Normal systolic function in hypertrophic cardiomyopathy: reality or myth?: reply

We would like to thank Efthimiadis et al. for their interest in our work. Indeed, it was long believed that patients with hypertrophic cardiomyopathy (HCM) had normal or supranormal systolic function despite mutations in genes encoding for sarcomeric proteins. This concept was, at least partly, based on the use of endocardial indices of systolic function such as ejection fraction. Ejection fraction is generally normal or supranormal in HCM patients. However, it is well known that ejection fraction is a poor surrogate for systolic function in the presence of left ventricular hypertrophy because a normal ejection fraction is maintained by the subnormal function of additional sarcomeres laid in parallel. Reduced shortening of extra parallel sarcomeres leads to the same thickening and ejection of blood as would normal shortening of fewer sarcomeres.1 Experimental data started to separate reality from myth by showing that there is myocardial dysfunction even before the development of left ventricular hypertrophy2 because normal ejection fraction is maintained in vivo by the subnormal function of additional sarcomeres. Reduced shortening of extra parallel sarcomeres leads to the same thickening and ejection of blood as would normal shortening of fewer sarcomeres.1

We concur that isolated systolic or diastolic dysfunction do not exist. One is coupled to the other. Studies have confirmed that parameters of systolic function are important determinants of peak blood pressure response with exercise \( r = 0.62, \ p < 0.01 \). Given a blunted blood pressure response to exercise, the identification of non-compaction in patients with dilated, hypertrophic, and restrictive cardiomyopathies suggests that non-compaction may be considered as a non-specific morphological trait rather than a distinct cardiomyopathy.3 In addition, not all non-compaction associated mutations are confined to genes that encode for a specific construct or functional element of the cardiomyocyte, but have been described in genes that encode for sarcomeric, cytoskeletal, and/or cell junctional proteins.1

References

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Non-compaction: a distinct cardiomyopathy or non-specific morphological trait?

With great interest, we have read the article of Hoedemaekers et al.1 on linking non-compaction cardiomyopathy to hypertrophic, restrictive, and dilated cardiomyopathies. The authors extensively describe two families in which variable severities of non-compaction of the myocardium segregated with mutations in the cardiac ß myosin heavy chain gene (MYH7).

Although genetic heterogeneity of traditional cardiomyopathies is well recognized, the concept was, at least partly, based on the use of endocardial indices of systolic function such as ejection fraction. Ejection fraction is generally normal or supranormal in HCM patients. However, it is well known that ejection fraction is a poor surrogate for systolic function in the presence of left ventricular hypertrophy because normal ejection fraction is maintained by the subnormal function of additional sarcomeres. Reduced shortening of extra parallel sarcomeres leads to the same thickening and ejection of blood as would normal shortening of fewer sarcomeres.1 Experimental data started to separate reality from myth by showing that there is myocardial dysfunction even before the development of left ventricular hypertrophy2 because normal ejection fraction is maintained by the subnormal function of additional sarcomeres. Reduced shortening of extra parallel sarcomeres leads to the same thickening and ejection of blood as would normal shortening of fewer sarcomeres.1

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References
Non-compaction: a distinct cardiomyopathy or non-specific morphological trait?: reply

With great interest I read the letter by Germans et al., as a reaction to our manuscript titled ‘cardiac β-myosin heavy chain defects in two families with non-compaction cardiomyopathy: linking non-compaction to hypertrophic, restrictive, and dilated cardiomyopathies. Eur Heart J 2007; 28:2732–2737.

We agree that it is essential to standardize the diagnosis of non-compaction cardiomyopathy (NCCM) in the context of the cardiac myopathies, which was the main purpose of our study. We also agree that echocardiography, both quantitative and qualitative, is the most valuable tool for the diagnosis of NCCM. However, our approach to standardization was different from that of Germans et al. We aimed to define the diagnostic criteria of NCCM in the clinical setting, whereas Germans et al. aimed to define a pathological equivalent in the context of heart failure.

We acknowledge the contributions of Petersen et al. and Biagini et al. to the standardization of the diagnosis of NCCM. Petersen et al. identified a limited number of seven NCCM patients, developed diagnostic criteria for NCCM, and suggested that cardiac magnetic resonance imaging (MRI) should be used to determine whether NCCM can be considered a distinct cardiomyopathy or as a non-specific morphological trait. Biagini et al. suggested that cardiac magnetic resonance imaging may have a role in the diagnosis of NCCM.

We believe that the discussion on the diagnosis of NCCM is ongoing and that further studies are needed to better understand the pathophysiology of this condition. We also agree that the identification of NCCM-like crypts in asymptomatic HCM mutation carriers as described by Germans et al. is a valuable contribution to the field.

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