Noncompaction cardiomyopathy, a frequently overlooked entity (...but beware of over diagnosis!)

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Noncompaction cardiomyopathy (NCCM) is recognised as a separate disease entity since the first report in 1984 of a rare case with persistent myocardial sinusoids and a series of 8 paediatric and adolescent patients in 1990 with increased trabeculation of the left ventricular endocardium [1, 2]. Since then, NCCM has been the subject of an increasing number of reports in the medical literature (July 2012: 1127 publications; source www.ncbi.nlm.nih.gov/pubmed) and is now recognised as a primary, predominantly genetic disorder of the myocardium [3]. Increased awareness of this disease entity made us recognise more and more cases of noncompaction cardiomyopathy, especially with the help of modern imaging modalities such as contrast echocardiography and magnetic resonance imaging (MRI), allowing better visualisation of the left ventricular cavity [4].

The classic clinical presentation of NCCM includes severe heart failure, malignant ventricular arrhythmias, thromboembolic events and sudden cardiac death [5]. It is characterised by an excessively prominent trabecular meshwork and deep intertrabecular recesses, as seen early in human embryogenesis. Compaction of the myocardium usually occurs between weeks five and eight of embryonic life and begins in the septum and base of the heart and from epicardium to endocardium [6]. Therefore, the primary pathophysiological hypothesis was that incomplete compaction of the loose myocardial meshwork during gestation resulted in a noncompacted heart, prone to heart failure, arrhythmias and intracardiac thrombus formation. The diagnosis of NCCM is established by imaging of the ventricular walls and cavities, classically by two-dimensional transthoracic echocardiography with colour Doppler flow. The frequently

used diagnostic criteria proposed by Jenni et al. include abnormally thickened ventricular walls with a two-layered structure, consisting of thickened, noncompacted (NC) endocardial myocardium and a thin compacted (C) epicardial myocardium (maximal end-systolic ratio $NC/C > 2$ at parasternal short-axis view) [5]. The abnormal structures of NCCM could be identified as deep intertrabecular recesses with colour Doppler flow as well as regional hypokinesia. Other imaging modalities such as left ventricular (LV) angiography, computed tomography, contrast echocardiography and MRI have also been used to visualise these recesses.

In the current issue of this journal, Luijckx et al. report the prevalence of hypertrabeculation in elite white and black athletes as seen at MRI [7]. They describe a greater degree of LV hypertrabeculation and lower LV and RV ejection fraction in elite black football players vs. white football players, which could be erroneously mistaken for NCCM. Interestingly, excess trabeculations ($NC/C > 1.0$) were only seen at the mid-ventricular level. However, as the authors also state, the sample size of black athletes was small (10 vs 28) and no non-athletic healthy controls were included. This study nevertheless contains welcome additional data, stimulating the discussion in this as yet new disease entity, where the danger is always over-diagnosis by us ‘overenthusiastic’ clinicians.

It should be well recognised that the trabecular meshwork of thin muscle bundles at the apical third of the left ventricle and thick muscle bundles aligning the myocardial wall are normal structures. Up to 70 % of hearts display at least one prominent LV trabeculation, with two or more present in 36 % [8]. Also, in pathology studies it has been shown that a hypertrabecularisation pattern was present in 43 % and 28 % of patients with dilated cardiomyopathy (DCM) and ischaemic heart disease, respectively [9]. Other subjects known with a high incidence of prominent trabeculations include

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those with chronic pressure or volume overload such as patients with valvular heart disease [10]. Therefore, an important limitation of current diagnostic criteria of NCCM is the fact that all definitions are based on morphological abnormalities as seen by an imaging modality [11]. The commonly used echocardiographic Jenni criteria were based on a post-mortem study in seven subjects with prominent trabeculations [5]. Echocardiographic views are operator-dependent and off-axis views may affect the morphological assessment of myocardial trabeculations. However, excellent contrast of MRI, as used in the study by Luijckx et al., allows better visualisation of trabeculations, in particular when echocardiography windows are poor [7]. One MRI diagnostic criterion based on an end-diastolic ratio of compacted to noncompacted myocardium >2.3 in long-axis views was used for the diagnosis of NCCM [12]. Another proposed diagnostic MRI criterion is $>20\%$ of LV trabecular mass compared with global LV mass [13]. The last data are not reported by Luijckx et al.

A new diagnostic possibility in this challenging issue would be measurement of ‘rigid body rotation’, a very promising *functional* criterion for the diagnosis of NCCM [14]. We recently studied the diagnostic value of rigid body rotation in a large group of patients with prominent trabeculations, including healthy subjects, subjects with prominent trabeculations but not fulfilling the NCCM diagnostic criteria, typical NCCM patients and DCM patients. The majority of healthy subjects had completely normal rotation (98 %; initial counterclockwise basal and clockwise apical rotation, followed by end-systolic clockwise basal and counterclockwise apical rotation), whereas the subjects with hypertrabeculation not fulfilling diagnostic criteria for NCCM predominantly had partly normal rotation (71 %; normal end-systolic rotation but absence of initial rotation in the other direction), and the patients with NCCM usually had abnormal rotation with the basal and apical level predominantly in the same direction (88 %). None of the patients with DCM showed rigid body rotation. Sensitivity and specificity of rigid body rotation for differentiating NCCM from ‘hypertrabeculation’ were 88 % and 78 %, respectively. It would be very interesting to use this new functional diagnostic possibility in these challenging groups with prominent trabeculations.

In conclusion, as Luijckx et al. conclude, prominent or excess trabeculations could indeed erroneously been mistaken for noncompaction cardiomyopathy in professional (especially black) athletes [7]. Given the possible psychological, social, legal, insurance or employment consequences, we clinicians must be very cautious about too ‘easily’ making the diagnosis of NCCM. However, the flip-side of the coin is missing the opportunity of pre-symptomatic

diagnosis and treatment of this potentially grave prognosis with a too reluctant attitude to diagnose NCCM.

Conflict of interest None.

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