REVIEW

Surgical management of left ventricular outflow obstruction in hypertrophic cardiomyopathy

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Abstract

Hypertrophic cardiomyopathy is the single most common form of inherited heart disease. Left ventricular outflow tract obstruction (LVOTO) is a recognised feature of this condition which arises when blood leaving the outflow tract is impeded by systolic anterior motion of the mitral valve. In an important minority of patients, breathlessness, chest pain and syncope may result and persist despite the use of medications. In suitable candidates, surgery may relieve obstruction and its associated symptoms, and normalise life expectancy. Refinements in surgical techniques have marked improvements in the understanding of mechanisms underlying LVOTO. In this review, we hope to provide the reader with an understanding of how contemporary surgical practice has developed, which patients should be considered for surgery, and what results are anticipated. The role echocardiography plays in this area is highlighted throughout.

Historical perspective

Soon after left ventricular outflow tract obstruction (LVOTO) was first described in individuals with hypertrophic cardiomyopathy (HCM), it was posited that it was primarily due to the physical obstructive effects of the hypertrophied septum. The movement of the mitral valve leaflets anteriorly and superiorly towards the LVOT and aortic valve (termed systolic anterior motion or SAM) (1) was felt to be a secondary phenomenon due to the Venturi effect. The proposed solution to this was therefore surgical resection of the obstructive muscle bundle. After preparing by carefully examining histological specimens, Cleland (2) undertook and reported the first transaortic resection in 1958. The technique was developed and later popularised by Morrow (3).

Later it was hypothesised that the subvalvular apparatus of the mitral valve, and in some cases the mitral valve itself, were abnormal in these patients. Cooley et al. (4, 5) therefore proposed mitral valve replacement in addition to septal myectomy.

Contemporary understanding

The idea that abnormalities of the papillary muscles and chordal attachments might lead to the initiation of SAM of the mitral valve by active displacement of the valve into the blood stream, rather than an attracting power generated by high-flow velocity, was first proposed in the late 1980s (6) and confirmed by work two decades later (7).

Echocardiography has shown that mitral valve leaflets in individuals with HCM are longer (8) and have a greater area (9) than those in normal controls. The zone of coaptation also occurs in the body of the leaflets, as opposed to the tips (8). This leads to laxity in the tip of the anterior mitral valve leaflet, and less commonly the posterior leaflet (Fig. 1).

When severe, SAM may occur to the extent that the tip of the anterior mitral valve leaflet is brought into contact with the basal anteroseptal wall (so called mitral leaflet–septal contact). In some cases, repetitive contact creates a lesion visible with the naked eye and on echocardiography.
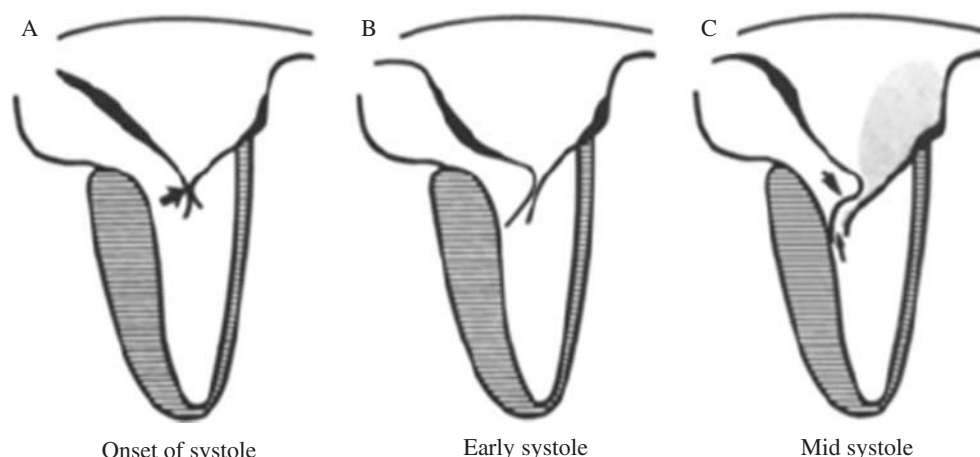
A — Onset of systole
B — Early systole
C — Mid systole

Figure 1

Scheme portraying how SAM evolves over systole (A, B and C) and why posteriorly directed mitral regurgitation (C) is seen. This image is licensed under an unspecified non-commercial open access CC licence, and is reproduced with permission from Elsevier, from Grigg LE, Wigle ED, Williams WG, Daniel LB & Rakowski H 1992 Transesophageal Doppler echocardiography in obstructive hypertrophic cardiomyopathy: clarification of pathophysiology and importance in intraoperative decision making. *Journal of the American College of Cardiology* 20 42–52 (8).

The presence of LVOTO has been found to be related to the leaflet area as measured by three-dimensional transthoracic echocardiography. In addition, a reduced distance between papillary muscles is also a strong predictor of LVOTO (9). Inter-papillary muscle distance will be reduced in HCM when the papillary muscles are anchored to more apical myocardium than normal. This leads to the papillary muscles being anteriorly and medially displaced compared to normal, and closer to one another. This malposition has the effect of bringing the mitral valve leaflets within the path of ejected blood flow, in contrast to the normal heart where the mitral valve leaflets remain well away from the LVOT during systole.

The combination of a contracting hypertrophied basal anteroseptal wall and SAM causes a progressive diminishment in the size of the LVOT throughout systole. Three-dimensional echo-measured LVOT narrowing is strongly related to the degree of obstruction (10) such that all patients with a minimal LVOT area $\leq 2\,cm^2$ had a peak gradient ≥ 50 mmHg. Even when there was mitral–septal contact, complete obliteration of the LVOT did not occur.

In a more recent study, the minimal LVOT area has was $0.56 \pm 0.31\,cm^2$ in individuals with HCM and basal obstruction, vs $2.75 \pm 0.66\,cm^2$ in those with non-obstructive HCM vs $4.05 \pm 0.70\,cm^2$ in controls (9). Determinants of minimal LVOT area were end-systolic left ventricle (LV) volume, leaflet area, annular height, the position of the papillary muscles and the degree to which the LVOT was hypertrophied.

Turbulent blood flow arises where the LVOT narrows and can persist upstream until it strikes the underside of the aortic valve leaflets. This causes a fluttering motion of the aortic valve leaflets detectable on M-Mode (1). Of the two leaflets, the anterior mitral valve leaflet is disproportionately affected in SAM (1). As it is pushed anteriorly and superiorly, the leaflet becomes separated from the posterior leaflet until the zone of coaptation, and valve competency is lost. The result is a posteriorly directed regurgitant orifice (8) which opens in mid systole (Fig. 1). This form of mitral regurgitation has been defined as type IV dysfunction within a revised Carpentier classification (11).

Echocardiographic assessment

SAM of the mitral valve and its consequences

Views of the heart which are orientated in an anterior–posterior projection and section the anteroseptal wall and mitral valve best demonstrate SAM. For transthoracic echocardiography, the parasternal long-axis and apical three chamber views should be sought, whilst in tranoesophgeal echocardiography, the mid-oesophageal long-axis view is optimal (Fig. 2). Rotation of the probe may be required to section the widest part of both mitral valve leaflets and identify the full extent of SAM. Although not perfectly aligned to the direction of mitral valve movement, SAM can also be appreciated in the transthoracic five chamber and deep transgastric five chamber and the
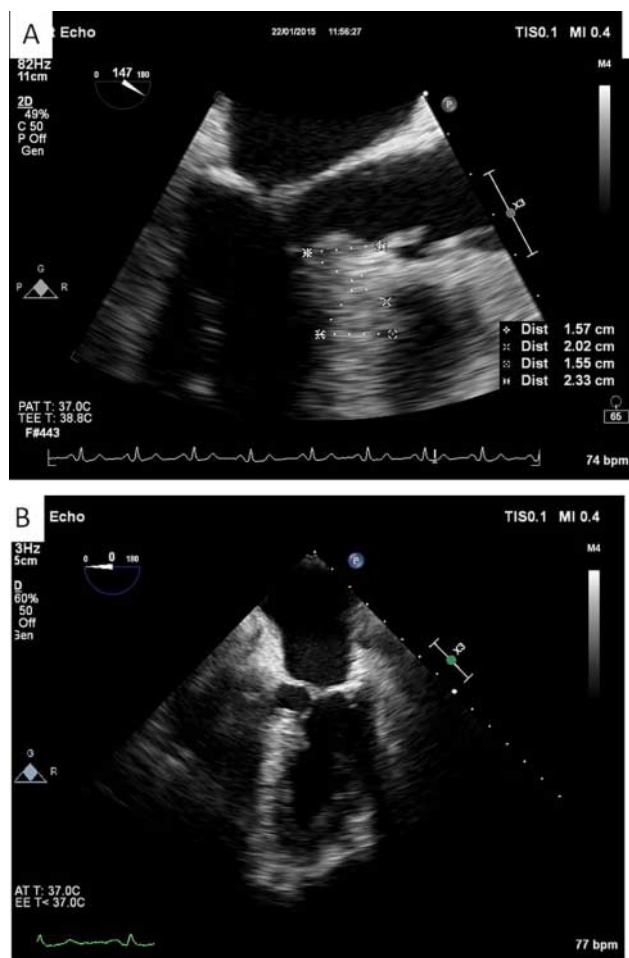
Figure 2
Systolic anterior motion of the mitral valve as seen by transoesophageal echocardiography in the mid-oesophageal long-axis (A) and five-chamber views (B). SAM–septal contact is seen in both. Measurements are used to describe septal anatomy are shown in (A). See main text for further details.

short-axis views (Fig. 2). En-face views of the mitral valve show the movement of the valve leaflet towards the basal anteroseptal wall.

LVOT turbulence can be recognised by the presence of mosaic colour flow. One can also determine the parts of the valve involved in the process (anterior leaflet, both leaflets and or chordae), the duration of SAM and its severity.

Quantifying the outflow tract gradient

To measure the peak gradient across the left ventricular outflow tract, one needs to find a plane that sections the site of obstruction and the areas immediately proximal and distal to it. Continuous Wave Doppler should lie parallel to direction of turbulent blood flow.

The transthoracic apical five and to a lesser extent the three chamber and transoesophageal deep gastric five chamber are ideally suited to achieve this (Fig. 3). Using trasnthoracic studies, the gradient should always be measured after provocation maneuvers such as Valsalva or with the patient in the seated and standing position because these actions may unmask obstruction by reducing preload. Exercise echocardiography is recommended to see whether a labile gradient is present when patients remain symptomatic, but the peak gradient does not exceed 50 mmHg either at rest, or with these manouevres.

It should be acknowledged that there are no universally approved protocols for exercise echocardiography
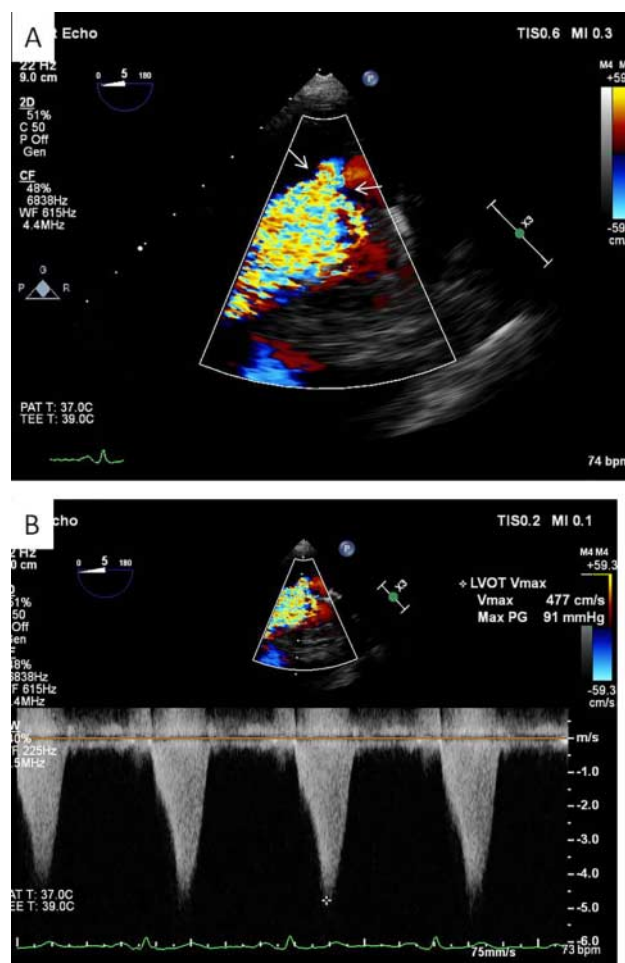

Figure 3
Assessment of LVOT obstruction using transoesophageal echocardiography from the deep transgastric position. The point of obstruction is denoted by the narrowest part of the jet seen on colour Doppler (A, arrows).
By directing continous wave Doppler through the centre of the jet, a clear late peaking gradient can be attained (B). In this case the peak gradient was 91 mmHg.
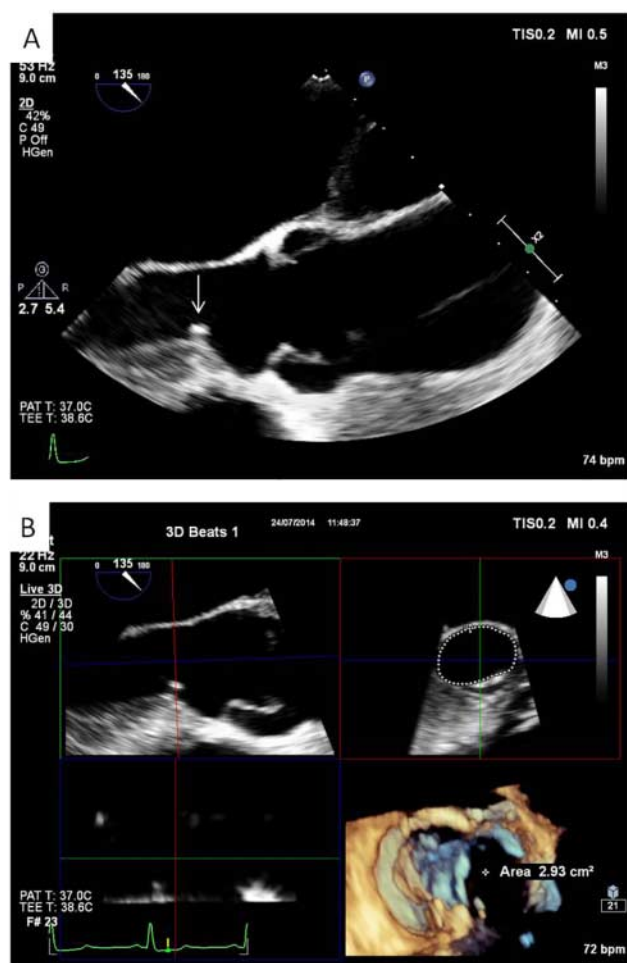
Figure 4
A fibrous ridge causing subaortic obstruction as visualised using transoesophageal echocardiography (A, arrow). The minimal area during systole has been quantified by three-dimensional analysis (B).

in HCM. Performing the test in the upright position and in the fed state has been shown to have value.

One has also to be cautious about mistaking LVOT obstruction for other entities including subaortic obstruction (Fig. 4), mitral regurgitation (particularly when the jet is directed centrally or anteriorly) and aortic stenosis. These conditions can be distinguished by the two-dimensional appearances of the LVOT, aortic and mitral valve and the onset and shape of the Doppler signal. Central mitral regurgitation can be avoided by keeping the Doppler position as medial as possible within the LVOT.

Additional forms of obstruction

Obstruction can occur remote to the LVOT, in the LV mid cavity, apex or right ventricular outflow tract due to

apposition of the opposing walls (Fig. 5). In practical terms, the search for obstruction should begin with a sweep of pulsed wave Doppler and colour in the three or five chamber views from the apex to the base followed by Continuous Wave Doppler through the area of flow turbulence to identify the highest gradient.

When workers at the Mayo Clinic reviewed the reasons leading to redo myectomy being performed in a large cohort of operated patients (12), the commonest was inadequate resection of the hypertrophied septum. Mid-ventricular obstruction due to septal hypertrophy was the second most important cause with the remainder comprising mitral valve abnormalities including medially displaced papillary muscles, anomalous chordal attachments to the septum and accessory papillary muscles.

Indication for surgery

There is no indication to reduce LVOT obstruction in asymptomatic patients. The recent European Society of Cardiology guidelines has recommend invasive septal reduction for patients with LVOTO gradient >50 mmHg (at rest or with provocation), New York Heart Association Class III–IV symptoms and/or recurrent exertional syncope in spite of maximally tolerated drug therapy (13). The same guidelines also suggest a place for invasive therapy when patients have less severe (New York Heart Association Class II) symptoms, dynamic gradients >50 mmHg, and moderate-to-severe SAM-related mitral regurgitation, atrial fibrillation, moderate-to-severe left atrial dilatation, although the lack of evidence to support such an approach is recognised.

Once the patient has met criteria for interventional treatment, the decision whether surgery or alcohol ablation is pursued is best decided in a dedicated multi-disciplinary setting in experienced HCM centres undertaking both procedures. No randomised controlled trials have been performed in this area as the relatively small numbers of patients requiring septal reduction intervention makes such an undertaking impractical. Both procedures have a similar impact on symptoms and are associated with a similar risk of death (13). The following features therefore play an important role in deciding which intervention is best suited to the patient:

1. The septal anatomy as extreme hypertrophy cannot be dealt with by alcohol ablation. Basal septal hypertrophy is described by measuring i) maximum wall thickness, ii) insertion of the right coronary leaflet to the point of maximal wall thickness,
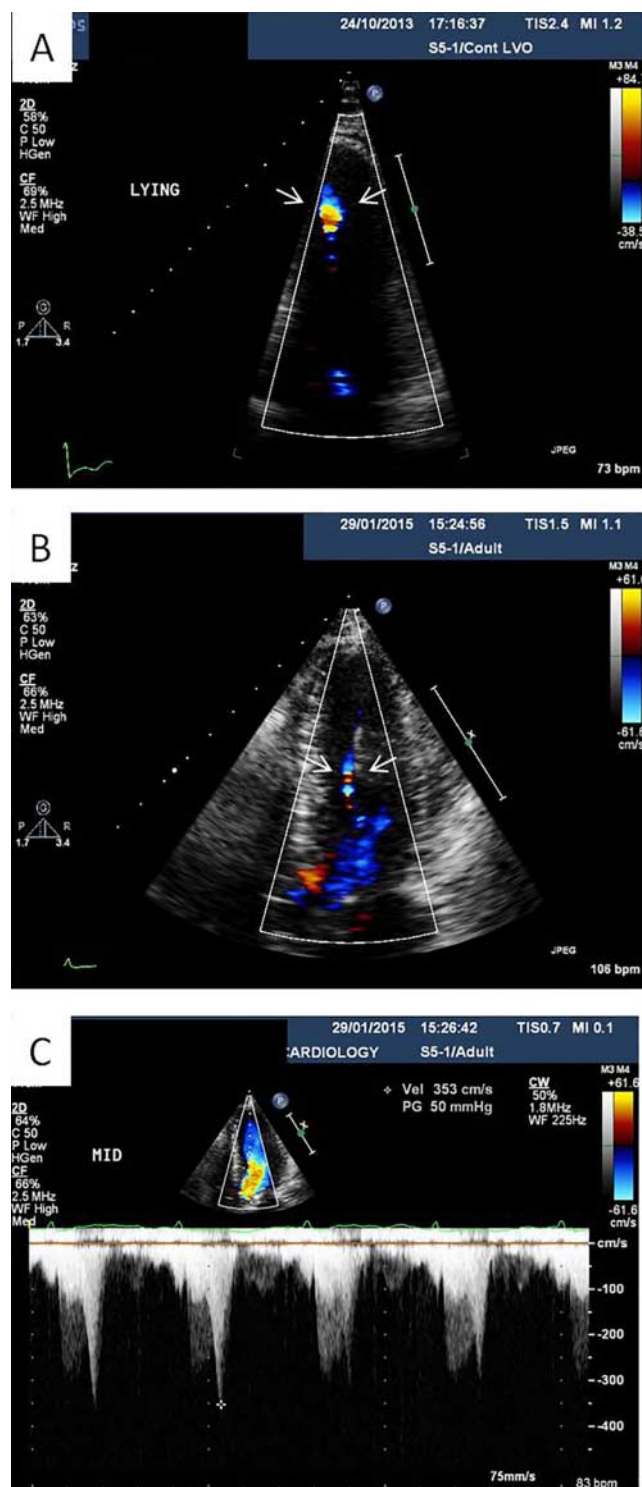
iii) thickness at point where basal septum tapers to thinner wall, and iv) distance of this point to the insertion of the right coronary leaflet (Fig. 2).

2. The presence of additional sources of obstruction which cannot be dealt with by alcohol septal ablation (ASA).

3. The presence of non-HCM indication for surgery i.e. flail mitral valve leaflet, coronary artery bypass graft.

4. The absence of suitable coronary anatomy by which alcohol can be delivered to the target area of myocardium.

Surgical technique

Extended transaortic myectomy

The septum is exposed through the aortic valve. Two parallel longitudinal incision are then made 6 mm inferior to the aortic valve annulus to both maintain annular integrity and avoid complete heart block; one directly below the right coronary ostia, the other below the commissure between left and right coronary cusp. These are then joined and a myectomy performed by sharp dissection to a level below the anterior mitral valve leaflet. Dissection can be aided by insertion of a sharp hook into the ventricle pulling the hypertrophied septal muscle superiorly as described by Messmer (14). Further dissection can be performed at the junction of the septum and lateral left ventricular wall as well as in the mid-ventricular area, where the septum and posterior wall meet.

Papillary muscle mobilisation

Abnormal papillary muscle architecture including malposition and mis-insertion and abnormal septal chordal attachments are common and therefore careful inspection of the subvalvar apparatus is always undertaken. Abnormal attachments between the ventricular wall and papillary muscles can then be divided as necessary.

Anterior mitral leaflet extension

To potentially increase both mitral coaptation and LVOT volume, the anterior leaflet of the mitral valve can be augmented with an oval patch (15). The patch extends the width but not the length of the leaflet by shifting the centrally attached chordae laterally, resulting in stretched cords that will enhance leaflet coaptation. The force produced by blood flow against the leaflet is proportional to its area and so the augmented leaflet will be directed posteriorly decreasing SAM and mitral regurgitation.

Figure 5
LV obstruction remote to the outflow tract assessed by transthoracic echocardiography: apical obstruction (A) and mid ventricular obstruction (B) identified by colour Doppler (arrows). In the patient in B, a peak gradient of 50 mmHg was derived (C).

From a transaortic approach, the midpoint of the anterior leaflet is identified and a longitudinal incision is made inferiorly and superiorly to within 2 mm of the free edge and annulus respectively. An oval patch is then trimmed to size and sutured into the valve leaflet using a continuous 5'0 Prolene suture.

Trans-mitral and minimal access approach

The mitral valve can be approached using a right lateral mini-thoracatomy. All native chordae of the anterior leaflet are completely excised and then the anterior leaflet is mobilised. A myectomy can then be performed with sharp dissection with the aid of stay sutures on the hypertrophied septum. Following myectomy, the anterior leaflet is resuspended using multiple neo-chordae, and then the mitral valve reconstruction completed with an annuloplasty (15, 16).

Contemporary European results

Whilst surgical myectomy for HCM in the USA has proved to be a durable treatment option, the rise of ASA procedures has limited the development of such programmes in Europe. A number of centres have however published excellent results.

Iacovoni et al. (17) published the results of 124 consecutive patients who underwent septal myectomy. In this series, almost all patients had additional procedures on the sub-valvular apparatus, with all patients having resection of fibrous-muscular attachments between papillary muscle and ventricular septum, a further 12% undergoing excision of abnormal chordal attachment between mitral valve leaflets and the ventricular septum or LV free wall, and ~5% requiring resection of anomalous attachment of the papillary muscle into the anterior mitral valve leaflet. Patients with paroxysmal or persistent atrial fibrillation also underwent concomitant atrial fibrillation ablation using bipolar radiofrequency energy device. There was one early death (0.8%). Patients were followed up in a dedicated HCM clinic. LVOT gradient decreased from 95 ± 36 mmHg to 12 ± 6 mmHg. No patient had dynamic gradient >30 mmHg and all patients who underwent AF ablation were in sinus rhythm at latest follow-up.

The Erasmus Medical Center has also recently published both their surgical and alcohol ablation outcomes for patients with obstructive HCM, and compared their result with the age-matched Dutch population (18). They reviewed 343 patients with obstructive HCM. Among them, 139 (41%) underwent surgery, 97 (28%) underwent alcohol ablation and 107 (31%) were managed medically.

In their surgical cohort, 98 consecutive patients underwent isolated surgery for HCM with the remainder undergoing combined procedures. Of these, 17% underwent isolated myectomy with the remainder undergoing concomitant mitral valve procedures, with 72% undergoing anterior leaflet extension and division of abnormal cords. There were no in-hospital deaths and the rate of repeat surgery for mitral valve replacement, redo procedures for residual obstruction, patch dehiscence or bleeding $<5\%$. Four patients required a permanent pacemaker for complete heart block and a further 17 received primary prevention implantable cardioverter defibrillator.
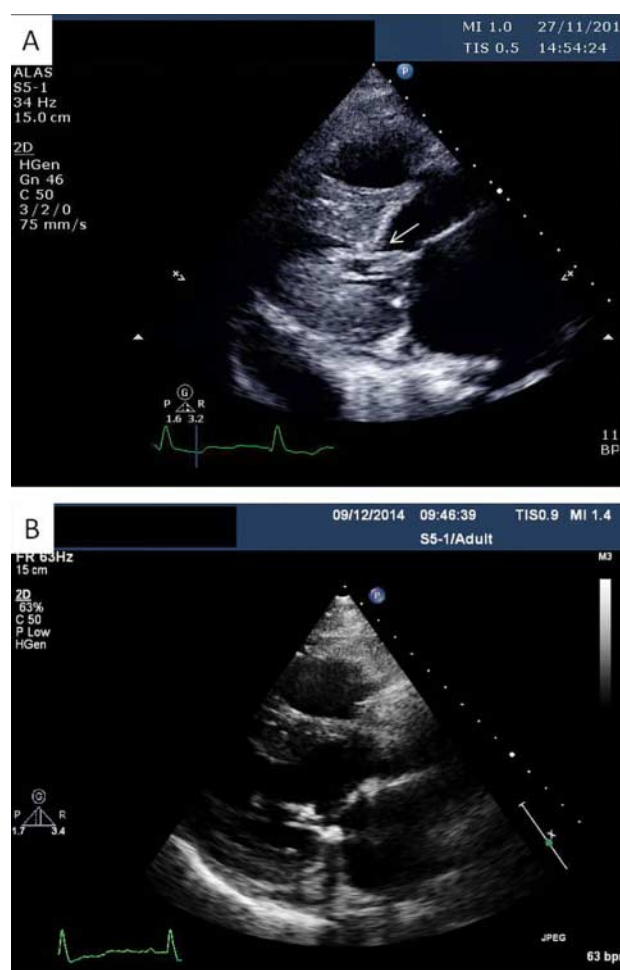

Figure 6
The effect of myectomy on LVOT anatomy: pre-myectomy in an individual who had previously undergone alcohol septal ablation (A). Severe mitral regurgitation due to endocarditis (not shown) had necessitated emergency surgery. Note how the chordate contact the hypertrophied septum (arrow). Post-operative images following mitral valve repair and myectomy (B) show how the LVOT is wider with chordae positioned well away from the ventricular septum. A mitral valve annuloplasty ring is also present.

Late survival was available up to 8 years when 88% of patients were free of repeat procedures. The patients undergoing surgery experienced significant improvements in New York Heart Association functional state. Pre-operatively 73 patients were in New York Heart Association III/IV compared with only two at last follow-up. The 1-, 5- and 10-year survival was reported as 98, 92 and 86% respectively, which was not different from the age-matched survival of the general population.

When they compared the results of surgery with ASA (18), the 1-, 5- and 8-year survival freedom for the end point of cardiac death and aborted sudden cardiac death was 100, 96 and 96% vs 96, 86 and 67%. They found that ASA was an independent predictor of this end point and in a propensity score adjusted HR 6.1; 95% CI 1.4–27; $P=0.02$. They concluded that when surgery for obstructive HCM included both septal myectomy and mitral valve surgery for patients with advanced symptoms and high gradients, surgery significantly improved both quality-of-life and delayed the onset of heart failure normalising the late survival in this cohort of patients.

Complications following surgical myectomy

Peri-procedural echocardiography is used to confirm the adequacy of septal resection (Fig. 6). The main surgical complications encountered are atrioventricular block, ventricular septal defect (Fig. 7) and aortic regurgitation. Mitral regurgitation and perforation of the anterior mitral

Figure 7
Iatrogenic post-myectomy ventricular septal defect. Colour flow is seen crossing a ventricular septal defect (arrows) sited between the left ventricle (LV) and right ventricle (RV) in a modified four chamber view using transthoracic echocardiography.

valve leaflet and coronary–caval fistulae due to transected septal perforators may also be encountered.

In most series, atrioventricular (AV) block is uncommon except when surgery follows a failed ASA, compared with ASA itself where there is a 20% risk of this complication. Ventricular septal defects are uncommon and in most series occur in <1%. When they do occur, they are often restrictive and can be conservatively managed. Aortic valve regurgitation can be eliminated entirely by starting the myectomy at least 6 mm inferior to the ventriculo-aortic junction allowing adequate annular tissue to support the aortic valve and taking appropriate care when passing instruments through the annulus.

Following surgery, a residual gradient of <15–20 mmHg is felt to be optimal. Mitral valve replacement to address significant mitral regurgitation is rarely required.

Early mortality is low with <1% quoted from most contemporary series. Higher operative mortality may be seen in elderly patients with concomitant coronary artery disease and impaired ventricular function. However, even in this group results appear favourable and this should be no barrier to offering surgical intervention.

Conclusion

Surgery for LVOT obstruction in the setting of HCM comprises a number of techniques used either in isolation or in combination. These provide good long-term outcome with low perioperative complications. Echocardiography is a key modality to determining the aetiology and severity of obstruction, excluding additional abnormalities and assessing the adequacy of resection and any complications.

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