median age 82 years; range 70 to 88 years). Four patients were symptomatic for dyspnea (New York Heart Association functional class II); 1 had a pacemaker; 2 were receiving antihypertensive therapy; carpal tunnel syndrome had been previously diagnosed in 3. None had overt neurologic symptoms. ECG was abnormal in all cases: atrial fibrillation in 3 cases, left anterior hemiblock in 2, isolated ST-T abnormalities in 4, abnormal Q waves in 3, and low QRS voltage in 2. Increased left ventricular (LV) wall thickness was detected in all patients (mean LV wall thickness, 14 mm; interquartile range: 13 to 15 mm), and LV ejection fraction was 58% (interquartile range: 54% to 67%). Other echocardiographic abnormalities included mild pericardial effusion (n = 6), A-V valve thickening (n = 5), and myocardial granular sparkling (n = 8). LV "hypertrophy" was completely unexplained in 10 patients and was out of proportion in 4 (moderate systemic hypertension with nondilated LV and ascending aorta). Genetic analysis was performed in 6 cases and documented an *Ile68Leu* TTR mutation in a single patient. Endomyocardial biopsy was performed in the remaining 5 patients and detected TTR-related amyloidosis in all, leading to a final diagnosis of wild-type TTR amyloidotic cardiomyopathy (senile systemic amyloidosis [SSA]).

In this large cohort of subjects undergoing $^{99m}$Tc-DPD scintigraphy for different reasons, 45 (0.36%) showed unexpected myocardial tracer uptake. We cannot exclude a slight underestimation of the real prevalence because of the retrospective nature of the study. The subsequent cardiological evaluation revealed an unexplained increase of LV wall thickness in all the analyzed cases, and endomyocardial biopsy confirmed the diagnosis of TTR-related amyloidosis in all the patients who underwent the procedure. The impact of our study, albeit small, mainly relies on the possibility of an early (pre-clinical) identification of patients affected by TTR-related amyloidotic cardiomyopathy, mainly the form related to the deposition of wild-type TTR, a condition that is believed to be highly underdiagnosed. There are currently no reliable studies regarding the prevalence of SSA. If we consider all our patients with myocardial $^{99m}$Tc-DPD uptake to be affected by TTR-related cardiomyopathy (mainly SSA), the prevalence of the disease would reach 1.4% among men in the ninth decade. It is noteworthy that although SSA is known to mainly affect elderly men, a relevant number of women showed asymptomatic myocardial tracer uptake. Finally, our data require confirmation through prospective studies, but, if confirmed, they would suggest the possibility of using $^{99m}$Tc-DPD scintigraphy as a screening tool in populations at risk. With the advent of new drugs aimed at halting TTR deposition that are currently under clinical evaluation (4), an early diagnosis of the disease is highly encouraged and should be pursued.

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# Diagnostic Problem of LV Hypertrabeculation/ Noncompaction?

With interest we read the article by Stacey et al. (1) about systolic and diastolic criteria for left ventricular hypertrabeculation/noncompaction (LVHT). Uniform diagnostic criteria for LVHT are a still unsolved problem in echocardiography as well as other imaging modalities like cardiac magnetic resonance (CMR). Whether the results of their investigations will lead to more clarification is questionable due to the following reasons: 1) No pathoanatomic gold standard is provided; thus, neither sensitivity nor specificity of the proposed criteria can be assessed. 2) It remains uncertain in how many patients LVHT was diagnosed by echocardiography. There is a need to calculate the percentage of LVHT patients in whom LVHT was diagnosed on echocardiography and CMR, on CMR but not on echocardiography and on echocardiography but not on CMR. 3) The duration and quality of follow-up remain uncertain. Were follow-up data obtained for each of the included patients? 4) Differentiation between LVHT on the one hand and papillary muscles, false tendons, and aberrant bands on the other is a difficult issue because these structures are seen frequently, and there is considerable anatomic variability (2,3). To our knowledge, the proposed "papillary muscle classification system" is not based on any pathoanatomic classification. Furthermore, it seems rather difficult to differentiate between papillary muscles and trabeculations when only short-axis views are considered. Only by using longitudinal views will it be possible to visualize the communication of the papillary muscles with the mitral valve leaflets via the chordae tendineae. Not to differentiate between LVHT and papillary muscles is not acceptable because LVHT diagnostic criteria definitions clearly exclude papillary muscles from the evaluation. 5) There is no need to distinguish between "myopathic LVHT" and "normal variants" because they are morphologically the same and have a similar complication rate and outcome. Normal variants may have subclinical myopathy or may have chromosomal abnormalities, which manifest only in the heart. This is why we recommend referring all LVHT patients to a myologist to also detect neurological abnormalities which are clinically inapparent for the cardiologist. As an initial step, the authors should provide information about how many of their patients had an elevated creatine kinase level and in how many patients was LVHT familial. Familial LVHT may suggest hereditary disease, including neuromuscular disorders.

Additionally, we have the following questions regarding the presented data. 1) It was previously reported that echocardiographically

diagnosed LVHT is more often visible on CMR in patients with an enlarged left ventricle and systolic dysfunction than in those with normal-size, well-contracting left ventricles (4). Did any of the patients undergo follow-up CMR studies and did the ratios of noncompacted to compacted layers and the trabecular mass change? 2) From pathoanatomic investigation we know that endocardial fibrosis is frequently found in LVHT patients (5). Was that phenomenon also visible on CMR? 3) Because of unknown reasons, LVHT was diagnosed more frequently in male than female patients. How can the relatively high proportion of female patients in the present study be explained?

In conclusion, only close cooperation between cardiologists, radiologists, neurologists, and cardiac pathologists will solve the enigmas of LVHT.

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## REPLY: Diagnostic Problem of LV Hypertrabeculation/Noncompaction?

We thank Drs. Stollberger and Finsterer for their interest in our recent publication (1). They raised several points that will help clarify future discussions regarding left ventricular noncompaction (LVNC).

Although the criteria for LVNC cardiomyopathy are evolving, the phenotypic characterization has been previously reported. We used standard criteria based on the end-systolic (2), end-diastolic (3), trabecular mass (4) ratio and ensured the presence of apical trabeculations with blood noted in trabecular recesses. Furthermore, we observed 88% concordance between systolic criteria with cardiac magnetic resonance and interpretable echocardiography in our patient cohort. In our experience, the most common cause of overdiagnosis is the singular dependence on the long-axis views. An obliquely imaged papillary muscle in the long axis may give the appearance of trabeculation instead of papillary muscle because the long-axis cardiac images are optimized for wall motion analysis and not papillary muscle anatomy. By using the short- and long-axis views together, an interpreter has the opportunity to distinguish between papillary muscle and trabeculation. As to whether some trabeculation may represent normal variants, 43% of the MESA (Multi-Ethnic Study of Atherosclerosis) population had 1 segment with an end-diastolic noncompacted to compacted ratio >2.3 (5). The clinical relevance of a single-segment pattern is uncertain. Our patients had multiple segments involved and occasional right ventricular involvement. Of note, no LVNC pattern criteria were associated with late gadolinium enhancement, making infiltrative or idiopathic disease such as endomyocardial fibrosis unlikely. Among the 8 patients who had serial cardiac magnetic resonance evaluation, no substantive changes in the pattern of LVNC were appreciated.

We agree that a pathoanatomic gold standard is lacking at this time; however, increased recognition and longitudinal clinical care may yield a pathway to obtaining tissue and address these concerns. Patients in our study did not have diagnoses of neuromuscular disorders or congenital heart disease and were not biologically related. Although a longer duration of clinical follow-up would be ideal, a mean follow-up of 500 days in our cohort does provide clinically useful short- and intermediate-term information. Concerns regarding genotypic myopathies as a clinical subset are not answered by our data, and future proposed collaboration may help to investigate these associations.

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