JACC: ADVANCES VOL. 3, NO. 3, 2024

EDITORIAL COMMENT

Watchful Waiting

Echocardiographic Surveillance of Childhood Left Ventricular Noncompaction*

John L. Jefferies, MD, MBA, MPH

"What is in your blood matters, but not as much as what is in your heart."

-Sonja Yoerg[1]

The awareness and diagnosis of left ventricular noncompaction (LVNC) have increased over the past decade. There are multiple possible drivers behind these changes. The field of pediatric cardiomyopathy has expanded greatly secondary to a variety of drivers including dedicated pediatric heart failure/cardiomyopathy/transplant training programs, publications, and interest from both pediatric and adult cardiologists. The downstream impacts have resulted in increased research around diagnostic and treatment strategies for less common pediatric cardiomyopathy phenotypes such as restrictive cardiomyopathy, arrhythmogenic cardiomyopathy, and LVNC cardiomyopathy.[2]

In this issue of the Journal, Kock et al[3] provide a much-needed perspective on changes in left ventricular (LV) function and morphology in children 2 to 4 years of age with and without LVNC, as well as describing the prevalence of LVNC in first-degree relatives. The authors assessed newborns participating in the Copenhagen Baby Heart Study. Of >25,000 newborns in the study, 16 were identified as meeting echocardiographic criteria for LVNC. Notably, these 16 newborns were found to have decreased LV systolic function as compared to matched newborns without LVNC. On follow-up at 2 to 4 years of age, these subjects were noted to have similar morphologic architecture with regards to the degree and location of LV trabeculations. They were also noted to have persistently lower left ventricular ejection fraction (LVEF) values as compared to age-matched controls without LVNC. There was no progression of LV dysfunction in the LVNC children as compared to baseline. In addition, the authors performed echocardiographic screening of the relatives of the children with LVNC. Of these 37 relatives, 11 (30%) fulfilled the LVNC criteria.

Although the patients in the study did not undergo genetic testing or advanced imaging in the form of cardiac magnetic resonance imaging, these findings have important implications for the current approach and future opportunities for patients with LVNC. In the newborns diagnosed with LVNC, the authors noted that LVEF was decreased in the LVNC cohort as compared to newborns without LVNC (49% vs 60%, $P < 0.001$). In addition, LV end-systolic volume was greater in the LVNC group (17 mL vs 13 mL, $P < 0.001$). This information has clinical relevance as it identifies targets for longitudinal surveillance. These findings also prompt the question of whether or not medical therapy may have utility in this setting. Future investigation will be required to define the potential benefits of medical therapy. At a minimum, these findings should compel providers to thoughtfully monitor for a further decrease in LVEF, worsening of LV volumes, and evidence of heart failure.

The authors highlight another very impactful finding, which is the importance of cascade screening. The testing of at-risk first-degree family members represents a significant opportunity to identify genetic triggers and/or phenotypic expression of disease. A practical approach to the

*Editorials published in *JACC: Advances* reflect the views of the authors and do not necessarily represent the views of *JACC: Advances* or the American College of Cardiology.

From the Division of Cardiovascular Diseases, Department of Medicine, University of Tennessee Health Sciences Center, Memphis, Tennessee, USA.

The author attests they are in compliance with human studies committees and animal welfare regulations of the author's institution and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

ISSN 2772-963X https://doi.org/10.1016/j.jacadv.2024.100828

appropriate use of genetic testing, interpretation of genetic testing results, and resultant cascade screening has been well outlined and can be implemented into clinical practice in both adult and pediatric population.[4] However, phenotypic screening in the form of imaging is another opportunity to identify disease. The current report by Kock et al underscores the importance of echocardiographic screening of first-degree family members. The investigators identified 30% of screened first-degree family members who met criteria for LVNC. As shown in Table 1, many of these relatives were adults with a median age of 31 years (4-38 years) and 46% being male. Furthermore, Figure 1 clearly demonstrates a significant difference in LVEF in relatives to children with LVNC fulfilling criteria for LVNC as compared to those relatives to children not fulfilling diagnostic criteria for LVNC. As a result of this screening, these relatives were made aware of clinically actionable information that can empower providers to develop directed surveillance and consideration of therapeutic strategies.

As a field, we continue to unearth additional learnings around LVNC. As more adult and pediatric patients are diagnosed, the broad phenotypic landscape is becoming better defined. The use of machine learning is providing valuable diagnostic and prognostic insights across a variety of diagnoses and cardiovascular medicine. This approach may provide an additional opportunity to diagnose LVNC and offer insights into prognosis. Algorithms have been reported leveraging machine learning to assist in diagnosis.[5,6] Machine learning has also been shown to aid in the prediction of major adverse cardiovascular events in patients with LVNC.[7,8] LVNC continues to be the subject of international discussions as complete alignment regarding morphologic development, diagnosis, and classification has not been realized. The addition of machine learning to the work presented in this issue of the journal may offer even greater opportunities to identify LVNC with greater accuracy and begin to better risk stratify newborns and children with this diagnosis.

The current report provides an important addition to the existing LVNC literature. As the pediatric population continues to expand, we must be better equipped as providers to ensure the best care possible for these patients and their families. A better understanding of the natural history of the diagnosis is essential in addressing this need. The recognition of LVNC at birth with subsequent echocardiographic follow-up in childhood described in this report helps shrink existing knowledge gaps and provides a foundation for future investigation in older children and adolescents. An equally important takeaway is the necessity of screening at-risk first-degree family members. Armed with this knowledge, providers now have the information needed to develop pathways directed at managing the entire family. Kock et al have given us a glimpse into the evolving world of pediatric LVNC. As a field, we should continue to build upon these findings with the aspirations of early diagnosis and timely intervention.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The author has reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr John L. Jefferies, The Cardiovascular Institute, 956 Court Avenue, Suite A312A, Memphis, Tennessee 38163, USA. E-mail: jjeffe15@uthsc.edu.

REFERENCES

1. Yoerg S. *All the Best People*. Thorndike Press; 2017.

2. Bogle C, Colan SD, Miyamoto SD, et al. Treatment strategies for cardiomyopathy in children: a scientific statement from the American heart Association. *Circulation*. 2023;148:174–195.

3. Kock TO, Børresen MF, Sillesen A-S, et al. Left ventricular noncompaction in childhood: echocardiographic follow-up and prevalence in first-degree relatives. *JACC: Adv*. 2024;3:100829.

4. Kontorovich AR. Approaches to genetic screening in cardiomyopathies: practical guidance for clinicians. *J Am Coll Cardiol HF*. 2023;11:133–142.

5. Izquierdo C, Casas G, Martin-Isla C, et al. Radiomics-based classification of left ventricular non-compaction, hypertrophic cardiomyopathy, and dilated cardiomyopathy in cardiovascular magnetic resonance. *Front Cardiovasc Med*. 2021;8:764312.

6. Rodriguez-de-Vera JM, Bernabe G, Garcia JM, Saura D, Gonzalez-Carrillo J. Left ventricular non-compaction cardiomyopathy automatic diagnosis using a deep learning approach. *Comput Methods Programs Biomed*. 2022;214:106548.

7. Han PL, Jiang ZK, Gu R, et al. Prognostic prediction of left ventricular myocardial non-compaction using machine learning and cardiac magnetic resonance radiomics. *Quant Imaging Med Surg*. 2023;13:6468-6481.

8. Rocon C, Tabassian M, Tavares de Melo MD, et al. Biventricular imaging markers to predict outcomes in non-compaction cardiomyopathy: a machine learning study. *ESC Heart Fail*. 2020;7:2431–2439.

KEY WORDS children, echocardiography, LVNC, noncompaction