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Does the Flow Know? Mitral Regurgitant Jet Direction and Need for Valve Repair in Hypertrophic Obstructive Cardiomyopathy

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Hypertrophic obstructive cardiomyopathy (HOCM) is characterized by primary changes of both left ventricular (LV) myocardium and mitral valve apparatus. During LV ejection, blood is forced to circumvent a bulging septum and redirected toward the posterior aspect of the mitral valve on its way to the LV outflow tract (LVOT). Papillary muscle displacement anteriorly and mitral leaflet and chordal elongation provide the leaflet slack necessary to allow anterior motion of the valve in response to the force of flow pushing it into the outflow tract and against the septum.^{1–7} Mitral apparatus changes also preposition the leaflets into the outflow stream at the onset of systole, setting the stage for this anterior push.⁸ Because the typically shorter posterior mitral leaflet (PML) cannot travel toward the septum as far as the anterior mitral leaflet (AML), systolic anterior motion of the mitral valve (SAM) frequently disrupts leaflet coaptation, causing both LVOT obstruction and mitral regurgitation (MR), augmented by the LVOT pressure gradient.⁹ The shorter the PML, the greater its disparity with the AML and the more regurgitation for comparable degrees of SAM.

Removing the septal bulge by myectomy achieves two geometric corrections: it rectifies the streamlines of flow, which are no longer diverted posteriorly but can take the straight path over the mitral valve, pushing it posteriorly, and it partially reverses anterior papillary muscle displacement by enlarging LV cavity size above the mitral valve and possibly allowing LV cavity expansion.¹⁰ By positioning the mitral valve apparatus more posteriorly, myectomy corrects one of the primary pathologies of the mitral valve apparatus in HOCM in addition to correcting the primary septal myocardial pathology.

In most patients, the bent AML and wing-shaped PML together form a flow path directing the regurgitant jet posteriorly (Figure 1A); this is augmented by a Coanda effect as the jet adheres to the PML and posterolateral atrial surfaces.^{11–13} Posteriorly directed MR is therefore the hallmark of SAM-mediated MR and, in the absence of additional

abnormalities, strongly predicts that adequate myectomy will successfully eliminate or at least substantially reduce MR, even if severe. This was confirmed by Hang *et al.*¹⁴ in a study reported in this issue of *JASE*, who showed a 97% probability of a posteriorly directed jet on prebypass transesophageal echocardiography being relieved by myectomy (95% for prebypass transesophageal echocardiography), although 9% had more than mild MR on predischARGE transthoracic echocardiography.

But what if the jet has an anterior or central direction? Given the high prevalence of primary pathology of the mitral apparatus in HOCM (in particular enlarged leaflets and elongated chordae, which play a central role in generating SAM itself), a nonposteriorly directed jet raises the specter of non-SAM-related intrinsic mitral valve disease with MR that may not be adequately corrected by myectomy.^{1-6,15-22}

Hang *et al.*¹⁴ present convincing data showing that two thirds of patients with intrinsic mitral valve disease, defined by non-SAM-related pathology, have central or anteriorly directed jets. However, 83% of patients with central or anteriorly directed jets on prebypass transthoracic echocardiography have relief of SAM by myectomy alone. This relates to most patients studied having SAM-related MR, defined as MR relieved by myectomy, 35% of whom have central or anteriorly directed jets. These results can be reconciled with the growing appreciation of intrinsic mitral valve apparatus abnormalities in HOCM.^{1-6,15-21} Most observed pathologic mitral changes, especially of the PML, are actually implicated in the mechanism of SAM-mediated MR. Except for structural deficiencies such as ruptured chordae, leaflet cleft or perforations, most primary leaflet and chordal changes play a role in SAM-mediated MR and may become less critical once SAM is abolished. For instance, in SAM of the AML, disrupted mitral coaptation may be increased by a relatively restricted PML or by concomitant prolapse of the PML,²³ moving it even further away from the AML. In both cases of such intrinsic PML changes, abolishing AML SAM is likely to eliminate or reduce MR by restoring sufficient coaptation length. This may be the reason for the effectiveness of myectomy in dealing with SAM-mediated MR even in the presence of PML pathology. Eliminating SAM might even diminish PML prolapse itself by reducing LV pressure and providing the PML a better coapting AML.

The authors correctly point out the pivotal role of PML geometry for the mechanism and severity of SAM-mediated MR. PML pathology and geometry of leaflet coaptation may also explain why SAM-mediated MR jets may be centrally or even anteriorly oriented: it all depends on the orientation of the SAM-generated funnel that steers the regurgitant jet into the left atrium with respect to the atrial leaflets (Figure 1). The excellent examples provided by Hang *et al.*¹⁴ demonstrate this clearly: in their Figure 2A, from a patient with SAM relieved by myectomy, we see a relatively long PML, which does not prolapse into the left atrium but instead can follow the AML to a very anteriorly located coaptation point. SAM of the distal free half of the AML generates a sharp leaflet bend. As a result, the atrial orifice of the funnel is posteriorly tilted, very close and virtually parallel to the atrial surface of the PML. These are ideal conditions for a Coanda effect: like flow emerging from a nozzle above an airfoil, the regurgitant jet will entrain fluid, causing a low-pressure zone that deflects the jet toward the leaflet and left atrial wall (see Figure 1A of this editorial). In their Figure 3A, from another patient with SAM relieved by myectomy, the AML bend appears

less pronounced, and the distal half of the PML parallels the LV inflow axis. The two leaflets therefore form a relatively vertically oriented funnel, parallel to the LV long axis, causing the jet to run parallel to the AML, to which it attaches along its full length (see Figure 1B of this editorial).

These examples further demonstrate that jet direction by the leaflet funnel will depend not only on PML length, but also on AML bend (sharp or obtuse), both functions of relative leaflet elongation.²⁴ Careful analysis of funnel geometry may permit distinguishing nonposterior MR jets that are SAM mediated from those related to intrinsic mitral apparatus pathology as well, especially with the improved echocardiographic resolution of transesophageal echocardiography. Criteria for diagnosing SAM-mediated MR in the presence of nonposterior MR jets may include the following: (1) the jet entering the regurgitant flow path near the mitral-septal contact, with proximity of obstructive and regurgitant proximal flow convergence zones, connecting the mechanism of MR with the mechanism of obstruction, and (2) relatively vertical coaptation position of the PML (parallel to the LV long axis) with an obtuse rather than sharp AML bend, funneling the jet away from the PML surface (Figure 1B).

Several additional points are worth noting. SAM relief by myectomy was evaluated at rest, whereas a greater appreciation for dynamic SAM related to intrinsic mitral valve disease comes from exercise testing^{6,19,25} Comprehensive echocardiographic imaging can readily reveal mitral apparatus abnormalities such as flail and papillary muscle malposition (apical or leaflet insertion) associated with greater SAM-related MR and improved benefit from repair strategies. In the study from the Mayo Clinic, indeterminate jet direction was present in 14.3% of patients, who were excluded from analysis; this may reflect partial jet deflection by a Coanda effect. Greater MR persistence despite relief of obstruction is seen with alcohol septal ablation, associated with persistent mitral apparatus abnormalities.²⁶ There is growing recognition from echocardiography and magnetic resonance imaging of great structural diversity of the mitral apparatus that can benefit from novel surgical approaches to reduce leaflet slack and positioning into the LVOT flow stream through leaflet and papillary muscle modification.^{5,22,27–29} Fundamentally, we need to understand the mechanism of mitral leaflet elongation in this disease caused by sarcomeric protein mutations that are not expressed in the leaflets; these may include stimulation by endothelial shear stress and paracrine valve growth factors released by interstitial cells in the LV walls.^{30–32}

The findings of Hang *et al.*¹⁴ have important clinical implications. A nonposterior jet direction is more than three times as likely to be associated with non-SAM-related mitral pathology and hence continues to require careful search for such intrinsic disease using prebypass echocardiography. However, nonposterior jets are frequent in SAM-mediated and myectomy-relieved MR. We believe nonposterior jets likely to be relieved by myectomy can be identified by careful analysis of coaptation geometry and “nozzle orientation” and (in the absence of structural deficiencies such as ruptured chordae, leaflet cleft or perforations) should not automatically trigger mitral intervention in patients in whom septal myectomy is planned. This is good news for patients who have benefited for decades from this surgical procedure. However, in patients in whom septal thickness is considered insufficient to permit safe and effective myectomy^{19,25} or in whom mitral leaflet abnormalities, whether SAM

related or not, make it unlikely that myectomy alone may result in a satisfactory result, combining myectomy with mitral repair techniques to correct the observed mitral valve pathology is warranted. Finally, as demonstrated in this study, careful preoperative analysis of mitral valve geometry using appropriate imaging techniques has made mitral valve replacement for HOCM unnecessary.

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REFERENCES

1. Jiang L, Levine RA, King ME, Weyman AE. An integrated mechanism for systolic anterior motion of the mitral valve in hypertrophic cardiomyopathy based on echocardiographic observations. *Am Heart J* 1987; 113: 633–44. [PubMed: 3825854]
2. Klues HG, Maron BJ, Dollar AL, Roberts WC. Diversity of structural mitral valve alterations in hypertrophic cardiomyopathy. *Circulation* 1992;85: 1651–60. [PubMed: 1572023]
3. Kim DH, Handschumacher MD, Levine RA, Choi YS, Kim YJ, Yun SC, et al. In vivo measurement of mitral leaflet surface area and subvalvular geometry in patients with asymmetrical septal hypertrophy: insights into the mechanism of outflow tract obstruction. *Circulation* 2010; 122: 1298–307. [PubMed: 20837895]
4. Cavalcante JL, Barboza JS, Lever HM. Diversity of mitral valve abnormalities in obstructive hypertrophic cardiomyopathy. *Prog Cardiovasc Dis* 2012;54:517–22. [PubMed: 22687594]
5. Sherrid MV, Balaram S, Kim B, Axel L, Swistel DG. The mitral valve in obstructive hypertrophic cardiomyopathy: a test in context, *J Am Coll Cardiol* 2016;67:1846–58. [PubMed: 27081025]
6. Maron MS, Olivetto I, Harrigan C, Appelbaum E, Gibson CM, Lesser JR, et al. Mitral valve abnormalities identified by cardiovascular magnetic resonance represent a primary phenotypic expression of hypertrophic cardiomyopathy. *Circulation* 2011;124:40–7. [PubMed: 21670234]
7. Levine RA, Vlahakes GJ, Lefebvre X, Guerrero JL, Cape EG, Yoganathan AP, et al. Papillary muscle displacement causes systolic anterior motion of the mitral valve. Experimental validation and insights into the mechanism of subaortic obstruction. *Circulation* 1995;91:1189–95. [PubMed: 7850958]
8. Sherrid MV, Gunsburg DZ, Moldenhauer S, Pearle G. Systolic anterior motion begins at low left ventricular outflow tract velocity in obstructive hypertrophic cardiomyopathy, *J Am Coll Cardiol* 2000;36:1344–54. [PubMed: 11028493]
9. Schwammenthal E, Nakatani S, He S, Hopmeyer J, Sagie A, Weyman AE, et al. Mechanism of mitral regurgitation in hypertrophic cardiomyopathy: mismatch of posterior to anterior leaflet length and mobility. *Circulation* 1998;98:856–65. [PubMed: 9738640]
10. Nakatani S, Schwammenthal E, Lever HM, Levine RA, Lytle BW, Thomas JD. New insights into the reduction of mitral valve systolic anterior motion after ventricular septal myectomy in hypertrophic obstructive cardiomyopathy. *Am Heart J* 1996; 131:294–300. [PubMed: 8579024]
11. Yeo TC, Miller FA Jr., Oh JK, Schaff HV, Weissler AM, Seward JB. Hypertrophic cardiomyopathy with obstruction: important diagnostic clue provided by the direction of the mitral regurgitation jet. *J Am Soc Echocardiogr* 1998;11:61–5. [PubMed: 9487471]
12. Grigg LE, Wigle ED, Williams WG, Daniel LB, Rakowski H. Transesophageal Doppler echocardiography in obstructive hypertrophic cardiomyopathy: clarification of pathophysiology and importance in intraoperative decision making, *J Am Coll Cardiol* 1992;20:42–52. [PubMed: 1607537]
13. Yu EH, Omran AS, Wigle ED, Williams WG, Siu SC, Rakowski H. Mitral regurgitation in hypertrophic obstructive cardiomyopathy: relationship to obstruction and relief with myectomy, *J Am Coll Cardiol* 2000;36: 2219–25. [PubMed: 11127464]

14. Hang D, Schaff HV, Nishimura RA, Lahr BD, Abel MD, Dearani JA, et al. Accuracy of jet direction on Doppler echocardiography in identifying the etiology of mitral regurgitation in obstructive hypertrophic cardiomyopathy. *J Am Soc Echocardiogr* 2018;32:333–40. [PubMed: 30598365]
15. Hagege AA, Dubourg O, Desnos M, Mirochnik R, Isnard G, Bonne G, et al. Familial hypertrophic cardiomyopathy. Cardiac ultrasonic abnormalities in genetically affected subjects without echocardiographic evidence of left ventricular hypertrophy. *Eur Heart J* 1998; 19:490–9. [PubMed: 9568454]
16. Kaple RK, Murphy RT, DiPaola LM, Houghtaling PL, Lever HM, Lytle BW, et al. Mitral valve abnormalities in hypertrophic cardiomyopathy: echocardiographic features and surgical outcomes. *Ann Thorac Surg* 2008;85: 1527–35. [PubMed: 18442532]
17. Hagege AA, Bruneval P, Levine RA, Desnos M, Neamatalla H, Judge DP. The mitral valve in hypertrophic cardiomyopathy: old versus new concepts. *J Cardiovasc Transl Res* 2011;4:757–66. [PubMed: 21909825]
18. Teo EP, Teoh JG, Hung J. Mitral valve and papillary muscle abnormalities in hypertrophic obstructive cardiomyopathy. *Curr Opin Cardiol* 2015;30: 475–82. [PubMed: 26192489]
19. Patel P, Dhillon A, Popovic ZB, Smedira NG, Rizzo J, Thamilarasan M, et al. Left ventricular outflow tract obstruction in hypertrophic cardiomyopathy patients without severe septal hypertrophy: implications of mitral valve and papillary muscle abnormalities assessed using cardiac magnetic resonance and echocardiography. *Circ Cardiovasc Imaging* 2015;8: e003132. [PubMed: 26082555]
20. Hong JH, Schaff HV, Nishimura RA, Abel MD, Dearani JA, Li Z, et al. Mitral regurgitation in patients with hypertrophic obstructive cardiomyopathy: implications for concomitant valve procedures. *J Am Coll Cardiol* 2016;68:1497–504. [PubMed: 27687190]
21. Groarke JD, Galazka PZ, Cirino AL, Lakdawala NK, Thune JJ, Bundgaard H, et al. Intrinsic mitral valve alterations in hypertrophic cardiomyopathy sarcomere mutation carriers. *Eur Heart J Cardiovasc Imaging* 2018;19:1109–16. [PubMed: 30052928]
22. van der Lee C, Kofflard MJ, van Herwerden LA, Vletter WB, ten Cate FJ. Sustained improvement after combined anterior mitral leaflet extension and myectomy in hypertrophic obstructive cardiomyopathy. *Circulation* 2003;108:2088–92. [PubMed: 14517170]
23. Petrone RK, Klues HG, Panza JA, Peterson EE, Maron BJ. Coexistence of mitral valve prolapse in a consecutive group of 528 patients with hypertrophic cardiomyopathy assessed with echocardiography. *J Am Coll Cardiol* 1992;20:55–61. [PubMed: 1607539]
24. Klues HG, Roberts WC, Maron BJ. Morphological determinants of echocardiographic patterns of mitral valve systolic anterior motion in obstructive hypertrophic cardiomyopathy. *Circulation* 1993;87:1570–9. [PubMed: 8491013]
25. Alhaj EK, Kim B, Cantales D, Uretsky S, Chaudhry FA, Sherrid MV. Symptomatic exercise-induced left ventricular outflow tract obstruction without left ventricular hypertrophy. *J Am Soc Echocardiogr* 2013;26: 556–65. [PubMed: 23534983]
26. Delling FN, Sanborn DY, Levine RA, Picard MH, Fifer MA, Palacios IF, et al. Frequency and mechanism of persistent systolic anterior motion and mitral regurgitation after septal ablation in obstructive hypertrophic cardiomyopathy. *Am J Cardiol* 2007;100:1691–5. [PubMed: 18036370]
27. McIntosh CL, Maron BJ, Cannon RO III, Klues HG. Initial results of combined anterior mitral leaflet plication and ventricular septal myotomy-myectomy for relief of left ventricular outflow tract obstruction in patients with hypertrophic cardiomyopathy. *Circulation* 1992;86:1160–7.
28. Song HK, Turner J, Macfie R, Kumar S, Mannello MJ, Smith D, et al. Routine papillary muscle realignment and septal myectomy for obstructive hypertrophic cardiomyopathy. *Ann Thorac Surg* 2018; 106:670–5. [PubMed: 29753818]
29. Halpern DG, Swistel DG, Po JR, Joshi R, Winson G, Arabadjian M, et al. Echocardiography before and after resect-plicate-release surgical myectomy for obstructive hypertrophic cardiomyopathy. *J Am Soc Echocardiogr* 2015;28:1318–28. [PubMed: 26272699]
30. Judge DP, Neamatalla H, Norris RA, Levine RA, Butcher JT, Vignier N, et al. Targeted Mybpc3 knock-out mice with cardiac hypertrophy exhibit structural mitral valve abnormalities. *J Cardiovasc Dev Dis* 2015;2:48–65. [PubMed: 26819945]

31. Levine RA, Hagège AA, Judge DP, Padala M, Dal-Bianco JP, Aikawa E, et al. Mitral valve disease —morphology and mechanisms. *Nat Rev Cardiol* 2015;12:689–710. [PubMed: 26483167]
32. Teekakirikul P, Eminaga S, Toka O, Alcalai R, Wang L, Wakimoto H, et al. Cardiac fibrosis in mice with hypertrophic cardiomyopathy is mediated by non-myocyte proliferation and requires Tgf-beta. *J Clin Invest* 2010; 120: 3520–9. [PubMed: 20811150]

Figure 1.

Systolic anterior motion of the mitral valve geometry and mitral regurgitant jet orientation in hypertrophic obstructive cardiomyopathy. **(A)** Typical posterior jet geometry: anterior mitral leaflet (AML) with sharp bend, posterior mitral leaflet (PML) reaching the anterior coaptation point in an almost horizontal position, both leaflets creating a posteriorly tilted nozzle parallel to the PML atrial surface to which the jet is directed and becomes attached. **(B)** Atypical nonposterior jet geometry: relatively obtuse AML bend with leaflet generally parallel to the long inflow axis of the left ventricle; AML and PML form a relatively vertically oriented funnel, creating a superiorly oriented nozzle parallel to the AML atrial surface, to which flow attaches.