

particular, we see huge possibilities for future therapeutic interventions and thus improvement of cardiovascular function and, thereby, quality of life in patients with cancer. With regard to spirometry assessment, a cutoff value for the RER value was indeed ≥ 1.10 in a number of studies, as this supposedly indicates maximal effort and prognostic sensitivity. This is, however, not the only cutoff used in previous studies. Although some authors have used a cutoff >1.05 or >1.00 (2), others have suggested that a cutoff >1.00 or >0.95 could be acceptable if this represents a change of at least 0.15 over baseline (3,4). Using data from more than 1,700 patients with heart failure with reduced ejection fraction, Chase et al. (5) recently reported that both peak $\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ slope remained significant predictors of major adverse cardiac events in all subgroups of RER, even in those with an RER <1.00 . We, therefore, strongly believe in the methodology that we applied in this prospective study of cardiovascular function and exercise capacity in patients with colorectal cancer.

Additional analyses are always welcome, but due to the overwhelming amount of data that our study produced, we had to limit ourselves to those parameters that we considered most important.

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The Importance of the Cardiac Cycle in the Imaging Criteria for Left Ventricular Noncompaction



We read with great interest the recent review by Arbustini et al. (1) highlighting the different aspects of the left ventricular noncompaction (LVNC). In this paper, the authors review pathophysiology, anatomy, epidemiology, genetics, and the imaging for diagnosis and other aspects related to this interesting and not well known entity. However, 1 limitation of the review, especially regarding the imaging diagnosis with cardiac magnetic resonance, should be also brought to the readers' attention.

The authors stated that for an echocardiography diagnosis after careful evaluation of all criteria, the most important echocardiographic criterion remains a noncompacted/compacted ratio greater than 2.0 in end-systole, well known as the Jenni criteria (2). One important detail in this case is that the measurement must be performed during the end-systolic phase of the cardiac cycle.

The authors do not provide by the other side a completely clear criteria for the measurement on CMR that they consider the technique that confirms diagnosis in the central illustration. They mentioned a noncompacted/compacted ratio greater than 2.3 on CMR be considered the cutoff for an LVNC diagnosis (3), the Petersen criteria, but they neglected to mention when we must perform this measurement, something of importance due to the different moment in the cardiac cycle at which it must be performed compared with echocardiography. The diagnosis with CMR is suggested when the noncompacted/compacted ratio is greater than 2.3 during end-diastole.

In our opinion, there is a lot of room for improvement in the diagnosis of this entity due to the important differences that an incorrect measurement could cause and also whether we need to take into account a different moment in the cardiac cycle at which to perform the measurements, depending on what imaging technique we use for the diagnosis or even where we must make the measurement (4). Maybe it is time to add genetics to improve this

imaging-based suspect diagnosis, as highlighted in the editorial by Garcia-Pavia and de la Pompa (5) with a review of all the imaging criteria available to the date.

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REPLY: The Importance of Cardiac Cycle in the Imaging Criteria for Left Ventricular Noncompaction



We appreciate the letter by Dr. Vidal-Perez and colleagues as it highlights the current lack of consensus on nosology and diagnostic criteria of left ventricular noncompaction (LVNC). In daily clinical practice, the presence of noncompaction in the absence of dilated cardiomyopathy (DCM) or left ventricular hypertrophy (LVH) is often annotated as a descriptive finding but not systematically labeled as cardiomyopathy, especially when identified as an incidental finding in otherwise functionally normal hearts. In clinical reports, the term *hypertrabeculation* or *increased trabeculation* followed by topographic indications is far more common than the diagnosis of LVNC. The question remains as to when should LVNC also be diagnosed as LVNC cardiomyopathy (1)?

Imaging provides quantification on the anatomy of the layers of the left ventricle as well as the possibility of measuring ratios between compacted and non-compacted layers. The thickness of the left ventricular layers are taken in end-diastole with cardiac magnetic resonance (2). However, thickness of the left ventricular layers can be measured with echocardiography in both end-systole and end-diastole, as indicated by Jenni et al. (3) and Paterick et al. (4). Paterick et al. (4) selected to measure in end-diastole because the thickness of compacted and non-compacted layers was deemed more precise in end-diastole. Chamber wall thickness measurements performed with echocardiography in end-diastole is currently consistent with the convention of the American Society of Echocardiography. The absence of consensus criteria is partly explained by the still limited knowledge on the natural history of the disease, namely, the evolution of LVNC with normal left ventricular size and function at onset and later developed left ventricular dilation and eventually dysfunction or LVH.

The point raised by Vidal-Perez and colleagues about genetics is appropriate more as a question rather than an answer as genes only causing LVNC and not associated with DCM or hypertrophic cardiomyopathy have not been identified. Although we strongly support genetic testing in all cardiomyopathies, a key problem remains the definition of LVNC and consequently its diagnosis and distinction with features of prominent, increased trabeculation. The measurement of the thickness of the epicardial compacted layer could add information to the ratio of compaction/noncompaction. For example, a thick epicardial layer could guarantee a normal function whatever the noncompaction is.

A major clinical problem specifically associated with LVNC is the risk of mural endocardial thrombotic stratification and thromboembolic complications. The presence of deep recesses may favor the formation of mural thrombi, but this only occurs in dysfunctional hearts. No case to date with LVNC and normal cardiac function has been associated with mural thrombosis or embolic complications. These latter cases occur typically in dilated and dysfunctional hearts with LVNC, which is DCM with LVNC. The open question is when to start anticoagulant treatment in these patients.

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