Role of Preoperative Cardiovascular Magnetic Resonance in Planning Ventricular Septal Myectomy in Patients With Obstructive Hypertrophic Cardiomyopathy

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In obstructive hypertrophic cardiomyopathy (HC), extreme heterogeneity of septal morphology makes septal myectomy particularly challenging. Although cardiovascular magnetic resonance (CMR) reconstructs ventricular anatomy with high spatial resolution, CMR is not used systematically to plan preoperatively septal myectomy. In this study, we report our results with using CMR to plan the extent of septal excision in 112 consecutive HC patients who subsequently underwent myectomy. Depth and length of the myectomy planned at CMR were compared with those of the septal muscle excised in a single piece in all patients. Anterior septum maximal thickness at CMR was 22 ± 5 mm and excised muscle thickness 9 ± 3 mm. Planned myectomy length was 35 ± 11 mm (range 17 to 65) and excised muscle length 38 ± 10 mm (range 10 to 70), indicating extension of septal resection to mid-cavity. Thickness and length of the planned myectomy showed a significant correlation with the excised muscle ($R^2 = 0.345$; $p < 0.001$; and $R^2 = 0.358$; $p < 0.001$, respectively). Deep septal crypts were identified at CMR in 12(11%) patients, preventing muscle excision from areas at increased risk of iatrogenic septal defect. Large aberrant muscle bundles that could decrease mid-cavity dimension were identified at CMR and excised in 26(23%) patients. In the 55 patients with postoperative CMR, qualitative comparison of pre and postoperative ventricular morphology showed a smooth and apically extended myectomy. In conclusion, CMR planning of septal myectomy provided high resolution images of septal morphology and allowed us to perform a standardized and apically extended septal excision that was associated with favorable outcome. Our novel approach could make myectomy more accessible to cardiovascular surgeons. **(Am J Cardiol 2019;123:1517−1526)**

Extended septal myectomy relieves the left ventricular (LV) outflow tract gradient and heart failure symptoms, and prolongs survival in patients with obstructive hypertrophic cardiomyopathy (HC).[1−9] However, the extreme heterogeneity in the magnitude and distribution of septal hypertrophy in HC makes this procedure particularly challenging.[10,11] Although cardiovascular magnetic resonance (CMR) has the unique potential to characterize ventricular anatomy with high spatial resolution in patients with HC,[11,12] CMR is not systematically used to plan preoperatively the septal myectomy. For several years, we have been using CMR at our surgical HC center to acquire a preoperative tomographic reconstruction of septal anatomy and plan the extent of the septal myectomy in patients with obstructive HC who subsequently underwent this procedure. In the present study, we describe in detail our CMR planning of septal resection and report the clinical results of our combined preoperative CMR imaging and surgical intervention in a consecutive cohort of over 100 patients with obstructive HC who underwent septal myectomy at our center over a period of 2 years. Purpose of our investigation was to determine the accuracy of preoperative CMR in reconstructing septal anatomy and usefulness in reducing the technical challenges posed by extended septal myectomy.

Methods

Between January 2015 and December 2016, 142 consecutive patients with obstructive HC underwent septal myectomy, performed by a single surgeon (P.F.), at the Policlinico di Monza, Italy. Of these 142 patients, 30 were excluded from the study on the basis of the following criteria: prior implantation of a cardioverter-defibrillator or other device incompatible with CMR, prior surgical myectomy or alcohol septal ablation, or aortic valve replacement

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at the time of the myectomy. The remaining 112 patients had a preoperative CMR and were enrolled in the study. Each of these patients had an LV outflow gradient ≥50 mm Hg at rest or with physiologic provocation and disabling symptoms unresponsive to medications. The criteria used for the diagnosis of HC in the present investigation have been previously reported.[6,13] Peak LV outflow tract gradient was measured as previously described.[13] The degree of MV regurgitation was assessed using multiple Doppler echocardiographic criteria, including jet area, jet width and spectral Doppler intensity, and was graded on a scale from 0 to 4 (0 = none, 1 = mild; 2 = moderate; 3 = moderate to severe; and 4 = severe).[7,14] This investigation was approved by our institutional review committee. All study patients were fully informed of the nature and risks of their condition, the therapies currently used to treat it, as well as the surgical procedure they were offered, and gave a written informed consent.

In each of our 112 study patients, CMR imaging was performed (GE Optima MR450w 1.5 Tesla scanner) with an electrocardiography-gated steady-state free procession breath-hold in cine 3 and 4 long-axis views, and sequential 6-mm short-axis slices from the atrio-ventricular ring to apex. In our study, 6-mm contiguous slices (without spacing between slices) rather than the standard 8-10 mm slices were used to acquire more detailed tomographic reconstruction of septal anatomy for surgical purposes.

In each patient, the initial point at which to measure the thickness of the anterior septum was identified in the 3-chamber long-axis view from the first CMR ventricular slice (Figure 1, line 1). Because the proximal portion of the posterior septum incorporates the atrio-ventricular conduction system,[10] the initial point at which to measure the thickness of the posterior septum was selected at 2.5 to 3.0 cm below the mitral annulus, in the 4-chamber long-axis view (Figure 1, line 4). Subsequent measurements of maximal septal thickness, from the basal ventricular septum to the papillary muscle level, were obtained from stacked contiguous 6-mm short-axis slices for the purpose of reconstructing the distribution of hypertrophy at different septal levels (Figure 1, lines 2 to 6). At surgery, this detailed CMR reconstruction of septal anatomy was used as a guide to reduce septal thickness in each segment, in proportion to its thickness, and perform a smooth myectomy.

Measurements of the maximal length (apical extension) of the muscular resection of the anterior septum and distal portion of the posterior septum were obtained by adding the number of stacked contiguous 6-mm short-axis slices from which a septal excision had been planned. Because CMR measurements of the planned length (apical extension) of the septal excision may be less accurate than the measurements of the depth of the excision, the final decision regarding the apical extent of the septal excision was integrated in some patients with measurements derived from the intraoperative transesophageal echocardiogram (TEE) and direct surgical inspection.

Stacked contiguous short-axis images were also carefully examined to identify the presence of septal crypts (i.e., focal areas in which septal thickness was markedly decreased) at different levels in the ventricular wall, to reduce the risk of iatrogenic septal defect at the level of the crypt. For surgical purposes (i.e., reducing the risk of iatrogenic septal defect) septal crypts were defined as one or more narrow and deep blood-filled invaginations contiguous with the LV cavity, extending by visual assessment >30% of the wall thickness of the adjacent myocardium, and identified in the short-axis images at end-diastole.[15] In patients in whom aberrant ventricular muscle bundles were identified at CMR, the location of the bundles in relation to the septum and ventricular free wall was assessed by integrating images obtained from the long-axis and short-axis CMR views.

After induction of general anesthesia, intraoperative TEE was performed to visualize the ventricular septum and assess the MV morphology and associated MV abnormalities.[6,14] In each of the 112 study patients, a septal muscular excision was performed in the anterior septum and, in most patients, was extended to the contiguous portion of the posterior septum (Figure 1). In each of the study patients, this portion of the septum was excised in a single piece.[6,14] In those patients in whom septal hypertrophy also involved the distal portion of the posterior septum, close to the junction between septum and right ventricle,[10] a second myectomy was performed, as planned at CMR (Figure 1), to extend the muscular excision more distally in the ventricular cavity and increase mid-cavity dimension.

In all study patients, great care was taken to ensure that the muscular resection went beyond the point of mitral-septal contact. In each of the 112 study patients, thickness and length of the muscle excised from the anterior septum were measured in the operating room and included in the operative report. Photographs of the resected muscle were taken in most patients.

The standard reference points were used for the initial incision in the anterior septum.[16] The depth of the initial incision was assessed by the surgeon and, if less than that planned at CMR, was appropriately increased. The anterior septal myectomy was then completed in a single piece, using scissors, following the preoperative CMR plan. In those patients in whom a muscle resection in the distal portion of the posterior septum had been planned at CMR, the septal excision was extended toward this area and again completed in a single piece, with the same surgical technique used for the anterior septum.

Fibrous or muscular structures connecting the papillary muscles to the ventricular septum or LV free wall were excised to increase papillary muscle mobility.[6,17] Fibrotic and retracted secondary chordae judged to play an important role in tethering the anterior mitral leaflet toward the LV outflow tract and ventricular apex were cut selectively, as previously described.[14] In patients with particularly elongated anterior or posterior leaflets, the excessive tissue at the free margin of the leaflet was plicated.

Statistical analyses were aimed at describing and comparing pre and post-operative clinical characteristics of the 112 study patients, and assessing the correlation between the measurements of septal thickness and length evaluated preoperatively with CMR and those obtained from the resected muscle at surgery. Variables were presented as means with standard deviations, or frequencies with proportions. Differences between pre and post-operative values were assessed for statistical significance using the paired

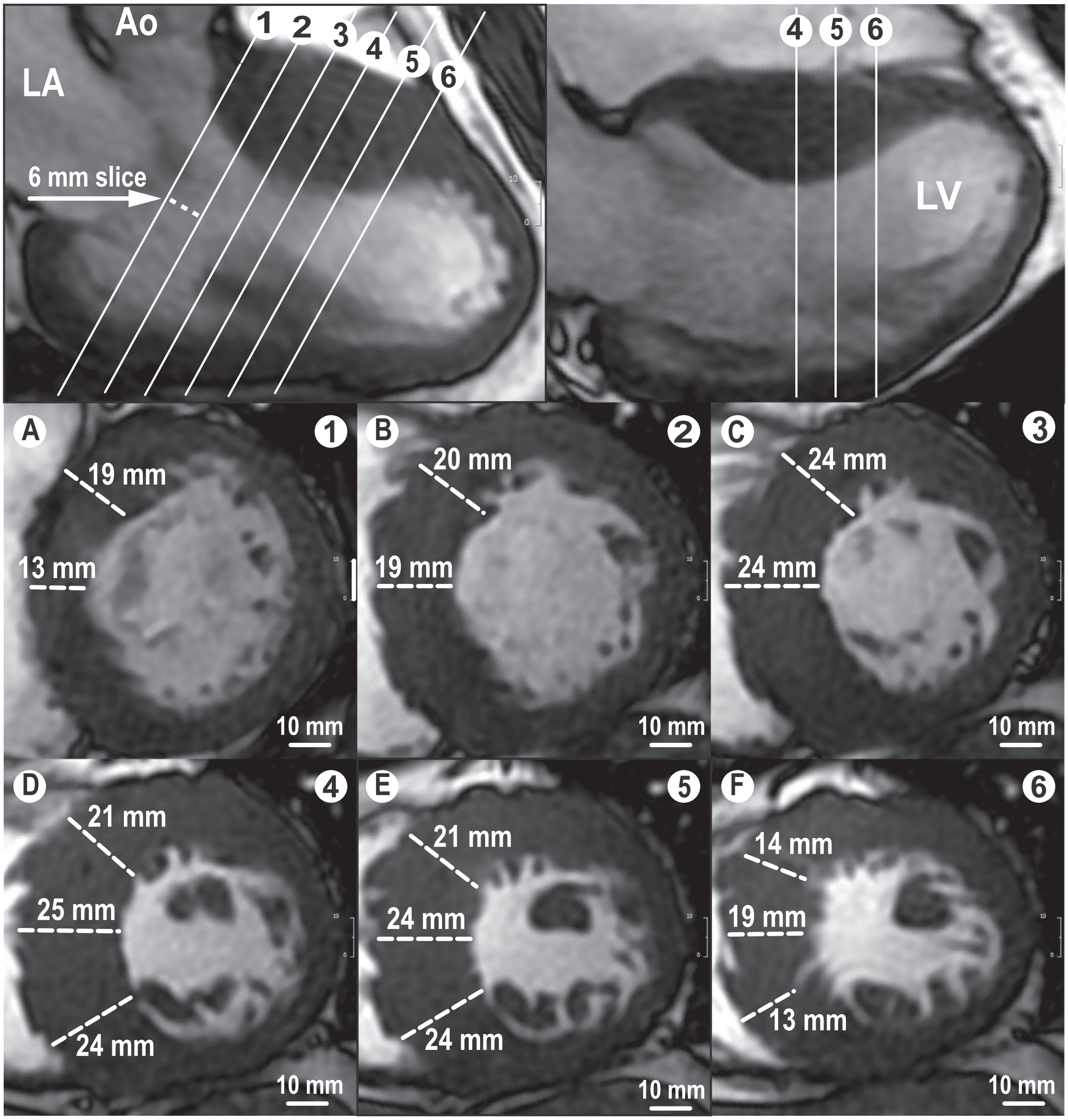

Figure 1. **Preoperative tomographic CMR reconstruction of septal morphology.** In a study patient**,** measurements are shown of maximal septal thickness assessed from CMR at different ventricular levels. The level at which short-axis measurements were obtained was simultaneously verified from the 3 and 4-chamber long-axis views. Measurements of anterior septum maximal thickness and contiguous portion of posterior septum were obtained from the 3-chamber long-axis view **(lines 1-6)** and 6-mm short-axis slices *(A-F)*. Measurements of maximal thickness of the posterior septum distal portion were obtained from the 4-chamber long-axis view **(lines 4-6)** and 6-mm short-axis slices *(D-F)*. Final CMR reconstruction of thickness and length of the hypertrophied portion of septum was obtained by integrating the information derived from the short-axis and long-axis views.

Student-*t* test or chi-square test, as appropriate. Relation between variables was determined by linear regression analyses, and regression coefficients and Pearson correlation coefficients were reported. p values <0.05 were considered statistically significant. Computations were performed with IBM SPSS 23.0 statistical software (SPSS, Inc., Chicago, IL).

Results

Baseline clinical characteristics in the 112 study patients with obstructive HC are summarized in Table 1. Of these patients, 1 (0.9%) died of sepsis during hospitalization 60 days after surgery, none had iatrogenic septal defect. Of the remaining 111 patients, each underwent clinical and echocardiographic evaluation and 55 (50%) underwent CMR at our center 8 $\pm$ 6 months after surgery. Clinical outcome is summarized in Table 2. At most recent evaluation, 80 (72%) patients were asymptomatic, 27 (24%) in NYHA class II, and 4 (3.6%) in class III (p <0.0001). Peak LV outflow gradient at rest was 67$\pm$ 41 mm Hg preoperatively and 6 $\pm$ 7 mm Hg at most recent evaluation (p <0.0001). No patient had a residual resting outflow gradient $\geq$30 mm Hg. In the 55 patients

Table 1
Baseline clinical characteristics in 112 patients in whom septal myectomy was planned preoperatively at CMR.

Preoperative variable	
Age (years)	53 ± 16
Male	60 (54%)
NYHA functional class	
I	0
II	20 (18%)
III-IV	91 (82%)
Atrial fibrillation	22 (20%)
Echocardiographic data	
LVOT gradient at rest (mm Hg)	67 ± 41
Maximum septal thickness (mm)	23 ± 5
Mitral valve regurgitation grade	
0-1	43 (40%)
2	50 (48%)
3	12 (11%)
4	2 (2%)

Values are expressed as mean ± SD, or number (%).
Abbreviations: CMR = cardiovascular magnetic resonance; LV = left ventricular; LVOT = left ventricular outflow tract; NYHA = New York Heart Association; SD = standard deviation.

Table 2
Outcome after septal myectomy in 112 patients in whom the extent of the septal excision was planned preoperatively at CMR.

Variable	Before surgery	After surgery	p value*
No. of in-hospital deaths	–	1 (0.9%)	–
No. of iatrogenic septal defect	–	0	–
NYHA functional class†			<0.0001
I	0	80 (72%)	
II	20 (18%)	27 (24%)	
III-IV	91 (82%)	4 (3.6%)	
Atrial fibrillation†	22 (20%)	10 (9%)	<0.001
Echocardiographic data†			
LVOT gradient at rest (mm Hg)	67 ± 41	6 ± 7	<0.0001
Post-op resting gradient ≥ 30 mm Hg (n.)	–	0	
Maximum septal thickness (mm)	23 ± 5	15 ± 3	<0.0001
Mitral valve regurgitation grade‡			<0.0001
0-1	43 (40%)	88 (82%)	
2	50 (48%)	17 (15%)	
3	12 (11%)	2 (2%)	
4	2 (2%)	0	
Mitral valve replacement	–	4 (3.6%)	

Values are expressed as mean ± SD, or number (%).
Abbreviations: CMR = cardiovascular magnetic resonance; EF = ejection fraction; LV = left ventricular; LVOT = left ventricular outflow tract; NYHA = New York Heart Association; post-op = postoperative; SD = standard deviation.
Symbols:
* Student *t* test, chi-square test, or Fisher's test, as appropriate.
† Assessed at most recent evaluation in 111 study patients.
‡ Assessed in the 107 patients without MV replacement at surgery.

with CMR performed at our center during follow-up, LV volume increased postoperatively from 68 ± 17 ml/m^2 to 73 ± 12 ml/m^2 (p <0.0001) and ejection fraction decreased from 74 ± 9% to 67 ± 8% (p = 0.023).

Of the overall 112 study patients, 4 (3.6%) underwent MV replacement because of valve abnormalities that could not be corrected by valve repair. Each of these 4 patients were >70 years of age. Of the 107 who did not undergo MV replacement, 2 (2%) had postoperative moderate-to-severe MV regurgitation, and none had residual severe MV regurgitation.

Septal myectomy. In the 112 study patients, maximal thickness of the anterior septum assessed preoperatively at CMR was 22 ± 5 mm, and maximal thickness of the muscle excised from the anterior septum at surgery was 9 ± 3 mm. A significant positive correlation was identified between maximal anterior septal thickness at CMR and maximal thickness of the muscle excised from the anterior septum ($R^2 = 0.345$; p <0.001) (Figure 2). The close relation between thickness of the muscle resection planned at CMR and that of muscle excised at surgery is illustrated in a patient (Figure 3).

Length of the anterior septum myectomy, planned preoperatively at CMR, was 35 ± 11 mm (range 17 to 65 mm), and length of the muscle excised from the anterior septum was 38 ± 10 mm (range 10 to 70 mm). A significant positive correlation was identified between length of the myectomy planned at CMR and that of the muscle excised at surgery ($R^2 = 0.358$; p <0.001) (Figure 2), although the pattern of this relation showed important variation because CMR measurements of length of the septal excision were integrated in some patients with measurements derived from the intraoperative TEE and direct surgical inspection.

In the 76 (68%) study patients in whom septal hypertrophy included the distal portion of posterior septum, close to the junction between septum and right ventricle,[10,11] the muscular excision was extended to this more distal area of the septum. CMR images in a study patient before and after a smooth myectomy that extended to mid-ventricular cavity and included both the anterior septum and distal portion of the posterior septum are shown in Figure 4. CMR videos before and after surgery are also shown (Online Videos 1 and 2).

Preoperative CMR images allowed the identification of deep septal crypts in 12 (11%) of the study patients. The number of crypts varied from 1 to 4 in the individual patient. Preoperative and postoperative CMR short-axis images in a patient with a crypt in the anterior septum are shown in Figure 5. CMR images also allowed the identification of large aberrant muscle bundles connecting the basal ventricular septum to the distal portion of the septum or free wall (Figure 3). Large bundles judged to reduce mid-cavity dimension and/or papillary muscle mobility were resected in 26 (23%) of the study patients at the time of myectomy.

Discussion

The results of our study show that meticulous preoperative CMR tomographic reconstruction of septal morphology can play a novel and important role in planning the site and extent of the muscular excision in septal myectomy in patients with obstructive HC. This method allowed us to perform a standardized, smooth and apically extended septal resection that uniformly reduced septal thickness. CMR guided septal myectomy, in association with papillary

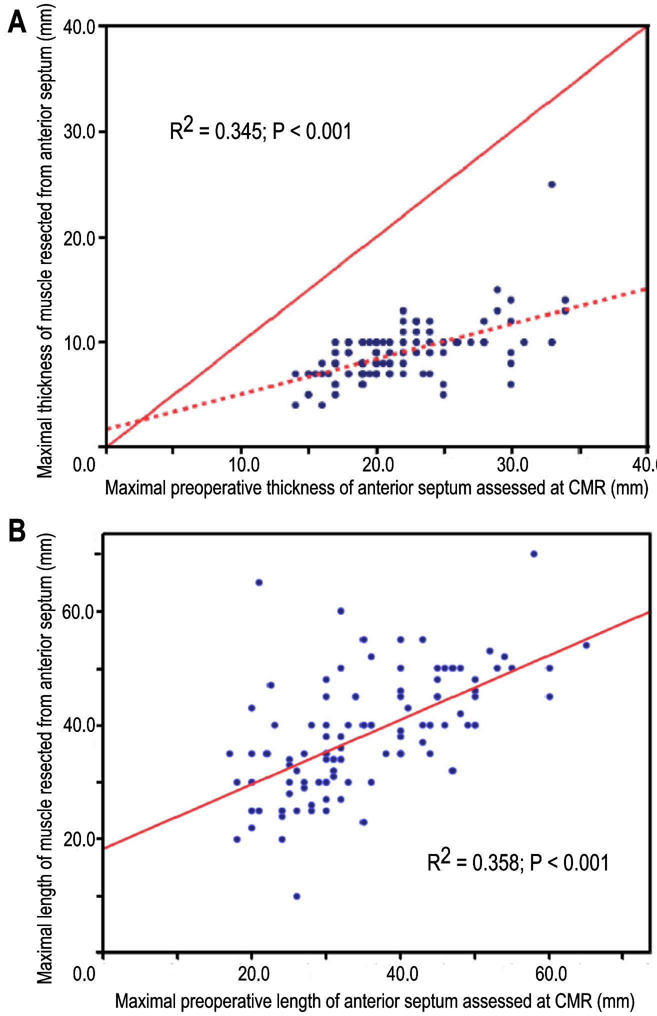

Figure 2. **Correlation between extent of muscular septal resection planned at CMR and size of septal muscle excised at myectomy.** A statistically significant positive correlation was identified between preoperative CMR maximal anterior septal thickness and maximal thickness and length of the muscle resected from the anterior septum at surgery (Figure 2A and B).

muscle mobilization, retracted secondary MV chordal cutting and elongated MV leaflet plication, abolished the LV outflow gradient in each study patient, and significantly reduced or abolished heart failure symptoms and MV regurgitation in >95% of patients, with a total perioperative mortality <1%.

Maximal thickness of the septal muscle excised at surgery showed a significant correlation with that of the septal resection planned at CMR, the extent of the muscular resection increasing progressively in direct relation to the maximal septal thickness measured at CMR. In the majority of our study patients, septal hypertrophy also involved the mid/distal portion of the posterior septum, i.e., the area close to the junction between posterior septum and right ventricle. In these patients, CMR planning of the surgical myectomy allowed us to extend the muscular excision to the distal posterior septum, uniformly reducing septal thickness up to or below the ventricular equator. Extension of the myectomy to mid-ventricular level, by further enlarging the mid-ventricular cavity, may contribute to redistribute LV wall stress more favorably.[18]

In previous investigations, CMR reconstruction of septal morphology has shown that septal hypertrophy in patients with obstructive HC frequently has a spiral distribution, with a progressive decrease in anterior septal thickness and increase in posterior septal thickness from the aorta to the apex.[19,20] Indeed, in our study patients in whom the muscular excision extended to the area of posterior septum close to the junction with the right ventricle, the excised septal muscle tended to have a spiral shape that reproduced the preoperative spiral pattern of hypertrophy, indicating that the apically extended myectomy followed evenly the hypertrophied portion of the original septum along the entire LV septal contour, generating a smooth and uniform increase in cavity dimension (Figure 6).

In recent years, the high spatial resolution of CMR has allowed the identification of narrow invaginations in the myocardium which has been defined as “crypts” and appears to be a unique morphologic feature of patients with HC, as well as family members who carry a HC-causing mutation in the absence of phenotypic expressions of the disease.[15] Septal crypts were detected preoperatively

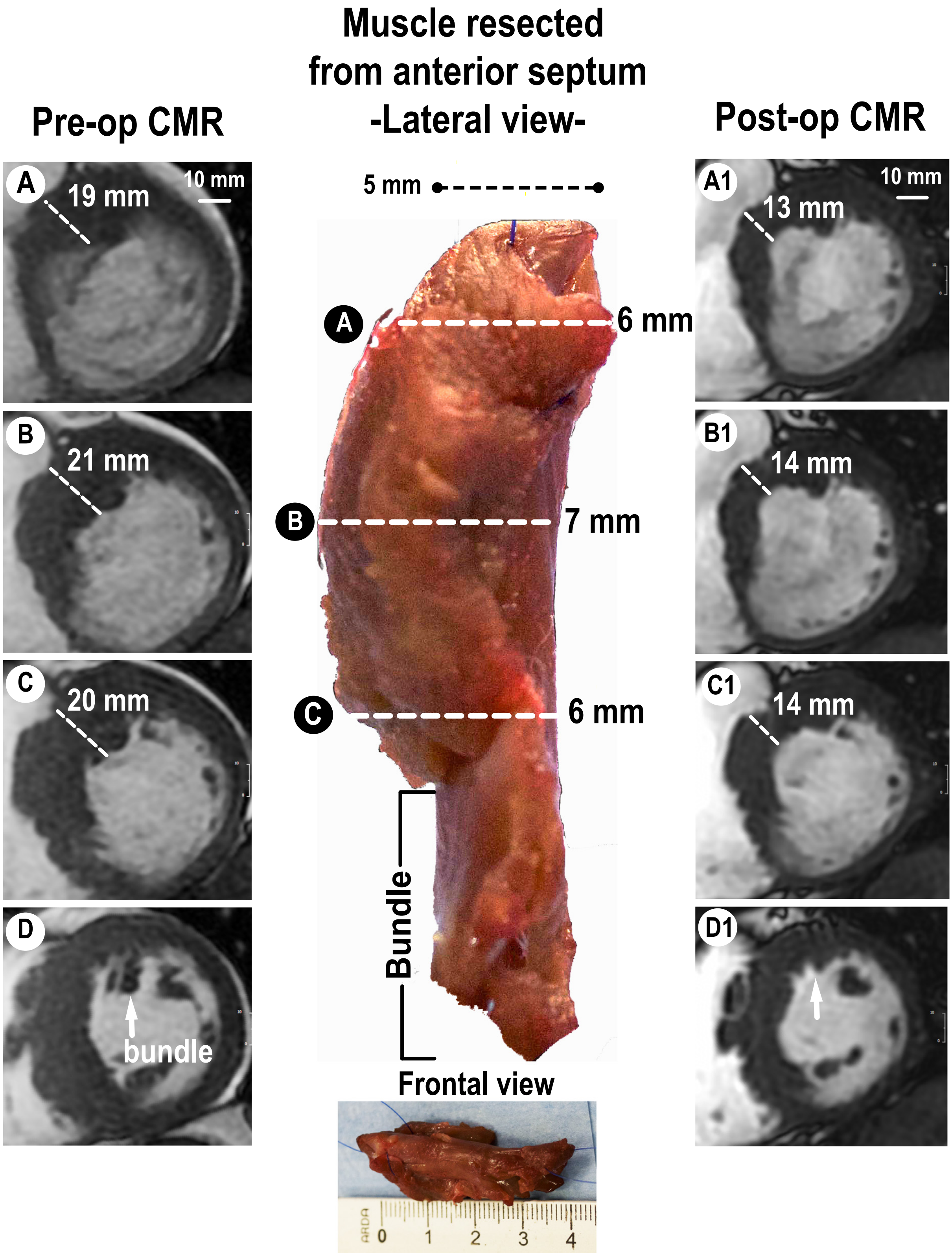

Figure 3. **In a study patient, the close correlation is shown between the muscular resection planned at CMR and septal muscle resected at myectomy.** *(A-C)* On the left, preoperative CMR measurements of anterior septal thickness obtained from contiguous 6-mm short-axis slices. The anterior septum muscular resection is planned at different septal levels on the basis of CMR wall thickness measurements. *(D)* Preoperative CMR images show a muscle bundle at the level of the anterior septum middle portion *(arrow)*. *(Center)* The thickness of the muscle resected from the anterior septum at surgery shows a good correlation, at each level, between anterior septum thickness measured at CMR and resected muscle thickness. *(A1-C1)* On the right, postoperative CMR shows the myectomy at the level of the anterior septum. *(D1)* Postoperative CMR images show that the muscle bundle at the level of the anterior septum has been resected *(arrowhead)*.

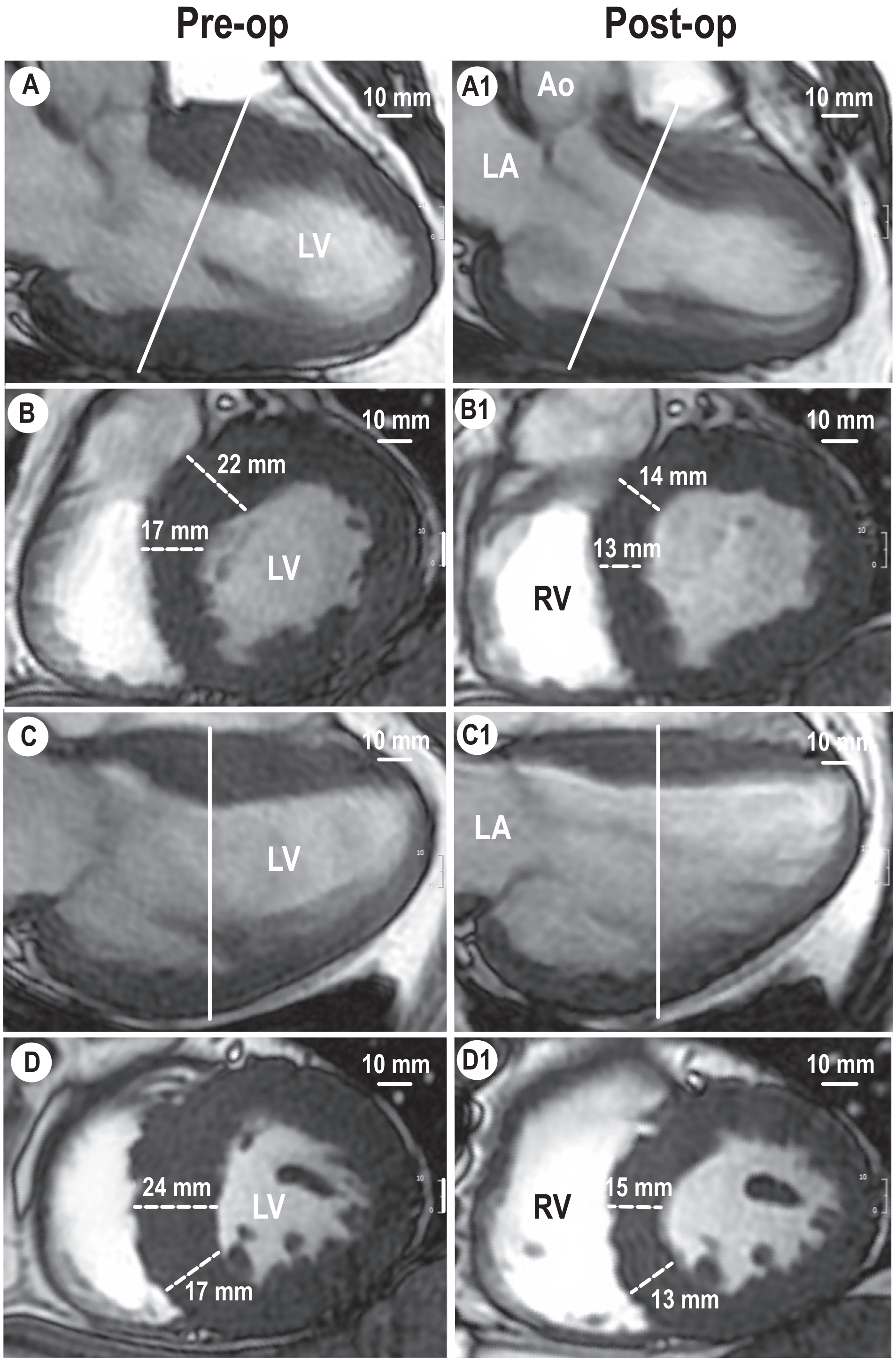

Figure 4. **Preoperative and postoperative CMR long-axis and short-axis images in a study patient.** A smooth and apically extended myectomy has been performed at the level of anterior septum and distal portion of posterior septum. Preoperative *(A to D)* and postoperative *(A1-D1)* CMR imaging.

at CMR in about 10% of our study patients, with multiple septal crypts being present in several patients. Although the clinical and prognostic significance of myocardial crypts remains to be determined, these focal areas of marked septal thinning, if not identified, may increase the risk of iatrogenic septal defect at the time of septal myectomy. Therefore, identification of these crypts played an important role in our preoperative CMR planning of the myectomy, the excision of septal muscle in the area of the crypts being carefully avoided.

The CMR high resolution images also allow identification of aberrant muscle bundles that, in patients with HC, often connect the hypertrophied basal ventricular septum to the distal portion of the septum or free wall and may further

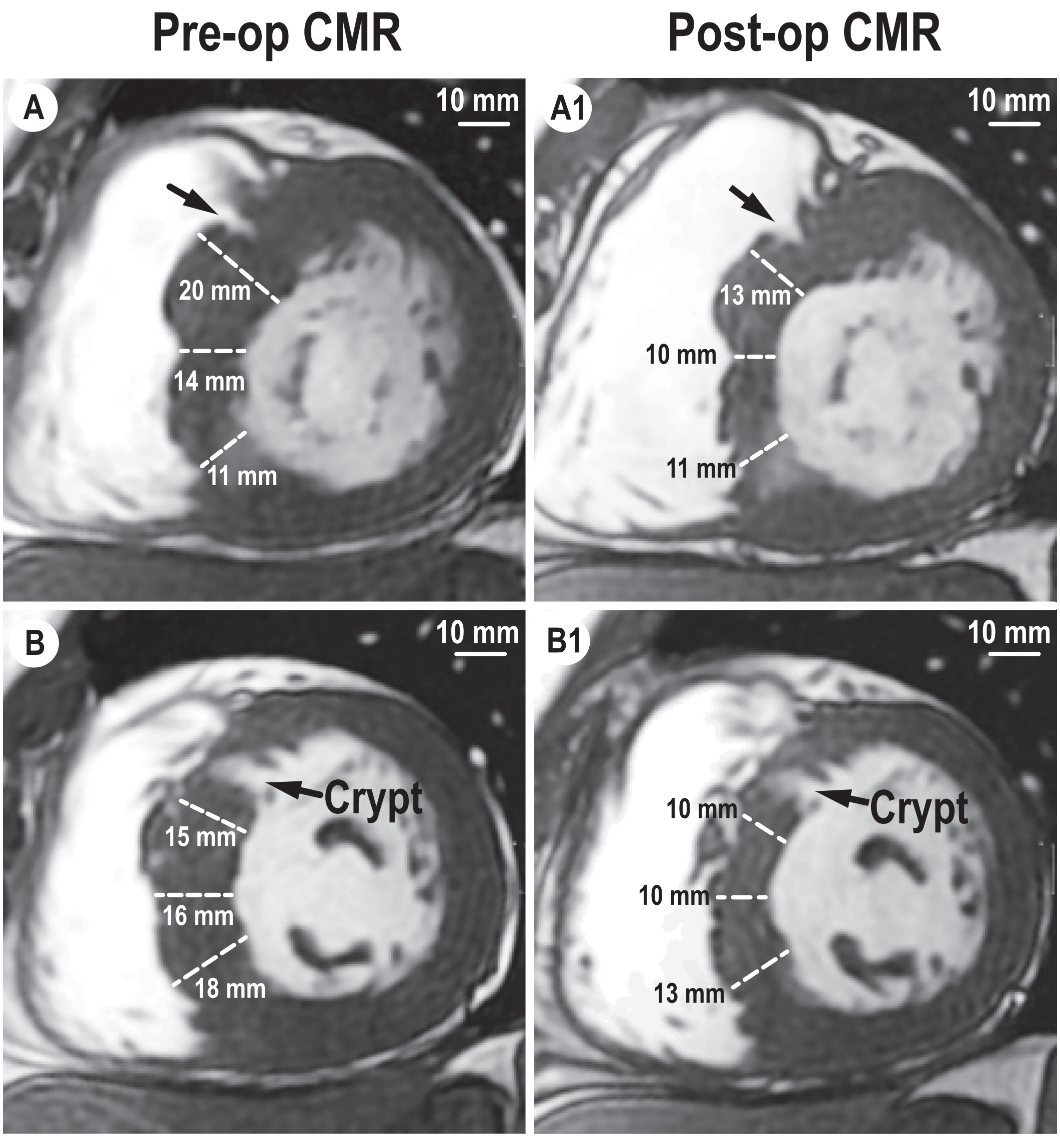

Figure 5. Preoperative and postoperative CMR Short-axis Images in a Study Patient with a Large Crypt in the Anterior Septum, at Papillary Muscle Level. *(A and A1)* Pre and postoperatively, a focal area of septal thinning (small crypt) is present at MV level on the right side of the anterior septum (arrow). *(B and B1)* Pre and postoperatively, a large deep crypt is present at papillary muscle level in the anterior septum *(arrow)*. Septal muscular resection has been carefully avoided in the area of the crypt. *(A1 and B1)* A smooth and apically extended septal myectomy has been performed in the anterior septum and distal portion of posterior septum. MV = mitral valve.

decrease mid-ventricular cavity dimension, or displace the papillary muscles anteriorly toward the LV outflow tract.[20] The proximal and distal points of attachment of large muscle bundles to the septum or free wall are clearly seen at CMR and their course within the ventricle can be reconstructed by combining images from different views. Such imaging potentials are unique to CMR. These muscle bundles usually emerge from the septum in the area at which septal thickness begins to decrease. Therefore, the location of the bundles may help the surgeon in the spatial orientation within the ventricular cavity and septal excision. Muscle bundles initially identified at CMR were excised in about 20% of our study patients on the basis of direct surgical inspection indicating their potential to decrease cavity dimension, particularly at mid-cavity level, and/or contribute to displace the papillary muscles toward the ventricular septum and outflow tract. Therefore, myocardial crypts and aberrant muscle bundles further justify attentive preoperative CMR reconstruction of LV morphology before surgical myectomy.

At present, because of the technical challenges posed by the standard extended septal myectomy, only a small number of highly experienced cardiovascular surgeons at a few North American and European HC centers can offer optimal hemodynamic and clinical results for myectomy, with an exceptionally low perioperative mortality (<1%).[2–9] Indeed, attention has been recently focused on the need for more myectomy surgeons that could guarantee satisfactory results for septal myectomy to a higher number of eligible HC patients.[21–23] Planning preoperatively the septal myectomy with CMR provides high resolution images of septal morphology and offers the surgeon the advantage

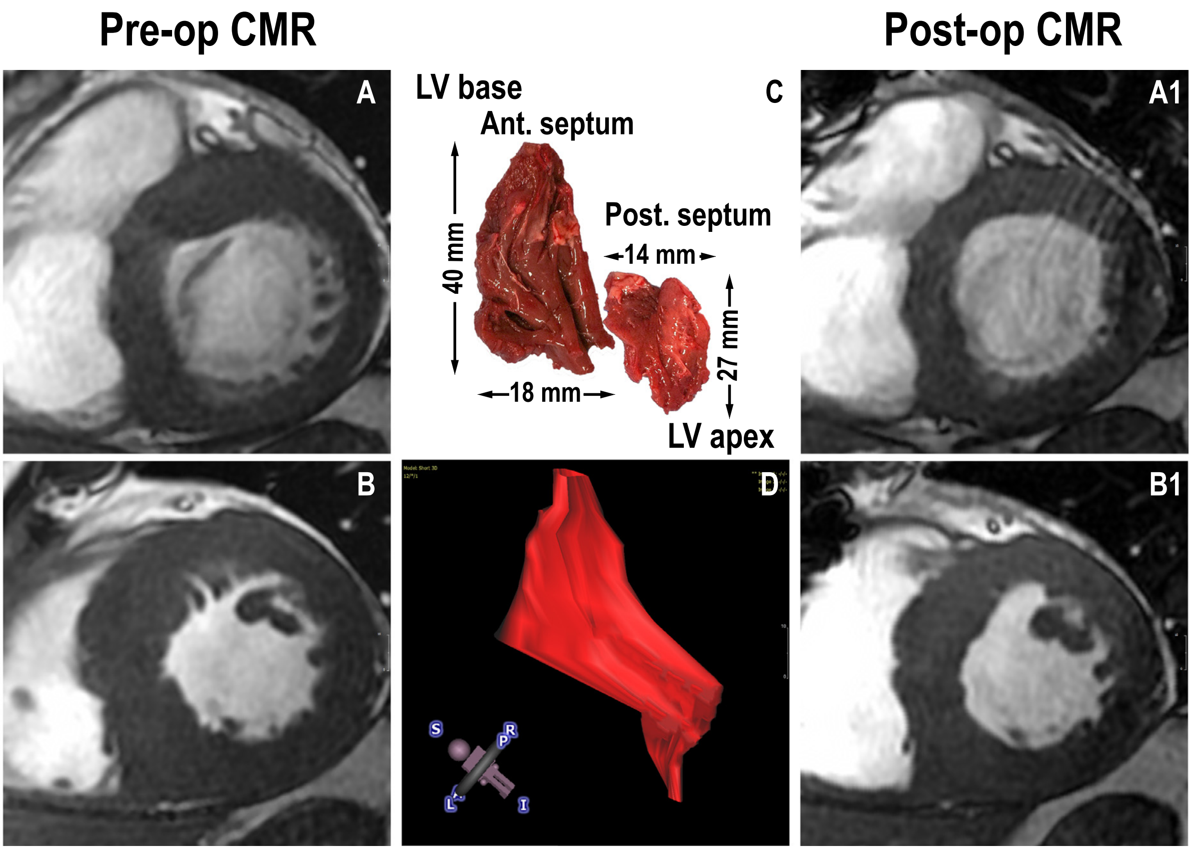

Figure 6. **3-Dimensional CMR reconstruction of the resected septal muscle.** *(A and B)* In a study patient, preoperative CMR short-axis images at MV and papillary muscle level are shown. *(C)* Resected muscle from the anterior septum and distal portion of posterior septum. *(D)* 3-Dimensional CMR reconstruction of the resected muscle from the anterior and posterior septum reproduces the preoperative spiral distribution of septal hypertrophy. *(A1 and B1)* Postoperative CMR short-axis images at MV and papillary muscle level. MV = mitral valve.

of entering the operating room with a more precise understanding of the septal anatomy and more accurate operative plan for the site and extent of the muscular resection than those traditionally offered by transthoracic echocardiography and intraoperative TEE. Therefore, our novel approach to septal myectomy could reduce the technical challenges of the muscular excision and, by increasing the number of surgeons that can perform appropriately an extended myectomy, could make this procedure available to eligible patients who cannot be referred to HC surgical centers of excellence.

A limitation of our study is the absence of a control group of patients who underwent myectomy without preoperative CMR planning of the septal excision. Such a group could not be included in our investigation, because CMR planning of the myectomy was progressively optimized at our center between July 2013 and 2014 in about 150 HC patients and gradually became a standardized procedure. Therefore, a control group without CMR guide for myectomy would not have taken into account the increased experience acquired by our HC team from almost 300 patients who underwent myectomy between our initial use of CMR to plan the septal excision and the end of patient enrollment for the present study (December 2016). Nevertheless, on the basis of our accumulated experience with CMR, we believe that detailed preoperative tomographic reconstruction of septal morphology would enable a higher number of surgeons to perform a more accurate and safer ventricular septal excision."

In conclusion, systematic implementation of preoperative tomographic CMR reconstruction of septal anatomy and detailed planning of septal resection allowed us to perform a standardized and apically extended myectomy that, in association with papillary muscle mobilization and selected secondary MV chordal cutting, abolished the LV outflow tract gradient in each of our study patients, and significantly reduced or abolished heart failure symptoms and MV regurgitation in the great majority of patients. Preoperative CMR also prevented muscular excision from focal areas of marked septal thinning due to crypts. These results suggest a novel role for CMR that could make extended septal myectomy more accessible to surgeons and reduce the number of inappropriate MV replacements.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.01.041.

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