Indications for Surgery in Obstructive Hypertrophic Cardiomyopathy

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Systolic anterior motion of the mitral valve is caused by an abnormal overlap of the inflow and outflow portions of the left ventricle (LV). Thickening of the septum and anterior position of the mitral valve in the LV cavity caused by mitral/submitral anomalies preposition the tip of the leaflets into the LV ejection stream, where they are swept by flow into the septum. Once they hit the septum, they are forced further into the wall by the pressure difference across the outflow tract. Abolishing or delaying systolic anterior motion is the goal of all treatment for obstructive hypertrophic cardiomyopathy (HCM). Pharmacotherapy with negative inotropes decreases early systolic ejection acceleration, decreasing drag forces on the leaflets, thus allowing the restraining force of the chordae and papillary muscles to reassert their posteriorly directed restraint. Extended surgical septal myectomy, often now performed with ancillary mitral repair, is the most complete and durable method to separate the inflow and outflow portions of the LV. There is no question that it is highly effective at relieving symptoms; in our practice, 550 patients with moderate or severe symptoms have had surgery. The questions posed by the current article by Alashi et al in this issue of the Journal of the American Heart Association (JAHA) are which patients with obstruction should have surgery and whether surgery should be applied early in their course for New York Heart Association I or II symptoms, or later when symptoms are moderate or severe.

DOES EARLY SURGERY PROLONG LIFE IN MILDLY SYMPTOMATIC PATIENTS?

If there were no human costs to surgery, or if early surgery was shown to have better survival outcomes in unselected mildly symptomatic patients, it should be applied earlier. The authors performed a retrospective analysis of their selected surgical cohort and found a lower mortality after a mean follow-up of 6.2 years in patients operated on when they had only mild or no symptoms. But, invariably, surgery exacts an early toll of mortality and morbidity in these mildly symptomatic or asymptomatic patients. In the article by Alashi et al, in-hospital deaths occurred in 0.6%, stroke occurred in 0.6%, and prolonged hospital stays >14 days occurred in 6%, including 3.8% for respiratory failure, 0.6% for poststroke recovery, and 2% for other causes. The present study did not randomize unselected patients to surgery for no/mild symptoms versus moderate/severe symptoms, so the observed difference in survival is subject to selection bias. In a retrospective study, there are always unmeasured confounders that no analysis can control for. This is also true of other reports comparing surgery with medical therapy, where in some, even

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See Article by Alashi et al.

There are only 2 reasons to operate on patients with heart disease. The first is to prolong life, and the second is to alleviate symptoms. On both counts, this article fails to convince this author that early surgery is preferable to stepped management comprised of aggressive pharmacotherapy followed by surgery, if needed, for patients with resistant symptoms.
age was not controlled as a comorbid condition. Thus, one cannot generalize from the results of such a surgical series, where patients have traveled for operations, to recommend surgery on all patients with mild or asymptomatic obstructive HCM. To recommend that, one would have to perform a randomized study of all mildly symptomatic patients to surgery or not.

In the present study, there were 174 sudden death events at follow-up in the 2268 operated on patients (7.7%) during a mean follow-up of 6.2±4 years. This will not differ from the sudden death incidence of all patients with HCM, irrespective of treatment, reported as 0.8%/year. Surgery has been advanced as preventing sudden death by dint of its removing LV outflow tract obstruction, and thereby lowering afterload, ischemic and energetic burdens from the myocardium. The report from Alashi et al throws afterload, ischemic and energetic burdens from the myocardium.9 The report from Alashi et al throws afterload, ischemic and energetic burdens from the myocardium.9 The report from Alashi et al throws afterload, ischemic and energetic burdens from the myocardium.9 The report from Alashi et al throws afterload, ischemic and energetic burdens from the myocardium.9 The report from Alashi et al throws afterload, ischemic and energetic burdens from the myocardium.9

The sudden deaths are pertinent clinically because there has been reticence to place implantable cardioverter-defibrillators in patients with risk factor(s) who have had successful surgery performed for symptoms. It is our recent practice to place defibrillators as primary prevention in postmyectomy patients when our judgement indicates significant hazard based on the presence of risk factors even if they have had successful surgery. It would be of interest for the authors of the current article to analyze the risk factor profile of the 174 patients who experienced postoperative sudden death.

The argument is made that early surgery improves prognosis in mitral and aortic regurgitation; should this be the case also in obstructive HCM? But mitral and aortic regurgitation are fixed lesions; load cannot be reduced or abolished in aortic regurgitation or mitral regurgitation. In contrast, the severity of obstruction in HCM decreases with pharmacotherapy. So, the analogy is not appropriate.

STEPPED MANAGEMENT OF SYMPTOMS IN OBSTRUCTIVE HCM

If medical therapy always failed to relieve symptoms, or if it was associated with frequent adverse outcomes, surgery should be applied earlier in the patient’s course. The combination of disopyramide given with either β blocker or verapamil is considered by physicians experienced with its use to be the most effective combination for symptom relief, reducing resting gradients by >50% and improving limiting symptoms in 50% to 65% of patients long-term. It has a class I recommendation by the most current published HCM guidelines, that of the European Society in 2014 and of the American Heart Association/American College of Cardiology in 2020. In recent years, the safety concerns about disopyramide have abated. It is not a typical type la sodium channel blocker and should not be tarred with the same brush as those agents. Rather, in HCM cardiomyocytes, it is best characterized as a multichannel blocker, also blocking the late sodium channel, the calcium channel, stabilizing the ryanodine receptor release of calcium from the sarcoplasmic reticulum, and markedly decreasing cytosolic calcium. In vitro, it decreases early and late after depolarizations.10

Disopyramide joins with other agents that prolong the QT, like amiodarone and ranolazine, which, despite their electrocardiographic effects on the QT, rarely provoke torsade de pointes. This explains its safety, clinically shown in studies from Toronto and New York.11,12 Most recently, Adler et al showed no risk for 168 patients started on disopyramide as outpatients.13 As with all medications, prudent patient education is appropriate; patients are advised to not take disopyramide along with other agents that prolong QT, and to take potassium commitment with diuretics, if they are begun. Long-term, the risks of disopyramide have been extremely low, consistent with its multichannel blockade, and particularly by its blockade of the late sodium channel. Consistent with its safety profile, authors from Toronto showed no difference in HCM-related mortality compared with surgery in patients treated medically, 65% who received disopyramide11 (Figure 1). If the disopyramide–β blocker trial fails to relieve symptoms, or if intolerable adverse effects occur, patients are promptly referred for surgery. We have termed this approach stepped management which is most often our real-practice scenario. The effect on mortality of stepped management is shown in Figure 2, a study where 74% of patients received disopyramide. There was no difference in mortality of patients treated in this staged manner compared with age- and sex-matched US population.12 Patients do not die more frequently if given a trial of aggressive pharmacotherapy before referral to surgery if, and when, they fail to improve. It is inaccurate to characterize patients who receive highly active gradient-lowering pharmacotherapy as undergoing “watchful waiting.” In the study by Alashi et al despite their statement that maximal pharmacotherapy was prescribed, only 4% of the patients were given disopyramide to relieve their symptoms. We have observed this geographic heterogeneity before. Centers in New York, Toronto, Boston, Los Angeles, London, and elsewhere use disopyramide extensively. Geographically remote
surgical referral centers may be more likely to operate because long distances make follow-up difficult and expensive. Also, there may be unfamiliarity with disopyramide among physicians in patient’s home communities. A primer on the use of disopyramide in obstructive HCM for practicing cardiologists has been published.14

Because of the lack of randomization, paucity of effective pharmacotherapy, the sudden deaths, and conflicting data from other investigators, we question the conclusion that “In oHCM patients, earlier versus surgery for Class I indication had a better long-term survival.” We would characterize this conclusion with the old Scottish verdict: “not proven.”

Stepped management will assume increased prominence in the care of patients with obstructive HCM if trials of 2 myosin ATPase inhibitors, or another, of a modification of the cibenzoline molecule are shown to be safe and effective, and achieve US Food and Drug Administration approval. We need more, and multiple, effective medications for HCM. Most patients will prefer a trial of these agents before moving on to surgery.

**EVOLUTION OF SURGICAL TECHNIQUE FOR OBSTRUCTION IN HCM**

Three major developments in surgical technique have occurred during the past 2 decades in parallel with improved preoperative echocardiography and planning. First, in response to an altered understanding of the pathophysiology of obstruction, the myectomy for most patients has been extended toward the apex to the level of the papillary muscles to redirect the direction of flow anteriorly and medially away from the mitral valve.6,7,15,16 Second, mitral repairs performed at the same time as myectomy have increasingly been applied by more surgeons and in more patients. Mitral and papillary muscle anomalies are identified on echocardiography preoperatively or by the surgeon by direct inspection, including leaflet elongation, anterior position of the valve in the LV chamber caused by anterobasal displacement of the papillary muscles, and shortened chordae or anomalous papillary muscles that tent the mitral valve into the flow stream.17 In the present report by Alashi et al, 38% had mitral repair for these detected abnormalities, which included plication of the anterior leaflet, chordal cutting/release, papillary muscle release, resection, or reorientation. Only 5% required mitral valve replacement (in our experience, performed because of leaflet or annular dense calcification). The patient with flexible leaflets is better off leaving the operating room with his/her own native valve. To this impressive list of new armamentarium, Dr Daniel Swistel of our institution has recently added residual leaflet excision, termed ReLex, which is now his preferred method of shortening a long anterior leaflet.18 Third, surgeons now successfully perform HCM surgery on patients with septal thickness <18 mm. These patients almost invariably have concomitant repairable mitral valve anomalies that predispose to obstruction even in the absence of significant septal thickening. A new echocardiographic modality, on-pump intracardiac echocardiography, “OPIE,” allows
online monitoring of septal thickness by the operating surgeon during the actual resection; this is a time when transesophageal echocardiography cannot visualize the heart, because it is empty of blood. This slender handheld device permits the surgeon to more accurately tailor the exact site and depth of the myectomy.\(^1\)

Will the advent of new pharmacologic agents decrease the number of surgeries performed for obstructive HCM? We are skeptical about that here. Rather, we expect an increased diagnostic recognition of HCM because of its higher profile in the medical community and better imaging. HCM is no longer a poor-prognosis disease because of modern application of lifesaving therapy with the implantable cardioverter-defibrillator, and because of quality-of-life improving therapies.\(^2\)

We expect increased referrals to HCM centers, and that a “rising tide will lift all boats” with robust referrals for both medical care and appropriate surgical referral in a stepped manner. Regardless how the mix of therapies pans out, the future is bright for patients with obstructive HCM.

ARTICLE INFORMATION

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Disclosures
Dr Sherrid has served as a consultant to Celltrion, Inc.

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