did not observe regression in LVNC. Some patients did progress from dilated to hypertrophic cardiomyopathy.

9. Only one patient had magnetic resonance imaging to delineate the cardiac diagnosis, as echocardiography is sufficiently sensitive for diagnosis of LVNC.
10. Acetyl-salicylic acid was used to minimize the risk of thrombosis.
11. Undulating phenotype clearly occurs in children. Left ventricular systolic function commonly improves and end-diastolic dimension commonly improves.

In summary, LVNC is relatively common in young children, has various etiologies, and in some children mitochondrial dysfunction and an undulating phenotype are noted. In addition, young children behave differently than adults.

Ricardo Pignatelli, MD
Colin J. McMahon, MB, MRCPI
William J. Dreyer, MD
Susan W. Denfield, MD
Jen Wu, MD
Jack Price, MD
Howaida El Said, MD, PhD
Louis I. Bezold, MD
Sarah Clunie, RN
Susan Fernbach, RN
Neil E. Bowles, PhD
Jeffrey A. Towbin, MD

Lillie Frank Amherst Division of Pediatric Cardiology
Texas Children’s Hospital and Baylor College of Medicine
Houston, Tex

---

Left Ventricular Noncompaction Suggests Myopathy
Josef Finsterer, Claudia Stöllberger and Gerhard Blazek

Circulation. 2004;109:e201-e202
doi: 10.1161/01.CIR.0000127124.84124.0E
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/109/16/e201

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/