Appendix 1: Materials and methods

Analysis of LV flow components

Analysis was performed using a method previously validated by Eriksson *et al.* (14). The raw 4D-flow data first underwent preprocessing, which included phase offset and anti-aliasing corrections. Phase offset corrections addressed errors induced by eddy current fields, Maxwell terms, and gradient field inhomogeneity. A static tissue mask was applied to cover uniformly distributed voxels while excluding those representing vessels, noise, or spatial aliasing. A polynomial surface was fitted to the velocities within the static tissue mask and subtracted from the entire image, based on the assumption of no flow in static tissue. Anti-aliasing correction was applied to adjust velocities exceeding the set VENC, where the VENC was relatively low.

For LV analysis, precise valve definition was crucial. Valve modeling consisted of two components: valve planes and valve contours. The mitral and aortic valve planes were automatically detected by a machine learning algorithm and tracked throughout the cardiac cycle using 3-chamber long-axis cine images. Valve contours were initially detected by a non-machine learning algorithm and were subsequently manually verified and corrected by the user to ensure accuracy. After confirming the valve positions, they were matched to the segmented geometric model to achieve automatic image registration between the cine and velocity magnitude images. Manual adjustments to valve position and size were performed when necessary.

Blood flow components were classified based on pathline analysis. The LV endocardium was segmented based on particles that enter the LV through the mitral valve and exit through the aortic valve. Particles were emitted during the isovolumetric contraction phase and traced both forward and backward until the isovolumetric relaxation phase. The resulting pathlines were compared against the defined aortic and mitral valve contours. Based on whether and when particles passed through the valves, pathlines were automatically classified into four distinct blood flow components: (I) DF: blood that enters the LV during diastole and leaves during systole within the same cardiac cycle; (II) RIF: blood that enters the LV during diastole but is not ejected during systole within the same cycle; (III) DEF: blood already present in the LV at the beginning of diastole that is ejected during systole; and (IV) RV: blood that remains within the LV for at least two consecutive cardiac cycles.

The total blood volume for each flow component was calculated by multiplying the number of particles belonging to that component by the volume represented by a single particle. For the flow component visualization presented in *Figure 2* of this study, a pathline seeding density of 80% was applied.

Regarding specific technical considerations: To minimize respiration-induced motion artifacts in free-breathing scans, navigator-based respiratory gating (using a diaphragmatic navigator) was applied during scan acquisition. No additional post-processing for respiratory motion correction was performed during the flow analysis itself. The reported volumes of the flow components are absolute values and were not indexed to LV volume or SV.

Cardiac surgery

Modified extended morrow procedure

Preoperative assessment: all patients underwent transthoracic echocardiography and CMR imaging before surgery to accurately evaluate the location, extent, and degree of myocardial hypertrophy, as well as the anatomy of the mitral valve apparatus and hemodynamic status.

Core surgical technique: the resection primarily focused on the hypertrophied myocardium on the LV aspect of the interventricular septum responsible for LVOT obstruction and SAM of the mitral valve. The resection extended from below the aortic valve toward the cardiac apex, medially from the area corresponding to the anterior mitral leaflet to laterally approximately 3–5 mm below the left edge of the right coronary cusp. The length (typically 35–50 mm) and depth of resection were adjusted according to the individual morphology of hypertrophy, aiming to completely relieve the obstruction while ensuring the residual septal thickness was not less than 50% of its original thickness to maintain structural integrity.

Concomitant procedures: concurrently, abnormal structures that could contribute to obstruction were addressed, including resection of anomalous muscle bundles and release of papillary muscles. Mitral valve repair was performed concurrently in cases with moderate-to-severe mitral regurgitation or abnormalities of the valve apparatus.

Intraoperative assessment and documentation: immediately after resection, transesophageal echocardiography was used to assess the LVOT gradient, SAM of the mitral valve, and regurgitation, with further adjustments made as necessary.

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Table S1 Detailed surgical information for all HOCM patients in myectomy group (including extent of resection, resected myocardial mass, management of mitral apparatus, etc.)

Patient	Myocardial resection				Mitral valve apparatus management		
	Length (cm)	Width (cm)	Thickness (cm)	Mass (g)	Mitral valve leaflet	Papillary muscle	Secondary chordae
A	4.3	3.0	1.0	10.2	Mitral valve repair	Papillary muscle release	–
B	3.4	2.5	0.5	3.1	Mitral valve repair	–	Resection of abnormal secondary chordae
C	2.0	3.0	0.5	5.0	Mitral valve repair	–	–
D	3.5	2.2	0.5	3.0	–	–	–
E	4.0	2.0	1.0	4.5	Mitral valve repair	–	–
F	4.2	4.3	0.95	8.9	Mitral valve repair	Papillary muscle release	–
G	5.0	3.0	1.0	5.3	Mitral valve repair	–	–
H	3.0	2.0	1.0	8.6	Mitral valve leaflet plication	–	–
I	3.0	2.0	1.0	3.0	–	–	–
J	4.0	3.0	1.0	7.2	Mitral valve repair	–	–

HOCM, hypertrophic obstructive cardiomyopathy.

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Table S2 Statistical significance of pairwise comparisons in LV parameters between the septal myectomy, mavacamten, and healthy control

LV parameters	Baseline		30 weeks		Controls (n=10)	P value (at baseline), mavacamten *vs.* myectomy	P value (for HOCM *vs.* controls at baseline)	
	Mavacamten	Myectomy	Mavacamten	Myectomy			Mavacamten	Myectomy
CMR parameters								
LVMWT (mm)	25.10±6.40	22.90±4.36	20.90±5.30	19.70±4.42	8.55±1.13	0.764	<0.001	<0.001
LVMI (g/m^2)	113.30±43.13	92.83±29.69	89.40±34.91	74.61±26.22	43.82±5.50	0.551	0.002	0.002
LVEDVI (mL/m^2)	106.10±21.78	82.16±11.23	92.70±18.04	70.35±10.96	74.09±5.54	0.025	0.003	0.175
LVESVI (mL/m^2)	34.50±7.69	28.14±4.25	30.70±7.49	24.72±4.18	27.87±3.53	0.110	0.082	0.416
LVEF (%)	69.9±3.14	66.75±3.26	64.6±2.07	63.58±3.65	60.78±2.81	0.118	<0.001	0.001
CO (L/min)	8.66±2.77	6.45±1.56	6.71±1.33	5.56±1.46	5.44±0.93	0.130	0.015	0.271
SV (mL)	121.80±26.51	92.41±18.28	97.80±21.61	74.75±18.55	75.92±11.06	0.032	0.001	0.081
Strain parameters								
GLS (%)	−8.02±2.92	−8.07±2.66	−10.56±3.06	−10.84±3.02	−16.48±0.97	0.969	<0.001	<0.001
GCS (%)	−16.00±2.04	−14.31±2.70	−17.46±1.84	−17.63±3.67	−21.07±2.85	0.350	0.001	<0.001
GRS (%)	27.02±4.85	24.71±6.37	30.36±5.46	33.12±9.28	38.91±2.76	0.757	<0.001	<0.001
Flow components								
DF (%)	23.51±4.72	25.00±5.5	29.05±2.92	34.43±5.84	37.07±3.22	0.892	<0.001	<0.001
DEF (%)	21.50±3.63	19.42±3.64	22.91±2.81	21.31±3.27	20.87±2.55	0.520	0.960	0.682
RIF (%)	17.50±1.99	18.03±3.98	17.99±2.79	19.89±4.29	19.15±1.82	0.977	0.194	0.817
RV (%)	37.49±4.60	37.55±6.77	30.27±2.19	24.08±6.75	22.91±3.10	0.981	<0.001	<0.001
Echocardiographic parameters								
LVOT gradient (mmHg)	107±53	87.90±18.26	39.70±21.26	8.10±3.14	–	0.288	–	–

Data are presented as mean ± SD. CMR, cardiac magnetic resonance; CO, cardiac output; DEF, delayed ejection flow; DF, direct flow; GCS, global circumferential strain; GLS, global longitudinal strain; GRS, global radial strain; HOCM, hypertrophic obstructive cardiomyopathy; LV, left ventricular; LVEDVI, left ventricular end diastolic volume index; LVEF, left ventricular ejection fraction; LVESVI, left ventricular end systolic volume index; LVMI, left ventricular mass index; LVMWT, left ventricular maximum wall thickness; LVOT, left ventricular outflow tract; RIF, retained inflow; RV, residual volume; SD, standard deviation; SV, stroke volume.

Table S3 Intra- and interobserver reproducibility of LV global strains and flow components by using ICC analysis

Parameters	Intraobserver		Interobserver	
	ICC	95% CI	ICC	95% CI
GLS (%)	0.88	0.70, 0.96	0.84	0.46,0.96
GCS (%)	0.94	0.84, 0.98	0.90	0.74, 0.97
GRS (%)	0.82	0.56, 0.93	0.83	0.58, 0.94
DF (%)	0.84	0.59, 0.94	0.82	0.56, 0.93
DEF (%)	0.95	0.86, 0.98	0.83	0.47, 0.96
RIF (%)	0.85	0.63, 0.95	0.71	0.22, 0.92
RV (%)	0.96	0.90, 0.98	0.84	0.46, 0.96

CI, confidence interval; DEF, delayed ejection flow; DF, direct flow; GCS, global circumferential strain; GLS, global longitudinal strain; GRS, global radial strain; ICC, intraclass correlation coefficient; LV, left ventricular; RIF, retained inflow; RV, residual volume.