Echocardiography in the treatment of hypertrophic cardiomyopathy

Hipertrofik kardiyomiyopati tedavisinde ekokardiyografi

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ABSTRACT

Echocardiography is the best technique to diagnose, evaluate, follow-up and guide the treatment of hypertrophic cardiomyopathy (HCM). Diagnosis of HCM depends on left ventricular wall thickness ≥15 mm. Also noted are mitral valve systolic anterior motion, anteriorly positioned mitral valve leaflet coaptation, anomalous anterior insertion of papillary muscles, and diastolic dysfunction. Resting left ventricular outflow tract (LVOT) gradient occurs in 25% of patients and provocable gradients may be demonstrated in more than half of patients. Echocardiography is important for sudden death risk assessment; patients with a wall thickness more than 30 mm have a higher risk of sudden cardiac death, as often as 2%/year. Two thirds of the symptomatic obstructed patients can be successfully managed long term with medical treatment alone (beta-blockers, disopyramide, verapamil) guided by transthoracic echocardiography (TTE) response and follow-up. Obstructed patients, who fail medical therapy, are usually offered invasive treatment: surgical septal myectomy, alcohol septal ablation, or DDD pacemaker. Preoperative TTE is a necessary guide for the surgeon in planning the operation. It gives the surgeon precise measurements of septal thickness, mitral valve leaflets length and floppiness and papillary muscle anomalies. Intraoperative transesophageal echocardiography is a very important tool for evaluating surgical results. Persistent SAM, resting outflow gradient more than 30 mm Hg or more than 50 mmHg with provocation, moderate to severe mitral regurgitation are indications for immediate revision. For patients > 40 years old, and also not suitable for surgery because of comorbidities, alcohol septal ablation is viable alternative therapy for relief of obstruction and improvement of symptoms. Echocardiography is a valuable tool to choose the site of ablation (using myocardial contrast echocardiography), as well as for evaluation of results. *(Anadolu Kardiyol Derg 2006; 6 Suppl 2: 18-26)*

Key words: Hypertrophic cardiomyopathy, obstructive HCM treatment, disopyramide, septal myectomy, alcohol septal ablation, echocardiography

ÖZET

Hipertrofik kardiyomiyopati (HKM) tanısında, değerlendirmesinde, takibinde ve tedavi kılavuzluğunda en iyi teknik ekokardiyografidir. Hipertrofik kardiyomiyopati tanısı sol ventrikül duvar kalınlığı >=15mm olduğunda konulmaktadır. Bununla birlikte mitral kapağın öne sistolik hareketi (SAM), mitral kapakçıkların koaptasyonunun anteriyor konumu, papiller adalelerin anormal anteriyor lokalizasyonu ve diyastolik disfonksiyon görülebilir. İstirahat sol ventrikül çıkış gradiyenti (SVÇG) hastaların %25 inde ve provokasyonla ortaya çıkan gradiyentler hastaların >%50 görülmektedir. Ekokardiyografi ani kardiyak ölümün risk değerlendirmesi için önemli bir yöntemdir ve 30 mm den fazla duvar kalınlığı olan hastalarda ani ölüm riski daha yüksektir, yılda %2 prevalansı vardır. Semptomatik obstrüksiyonu olan hastaların 2/3 ekokardiyografi kılavuzluğunda ve takibinde sadece uzun süreli medikal tedavi ile (beta-blokerler, disopiramid, verapamil) başarılı olarak takip edilebilirler. Medikal tedaviye cevap vermeyen ve obstrüksiyonu olan hastalara genellikle cerrahi septal miyektomi, alkol septal ablasyonu veya DDD pacemaker önerilir. Preoperatif transtorasik ekokardiyografi (TTE), ameliyatı planlayan cerrah için vazgeçilmez bir kılavuzdur. Ekokardiyografi cerraha septal kalınlığının kesin ölçümlerini, mitral yaprakçıkların uzunluğunu, sarkmasını ve papiller adale anomalilerini gösterir. Cerrahi sonucunun değerlendirmesinde intraoperatif transözofajiyal ekokardiyografi çok önemli bir araçtır. Acil revizyon için endikasyonlar şunlardır: persistan SAM, 30 mmHg'dan fazla olan istirahat veya provokasyonla 50 mmHg çıkış yolu gradiyenti ve orta/şiddetli mitral regürjitasyonu. Yaşı 40 tan fazla olan veya komorbiditeler nedeni ile cerrahi için uygun olmayan hastalarda obstrüksiyonun hafifletilmesi ve semptomların iyileşmesi için alkol septal ablasyonu canlı bir alternatif terapidir. İşlemin sonuçlarını değerlendirmede ve ablasyonun yerini belirlemede (miyokardiyal kontrast ekokardiyografi aracı ile) ekokardiyografi çok değerli bir yöntemdir. *(Anadolu Kardiyol Derg 2006; 6 Özel Sayı 2: 18-26)*

Anahtar kelimeler: Hipertrofik kardiyomiyopati, obstrüktif HKM tedavisi, disopiramid, septal miyektomi, alkol septal ablasyonu, ekokardiyografi

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Role of echocardiography in diagnosis of hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is clinically defined by a hypertrophied non-dilated left ventricle in the absence of another cardiac or systemic disease capable of producing the degree of left ventricular hypertrophy observed (1). Echocardiography (echo), widely available, noninvasive, of relatively low cost and with no contraindications (except sometimes for poor imaging quality) has proved over the years, to be the best technique to diagnose, evaluate, follow-up and guide the treatment of HCM (2-5). Most recent advances towards understanding the pathophysiology, and developing treatments have employed echo (6,7).

Early echo studies of HCM had used M-mode. A septal to posterior wall thickness ratio of 1.3:1 was considered evidence of inappropriate septal hypertrophy. With two-dimensional echo the presence, magnitude, and distribution of left ventricular hypertrophy can now be accurately determined. When combined with color flow and spectral Doppler imaging, echo can fully delineate the entire spectrum of hemodynamic abnormalities seen in HCM (8).

Currently, HCM is identified by virtue of a maximal left ventricular wall thickness of 15 mm in adult patients or the equivalent wall thickness relative to body-surface area, in children (1). This represents an unambiguous and conservative cutoff value. Other features, useful but not necessary in diagnosing HCM, are: 1) mitral valve systolic anterior motion (absent or mild in nonobstructed pattern) (9); 2) anteriorly positioned mitral valve leaflet coaptation (10,11); 3) anomalous anterior insertion of papillary muscles (12,13), 4) diastolic dysfunction. When a patient is referred for evaluation and diagnosis of HCM, echo is useful for assessing the anatomic type, presence of obstruction, and future risk for sudden cardiac death.

Echocardiography role in defining types and assessing obstruction in HCM

Classical HCM is described as asymmetric hypertrophy of the septum involving the subaortic area of the LV outflow tract. Besides this pattern, HCM can present with hypertrophy in any segment. According to the degree and distribution of hypertrophy in left ventricular (LV) short axis views, Gregor et al described 5 types of HCM: 1) type I - hypertrophy affecting only the interventricular septum; 2) type II - hypertrophy involving besides the septum, also the left ventricular (LV) anterior or lateral wall; 3) type III - hypertrophy of the LV posterior wall; 4) type IV - distinct hypertrophy of the whole apical LV and septum; and 5) type V - concentric hypertrophy of the LV and septum (14). Type II pattern is the most frequent (67%) followed by type I (14%), with least encountered being the type III (4%). Other studies have confirmed that HCM mainly occurs in one of the three major areas: septum, mid cavity or apical (15-18). There was no evidence of a transformation from one form of hypertrophic cardiomyopathy to the other (15). All three forms could present with or without obstruction, though obstruction is uncommon in the mid and apical variants.

During the echo evaluation of patients with HCM it is important to assess for obstruction, both by evaluating anatomy - i.e. mitral-septal contact or systolic wall apposition - and by Doppler (19). Obstruction in HCM is a dynamic phenomenon, depending on the loading conditions and contractility. Resting left ventricular outflow tract (LVOT) gradient occurs in 25% of patients but provocable gradients are more prevalent and obstruction may be demonstrated in more than half of patients after exercise (20). In non-obstructive patients it is important to try provocative maneuvers to elicit obstruction because obstruction offers a target for treatment of symptoms. Provocative maneuvers are done during pulsed or continuous wave Doppler in 5-chamber and 3-chamber apical views (21), and include: Valsalva's maneuver (22-24), standing up from a lying down position (22), postprandial (25), treadmill exercise (20), amyl nitrite inhalation (20,26). Amyl nitrite and dobutamine are not physiologic stimuli, which do not mimic activities of daily life and generally are not recommended. Also, dobutamine may cause obstruction in normals.

Echocardiography and risk for sudden cardiac death assessment

Several factors are known to be indicators of a risk of sudden death: a previous aborted cardiac arrest, one or more episodes of non-sustained ventricular tachycardia, unexplained syncope, and a history of sudden death in young family members (27-31). Using 2D echocardiographic measurements Spirito et al showed that the risk of sudden death increased progressively in direct relation to wall thickness (P=0.001). The risk of sudden death was less than 2.6 per 1000 person-years in those with a wall thickness less than 19 mm, and went up to 18.2 per 1000 person-years (1.8%/year) in those with a wall thickness of 30 mm or more (31) (Fig. 1). Some patients deemed to be at increased risk for sudden cardiac death because of massive thickening may be offered prophylactic implantable cardioverter defibrillator (ICD) placement.

Treatment of symptoms

Treatment of HCM patients is guided by patient's symptoms and echo findings. In patients with no or only mild symptoms the approach of watchful waiting is often appropriate (19). Though

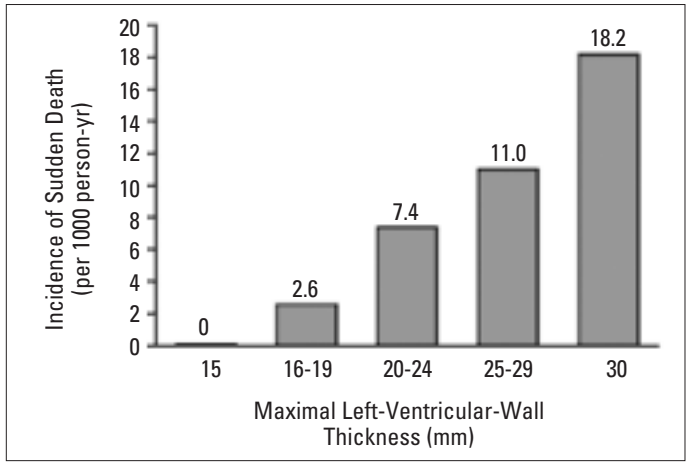

Figure 1. Relation between maximal left-ventricular-wall thickness and the risk of sudden death in 480 patients with hypertrophic cardiomyopathy. The incidence of sudden death increased progressively and in direct relation to maximal wall thickness (P=0.001 by the Chi-square test for trend) (31)

(Reproduced from Spirito P, Bellone P, Harris KM, Bernabo P, Bruzzi P, Maron BJ. Magnitude of left ventricular hypertrophy and risk of sudden death in hypertrophic cardiomyopathy. N Engl J Med 2000;342:1778-85 : Copyright © 2000 with permission of Massachusetts Medical Society).

patients with non-obstructive HCM are empirically offered verapamil and beta blockade to improve symptoms, relief of ischemia by limiting heart rate rise may be their main action.

Echocardiography is a valuable tool to understand the pathophysiology of obstruction. Echocardiography data indicates that systolic anterior motion (SAM) of the mitral valve is initiated by flow drag; the mitral valve is swept toward the septum by the pushing force of flow (Fig. 2). After mitral-septal contact, obstruction begets further obstruction as the pressure gradient pushes the mitral valve into the septum. The obstruction is best described as: flow drag triggered, time dependent, amplifying feedback loop (32-34) (Figures 3-5).

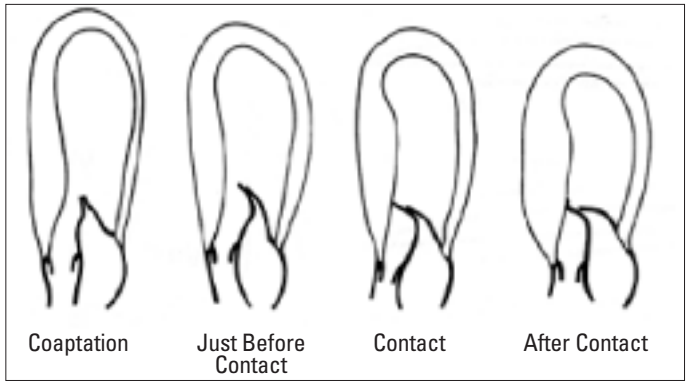

Figure 2. From the two-dimensional echocardiogram, four frames were identified: initial mitral leaflet coaptation, just before mitral-septal contact, mitral-septal contact and immediately after mitral-septal contact. The protruding mitral leaflet moves in an arc toward the septum until its tip contacts the septum. In the frame after contact, a portion of the body of the leaflet usually comes into apposition as well

(Reprinted from the Journal of the American College of Cardiology, Vol 22, number 3, Sherrid MV, Chu CK, Delia E, Mogtader A, Dwyer EM, Jr. An echocardiographic study of the fluid mechanics of obstruction in hypertrophic cardiomyopathy., Pages No. 816-25, Copyright (1993), with permission from the American College of Cardiology Foundation).

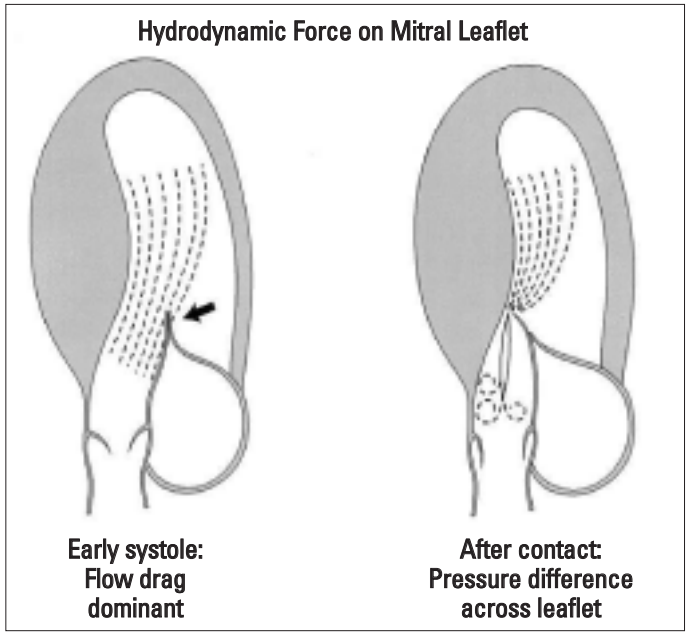

Figure 3. Early in systole flow drag is the dominant hydrodynamic force on the mitral leaflet. After mitral-septal contact the pressure difference is the force that pushes the mitral leaflet further into the septum.

(Modified from references 32 and 33)

Two thirds of the symptomatic obstructed patients can be successfully managed long term with medical treatment alone without any other intervention (35). Drugs that are useful in treatment of obstruction are the negative inotropes (β-blockers, verapamil, disopyramide). By reducing ejection acceleration of early

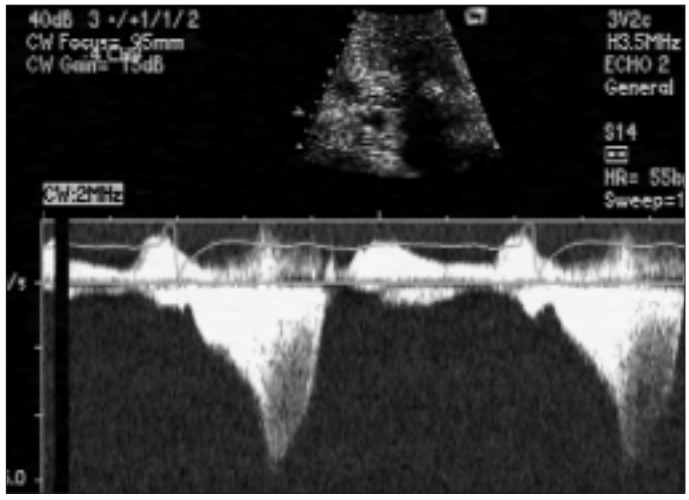

Figure 4. CW Doppler through jet is concave to the left, "dagger shaped" due to amplifying feedback loop exponentially increasing the obstruction

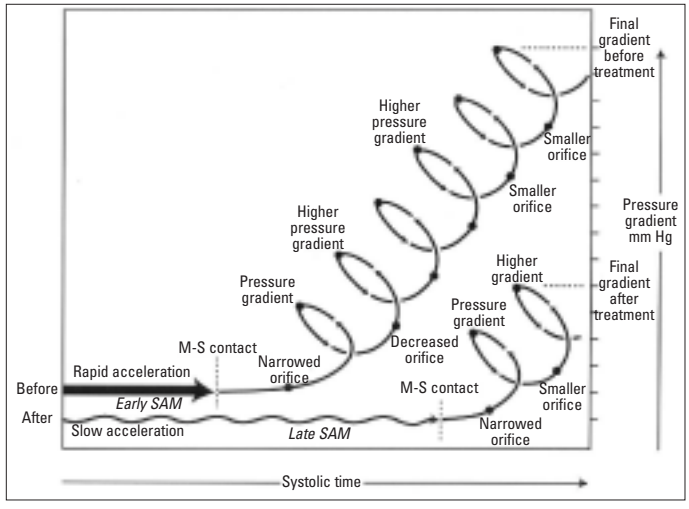

Figure 5. Proposed explanation of pressure gradient development before and after treatment of obstruction. Before treatment (top tracing), rapid left ventricular acceleration apical of the mitral valve, shown as a horizontal thick arrow, triggers early systolic anterior motion (SAM) and early mitral-septal (M-S) contact. Once mitral-septal contact occurs, a narrowed orifice develops, and a pressure difference results. The pressure difference forces the leaflet against the septum, which decreases the orifice size and further increases the pressure difference. An amplifying feedback loop is established, shown as a rising spiral. The longer the leaflet is in contact with the septum, the higher the pressure gradient. After treatment (bottom tracing), negative inotropes slow early SAM (shown as a horizontal wavy arrow) and may thereby decrease the force on the mitral leaflet, delaying SAM. Mitral-septal contact would occur later, leaving less time in systole for the feedback loop to narrow the orifice. This would reduce the final pressure difference. Delaying SAM may also allow more time for papillary muscle shortening to provide countertraction. In the figure, for clarity, the "before" arrow is positioned above the "after" arrow, although at the beginning of systole they both actually begin with a pressure gradient of 0 mm Hg

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flow, the early systolic pushing force on the protruding mitral leaflets is reduced, thus delaying the SAM and mitral-septal contact (33) (Fig. 6).

Finding the right medication and the right dosage for symptomatic patients can be challenging for the treating physician. The first step in medical treatment is stopping medications that may worsen obstruction: angiotensin converting enzyme inhibitors, angiotensin receptor blockers, nifedipine, amlodipine, long and short acting nitrates and β-blockers (36). The first medication to be tried in symptomatic patients are β-blockers. After IV or oral β-blocker administration, Doppler gradient is checked. If good response is achieved, with reduction of the gradient to less than 30 mmHg, β-blockers are used as single therapy with a goal of resting heart rate between 55 and 60 bpm. Addition of disopyramide, or verapamil substitution is considered if symptoms persist and gradient remains more than 30 mmHg (36). At our institution the preference is to add disopyramide to β-blockers for a synergistic effect. Repeat echo is done 2.5 hours after a single dose of 250 mg disopyramide, or 2 days after disopyramide controlled release (CR) 250 mg every 12 hours, has begun to assess acute response. Patients who respond to disopyramide with a gradient less than 30 mm Hg are continued on the combination. Amiodarone or any other antiarrhythmic drug are stopped when disopyramide is begun. In patients with contraindication to disopyramide, oral verapamil is begun at 240-360 mg/day in divided doses. When the gradient remains greater than 30 mmHg and patients are still symptomatic despite medication manipulation, Doppler examinations of left ventricular acceleration may help the clinician to decide further management (Fig. 6). If left ventricular acceleration is not significantly slowed by medical treatment, or if heart rate has not slowed, then the medication can be increased. If acceleration in the left ventricle has slowed but there is still significant obstruction, medication alone may not be adequate to eliminate obstruction because of adverse anatomy and further non-pharmacologic interventions are required (36, 37) (Fig. 7).

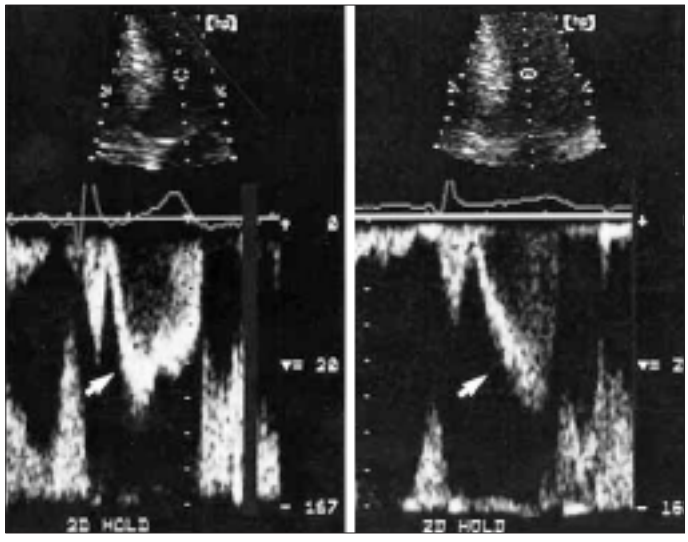

Figure 6. Comparison of left ventricular pulsed Doppler tracings, before treatment (left panel) and after successful medical treatment (right panel). The sample volume was 2.5 cm apical of mitral valve coaptation point. Before treatment, ejection acceleration was rapid (arrowhead) and velocity peaked in the first half of systolic. After treatment, ejection acceleration was slowed (arrowhead) and velocity peaked in the second half of a systole. Systolic anterior mitral motion was delayed and a 96 mm Hg gradient was eliminated. Note, that though acceleration slowed, peak velocity remained virtually unchanged. This contrast highlights the importance of acceleration and the timing of ejection in successful medical therapy. The velocity calibration is identical in both panels. The scale is 20 cm/sec between white marks

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Echocardiography is extremely helpful for close monitoring of intravenous β-blocker treatment of critically ill HCM patients with severe acute obstruction and congestive heart failure, where parameters can be followed in real time. The best pharmacologic combination for patients in shock due to obstruction is phenylephrine for pressure support and β-blockers for decrease in gradient (33,36). Dobutamine or dopamine or epinephrine should be avoided as they usually will worsen precarious situations.

Echocardiography role in surgical septal myectomy

Obstructed patients who fail medical therapy, defined as lack of gradient reduction below 50 mmHg and persistent disabling symptoms, are usually offered invasive treatment: surgical septal myectomy, alcohol septal ablation, or DDD pacemaker. Surgical septal myectomy is the gold standard for obstructed patients refractory to treatment. It results in immediate relief of obstruction and improvement of mitral regurgitation. In specialized centers operative mortality is 1% and the rate of surgical success > 95% in those without comorbid cardiac or medical conditions. Postoperative resting gradients are abolished and parallel improvement in symptoms are achieved (5, 38-45).

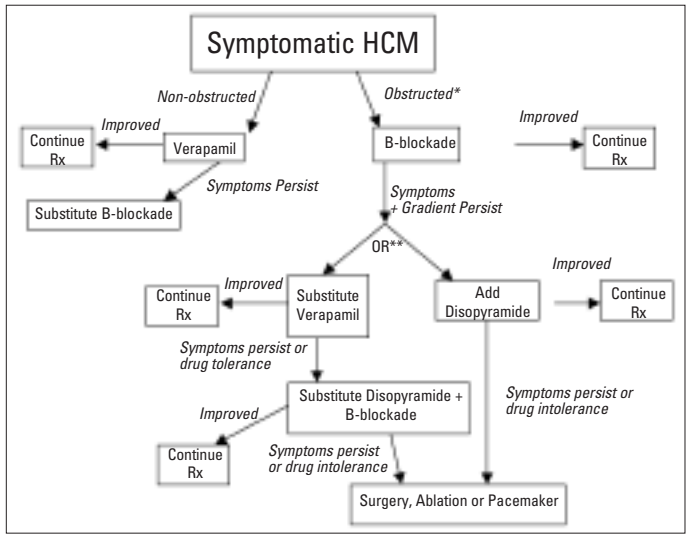

Figure 7. Proposed algorithm for medical therapy of symptomatic hypertrophic cardiomyopathy

Patients are considered for medical therapy of obstruction if they have a gradient greater than 30 mmHg at rest or after provocation with Valsalva maneuver or exercise. The criterion of 30 mmHg may prompt medical therapy; surgical or ablation interventions is usually reserved for patients who fail medical therapy but have gradients at rest or after provocation greater than 50 mmHg. Either disopyramide or verapamil may be selected as the second-line agent. Disopyramide is added to β-blockade, while verapamil is generally substituted for β-blockade

(Adapted from reference 36)

Surgical intervention to relieve obstruction in HCM is technically challenging because in HCM multiple anatomical factors may play a role in gradient development and symptomatology. Key factors leading to SAM with mitral-septal contact are:

1. prominent septal bulge which directs the blood flow behind mitral valve coaptation (5, 32, 34),

2. large, slack mitral valve and anteriorly positioned coaptation plane (5, 10, 46-48),

3. anterior position and agglutination of the papillary muscles to the anterior left ventricular wall contributing to anterior position of coaptation plane (5, 49).

The surgeon may need to address all three anatomical abnormalities, which lead to a very crowded base of left ventricle and crucial overlap between the inflow and outflow portions of the left ventricle (5). McCully et al suggested, in a series of 47 patients who underwent septal myectomy alone, that asymmetric hypertrophy, severe systolic anterior motion of the mitral leaflet(s) on preoperative echocardiography can identify patients who are most likely to benefit from septal myectomy (50).

Technical difficulties are due especially to a very small and deep operative field offered by the aortotomy and small left ventricle chamber dimensions. Visualization is accessible only to the principal surgeon, and the anatomy of the empty heart can be ambiguous, leading to imprecision in the extent of myectomy that may result in either an inadequate small resection with persistent obstruction (51), or too large, and a ventricular septal defect (0% to 2%), or complete heart block (5, 38-45).

Preoperative TTE is a necessary guide for the surgeon in planning the operation. It gives the surgeon precise measurements on septum thickness and how deep he needs to go into the left ventricle to excise the midseptal bulge, as well as to evaluate the length and floppiness of the mitral valve leaflets, papillary muscle abnormalities and/or anomalous insertion (better evaluated by TEE). If the TTE imaging is inadequate transesophageal echocardiography (TEE) is required. Important information is also provided by the TEE pre-bypass, as real-time measurements and assessment of the whole picture are evident. New unsuspected findings (patent foramen ovale, mitral valve prolapse and flail mitral valve leaflet, abnormal papillary muscles, etc) have been reported by Ommen et al in 17% of 256 patients undergoing septal myectomy. These findings resulted in an alteration of the surgical plan for 9% of the patients (5, 52, 53).

Persistent SAM, resting outflow gradient more than 30 mm Hg or more than 50 mmHg with provocation (intravenous inotropic agents or post-PVC), moderate to severe mitral regurgitation are indications for placing the patient back on heart-lung bypass for revision (5, 18, 54). Using these criteria 7 - 20% of the patients were found to need revision: either additional resection, or further mitral valve repair (5, 53, 54). In successful cases of extended septal myectomy, mitral valvuloplasty and papillary muscle release (Fig. 8.), as seen in a R-P-R (resection - plication - release) operation described by Swistel (55), the post-surgical study will show: 1) a dramatic thinning of the septum, with widening of the left ventricular outflow tract to a width similar to that in the normal subjects, 2) resolution of systolic anterior motion and the left ventricular outflow tract gradient, 3) marked reduction or abolition of mitral regurgitation, 4) decreased anterior mitral leaflet length and 5) more posterior mitral leaflet coaptation point (5, 53, 55).

Late recurrent obstruction can be rarely encountered. Minakata et al reported 13 patients needing repeat myectomy in a series of 610 patients after classic myectomy operations, which included 7 patients from outside institutions. Mechanisms included too limited myectomy at the initial operation, mid-ventricular obstruction, unrecognized anomalies of papillary muscles, and ventricular remodeling (especially in pediatric patients) (56). Repeat myectomy can be performed with excellent outcomes. Need for re-operation may be reduced with current surgical approaches that include a more extended resection of the mid-ventricular septum, relief of papillary muscle anomalies, mitral valve plication, and routine use of intraoperative transesophageal echocardiography (5, 56).

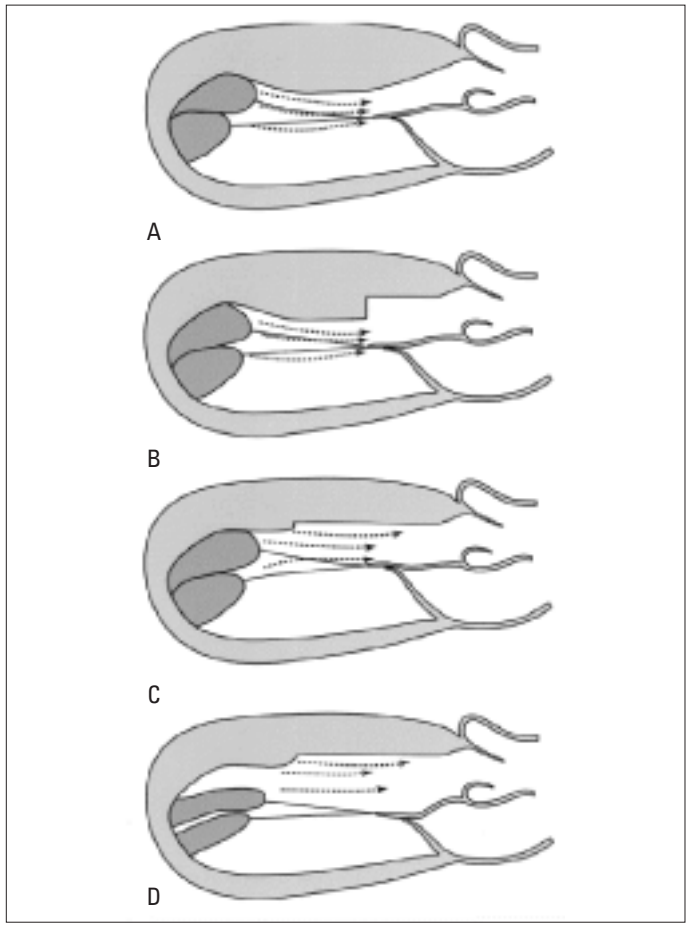

Figure 8. Surgical separation of ventricular inflow from outflow in obstructive hypertrophic cardiomyopathy, and extended myectomy and papillary muscle mobilization. (A) Illustration of outflow relative to the mitral valve in early systole. Note the anterior position of the mitral valve coaptation. The prominent midseptal bulge redirects outflow so that it comes from a relatively posterior direction, catching the anteriorly positioned mitral valve and pushing it into the septum. (B) After subaortic septal resection. The subaortic septum has been resected, but only down to the tips of the mitral leaflets. Flow is still redirected by the remaining septal bulge so that it comes from a posterior direction. It still catches the mitral valve; systolic anterior motion persists, as does the obstruction. (C) The septal bulge below the mitral leaflet tips has been resected, an extended myectomy. Now, flow tracks more anteriorly and medially, away from the mitral leaflets. (D) Mobilization and partial excision of the papillary muscles is added to extended myectomy. The mitral coaptation plane is now more posterior, explicitly out of the flow stream

(Reprinted from the Annals of Thoracic Surgery, Vol 75, number 2, Sherrid MV, Chaudhry FA, Swistel DG. Obstructive hypertrophic cardiomyopathy: echocardiography, pathophysiology, and the continuing evolution of surgery for obstruction, Pages No. 620-32, Copyright (2003), with permission from the Elsevier)

Echocardiography in DDD pacemaker treatment of HCM

Historically the next intervention that was applied to reduce LVOT obstruction was DDD pacing with atrioventricular (AV) delay (57-59). Though pacing cannot be considered a primary strategy to treat obstruction it appears useful in certain patients. The mechanism of the therapeutic effect derived from pacing is unclear. It is proposed that the initiation of the electrical impulse in the apex of the right ventricle alters the LV systolic contraction sequence leading to a reduction in the outflow gradient (57). Echocardiography has been an important technique in the evaluation and follow-up of response to this intervention. Fananapazir in a study of 44 patients with obstructive HCM showed that implantation of a DDD pacemaker improved symptoms and was associated with significant reduction in LVOT gradient (59). M-mode in the parasternal long axis and Doppler measurements (continuous or pulsed wave) of the LVOT in apical 3 or 5 chamber views were used to demonstrate the response to pacing with reduction in SAM and LVOT velocity. The response was simultaneous with the start of atrioventricular pacing (59) (Fig. 9). Doppler considerations may aid selecting optimal AV delay (60).

Initial observational findings of relief of symptoms, reduction of the gradient and LV remodeling (61, 62) have not been reproduced in randomized clinical trials (63, 64). These showed a large placebo effect and no significant improvement in objective measures of exercise capacity, and incomplete gradient reduction (30 to 50 mm Hg average residual gradient after pacing) (63, 64). Failure to relieve symptoms is common, with fewer than 40 % of patients still having improved symptoms at five years follow-up (57, 65). Also pacing may be detrimental to diastolic function (60).

Two particular groups of population had been shown to have a good long term clinical response to DDD pacemaker: elderly patients ≥ 65 years of age (64), and patients with normal septal curvature and preserved elliptical LV cavity shape (66). Knowing that degree of improvement is less than that achieved with the other therapies dual-chamber pacing should be limited to elderly patients (≥ 70 years of age), those with significant co morbidities preventing them from having other therapies, those who require pacing for bradycardia, or who receive devices for sudden death prevention (37).

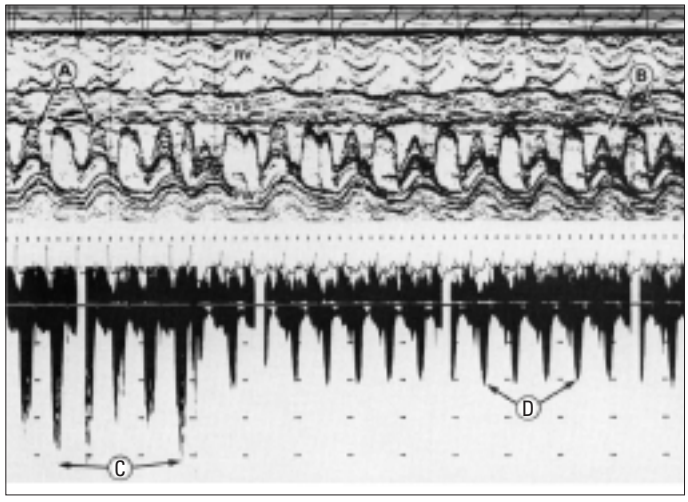

Figure 9. M-mode echocardiogram and continuous-wave Doppler recordings obtained during sinus rhythm and immediately after initiation of atrial synchronized ventricular pacing mode from a 24-year-old patient with obstructive hypertrophic cardiomyopathy. Top panel shows the M-mode echocardiographic tracing recorded at a paper speed of 50 mm/sec. At baseline, there is marked systolic anterior motion of the mitral valve with prolonged mitral-septal apposition (A); after initiation of dual-chamber (DDD) pacing, the magnitude of mitral systolic motion is significantly reduced with disappearance of the mitral-septal contact (B). Pacing is also associated with subtle paradoxical movement of the interventricular septum (VS). Bottom panel shows continuous-wave Doppler interrogation of left ventricular outflow tract velocities obtained at the same study and in the same patient and recorded at paper speed of 25 mm/sec. At baseline, peak velocity is 4.2 m/sec (C), corresponding to an estimated gradient of 70 mm Hg; with DDD pacing, peak velocity is reduced to 2.2 m/sec (D) (estimated gradient, 20 mm Hg)

PW- posterior left ventricular free wall, RV- right ventricle

(Reproduced from Fananapazir L, Cannon RO, 3rd, Tripodi D, Panza JA. Impact of dual-chamber permanent pacing in patients with obstructive hypertrophic cardiomyopathy with symptoms refractory to verapamil and beta-adrenergic blocker therapy. Circulation 1992; Vol 85, No. 6: pages 2149-61 Copyright (1992) with permission of LWW).

Role of echocardiography in alcohol septal ablation

For patients with refractory symptoms and high gradients on medication and not suitable for surgery because of comorbidities, percutaneous septal reduction via alcohol septal ablation (ASA) is an alternative therapy for relief of obstruction and improvement of symptoms. Absolute ethanol is infused into a septal branch of the left anterior descending coronary artery (LAD) to specifically induce necrosis of the hypertrophied septum (67). The technique has a periprocedural mortality of 1-2%, lower in experienced centers (68-70). Hypertrophic cardiomyopathy experts in the United States have expressed reservation about alcohol septal ablation because procedural complications occur at least as frequently as in surgical septal myectomy and long term results have not been yet been reported.

Alcohol septal ablation is a viable alternative to surgery in patients considered as high risk for surgery. Irreversible complete heart block requiring permanent pacemaker implantation occurs in 7-18% of the patients (68, 71). Also of concern is the scar that can be a substrate for late increased risk of ventricular arrhythmias. Alcohol septal ablation should therefore not be done in young patients < 40 years.

Echocardiography is a valuable tool to choose the site of ablation, as well as for evaluation of results. Myocardial contrast echocardiography (MCE) guides the targeted delivery of ethanol during ASA: there is a relation between the MCE risk area and infarct size determined by enzymatic and radionuclide methods (72,73). This technique to guide ASA was implemented in late 1990's in Europe by Faber and Seggewiss and in the US by Lakkis and Nagueh. Lakkis et al described their technique in 33 patients (72). After completion of initial angiography a balloon catheter is introduced into the first large septal perforator and inflated. With the balloon inflated echocardiography contrast is injected through the balloon lumen to delineate the area supplied by the septal branch, to assure that contrast does not go to the LV apex or lateral wall, papillary muscles, RV free wall or any other place not wanted (72) (Figures 10, 11). In the US dilute Definity is used; in Europe Levovist. Intra-procedural MCE guidance leads to a changes in interventional strategy in 15-20% patients; in 7-11% bubbles are seen distant from the expected septal target region is detected, leading to a target vessel change (68, 74). In 5-7% the procedure is aborted due inappropriate target vessel and patients are referred for surgery (68).

Depending on the septal artery size and the septal thickness, 1-3 mL of absolute ethanol is slowly instilled through the lumen of the inflated balloon catheter and left in place for 5 minutes. After balloon deflation and removal, angiography is performed to confirm the patency of the LAD and the occlusion of the target septal branch. Some groups will inject other septal branches during the same sitting if deemed necessary (72). Introduction of MCE as guidance in choosing the accurate septal branch was associated with a more targeted alcohol injection and a higher percentage of short (92% vs. 70%) (75), mid term (88%) (76) and 1 year success rate (99%) (69). In patients treated before the introduction of intraprocedural myocardial contrast echocardiography the main reason for unsatisfactory gradient reduction was suboptimal scar placement (74, 77).

Echocardiography offers insights into the mechanisms of benefit of ASA. It induces an acute decrease in septal thickening and decrease in acceleration of LV ejection (73). This translates into decrease in drag forces. Also, electromechanical changes after ASA with the development of bundle branch block (right bundle branch block alone in 60% and with left anterior hemiblock in 20%) lead to further inhomogeneity in LV contraction (78). There are no acute geometric changes, no immediate effect on the mitral valve apparatus (79).

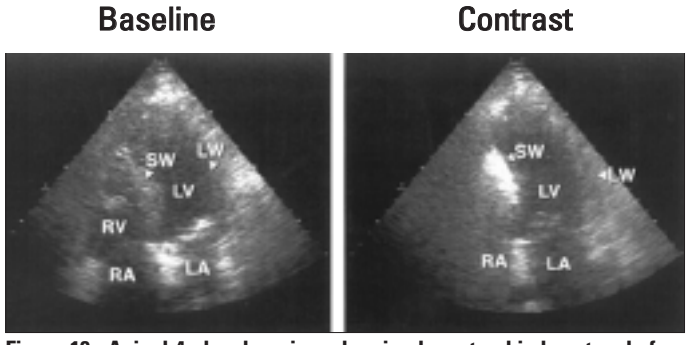

Figure 10. Apical 4-chamber view showing hypertrophied septum before (left) and after (right) contrast injection into target septal branch delineating area to be infarcted

LA- left atrium, LW- lateral wall, LV- left ventricle, RA- right atrium, RV- right ventricle, SW- septal wall

(Reproduced from Lakkis NM, Nagueh SF, Kleiman NS, Killip D, He ZX, Verani MS, et al. Echocardiography-guided ethanol septal reduction for hypertrophic obstructive cardiomyopathy. Circulation 1998; Vol 98, No. 17: pages 1750-5, Copyright (1998) with permission of LWW).

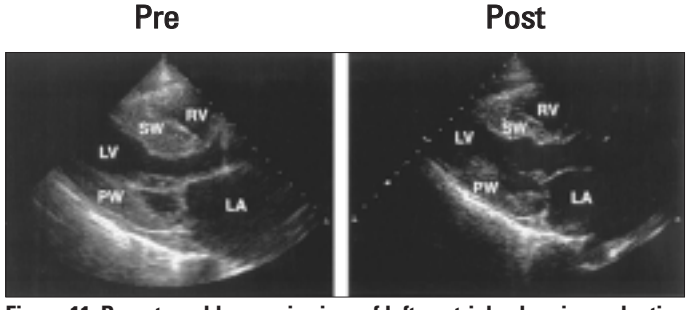

Figure 11. Parasternal long-axis view of left ventricle showing reduction of septal thickness after ethanol septal infarction. Septal basal thickness decreased from 2.1 cm (left) to 1.2 cm at 6 weeks (right)

LA- left atrium, LV- left ventricle, PW- posterior wall, RV- right ventricle, SW- septal wall

(Reproduced from Lakkis NM, Nagueh SF, Kleiman NS, Killip D, He ZX, Verani MS, et al. Echocardiography-guided ethanol septal reduction for hypertrophic obstructive cardiomyopathy. Circulation 1998; Vol 98, No. 17: pages 1750-5, Copyright (1998) with permission of LWW).

On the follow up echocardiography basal septal thickness decreases significantly, with decreased systolic excursion. Decreased acceleration persists acting in synergy with the decreased septal thickness (72, 79). The angle between ventricular flow and mitral valve leaflets decreases. Mitral regurgitation improvement parallels the improvement in LVOT obstruction. After six weeks, LVOT diameter and the distance between anterior mitral leaflet and the septum were greater in comparison to baseline. Further benefits beyond the acute response from ASA can be explained by LV remodeling (69).

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