Reply to: Consensus on unsolved issues of left ventricular hypertrabeculation/non-compaction is warranted

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Abstract

In reply to the letter by Finsterer and Stöllberger entitled “Consensus on unsolved issues of hypertrabeculation/noncompaction is warranted,” the authors reaffirm the need for a concordant opinion on the unsolved issues which still loom over the diagnostic and clinical facets of left ventricular non-compaction. Subjects known to have ventricular hypertrabeculation and who subsequently experience a thromboembolic event should still be meticulously screened for other commoner and possibly co-existent embolic sources. In the absence of systolic dysfunction left ventricular non-compaction alone is not an indication for oral anticoagulation in so far as the primary prevention for thromboembolism is concerned.
There exists no exact proof that the degree of inotropic dysfunction in hypertrabeculated hearts is directly and solely related to the extent of the non-compaction. Subendocardial perfusion deficits; diminished coronary blood flow reserve; trabecular fibrosis and aberrations at the cellular level may also be responsible for affecting ventricular systolic function.
Early neurological referral is indicated following the diagnosis of non-compaction with the aim of screening for the many disorders known to be associated with this condition and genetic screening tests are best resorted to only if clinical examination fails to expose a relevant syndrome.
The current cardiac magnetic resonance diagnostic criteria for non-compaction still have some important limitations which beckon a unifying consensus.

We are grateful to Prof. Finsterer and Dr. Stöllberger for their valuable letter underscoring the need for a consensus on the unsolved issues which still loom over the diagnostic and clinical facets of left ventricular non-compaction (LVNC).
An appreciable number of reports exist in the literature to date describing thromboembolic events (cerebrovascular accidents [1], [2], [3], transient ischaemic attacks [4], superior mesenteric artery occlusion [5], coronary artery embolism [6]) in patients found to have LVNC. We agree that the discovery of a non-compacted left ventricle in subjects who have sustained a thromboembolic event should not automatically license physicians to assume that the hypertrabeculation is wholly and uniquely responsible for the phenomenon. We concur with the need to conduct a more meticulous search for alternative, commoner and possibly co-existent embolic sources in these subjects (paroxysmal atrial fibrillation; patent foramen ovale etc.) even once the discovery of the non-compaction has been made. Analysis of larger case series conducted in 2005 and 2008, involving 62 [7] and 229 [8] LVNC patients

respectively, both rendered similar results which suggested that (in the absence of systolic dysfunction [8]) LVNC alone is not an indication for oral anticoagulation in so far as the primary prevention for thromboembolism is concerned.

We reported that the left ventricle afflicted by hypertrabeculation “generally demonstrates impaired systolic function” and that “LVNC may present with depressed systolic function of the non-compacted left ventricle resulting in heart failure” with the degree of systolic dysfunction being related to the extent of non-compaction. We agree that to date there exists no exact proof that the degree of inotropic dysfunction is directly and solely related to the extent of the trabeculations and indeed the altered myocardial contractility of non-compacted hearts may stem from a variety of other causes not least: subendocardial perfusion deficits [9]; diminished coronary blood flow reserve; trabecular fibrosis and aberrations at the cellular level. While several early studies did demonstrate a correlation between the degree of non-compaction and the extent of systolic dysfunction [10], [11], [12] more recent evidence suggests that other parameters such as the degree of trabecular delayed hyperenhancement on cardiac magnetic resonance imaging (CMR) and pathological tissue Doppler velocities [13] correlate more strongly with reductions in ejection fraction [14]. Interestingly Fazio et al. have recently reported no correlation between the number of non-compacted segments and the reduction in ejection fraction when considering a 16-segment ventricular model in 238 patients with isolated non-compaction being diagnosed using the Jenni echocardiographic criteria alone [15]. These findings invite us to rethink our understanding of the complex relationship between left ventricular hypertrabeculation and heart failure in this context.

The value of multiplane transoesophageal echocardiography in the diagnosis of LVNC [16] was indeed outlined in our paper. This modality can provide good views of the left ventricular free wall [17] but visualization of the apex is usually suboptimal partly because of its remoteness from the oesophagus and partly because sections across it may tend to be oblique. It is easier and perhaps better to resort to contrast echocardiography using second generation agents when interrogating the cardiac apex in the search for prominent myocardial trabeculations and when struggling to distinguish between hypertrophic cardiomyopathy and apical mural thrombi [18]. We agree that conditions like myocardial abscesses [19], haematomas, and the apical form of hypertrophic cardiomyopathy must also feature as contenders in the differential diagnosis of the disease.

Following a diagnosis of LVNC early neurological referral is indicated with the aim of screening for the many disorders known to be associated with this condition. A detailed history and physical examination should be followed by investigations as dictated by the clinical findings and these could take the form of blood tests for muscle enzymes, nerve conduction studies, electromyographies, lumbar punctures, fundoscopy, nerve and muscle biopsies and so on and so forth. We agree that genetic screening tests should be resorted to if clinical examination fails to expose a relevant syndrome and that even then, judicious planning and conscientious selection of genetic tests are crucial. The rationale behind offering echocardiographic screening to first degree relatives rests on the notion that up to 44% of affected patients in clinical series have a family history of cardiomyopathy [20].

Finally we thank the authors for highlighting the existing limitations of the current CMR diagnostic criteria for LVNC. When the Jenni et al. parameters are applied to CMR for instance, they are usually modified such that the end-diastolic vertical long-axis (2-chamber) view is employed in preference to the traditional end-systolic parasternal short-axis view used in transthoracic echocardiography. These

compromises allow for superior spatial resolution and better differentiation between compacted (C) and non-compacted (N) layers [9], [21] and would suggest pathological non-compaction with an N/C ratio of > 2.3 (a higher cut-off than that conventionally used in the end-systolic transthoracic measurements). Furthermore Fazio et al. recently suggested a cut-off of > 2.5 because inferior values threaten to increase the number of false positive diagnoses [22]. A unifying consensus on these and other CMR criteria is strongly solicited.
Misdiagnosis, overreaction and mistreatment of LVNC may persist till all avenues of its convoluted pathogenesis and diagnosis are explored, but the avid research efforts to date augur well for the future.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [23].

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