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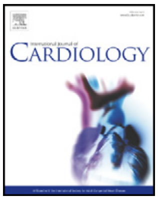

Reference values for left and right ventricular trabeculation and non-compacted myocardium[☆]

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ABSTRACT

Background: Since the differentiation between physiological and pathological trabeculation is challenging, we assessed its distribution in a reference population of selected healthy volunteers.
Methods: We studied 117 subjects (58 males) stratified into age tertiles and by gender. Cardiovascular magnetic resonance images were acquired using a standard SSFP-sequence. Left and right ventricular (LV/RV) end-diastolic (EDV), end-systolic (ESV) and trabeculated volumes indexed to the body surface area as well as ejection fraction (EF) were quantified in short-axis views. The maximum non-compacted-to-compacted (NC/C) ratio was measured in long-axis views.
Results: The trabeculated volumes were significantly larger in men than in women and decreased with age. The correlation between both was moderate ($r = 0.46$; $p < 0.001$). LV trabeculated volume was positively associated with EDV and ESV ($r = 0.74$; $r = 0.59$; both $p < 0.001$) and negatively with EF ($r = -0.27$; $p < 0.005$). It was no independent predictor for EF. The maximum NC/C ratio was >2.3 in 46.2% and >2.5 in 37.6% of the subjects, which is regarded as abnormal in current literature. The fraction of subjects with a maximum NC/C ratio >2.3 and the mean maximum NC/C ratio differed significantly between gender but not between age groups. An increasing NC/C ratio was associated with a significant decrease in EF ($r = -0.21$; $p < 0.05$).
Conclusion: A considerable amount of healthy volunteers fulfils the current diagnostic criteria of LV noncompaction with female subjects showing a higher fraction of false-positive results than males. LV trabeculated volume is more pronounced in young subjects and declines with age. The use of age- and gender-specific reference values as provided in this study may facilitate the delineation of physiological and pathological findings.

1. Reference values for left and right ventricular trabeculation and non-compacted myocardium

1.1. Background

The signification and distribution of cardiac trabeculation are poorly understood. Especially the differentiation between physiological and pathological forms as in left ventricular noncompaction (LVNC) is challenging. LVNC is characterized by pronounced intraventricular trabeculations and deep recesses that communicate with the cavity but not with the coronary artery system. Therefore, it shows a typical myocardial two-layer structure with a thin compacted outer layer and a thick non-compacted but trabeculated inner one [1,2].

In clinical routine, echocardiography (EC) is mostly used for the initial diagnosis of LVNC and several diagnostic criteria have been published. Yet, the concordance between the different definitions is poor [3]. Furthermore, some authors suggest that the present EC parameters were too sensitive, whereas others argue that several patients who may have a milder form of the disease fell short of fulfilling the criteria and thus remain undiagnosed [3,4].

Therefore, cardiovascular magnetic resonance (CMR) has gained importance due to its high spatial resolution, its excellent intrinsic soft tissue contrast and its good reproducibility. Studies comparing both imaging modalities indicated that CMR might be superior to EC with regard to the assessment of myocardial trabeculation [5,6]. Consequently, several CMR studies assessing the physiological extent of the left ventricular (LV) trabeculation have been performed and different diagnostic criteria applying the ratio of non-compacted to compacted (NC/C) myocardial thickness or the fraction of the trabeculated volume have been published [6–9].

Current population studies on LV trabeculation used standard two-dimensional measurements whereas volumetric assessments are only

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[☆] The authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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available from small cohorts [6–8]. Furthermore, the data about the RV trabeculation and function is still limited although it might play a significant role in LVNC [10].

Therefore, the aim of this study was to investigate the physiological distribution of the ventricular trabeculations with respect to age and gender in a population of proven healthy volunteers applying standard two-dimensional as well as volumetric measurements.

Furthermore, the right ventricular (RV) trabeculation and function and their relation to LV ones were assessed.

2. Methods

2.1. Study population

All subjects of this population study were preselected by interview, were completely asymptomatic and had no history of cardiac disease. They were screened for normal NT-proBNP values (<125 ng/l). Eligible candidates received a physical examination, an electrocardiography and an oral glucose tolerance test which needed to show no pathologic findings. Subjects were not allowed to take any drugs except for oral contraceptives or chronic thyroid hormone substitution. All participants were tested for normal levels of serum creatinine, aspartate aminotransferase, alanine aminotransferase, thyroid-stimulating hormone, haemoglobin concentration as well as normal leucocyte and platelet counts. Furthermore, high-sensitivity cardiac troponin T (hscTnT) levels were determined.

CMR stress examinations (adenosine or dobutamine) were performed in all participants to exclude a significant coronary artery disease.

Finally, 58 male and 59 female healthy volunteers of three age groups (1: 20–34 years, 2: 35–50 years, 3: >50 years) were included in the study.

The body height, weight and blood pressure were measured and the body surface area (BSA) was calculated using the Mosteller formula for BSA [11].

The study was approved by the institutional ethics committee and all subjects gave written informed consent. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki.

2.2. Image acquisition

Images were acquired in a 1.5 T whole body MRI scanner (Achieva, Philips Medical Systems, Best, The Netherlands) using a standard vector-ECG gated steady-state free precession (SSFP) sequence. Short-axis views from cardiac base to apex as well as 2-, 3- and 4-chamber (ch) views were obtained as usual.

All CMR examinations were transferred to a dedicated workstation (Philips Viewforum, Philips Medical Systems, Best, The Netherlands) and analyzed by two independent observers who were blinded to the clinical data.

Epicardial and endocardial contours, papillary muscles and the trabeculation-free LV volume were outlined manually on short-axis views (Fig. 1).

End-diastolic and end-systolic volumes (EDV, ESV) were derived from the endocardial borders of the compacted myocardium in the end-diastolic and end-systolic frames excluding the LV papillary muscles. Stroke volume (SV) was defined as the difference between EDV and ESV and ejection fraction (EF) was calculated as the ratio of SV/EDV. LV wall mass was assessed in end-diastole.

The LV and RV trabeculated volumes were measured in diastolic short axis views. They were defined as the volume between the endocardial border and a line, which was drawn between the trabeculation-free ventricular cavity and the ventricular volume which contained trabeculation and papillary muscles (Fig. 1).

Since in previous studies papillary muscles were excluded from analysis, we also measured the papillary muscle-free LV trabeculated volume (pfLVTV) which is defined as the LV trabeculated volume less the volume of the papillary muscles.

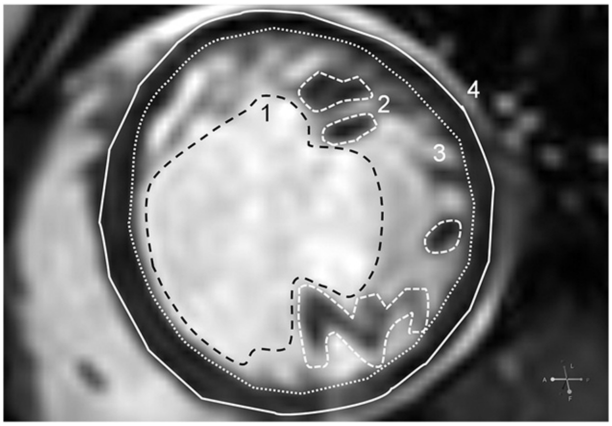

Fig. 1. Example of the image analysis in a LV short axis view. Line 1 encloses the trabeculation-free LV volume. Line 2 shows the segmentation of the papillary muscles. Line 3 represents the endocardial and line 4 the epicardial border.

EDV, ESV, SV, LV wall mass, trabeculated volumes and pfLVTV were indexed to the BSA. Compacted and non-compacted myocardial thickness was assessed in end-diastolic 2-, 3- and 4-ch views. The maximum NC/C ratio was used for analyses. As in previous studies the apex was excluded from measurements.

2.3. Statistics

Patients were divided into six subgroups with respect to age and gender.

Data was assessed for normal distribution applying the Kolmogorov–Smirnov test. Continuous data of two groups were analyzed using the Student's t-test for independent samples or the Welch test if the F-test showed unequal variances. For comparison of more than two groups a one-way analysis of variance (ANOVA) was applied. If the ANOVA was positive, a Student–Newman–Keuls test for pairwise comparison of the subgroups was performed. The Pearson correlation coefficient was employed for the analysis of the association between two variables. A stepwise multivariable regression model was applied to analyze the relationship between multiple variables. For the assessment of age-dependency a linear regression analysis was applied. For the comparison of categorical data we used the Fisher's exact test.

Statistical analyses were mostly carried out using MedCalc 12.5 (MedCalc Software bvba, Ostend, Belgium).

A p-value < 0.05 was regarded as statistically significant. All continuous data are presented as mean and standard deviation (SD).

3. Results

3.1. Study population

The mean age of the reference population was 41.8 years and did not differ between men and women in the entire cohort (41.8 SD 12.8 yrs. vs. 41.8 SD 13.3 yrs., p = n.s.) or in prespecified age tertiles (1: 27.8 SD 3.8 yrs. vs. 25.6 SD 3.2 yrs., 2: 42.0 SD 5.1 yrs. vs. 44.1 SD 3.8 yrs., 3: 56.5 SD 5.6 yrs. vs. 56.6 SD 4.2 yrs., all p = n.s.).

BSA was higher in men than in women in general (2.00 SD 0.19 m^2 vs. 1.76 SD 0.15 m^2, $p < 0.01$, Table 1) and in all age tertiles (1: 2.01 SD 0.15 m^2 vs. 1.75 SD 0.14 m^2, 2: 2.01 SD 0.19 m^2 vs. 1.74 SD 0.17 m^2, 3: 1.99 SD 0.22 m^2 vs. 1.79 SD 0.13 m^2, all $p < 0.01$). There was no significant age-dependency of BSA.

The systolic and diastolic blood pressure was significantly higher in male subjects than in female ones (130.2 SD 10.9/79.1 SD 8.7 mm Hg vs. 122.4 SD 10.6/73.3 SD 7.8 mm Hg, $p < 0.01$) and the diastolic values were higher in the elderly men in the third age tertile compared to the younger men in the first tertile (83.7 SD 8.3 mm Hg vs. 74.8 SD