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EDITORIAL COMMENT

The Mitral Valve in Hypertrophic Cardiomyopathy

Other Side of the Outflow Tract*

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Mitral valve and papillary muscle abnormalities are common in hypertrophic cardiomyopathy (HCM) patients and contribute to systolic anterior motion (SAM) and left ventricular outflow tract (LVOT) obstruction (1,2). The necessary conditions for SAM are anterior position of the mitral valve in the left ventricular (LV) cavity, LV flow striking the posterior aspect of the mitral leaflets, and leaflet slack that permits increased mobility (3,4). Without leaflet slack, the mitral leaflets will remain in their more or less central position in the LV, regardless of the hemodynamic force compelling them forward. Among the most common abnormalities observed are elongated mitral leaflets, producing an anterior leaflet residual leaflet tip that protrudes past the coaptation plane into the LV ejection flow (5). The normal leaflet is held in place by the LV-left atrial pressure difference; in contrast, the diaphanous residual leaflet is bounded only by LV flow, and LV currents easily sweep it toward the septum in early systole. In this issue of the *Journal,* Ferrazzi et al. (6) present observations in a subset of young HCM patients that have a developmental abnormality, consisting of a band of muscular tissue in the intervalvular fibrosa between the base of the mitral valve and the aortic valve. This novel observation may explain leaflet elongation in some young patients. Other investigators have previously described immunohistopathological findings in the residual mitral leaflet tip resected at the time of surgery that indicate a nonmuscular developmental abnormality in this portion of the leaflet (7).

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Another common anomaly is an anteriorly positioned head of the anterolateral papillary muscle or its chordae that pre-position the valve into the outflow tract by tenting the mitral leaflets anteriorly. This also reduces the posteriorly directed traction and restraint on the mitral leaflets that act to prevent SAM. Indeed, SAM is best thought of as the result of a dynamic disequilibrium between the restraining forces of the subvalvular apparatus and the displacing anteriorly directed pushing force of flow (8). Patients with LVOT obstruction who have no or only modest thickening of the septum invariably have abnormalities of their mitral valves that predispose to SAM.

What then is the role of the hypertrophied septal muscle? An early theory was that hypertrophy causes a narrowing of the LVOT and that high velocities there cause a Venturi underpressure that sucks the mitral leaflets into the septum. In contrast, the preponderance of current evidence is that drag, the pushing force of flow, catches the leaflets from behind and sweeps them into the septum. At the onset of SAM, LVOT velocities are low, precluding significant Venturi forces there, and LV flow behind the leaflets is observed early in systole (3,4). The principal role of the hypertrophied septum is that it redirects flow posteriorly and laterally in the LV cavity, so that its early systolic flow strikes the mitral valve on the wrong side. SAM is understood as an

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overlap between the inflow and outflow portions of the LV (3,9). Once mitral-septal contact occurs, it is the pressure difference itself (the gradient) that further narrows the orifice, producing the typical concave-to-the-left Doppler velocity tracing.

These observations have led to an altered surgical approach for obstructive HCM (10). Initially, with a limited resection, the subaortic septal bulge was excised with the trough myectomy described by Morrow (10). However, for many years myectomy was viewed as an unpredictable tool, plagued in the hands of the inexperienced surgeon by either inadequate relief of obstruction, or rarely the dreaded result of a ventricular septal defect. Because of the improved understanding of the pathophysiology of SAM, Messmer (11) introduced the extended myectomy that carries the septal resection more toward the apex to the level of the papillary muscles. This resection redirects ejection flow anteriorly and medially away from the mitral valve. In addition, when the papillary muscles are bound to the anterior wall, Messmer (11) introduced their release from the anterior wall of the LV, allowing the mitral valve coaptation plane to drop posteriorly in the LV cavity (11). The extended myectomy is now the operation that is most commonly performed at HCM surgical centers. It better separates the inflow and outflow portions of the LV with improved and more predictable outcomes (12–14).

When mitral leaflet and papillary muscle/chordal abnormalities are detected pre-operatively and by direct inspection in the OR, most HCM surgeons now address this pathology at the same time as the myectomy. These ancillary mitral procedures are not performed on every HCM patient who comes to surgery, only those with mitral abnormalities that predispose to SAM. Anterior leaflet plication with a row of horizontal mattress sutures both stiffens it and decreases its length (12,13). The residual leaflet may be safely directly excised when it does not contribute to coaptation, and when there is enough chordal support on either side to prevent prolapse (2,15). In addition, resection of anomalous papillary muscles or thickened secondary chordae that insert directly into the anterior mitral leaflet allow a posterior drop of the mitral leaflets explicitly out of the ejection flow stream. This has been termed chordal cutting, or papillary/chordal release. An experienced HCM surgeon who both understands the physiology and can confidently recognize the contributing mitral pathology will apply these ancillary procedures judiciously.

The advantage to addressing the mitral valve pathology at the same time as the myectomy is that the depth of the myectomy is inherently imprecise. Correcting the contributors to SAM on both sides of the outflow tract, at the same operation, provides insurance that patient will leave the operating room without obstruction. The advent of on-pump intracardiac echocardiography “OPIE” also allows real-time monitoring of septal thickness by the operating surgeon during the actual resection at a time when transesophageal echocardiography cannot visualize the heart, because it is empty of blood (16). This slim handheld device allows more accurate tailoring of the depth of the myectomy.

Stepping back, not every patient with obstructive HCM needs surgery, which by guidelines has been offered to patients with New York Heart Association functional class III symptoms resistant to maximum pharmacotherapy, and have rest or exercise gradients >50 mm Hg. We also recommend surgery to patients with syncope with less severe symptoms if their history suggests a gradient-related cause. Pharmacotherapy controls LVOT obstruction and symptoms in the majority of patients through stepped management with beta-blockade, disopyramide, or verapamil (17). Clinical trials of novel pharmacotherapy with myosin ATP-ase inhibitors are in progress and offer hope for new armamentarium (18). In Japan, cibenzoline has long been the therapeutic agent of choice for patients resistant to beta-blockade, and there currently is a phase 1 study of a modification of the cibenzoline molecule planned. Negative inotropes such as these decrease early LV ejection flow acceleration and thus decrease the hydrodynamic force on the valve (19). In SAM’s dynamic equilibrium, this decreases the pushing force on the mitral valve and allows the restraining structures to reassert themselves, delaying or abolishing SAM. In contrast, the Valsalva maneuver, standing, and/or eating a meal decrease the size of the LV cavity, increase the overlap, decrease restraint, and provoke gradients. A meal is also is a vasodilator provocation, decreasing systemic vascular resistance. Performing an exercise test after a meal and acquiring echocardiographic gradients in the upright posture is currently the most potent physiological maneuver to provoke obstruction. Termed the “SPEPP” test, standing post-exercise post-prandial stress testing is recommended for patients with a strong suspicion for obstruction when conventional exercise testing does not provoke a gradient. Many patients who have been initially diagnosed as nonobstructive HCM will actually turn out to have obstruction when post-prandial exercise is applied (20,21). These patients will then be candidates for treatment of obstruction for their symptoms.

Shah et al. (5,22) first observed SAM of the mitral valve by echocardiography in the late 1960s and also first reported the residual leaflet. Echocardiography

remains the principal tool for detecting mitral abnormalities in HCM. In 2-dimensional apical views, the mitral valve normally coapts near the plane of the mitral annulus. In stark contrast, in obstructive HCM, the mitral leaflets often extend deep into the LV toward the apex, coapting distant from the annulus (particularly on the apical 3-chamber view). This abnormality resembles an old-fashioned nightcap not only because of the length and protrusion, but because of the inherent mitral anterior mobility and floppiness. The anatomic protrusion of the valve is often overlooked because the eye is drawn to the SAM and the septal hypertrophy. Anterior displacement of the papillary muscles are best observed on the 2-dimensional short-axis view, particularly a head of the anterolateral papillary muscle. With foreknowledge, the surgeon begins the operation more precisely informed of the pathophysiology of the SAM, knowledge that is heightened by the pre-pump transesophageal echocardiogram (15). Careful inspection of the pre-operative echocardiogram, not only for the septum, but also for the mitral valve, detects therapeutic targets that may improve outcomes.

The observation of aortic-mitral discontinuity, the muscular band observed in the present study, is novel for our centers. We have not noticed it despite aggressive direct surgical examination, chordal cutting, and often horizontal plication of the anterior leaflet at this location as mainstays of our surgical strategy for many years. Because of the report of Ferrazzi et al. (6), HCM surgeons will be looking for this in young patients and assessing its frequency and its association with pathogenic variants.

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