Trabeculated (Noncompacted) and Compact Myocardium in Adults
The Multi-Ethnic Study of Atherosclerosis

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Background—A high degree of noncompacted (trabeculated) myocardium in relationship to compact myocardium (trabeculated to compact myocardium [T/M] ratio >2.3) has been associated with a diagnosis of left ventricular noncompaction (LVNC). The purpose of this study was to determine the normal range of the T/M ratio in a large population-based study and to examine the relationship to demographic and clinical parameters.

Methods and Results—The thickness of trabeculation and the compact myocardium were measured in 8 left ventricular regions on long axis cardiac MR steady-state free precession cine images in 1000 participants (551 women; 68.1±8.9 years) of the Multi-Ethnic Study of Atherosclerosis cohort. Of 323 participants without cardiac disease or hypertension and with all regions evaluable, 140 (43%) had a T/M ratio >2.3 in at least 1 region; in 20 of 323 (6%), T/M >2.3 was present in >2 regions. A multivariable linear regression model revealed no association of age, sex, ethnicity, height, and weight with maximum T/M ratio in participants without cardiac disease or hypertension (P>0.05). In the entire cohort (n=1000), left ventricular ejection fraction (β=-0.02%/P=0.015), left ventricular end-diastolic volume (β=0.01/mL; P<0.0001), and left ventricular end-systolic volume (β=0.01/mL; P<0.001) were associated with maximum T/M ratio in adjusted models, whereas there was no association with hypertension or myocardial infarction (P>0.05). At the apical level, T/M ratios were significantly lower when obtained on short- compared with long-axis images (P=0.017).

Conclusions—A ratio of T/M of >2.3 is common in a large population-based cohort. These results suggest re-evaluation of the current cardiac MR criteria for left ventricular noncompaction may be necessary. (Circ Cardiovasc Imaging. 2012;5:357-366.)

Key Words: cardiomyopathy ■ cardiovascular MRI ■ noncompaction ■ trabeculation

According to the American Heart Association, left ventricular (LV) noncompaction (LVNC) is classified as primary genetic cardiomyopathy and is characterized by the presence of a thin compact epicardial and a thick noncompacted endocardial myocardial layer in the region of the left ventricle.1,2 Heart failure, thromboembolism, and arrhythmias are known complications.3 LVNC is considered a congenital disease due to an arrest of the normal compaction process of the developing myocardium. However, it has been postulated that LVNC can also develop postnatally.4

Clinical Perspective on p 366

The large increase in publications for LVNC let Oechslin et al5 raise the question “…whether advances in noninvasive diagnostic technologies led to better delineation of the morphological appearance of the myocardium or whether LVNC is over diagnosed and the diagnostic criteria are too sensitive.” In the interpretation of advanced imaging studies, the question of LVNC arises for patients with prominently trabeculated myocardium without known reason for myocardial dysfunction and/or arrhythmia. Prominent LV trabeculations are known to occur in normal hearts, thus complicating the diagnosis of LVNC.5–7

The MRI criterion of a ratio of noncompacted (trabeculated) versus compacted myocardium (T/M) >2.3 (measured at diastole on long axis images) for LVNC has been suggested by Petersen et al.2 Using this cutoff value to distinguish pathological noncompaction, they demonstrated a high...
sensitivity, specificity, and positive and negative predictive values of 86%, 99%, 75%, and 99%, respectively.

The aims of this study were (1) to determine the specificity of the current MRI criterion for LVNC in a large population-based study; and 2) to determine if the T/M ratio and thickness of trabeculation vary with demographics, LV function, and clinical characteristics. We note that the terms “noncompacted myocardium” and “(prominent/hyper-) trabeculation” are used interchangeably in the literature. Because the term “noncompacted myocardium” implies LVNC cardiomyopathy, whereas “trabeculation” appears to be a more neutral expression indicating a normal anatomic variant, the latter is used in the discussion that follows.

Methods

Study Sample

The Multi-Ethnic Study of Atherosclerosis (MESA) study is a population-based longitudinal study initiated in July 2000. At enrollment, study participants were free of clinically recognized cardiovascular disease including LVNC. One thousand consecutive participants (characteristics are shown in Table 1) were chosen randomly from the “MESA 5” follow-up evaluation of the cohort, initiated in April 2010. The study was approved by the Institutional Review Boards of each of the 6 participating US field sites, and all participants provided written informed consent.

Cardiac MR

Cardiac MR (CMR) examinations were performed at the 6 MESA field centers (Baltimore, Winston-Salem, New York, Minneapolis, Los Angeles, Chicago) on 1.5-T MR scanners (Signa Excite; General Electric Medical Systems, Waukesha, WI; and Avanto/ESpree; Siemens, Erlangen, Germany). Retrospectively electrocardiography-gated long- and short-axis cine images were acquired using a steady-state free precession sequence with the following parameters for Siemens (and GE) scanners: TR/TE ≤3.8 ms (minimize/minimized (minimum full); flip angle 70° (45°); field of view 360×360 mm; matrix size 256×256 (256×192); slice thickness 8 mm, interslice gap 2 mm; bandwidth 1221 (977) Hz/pixel; parallel imaging GRAPPA: 2 (ASSET); number of segments 18 (16); temporal resolution 49 (48) ms. The presence of myocardial scar was evaluated in 665 participants who consented to contrast administration and without contraindication beginning 15 minutes after administration of 0.15 mmol/kg gadopentetate dimeglumine (Bayer) using a single-shot inversion recovery steady state free precession (SSFP) sequence.

Image Evaluation

CMR examinations were evaluated using WebPAX (Heart Imaging Technologies, LLC, Durham, NC). Horizontal and vertical long axis cine steady-state free precession images were used for measuring the thickness of the compact myocardium and of the trabeculation in the middle of 8 LV regions: anterior, inferior, septal, and lateral at midcavity (MidAnt, MidInf, MidSept, MidLat) and apical level (ApAnt, ApInf, ApSept, ApLat) at end-diastole (Figure 1). Measurements were not performed at the base of the heart because trabeculation was not typically observed in this region or showed only a very thin layer. As per Petersen et al, the apex was also excluded because myocardium is usually very thin and with prominent trabeculation in normal subjects. Compact myocardium was defined as a myocardial layer of homogeneous medium signal intensity on the steady-state free precession image without inclusion of blood of brighter signal intensity. Trabeculation was defined as a meshwork of the trabeculae carneae of medium signal intensity adjacent to compact myocardium interspersed with blood of bright signal intensity. Measurements of the thickness of the compact myocardium as well as of the adjacent trabeculation were obtained perpendicular to the compact myocardium (Figures 1A and C). Fifty percent of the thickness of the “black line” on the epicardial surface related to a

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Entire Study Cohort (n=1000)</th>
<th>Participants Without Cardiac Disease or Hypertension (n=367)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, no. (%)</td>
<td>551 (55)</td>
<td>192 (52)</td>
</tr>
<tr>
<td>Age, y, mean±SD (range)</td>
<td>68.1±8.9 (54–94)</td>
<td>65.4±8.3 (54–91)</td>
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<td>Ethnicity, no. (%)</td>
<td>White 503 (50)</td>
<td>187 (51)</td>
</tr>
<tr>
<td></td>
<td>Chinese 81 (8)</td>
<td>46 (13)</td>
</tr>
<tr>
<td></td>
<td>Black 252 (25)</td>
<td>65 (18)</td>
</tr>
<tr>
<td></td>
<td>Hispanic 164 (16)</td>
<td>69 (19)</td>
</tr>
<tr>
<td>Height, cm, mean±SD</td>
<td>167±9.6</td>
<td>167±9.7</td>
</tr>
<tr>
<td>Weight, kg, mean±SD</td>
<td>78.9±16.3</td>
<td>76.6±16.1</td>
</tr>
<tr>
<td>Hypertension, no. (%)</td>
<td>439 (44)</td>
<td>0</td>
</tr>
<tr>
<td>Participants with evaluation of all 8 regions, no. (%)</td>
<td>827 (83)</td>
<td>323 (88)</td>
</tr>
<tr>
<td>Participants excluded per region,* no. (%)</td>
<td>Midcavity anterior 125 (13)</td>
<td>34 (9)</td>
</tr>
<tr>
<td></td>
<td>Midcavity inferior 118 (12)</td>
<td>33 (9)</td>
</tr>
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<td></td>
<td>Midcavity septal 32 (3)</td>
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<tr>
<td></td>
<td>Midcavity lateral 36 (4)</td>
<td>5 (1)</td>
</tr>
<tr>
<td></td>
<td>Apical anterior 149 (15)</td>
<td>40 (11)</td>
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<tr>
<td></td>
<td>Apical inferior 141 (14)</td>
<td>38 (10)</td>
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<td></td>
<td>Apical septal 40 (4)</td>
<td>6 (2)</td>
</tr>
<tr>
<td></td>
<td>Apical lateral 38 (4)</td>
<td>5 (1)</td>
</tr>
<tr>
<td>LV EF, %, mean±SD</td>
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<td>62.4±5.9</td>
</tr>
<tr>
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<tr>
<td>LV EDV, mL, mean±SD</td>
<td>123±33†</td>
<td>124±31</td>
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<tr>
<td>LV ESV, mL, mean±SD</td>
<td>47±19†</td>
<td>47±15</td>
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<tr>
<td>Delayed gadolinium CMR performed, no. (%)</td>
<td>665 (67)</td>
<td>367 (100)</td>
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<tr>
<td>Myocardial infarction,‡ no. (%)</td>
<td>36 (4)</td>
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<tr>
<td>Nonischemic scar,§ no. (%)</td>
<td>25 (4)</td>
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<tr>
<td>Participants with focal myocardial thinning,</td>
<td></td>
<td>no. (%)</td>
</tr>
<tr>
<td>LV hypertrophy, no. (%)</td>
<td>14 (1)</td>
<td>0</td>
</tr>
</tbody>
</table>

*Participants without cardiac disease or hypertension—participants with a CMR examination including MDE imaging, no history of myocardial infarction, no evidence of an ischemic or nonischemic scar on CMR MDE images, left ventricular ejection fraction >50%, systolic blood pressure <140 mm Hg and no hypertensive medication, and LV myocardial thickness <15 mm at end-diastole.

†LV EF, LV EDV, and LV ESV were available for 990 participants only.
‡Based on clinical diagnosis and cardiac MRI.
§Based on cardiac MRI only; note that the presence of a nonischemic scar could be assessed only in participants whose examination included myocardial delayed enhancement imaging (n=665).
||Due to myocardial infarction; thinning of ≥50% of the thickness of the compact myocardium compared with adjacent myocardium in the area of measurement.

chemical shift artifact was included in the compact myocardium. Papillary muscles that were clearly observed as compact tubular structures were not included in the measurements. Short-axis views and cine mode were used additionally to separate papillary muscles from trabeculation. Regions with inadequate image quality were
excluded from further analysis. Regions with focal thinning >50% of the compact myocardium in the area of measurement as assessed visually due to myocardial infarction were also excluded.

Measurements were first made by a single primary reader. To assess intra- and interobserver agreement, measurements were repeated by the primary reader and also by a second reader in 100 (10%) randomly chosen participants. Furthermore, in a subset of 100 (10%) randomly chosen participants, measurements obtained on long-axis images were compared with measurements on corresponding short-axis views. To crossreference short- and long-axis views, images were transferred to QMass V.7.2 (Medis Medical Imaging Systems) and measured along a reference line displayed by that software. For those purposes, also measurements on long-axis images were repeated with QMass software. Because short-axis images showed blurring of trabeculation and compact myocardium at the apex, for the comparison, measurements were obtained 1 slice toward the midcavity from the middle of the apical level.

LV functional parameters were obtained using CIM software (cardiac image modeler) by 2 independent readers (Auckland, New Zealand). The presence of myocardial delayed enhancement was categorized as present or absent as defined by 2 additional independent readers.

**Statistical Analysis**

The thickness of the trabeculation and the T/M ratio were evaluated. Analysis was performed for the 1000 randomly chosen consecutive MESA participants (in the following referred to as the “entire/whole cohort”) as well as for a subset of these 1000 participants considered to be without cardiac disease or hypertension (in the following referred to as the “participants without cardiac disease or hypertension”). None of the 1000 participants was known to have LVNC. “Participants without cardiac disease or hypertension” (n = 367) were defined as participants with a CMR examination including myocardial delayed enhancement imaging, no history of myocardial infarction, no evidence of an ischemic or nonischemic scar on CMR myocardial delayed enhancement images, left ventricular ejection fraction >50%, systolic blood pressure <140 mm Hg and no antihypertensive medication, and LV myocardial thickness <15 mm at end-diastole.

For multivariable linear regression analysis, T/M ratio and thickness of trabeculation, which were normally distributed, were calculated as maximum of the measurements of all 8 regions in those participants only in whom all 8 measurements were obtained (83% of the entire cohort and 88% of the participants without cardiac disease or hypertension). Missing values of 1 of the independent variables led to exclusion of the participants for the respective model (10 of 1000 [0.01%] due to missing LV functional parameters).

For participants without cardiac disease or hypertension, multivariable linear regression models were developed to determine the relationship between the dependent variables T/M ratio and thickness of trabeculation and age, sex, ethnicity, height, and weight (Model 1). The relationship of T/M ratio and trabeculation thickness to LV function parameters (LV ejection fraction, LV end-diastolic volume [LVEDV] and LV end-systolic volume [LVESV]) was individually assessed after adjustment for parameters in Model 1: Model 2a (Model 1 + LV ejection fraction), Model 2b (Model 1 + LVEDV), and Model 2c (Model 1 + LVESV). Due to colinearity, LV parameters were not combined in the same model. For the entire cohort, the relationship of T/M ratio and thickness of trabeculation was additionally assessed in relationship to hypertension and myocardial infarction again adjusted for parameters in Model 1.

Intraclass correlation coefficient, Spearman correlation coefficient, and the Bland-Altman method were used to investigate intra- and interobserver agreement.

Measurements for the thickness of trabeculation, the compact myocardium, and the T/M ratio obtained on long- and short-axis images were compared using a paired t test for normal distributed variables (thickness of compact myocardium) and a Wilcoxon signed-rank test for nonnormally distributed variables (thickness of trabeculation and T/M ratio) for the midcavity level and the apical level separately.

Probability values <0.05 were considered statistically significant. All statistical analysis was performed using PASW statistical software (Version 19).

**Results**

Table 1 shows demographic characteristics of the entire cohort and the participants without cardiac disease or hypertension. Compared with the entire cohort, the participants without cardiac disease or hypertension were approximately 3 years younger, had 5 mg smaller LV mass, and were 3% more likely to be male.
In the whole cohort as well as in participants without cardiac disease or hypertension, trabeculation was most commonly detected and most prominent in the apical lateral (79%, 81%), midanterior (78%, 79%), midlateral (64%, 67%), apical anterior (62%, 65%), and apical inferior (60%, 63%) regions, respectively. Trabeculation was least common in the midseptal (3%, 4%) region (Figures 2 and 3).

Figure 2. Trabeculation thickness for the subset of participants without cardiac disease or hypertension for the midcavity anterior (A), inferior (B), septal (C), lateral (D), and the apical anterior (E), inferior (F), septal (G), and lateral (H) regions.

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Figure 3. Percent participants with trabeculation per region at the midcavity level (outer circle) and the apical level (inner circle) of the entire cohort (A) and the subset of participants without cardiac disease or hypertension (B).
In 564 of 7321 (8%) evaluable regions in the total cohort, a T/M ratio >2.3 was present. In 243 of 2936 (8%) evaluable regions in participants without cardiac disease or hypertension, a T/M ratio >2.3 was present. The distribution of the T/M ratios is shown in Figure 4. For 827 participants with all 8 evaluable regions, 309 of 827 (37%) had a T/M ratio >2.3 in at least 1 region and 18 (2%) had trabeculation in none of the regions. For 323 participants without cardiac disease or hypertension and with all 8 evaluable regions, 140 (43%) had a T/M ratio >2.3 in at least 1 region. Twenty of these 323 participants (6%) had a T/M ratio >2.3 in >2 regions and 5 (2%) had trabeculation in none of the regions. For 323 participants without cardiac disease or hypertension with all 8 evaluable regions, 140 (43%) had a T/M ratio >2.3 in at least 1 region. Twenty of these 323 participants (6%) had a T/M ratio >2.3 in >2 regions and 5 (2%) had trabeculation in none of the regions. For 323 participants without cardiac disease or hypertension with all 8 evaluable regions, 140 (43%) had a T/M ratio >2.3 in at least 1 region. Twenty of these 323 participants (6%) had a T/M ratio >2.3 in >2 regions and 5 (2%) had trabeculation in none of the regions. For 323 participants without cardiac disease or hypertension with all 8 evaluable regions, 140 (43%) had a T/M ratio >2.3 in at least 1 region. Twenty of these 323 participants (6%) had a T/M ratio >2.3 in >2 regions and 5 (2%) had trabeculation in none of the regions. For 323 participants without cardiac disease or hypertension with all 8 evaluable regions, 140 (43%) had a T/M ratio >2.3 in at least 1 region. Twenty of these 323 participants (6%) had a T/M ratio >2.3 in >2 regions and 5 (2%) had trabeculation in none of the regions. For 323 participants without cardiac disease or hypertension with all 8 evaluable regions, 140 (43%) had a T/M ratio >2.3 in at least 1 region. Twenty of these 323 participants (6%) had a T/M ratio >2.3 in >2 regions and 5 (2%) had trabeculation in none of the regions. For 323 participants without cardiac disease or hypertension with all 8 evaluable regions, 140 (43%) had a T/M ratio >2.3 in at least 1 region. Twenty of these 323 participants (6%) had a T/M ratio >2.3 in >2 regions and 5 (2%) had trabeculation in none of the regions. For 323 participants without cardiac disease or hypertension with all 8 evaluable regions, 140 (43%) had a T/M ratio >2.3 in at least 1 region. Twenty of these 323 participants (6%) had a T/M ratio >2.3 in >2 regions and 5 (2%) had trabeculation in none of the regions.

Association of Trabeculation With Demographic, Clinical, and LV Parameters

Table 2 shows the 5th, 50th, and 95th percentiles of the composite measures maximum T/M ratio and maximum trabeculation thickness. For participants without cardiac disease or hypertension, there was no relationship between T/M ratio and age, sex, race/ethnicity, height, or weight. Compared with white, Chinese (mean difference $\beta=1.5$ mm; $P=0.02$) and black ($\beta=1.3$ mm; $P=0.01$) race were associated with a higher maximum thickness of trabeculation in participants without cardiac disease or hypertension. Maximum thickness of trabeculation was also greater in men than women ($\beta=1.1$ mm; $P=0.04$).

In participants without cardiac disease or hypertension, lower ejection fraction ($\beta=-0.02/\% ; P=0.044$) and higher LVEDV ($\beta=0.01/\text{mL} ; P<0.0001$) were associated with a greater maximum T/M ratio after adjustment for age, sex, ethnicity, height, and weight. In addition, higher LVEDV ($\beta=0.03 \text{ mm/mL} ; P<0.0001$; and higher LVESV...
...were also associated with maximum thickness of trabeculation in participants without cardiac disease or hypertension after adjustment. Results in the entire cohort paralleled those of the participants without cardiac disease or hypertension for T/M ratio and maximum trabeculation thickness, except greater LV mass was additionally associated with trabeculation thickness in the entire cohort (â=0.02 mm/g; P=0.013) and remained significant after additional adjustment for hypertension (â=0.02 mm/g; P=0.014). The presence of hypertension or myocardial infarction was not associated with maximum T/M ratio or trabeculation thickness (P>0.05). This result regarding association with myocardial infarction remained unchanged after inclusion of the participants (n=7) who had been excluded previously due to focal thinning of the compact myocardium in the area of measurement related to myocardial infarction.

**Short-Axis Versus Long-Axis Myocardial Assessment**

By convention, MRI criterion of a ratio of noncompacted (trabeculated) versus compacted myocardium (T/M) >2.3 has been measured on long-axis images to avoid geometric distortion of the trabecular matrix.2 We additionally assessed short-axis measurements from 100 randomly selected participants to assess the degree of variation between long- and short-axis measurements.

At the apical level, trabeculation thickness and thickness of compact myocardium were significantly greater when obtained on short-axis images compared with long-axis images (trabeculation thickness, median [interquartile range], 6.0 mm [0–8.9 mm; short axis] and 5.8 mm [0–8.1 mm; long axis], respectively, P<0.01; thickness of compact myocardium, mean±SD, 6.2±1.7 mm [short axis] and 5.2±1.2 mm [long axis], respectively; P<0.0001). At the midcavity, there was a significant difference for thickness of compact myocardium (mean±SD, 7.1±2.0 mm [short axis] and 7.3±1.9 mm [long axis]; P<0.01), whereas there was no significant difference for thickness of trabeculation (P=0.8).

Correspondingly, the T/M ratios for short-axis images at the apical level were less than values obtained on long-axis images (median [interquartile range], 1.0 [0–1.4] and 1.1 [0–1.7], respectively; P=0.02). T/M ratios at the midcavity level measured on short axis were not different than long-axis measurements (P=0.13).

**Intra- and Interobserver Agreement**

Assessment of the intraobserver agreement revealed a Spearman correlation coefficient of 0.84 and a probability value of <0.001 for both thickness of trabeculation and T/M ratio and a correlation coefficient of 0.88 (P<0.001) for thickness of compact myocardium. By Bland-Altman method, bias (95% CI) for trabeculation thickness was 0.5 mm (0.3–0.6 mm) with lower limits of agreement (95% CI) of −3.4 mm...
Discussion

In the current study we demonstrated (1) that 43% of subjects without cardiac disease or hypertension had a T/M ratio > 2.3 in at least 1 myocardial segment; (2) T/M ratio was not associated with age, sex, race/ethnicity, height, or weight in subjects without cardiac disease or hypertension and not with hypertension and myocardial infarction in the entire cohort; (3) the maximum thickness of trabeculation was positively associated with Chinese and black races and with male sex; (4) in both the entire cohort and the subjects without cardiac disease or hypertension, there was a negative association of LV ejection fraction and a positive association of LVEDV and LVESV with the maximum T/M ratio, whereas LVEDV and LVESV were also positively associated with maximum trabeculation thickness; and (5) values for thickness of trabeculation and compact myocardium as well as T/M ratio vary with measurement technique.

The MESA study population is a well-characterized population cohort that was enrolled between the years 2000 to 2002. The study participants have no known diagnoses of left ventricular noncompaction. All study participants were free of clinical cardiovascular disease at baseline enrollment. At the time of this CMR examination (beginning 2010), 367 of 1000 of this substudy’s participants were free of clinical as well as CMR-defined cardiac disease and without hypertension or hypertension medication use. We focused our results on this “healthy” subpopulation of 367 participants to further exclude the potential of occult LVNC. We also noted that in both the “health participants” and the entire subpopulation of 1000 participants, lower LV ejection fraction, higher LVEDV, and higher LVESV were associated with slightly higher values of T/M ratio in adjusted models. In participants without cardiac disease or hypertension, a 10-mL higher LVEDV was associated with 0.1 higher T/M ratio. In these same participants, a 10-mL higher LVESV was associated with a 0.3 higher T/M ratio. Although these effects are small, clinicians should be aware that slightly higher T/M ratios may be present in participants with elevated LVEDV and LVESV. Alternatively, this could represent a subclinical cardiomyopathy, a hypothesis that may be addressed by the long-term outcome of these participants in future studies.

At autopsy in hearts free of cardiac disease, Boyd et al found prominent LV trabeculae in 323 of 474 (68%) of specimens. “Prominent trabeculation” was defined as “discrete muscle bundles, more than 2 mm in diameter,” whereas the thickness of the whole trabeculated layer is not mentioned. In an echocardiography-based study Kohli et al realized that also 8% of subjects free of cardiac disease fulfilled ≥1 of the echocardiographic criteria to diagnose LVNC. This result led them to the conclusion that the current echocardiographic criteria might be too sensitive. Similarly, our results suggest that the current CMR criterion for LVNC shows low specificity, because 43% of participants without cardiac disease or hypertension had a T/M ratio > 2.3 in at least 1 region. However, only 6% participants without cardiac disease or hypertension in the current study had a maximum T/M ratio > 2.3 in > 2 regions. Reconsideration of CMR criterion may improve specificity for LVNC diagnosis, but the effect on sensitivity is unknown.

Although according to the literature diagnosis with echocardiography and CMR is based solely on morphological criteria such as T/M ratio, in routine clinical practice, LVNC is usually also based on assessment of function. Dysfunction in addition to prominent trabeculation/noncompacted myocardium adjacent to thinned compact myocardium is sug-

### Table 2. Percentiles of Maximum Values

<table>
<thead>
<tr>
<th></th>
<th>Maximum T/M Ratio</th>
<th>Maximum Thickness of Trabeculation, mm, for All (men, women)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>5th</td>
<td>50th</td>
</tr>
<tr>
<td>Entire cohort (n=827)</td>
<td>0.9</td>
<td>2.0</td>
</tr>
<tr>
<td>Participants without cardiac disease or hypertension (n=323)</td>
<td>1.0</td>
<td>2.2</td>
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</table>

T/M ratio indicates thickness of trabeculation/thickness of compact myocardium.
gestive of LVNC. We therefore suggest evaluation of a multifactorial approach to diagnose LVNC in further studies including morphological criteria such as the T/M ratio, the number of affected regions, and assessment of function.

In the current study, trabeculation was most common at the apical lateral (81%) and midcavity anterior (79%) regions (Figure 3) and the highest ratios were measured at the apical lateral and anterior lateral regions (Figure 6). This result is similar to previous publications. Petersen et al.\(^2\) realized that in 91% of 45 healthy subjects, trabeculation was present at the apical level and in 78% at midcavity level. Dawson et al.\(^6\) also reported that trabeculation was present in \(\approx1\) segments in all of 120 healthy volunteers. Furthermore, 64% had an apical free wall trabecular layer at least as thick as the compact layer.\(^6\) We measured trabeculation on long-axis images similar to Petersen et al.,\(^2\) whereas Dawson et al. evaluated short-axis images. The cone shape of the left ventricular apex particularly tends to overestimate measurements of the thickness of compact myocardium in the

**Figure 7.** Steady-state free precession (SSFP) cine sequence at end-diastole acquired as vertical long-axis (A) and short-axis (C) views and the corresponding schematic diagrams (B, D). Example of triangular-shaped trabeculation along the lateral left ventricular wall. Measurements of the thickness of trabeculation and the compact myocardium were acquired perpendicular to the compact myocardium on long axis images (double arrows in B). Due to the conical shape of the left ventricle in the apical region and depending on the configuration of the trabeculation, measurements obtained at the corresponding short-axis image (D) as indicated by the gray double line (B) reveal a greater thickness of the compact myocardium and a smaller thickness of trabeculation (double arrows in D).

**Figure 8.** Steady-state free precession (SSFP) cine sequence at end-diastole acquired as vertical long-axis (A) and short-axis (C) views and the corresponding schematic diagrams (B, D). Example of a participant with prominent trabeculation, a normal ejection fraction (56.2%), and no history of hard or soft cardiovascular disease events. Measurements of the thickness of trabeculation and the compact myocardium were acquired perpendicular to the compact myocardium on long-axis images (double arrows in B). Due to the conical shape of the left ventricle in the apical region, measurements obtained at the corresponding short-axis image (D) as indicated by the gray double line (B) reveal a greater thickness of the compact myocardium and equal thickness of trabeculation (when measured until the middle of the left ventricular cavity; double arrows in D). The resulting T/M ratio is smaller when measurements were obtained on short axis images. T/M ratio indicates thickness of trabeculation/thickness of compact myocardium.
short-axis view in relationship to the cosine of the ventricular angulation with respect to the axis of the ventricle. Differences in MRI scanner pulse sequences, study population, or measurement technique also account for differences between studies. Papillary muscle separation from trabeculation is particularly challenging and is not described in other articles. We excluded papillary muscles when clearly visible as a tubular compact structure (Figures 1A and C). We realize that there is often a smooth transition between the compact papillary muscle and trabeculation (Figure 1A). It is challenging to clearly delineate between papillary muscle and trabeculation in this transition zone. To avoid inclusion of papillary muscles in measurements, it is useful to correlate orientation of the long-axis images with short-axis images. Software that provides a reference line of the acquisition plane is particularly helpful.

In the current study, a thicker maximum trabeculation was significantly associated with Chinese and black ethnicities, whereas the maximum T/M ratio did not show an association with ethnicity. Kohli et al demonstrated that more black individuals of their control groups fulfilled echocardiographic criteria for noncompaction compared with white individuals (13.3% versus 3.3%), whereas in a study by Peters et al, none of 54 control subjects of sub-Saharan African descent fulfilled echocardiographic criteria for LVNC. In the current study, male sex was also significantly associated with a higher maximum thickness of trabeculation. In another study in which the mean thickness of trabeculation was compared for each segment separately, there was no statistically significant difference between men and women. Both studies did not show a significant association between sex and the T/M ratio.

There was no association of trabeculation thickness or T/M ratio with age in the current study. Dawson et al did not find an age-related trend of T/M ratio. Only when study participants were divided into 2 age groups a significantly lower ratio of the older age group compared with younger individuals was present. In the current study, only older participants (age range, 54–94 years) were included. This might explain why no statistical relation between T/M ratio and trabeculation thickness was detected.

There are several limitations of the current study. No participant was known to have the diagnosis of LVNC but there was no gold standard of reference for the diagnosis of LVNC. However, the prevalence of LVNC in the general population has been estimated at 0.05%, which means that in the present cohort of 1000 subjects, only 0.5 participants might have nondiagnosed LVNC, which would not affect the result. The results apply only to measurements made by the techniques described in this study for the long-axis analyses. The mean age of study participants was 68 years, although no relationship of age to T/M ratio was present. Although we discuss the potential to understand the specificity of criteria for LVNC, this is hypothetical because LVNC participants were not studied by these methods. Strengths of the study include a large heterogeneous study population that allowed multivariable analysis of associations of trabecular measurements with clinical, LV, and demographic characteristics.

In conclusion, T/M ratio > 2.3 in at least 1 myocardial region is common, present in 43% of our study participants. The T/M ratio is dependent on measurement technique and thus dedicated guidelines with respect to measurement techniques are necessary. T/M ratio is a robust and reproducible measure that is independent of age, sex, ethnicity, height, and weight in participants without cardiac disease or hypertension.

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References

CLINICAL PERSPECTIVE

Diagnosis of left ventricular noncompaction cardiomyopathy remains challenging in daily practice. Using standard morphological cardiac MRI criteria of trabeculated and compacted myocardium (T/M ratio) of $>2.3$, overdiagnosis of left ventricular noncompaction cardiomyopathy has been suggested. The present study evaluated T/M ratio in a large population-based cohort of 1000 subjects; 323 of these subjects were free of cardiac disease. In the subset of individuals free of cardiac disease, 43% of subjects had at least 1 region with T/M ratio $>2.3$. This suggests that T/M ratio alone for left ventricular noncompaction cardiomyopathy diagnosis may have low specificity. Measurement of T/M ratio varied using different imaging planes (long axis versus short axis), indicating a standardized measurement is needed. T/M ratio did not vary with age, sex, ethnicity, height, or weight; therefore, no adjustment to these demographic parameters is required.
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