With the increasing accuracy of cardiac imaging techniques, new findings, not or rarely observed before, come to light. In particular, the improvement in high spatial resolution of a multiplanar imaging technique such as cardiac magnetic resonance (CMR), associated with its increased contrast between blood and endocardial border surface of current cine images, led the appreciation of subtle left ventricular (LV) wall structural features, not seen or neglected by 2-dimensional echocardiography. This is the case of myocardial clefts, described both in hypertrophic cardiomyopathy (HCM) and in healthy volunteers, thus providing another hot potato to the hands of the clinical cardiologist.

These myocardial invaginations have been variably called clefts, crypts, fissures, crevices, and atypical LV noncompaction. Although the etiopathogenesis remains a matter of debate, it is a common belief that they represent a failure to resorb the trabeculated part of ventricular wall during normal embryological development, as seen in isolated LV noncompaction.1,2 Before the development of coronary circulation, the myocardium consists of a spongy meshwork of intertwined myocardial fibers organized into trabeculae with deep recesses, the latter communicating with the LV cavity and enabling a direct blood supply to the myocardium.

Myocardial clefts have been described within the LV wall of patients with HCM since early postmortem studies.3-5 In particular, to the best of our knowledge, the first pathological description of a myocardial cleft dates back to 1958, in the historical publication of Donald Teare.6 Noteworthy, Teare observed clefts not only at gross examination (see Figure A) but at histology in case no. 1: “Microscopical examination of a section of the tumor shows a bizarre arrangement of bundles of muscle fibres running in diverse directions and separated by connective tissue and clefts…the clefts are lined with endothelium covering sparse elastic tissue which is similar to the structure of the normal endocardium,” and further, in case no. 3 (see Figure, B): “…the clefts or fissures between muscle bundles were greater than in any other specimen. These endothelial-lined channels communicated with the cavities of both ventricles, but pursued such tortuous and muscle-bound courses as to suggest that there could be no shift of blood from one ventricle to another during systole.”

Not surprisingly, these myocardial clefts with a slit-like shape remained largely unrecognized by pathologists for 2 main reasons. First, according to the well-known aphorism by Merrill C. Sosman, you see only what you look for and you recognize only what you know; second, heart specimens at postmortem are always in a contracted state and features are closer to end-systolic cardiac images than end-diastolic ones, thus explaining the narrowing or even obliteration of myocardial clefts at naked eye and their detectability only at histological examination.6

Two-dimensional echocardiography is able to detect these clefts, but the sensitivity and specificity of the pathological findings have been questioned. CMR has provided greater insight into these clefts and their potential pathological significance.

The first consecutive series of HCM mutation carriers systematically investigated by CMR demonstrated an 81% prevalence of so-called crypts in the inferoseptal LV myocardium, such that it was suggested that this finding may represent a preclinical marker of HCM. A subsequent report, highlighting the prevalence of crypts even in healthy volunteers (7 of 120; 6%), has toned down the initial enthusiasm.7 More recently, Maron et al demonstrated that none of the healthy volunteers (98 versus 120 patients with HCM) prospectively investigated exhibited crypts, whereas they had a high percentage, similar to Germans et al,8 in HCM mutation carriers without LV hypertrophy (61%). Overall, despite the differences in healthy volunteers, all studies confirmed a similar low prevalence of crypts in HCM patients with overt disease phenotype (ie, with LV hypertrophy). According to Maron et al,8 the observation that crypts are uncommon in patients with overt HCM suggests the possibility that they could regress with subsequent LV wall thickening and remodeling. But another possibility is that the more prominent the hypertrophy, the more common the virtual diastolic obliteration of these invaginations due to compression by the surrounding hypertrophied myocardium.6

To determine the real clinical significance of LV myocardial crypts, Petryka et al,9 in this issue of Circulation: Cardiovascular Imaging, investigated the prevalence of crypts in routine vertical long-axis plane cines in the largest population of consecutive patients undergoing CMR.9 Crypts, defined as invaginations penetrating >50% of the thickness of adjoining compact myocardium in diastole in the basal to mid-inferior LV wall,7 were identified in 46 of 686 patients (6.7%). Crypts were found to be most prevalent in patients...
with HCM (5 of 32; 15.6%), myocarditis (2 of 13; 15.3%), and arterial hypertension (3 of 22; 13.6%). The prevalence of crypts in phenotype-negative HCM family members was in keeping with previous results of the same group (5%), lower than that reported by Maron et al. As argued by Petryka et al, genetic difference between various HCM genotype-positive and phenotype-negative subjects could be one explanation. However, the location of crypts considered in the 2 studies could also account for the different results. In fact, although Petryka et al included only crypts located in the inferobasal LV wall, Maron et al extended the observation to crypts in the anterior and anteroseptal walls, in keeping with the original autopsy observations.

In general, when analyzing data on myocardial crypts coming from different CMR studies and registries, some essential issues should be defined a priori: first, whether the crypts are isolated or multiple, mimicking the presence of marked trabeculations characteristic of segmental LV noncompaction, where these findings are usually seen in the lateral wall; second, the location of crypts, useful to differentiate from spontaneously closed ventricular septal defects; third, the presence of late gadolinium enhancement (LGE); and finally, consideration should be given to differentiating from congenital diverticulum and aneurysm, facilitated by the presence of intertrabecular spaces lacking outpouching.

Given these shortcomings, in the setting of familial HCM, the identification of isolated crypts in patients undergoing CMR should prompt a screening of first-degree family members, and possibly genetic testing.

Pathological studies on heart specimens with HCM and hypertrophy of different etiologies as well as normal hearts are lacking and should be performed to gain an insight on this entity. In the past, we identified that myocardial bridges are a frequent component of HCM without clear significance. No follow-up data are yet available on whether crypts predict the development of HCM or portend an unfavorable outcome.

Prospective registries with uniform CMR protocols and definition of terms should include patients with different ethnicities, and these data may improve the knowledge of the real prevalence and significance of crypts in normal and HCM subjects. The results of such studies will help to determine whether these crypts represent a congenital defect due to maldevelopment, a genetic familial disorder, a prephenotypic HCM marker, or a benign structural variant.

Disclosures
None.

References

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