Prevalence of Inferobasal Myocardial Crypts Among Patients Referred for Cardiovascular Magnetic Resonance

Joanna Petryka, PhD; A. John Baxi, MD, PhD, MRCP; Sanjay K. Prasad, MD, FRCP; Dudley J. Pennell, MD, FRCP; Philip J. Kilner, MD, PhD

Background—Crypts or clefts in the left ventricular inferobasal myocardium have been detected by cardiovascular magnetic resonance (CMR), but the extent to which they represent prephenotypic markers of hypertrophic cardiomyopathy (HCM) or incidental structural variants remains controversial.

Methods and Results—We examined retrospectively the routine vertical long-axis cines in 686 consecutive patients (48±20 years, 55% men) referred for CMR. Crypts were identified in 46 (6.7%), 17 being among patients (8.7% of 196) with otherwise normal CMR findings and without a known family history of HCM. Higher percentages were found in patients with HCM (16%), myocarditis (15%), and hypertension (14%) but without reaching statistical significance (P=0.12). Only 1 (5%) of 20 phenotype-negative HCM family members had a visible crypt. Relative to those without, patients with crypts had lower indexed left ventricular end-systolic volumes (P=0.042) and higher indexed left and right ventricular stroke volumes (P=0.007 and P=0.015) and ejection fractions (P=0.003 and P=0.021). Crypts tended to narrow in systole, varying slightly in size, shape- and number, without obvious group-related features.

Conclusions—Single or paired inferobasal myocardial crypts were an occasional and by no means rare finding among patients referred for CMR without a pretest suspicion of HCM. This, together with similar previous findings in a cohort of healthy volunteers, supports their being regarded, in such individuals, as incidental variants of local myocardial structure, unlikely to require further investigation. However, a larger registry-type study may be justified to investigate the clinical implications of multiple crypts, especially if associated with HCM family history. (Circ Cardiovasc Imaging, 2014;7:259-264.)

Key Words: cardiomyopathy, hypertrophic ▼ cleft ▼ crypt ▼ diverticulum ▼ magnetic resonance imaging

Clefts or fissures were observed at autopsy between muscle bundles of the junctional regions between the left ventricle (LV) and right ventricle (RV) of the hearts of patients with hypertrophic cardiomyopathy (HCM) >20 years ago.1 Comparable recesses were later identified in vivo by cardiovascular magnetic resonance (CMR) in a small group of HCM carriers and termed crypts,2 although none was observed then in age- and sex-matched healthy volunteers. The authors therefore postulated potential pathological significance to the presence of crypts. In contrast, we had by then noticed inferobasal recesses in healthy volunteers as well as several patient groups referred for CMR in our unit. We retrospectively reviewed acquisitions in 120 healthy volunteers and found that 6% had single clefts or, in one case, a pair, visible inferobasally in the routine vertical long-axis (VLA) cines.3 We used the term cleft because it indicated their typically slit-like shape: V- or U-shaped as seen in diastolic long-axis cine frames, with narrowing or occlusion in systole, and crescentic in selected cases where image planes had been aligned through them, tangential to the local wall curvature.4 The terms cleft and crypt can perhaps be used interchangeably to describe such extensions of luminal blood into the otherwise compact myocardium, with a tendency to narrow or obliterate in systole, without local hypokinesia or dyskinesia.3 The typical location is in the basal to middle inferior wall of the LV, adjacent to the line of insertion of the RV.

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In 2012, Maron et al6 suggested that myocardial crypts could be regarded as a prephenotypic marker of HCM in patients with a family history of the condition, having found crypts to be present in 19 of 31 carriers of HCM, although none was identified in 98 subjects without cardiovascular disease. The absence of crypts in the latter group drew correspondence from 2 CMR centers based, like our own, in London, UK.5,7 Their experience, which accords with ours, was that clefts or crypts are occasionally visible in patients or volunteers with no other cause for suspicion of HCM. The uncertain clinical relevance of such findings is of potential concern in relation to large numbers of patients, their relatives, and volunteers likely to be studied by CMR in the coming decades. As the majority of recent authors have used the term crypts rather than clefts
for inferobasal recesses that we interpret as belonging to the same phenotypic spectrum, we will adopt the term crypts for the remainder of this article.

**Methods**

We examined retrospectively the routine VLA cines acquired in all 686 consecutive patients who had undergone clinically requested CMR studies at our institution (The Royal Brompton Hospital, London, UK) in the 2 months of October and November 2012. Because the study involved a retrospective review of patient images and records, individual patient consent was not required by our Ethics Committee who approved the study. All CMR studies were acquired using either 1.5 Tesla whole-body systems (Siemens Sonata, Erlangen, Germany, or Siemens Avanto, Erlangen, Germany) or a 3 Tesla system (Siemens Magnetom Skrya, Erlangen, Germany). Aspects of the CMR protocols varied individually depending on clinical indication but always included balanced steady-state free precession (bSSFP) cines in 3 LV long-axis planes and short-axis stack for the measurements of biventricular volumes and LV mass. The presence of myocardial crypts was assessed in SSFP cines in 2-chamber VLA plane aligned orthogonal to transaxial scouts through the apex and the mitral valve. Crypts were defined as a discrete approximately V- or U-shaped extension of blood signal, considered on cine viewing to penetrate >50% of the thickness of adjoining compact myocardium in diastole. Partial crypts extending only 25% to 50% of the thickness were also recorded. Two independent observers confirmed the presence of crypts.

Statistical analysis was performed using MedCalc statistical software (version 12.4, MedCalc Software, Ostend, Belgium). Volumetric and functional LV and RV parameters are presented as mean values±SD. For comparison of continuous data, Student t test was used to compare mean values. Nominal variables are expressed as number of subject and percentage in the analyzed group. χ² test was used to compare nominal data. Cohen κ coefficient was used to analyze the intra- and interobserver variability. All statistical tests were 2-tailed, and P<0.05 was regarded as significant.

**Results**

CMR studies of 686 consecutive patients (48.2±19.9 years of age, 55.4% men) were analyzed. The most common clinical indications for CMR were suspected cardiomyopathy other than HCM (25.8% of all referrals), congenital heart disease (19.2%), and coronary artery disease (16.3%). Just more than one quarter of the patients were considered to have normal CMR findings (196 patients, 28.6%). The most common categories of abnormality based on CMR result were congenital heart disease (131 patients, 19.1%) and coronary artery disease (82 patients, 12%; Table 1).

The 686 consecutive patients included 24 individuals (3.5%, 50% men, 28.6±14.0 years of age) screened for HCM. Among them, 2 patients were found to have CMR features of HCM, 1 patient was found to have a slightly atypical single crypt (Figure; case 23), 1 patient was diagnosed with absent pericardium accounting for T wave changes on ECG, and 1 patient was found to have a subaortic membrane. The other 20 patients had no abnormalities on CMR; of these, only 1 patient had a single crypt (Figure; case 17). Overall, 32 patients (4.7%) had CMR findings consistent with HCM.

Crypts were identified in 46 patients (6.7%, 47.8±18.3 years of age, 59% men). The intra- and interobserver agreement in identifying the crypts was good (K=0.81 and 0.72, respectively). All crypts are illustrated, grouped according to diagnostic category, in the Figure. This shows some variability in crypt size and visible shape. However, all were located in the basal to middle inferior wall as seen in VLA cines and showed at least partial occlusion in systole (Movies I and II in the Data Supplement). To our eyes at least, qualitative comparison shows no consistent or characteristic differences of appearance between the diagnostic groups.

Four patients (50% men, 22.0±3.4 years of age) were found to have >1 crypt. Of these patients, 1 was diagnosed with congenital heart disease (Figure; case 24), and 3 had otherwise normal CMR studies (Figure; cases 3, 11, and 18). Patient 18, a 17-year-old female, had presented with atypical chest pain, and echocardiography had shown an inferior diverticulum

<table>
<thead>
<tr>
<th>Clinical Categories</th>
<th>Pre-CMR Diagnosis</th>
<th>Post-CMR Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>No significant structural cardiac abnormality*</td>
<td>46 (6.7%)</td>
<td>196 (28.6%)</td>
</tr>
<tr>
<td>Cardiomyopathy other than HCM</td>
<td>177 (25.8%)</td>
<td>82 (12.0%)</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>132 (19.2%)</td>
<td>133 (19.4%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>112 (16.3%)</td>
<td>82 (12.0%)</td>
</tr>
<tr>
<td>HCM</td>
<td>68 (9.9%) including 24 HCM family members</td>
<td>32 (4.7%) including 2 phenotype +ve HCM family members</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>41 (6.0%)</td>
<td>47 (6.8%)</td>
</tr>
<tr>
<td>Iron loading study</td>
<td>33 (4.8%)</td>
<td>18 (2.6%)</td>
</tr>
<tr>
<td>Disease of the aorta</td>
<td>22 (3.2%)</td>
<td>23 (3.3%)</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>18 (2.6%)</td>
<td>13 (1.9%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>15 (2.2%)</td>
<td>22 (3.2%)</td>
</tr>
<tr>
<td>Cardiac masses</td>
<td>10 (1.5%)</td>
<td>6 (0.9%)</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>8 (1.2%)</td>
<td>10 (1.4%)</td>
</tr>
<tr>
<td>Pericardial disease</td>
<td>4 (0.6%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>686 (100%)</td>
<td>686 (100%)</td>
</tr>
</tbody>
</table>

CMR indicates cardiovascular magnetic resonance; and HCM, hypertrophic cardiomyopathy.

*Referrals for CMR for arrhythmias, cardiac blocks, and unexplained symptoms or before noncardiac surgical procedures.
that was to be investigated by CMR. Her ECG was normal. The routine VLA cine, and also a 3-chamber view, showed 3 unusually large and rounded blood spaces extending inferiorly from the LV lumen between the base and the insertion of the inferior papillary muscle. These became narrower in systole as the compact muscle adjacent to and between them thickened. Comparison of the patient’s long-axis and short-axis cines showed evidence that contractile, circularly oriented muscle ridges separated the lobes of what we interpreted to be 3 unusually large crypts. In this patient, late gadolinium inversion recovery imaging showed relatively bright signal at the thinnest part of the outer boundary of the deepest crypt only. We considered this to be interpretable as either fibrosis of the myocardial layer where it was exceptionally thin, local thickening of the adjoining visceral pericardial layer, or both. In 2 patients (cases 22 and 29 in the Figure), midwall to epicardial streaks of bright blood signal in the middle inferior wall were attributed to encroachment of the RV lumen into the slice. These were not counted as crypts, whereas in each case more basal recesses that showed continuity with the LV cavity were.

Additionally but otherwise not included in our analyses, partial crypts penetrating 25% to 50% of the myocardial thickness were identified in further 26 patients (3.8%), distributed as shown in Table 2.

No significant differences in body surface area, sex, or age were found between patients with and without crypts. Crypts were found to be most prevalent in patients with HCM (15.6%), myocarditis (15.4%), and arterial hypertension (13.6%). Table 2 shows the percentages of patients with crypts in all groups of patients according to final CMR diagnoses. There was no statistically significant difference in crypt prevalence between the clinical groups of patients if all patient categories were included into the analysis ($P=0.12$). Nor were there differences between patients with no structural abnormality on CMR versus phenotype-negative HCM family members ($P=0.83$), versus patients with HCM ($P=0.76$), versus patients with hypertension ($P=0.41$), versus patients with myocarditis ($P=0.80$).

No significant differences in indexed LV and RV end-diastolic volumes, indexed LV mass, or RV end-systolic volume were found between patients with and without crypts. However, patients with crypts had statistically significantly lower indexed LV end-systolic volume (26.7±9.3 versus 35.1±28.0 mL/m²; $P=0.042$), higher indexed biventricular stroke volumes (LVSV, 55.8±10.4 versus 50.6±12.8 mL/m²; $P=0.007$; RVSV, 55.8±10.4 versus 50.6±12.8 mL/m²; $P=0.007$; RVSV,
52.7±11.1 versus 47.9±13.1 mL/m²; \( P=0.015 \)), and biventricular ejection fraction (LVEF, 68.0±6.8% versus 62.0±13.3%; \( P=0.003 \); RVEF, 62.3±9.7% versus 58.5±10.7%; \( P=0.021 \)) than patients without crypts on CMR (Table 3).

### Discussion

To our knowledge, this is the largest study of the prevalence of crypts visible in routine VLA cines performed in consecutive patients undergoing CMR. Although this approach may not be optimal for the identification and characterization of features whose three-dimensional shape, location, and orientation can vary among individuals, it has the advantage of applicability to routine CMR acquisitions, as in the retrospective study performed here and, potentially, for identification and follow-up in a larger cohort in a CMR registry. More crypts are likely to have been present than were apparent by this method, which nevertheless showed their presence in patients with otherwise normal CMR findings as well as patients with a range of cardiovascular pathologies. The proportion of cines showing crypts was slightly higher in patients with HCM and systemic hypertension than in other conditions but without reaching statistical significance.

Our results remain in keeping with previously published data on the prevalence of myocardial crypts in healthy volunteers and in patients with hypertension and congenital pulmonary stenosis undergoing CMR.1 The overall prevalence of myocardial crypts in our study (6.7%) was higher than in a study of 675 patients with known or suspected coronary artery disease or coronary artery anomaly undergoing cardiac computed tomography scan (2.2%); however, in the computed tomography study, crypts were identified from the clinical reports and not sought specifically.9 On the contrary, the percentage of crypts found in the subgroup of patients (n=82) with coronary artery

### Table 3. Volumetric Measurements in Patients With and Without Crypts With the Results of the Intergroup Comparison by the Student \( t \) Test

<table>
<thead>
<tr>
<th>Post-CMR Diagnosis</th>
<th>Patients With Crypts</th>
<th>Patients Without Crypts</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indexed LVEDV, mL/m²</td>
<td>82.5±16.1</td>
<td>85.5±31.3</td>
<td>NS</td>
</tr>
<tr>
<td>Indexed LVESV, mL/m²</td>
<td>26.7±9.3</td>
<td>35.1±28.0</td>
<td>0.042</td>
</tr>
<tr>
<td>Indexed LVSV, mL/m²</td>
<td>55.8±10.4</td>
<td>50.6±12.8</td>
<td>0.007</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>68.0±6.8</td>
<td>62.0±13.3</td>
<td>0.003</td>
</tr>
<tr>
<td>Indexed LV mass, g/m²</td>
<td>74.3±21.4</td>
<td>70.8±22.6</td>
<td>NS</td>
</tr>
<tr>
<td>Indexed RVEDV, mL/m²</td>
<td>86.7±24.1</td>
<td>83.3±24.3</td>
<td>NS</td>
</tr>
<tr>
<td>Indexed RVESV, mL/m²</td>
<td>33.9±17.2</td>
<td>35.5±17.4</td>
<td>NS</td>
</tr>
<tr>
<td>Indexed RVSV, mL/m²</td>
<td>52.7±11.1</td>
<td>47.9±13.1</td>
<td>0.015</td>
</tr>
<tr>
<td>RVEF, %</td>
<td>62.3±9.7</td>
<td>58.5±10.7</td>
<td>0.021</td>
</tr>
</tbody>
</table>

LV indicates left ventricle; LVEDV, LV end-diastolic volume; LVEF, LV ejection fraction; LVESV, LV end-systolic volume; LVSV, LV systolic volume; \( \text{NS}, \) not significant; RVEDV, right ventricular end-diastolic volume; RVEF, RV ejection fraction; RVESV, RV end-systolic volume; and RVSV, RV systolic volume.
disease in the present study (2.4%) came out similar to that in the cardiac computed tomography cohort, most of whom were investigated for known or suspected ischemic heart disease.

The prevalence among HCM patients seems to be slightly lower than in the study by Brouwer et al., in which a modified 2-chamber view through the inferior RV insertion point was used. Because most centers acquire routine CMR imaging planes without the additional 2-chamber plane, the rates of crypts visible in this study should be representative of the apparent prevalence in routine acquisitions. Although we include in Table 2 information on partial crypts, penetrating 25% to 50% of the wall thickness, it can be hard to decide whether these should be classed as crypts or just irregularities of endocardial contour related to trabeculation. Therefore, we only analyzed the prevalence of crypts considered on cine viewing to penetrate ≥50% of the local wall thickness.

We found the highest percentage of crypts in patients with HCM (15.6%), myocarditis (15.4%), and arterial hypertension (13.6%). High prevalence in patients with hypertension (33%) and myocarditis (22%) has also been reported previously. The very high prevalence of crypts (81% and 61%) observed by Germans and Maron et al. was in individuals with confirmed HCM gene mutations and without LV hypertrophy. However, Maron et al. reported lower prevalence of crypts in patients with overt HCM (4%) using the same methodology of assessing crypts in VLA cines as in our study (16%). Also, we found a high percentage of patients with crypts among 195 patients with normal CMR studies, whereas Maron et al. surprisingly reported no crypts in their control cohort of 98 patients referred for CMR in whom no CMR abnormalities were found. These discrepancies are difficult to explain, especially that the same criteria were used to define the control cohort of Maron et al. and our group of patients with no abnormal findings on CMR scan. Possibly genetic differences between these populations could explain varied crypt prevalence despite structurally normal cardiac appearances on CMR scan.

In contrast to previously studied groups, which were limited to patients with few cardiac conditions, more commonly seen in our study in patients with lower LV end-systolic volume, higher biventricular stroke volume, and ejection fraction. This finding may be attributed to the high percentage of crypts in patients with HCM and arterial hypertension, which are known to be associated with higher values of the above parameters. At the same time, it is possible that crypts are either more visible or genuinely more prevalent in patients with hyperdynamic biventricular systolic function.

It may be no coincidence that the characteristic location of crypts in the basal inferior wall of the LV is also the region of insertion between the free walls of the LV and RVs and the interventricular septum. This region is known to be subject to myocardial disarray, described postmortem in the hearts of some healthy individuals as well as those with HCM. We propose that crypt formation in this location may be secondary to the crossing and interdigitation of myocytes, which, although presumably structurally required in this location, may predispose to myocardial splitting. As illustrated in the Figure, basal myocardial crypts varied in size, shape, and number in the consecutively imaged patients analyzed.

The limitations of our study include its retrospective and a single center design and lack of genotype data. The absence of overt abnormality on CMR cannot exclude early or concealed stages of HCM or other cardiovascular disease. Although the percentage of patients carrying HCM-related genes in the cohort was unknown, it would seem unlikely to have approached the 6.7% of patients found to have visible crypts.

In conclusion, our results are in keeping with previous reports that single or paired myocardial crypts are an occasional and by no means rare CMR finding across groups of volunteers or patients undergoing CMR without pretest suspicion of HCM. We agree with Moon and Puntmann that, although crypts, particularly if multiple, may represent a significant CMR finding in the familial context where the pretest probability of HCM is 50%, they are unlikely to be of clinical significance in other clinical scenarios, where they may represent incidental variants of local myocardial structure. However, a multicenter prospective registry with a large number of patients imaged by CMR with a view to ongoing follow-up of clinical outcomes, such as EuroCMR registry, would be justified to investigate any potential clinical implications of LV inferobasal crypts, particularly in relation to HCM.

Sources of Funding

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Disclosures

Dr Pennell is a consultant to Siemens and a director of Cardiovascular Imaging Solutions. Royal Brompton Hospital has research collaboration agreements with Siemens AG Medical Solutions. The other authors report no conflicts.

References


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**CLINICAL PERSPECTIVE**

This study is important in relation to patients found incidentally to have inferobasal myocardial crypts without a pretest suspicion of hypertrophic cardiomyopathy or previous genetic characterization. This arises frequently in clinical cardiovascular magnetic resonance practice. The findings support our previous impression that single or paired crypts are occasional structural variants, unlikely in themselves to justify further investigation by imaging or genetic analysis. Although our study lacks genetic characterization, its design was straightforward and its findings unusually comprehensively illustrated. We included still images from all 46 considered to have 1 or more inferobasal crypt out of 686 consecutive patients referred for cardiovascular magnetic resonance, grouped according to diagnostic category. This and the text allows readers to appreciate the range of appearances that we interpreted as representing crypts, enabling appraisal of the variants seen and their distribution across diagnostic groups. However, the study lacks sufficient numbers or outcome data for firm conclusions to be drawn regarding clinical implications, particularly where multiple crypts are identified in association with a family history of hypertrophic cardiomyopathy. For this, the inclusion of crypts as a phenotypic category in a large ongoing cardiovascular magnetic resonance registry would be justified.
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Supplemental Material

**Movie 1.** Vertical long axis cine in a 65 year old woman referred with chest pain (patient 1 in the Figure). Apart from the relatively deep inferobasal crypt seen, her CMR study was normal. The location of the crypt, which narrows in systole, is typical. Additional blood signal in the mid inferior wall in late diastole is thought to represent encroachment the right ventricular cavity into the plane.

**Movie 2.** Vertical long axis cine in a 17 year old female who we considered to have a crypt-related left ventricular diverticulum (patient 18 in the Figure).