Discrete Membranous Subaortic Stenosis

Report of 31 Patients,
Review of the Literature, and Delineation of Management

NEVIN M. KATZ, M.D., MORTIMER J. BUCKLEY, M.D., AND RICHARD R. LIBERTHSON, M.D.

SUMMARY The presentation, management, and follow-up of 31 patients with discrete membranous subaortic stenosis (DMSS) is presented. DMSS comprised 16% of 185 patients with congenital left ventricular (LV) obstruction. Only one patient was older than 40 years. The rarity of DMSS in older patients in both our population and in the literature is noted, and possible explanations are discussed. One-quarter of these patients had dyspnea, chest pain, or syncope combined with electrocardiographic left ventricular hypertrophy (LVH) and strain, and these all had peak LV outflow gradients (PSG) greater than 85 mm Hg. One-quarter had neither symptoms nor electrocardiographic abnormalities and all had PSG < 90 mm Hg. Bacterial endocarditis was found in 13%, and in 13% an immediate family member also had congenital LV obstruction. Following surgical resection (25 patients), 18 were asymptomatic, two had residual fibromuscular obstruction, and four developed new fibromuscular obstruction after one to six years (leading in one to late sudden death). Thus, even after resection, these patients require continued re-evaluation for residual or new LV obstruction.

WHILE DISCRETE MEMBRANOUS SUBAORTIC STENOSIS (DMSS) has been well described,1-9 and is reported to comprise between 8 and 30% of patients with congenital obstruction of left ventricular (LV) outflow,1,9 a number of aspects concerning this entity warrant further clarification, emphasis, and delineation, including particularly its natural history, and its peri- and late postoperative course and management.

In this study, we report our experience with 31 patients with DMSS, present their history and clinical course, their diagnostic evaluation and management, their peri- and late postoperative complications, and review the reported literature.

Methods

Between 1949 and 1977, 31 patients with DMSS were managed at the Massachusetts General Hospital. In all pa-
patients, the diagnosis was established by cardiac catheterization and angiography, or by surgical exploration, and in all, previous history, presenting symptoms, physical examination, diagnostic studies, management, and short and long-term follow-up were evaluated.

Results

History and Presentation

These 31 patients ranged in age from 3 to 54 years at the time of cardiac catheterization (table 1). Sixteen patients were male. Correlation of cardiac symptoms, electrocardiographic findings and peak resting systolic left ventricular outflow tract gradients (PSG) is shown in table 2. In the 12 patients older than 20 years, PSG were between 60 and 160 mm Hg, mean 97 mm Hg, chest pain, dyspnea or syncope was reported in 10, and LVH and strain was present in six. Four patients developed subacute bacterial endocarditis (ages 13, 20, 22, 25 years), and one patient, age 37 years, had a cerebral embolus. In four patients (13%), immediate family members also had congenital LV obstructive lesions which included coarctation of the aorta in one, valvular aortic stenosis in another, and DMSS in the remaining two. One previously reported patient had an unusual facial syndrome. Details of the physical examination and chest X-ray in these patients are shown in table 3.

Cardiac Catheterization

Peak resting systolic LV outflow tract gradients in these 31 patients were between 25 and 188 mm Hg, mean 87 mm. In three patients PSG were less than 40 mm Hg, in 13 between 40 and 80 mm, and in 15, greater than 80 mm Hg. Left ventricular angiography was performed in 28 patients and demonstrated a definite discrete subaortic membrane in 25, no definite membrane in one, and in two, a broader obstruction similar to type II subaortic stenosis described by Kelly et al. The membranes appeared to vary in thickness from 2 to 4 mm, and varied in position from just beneath the aortic valve to approximately 4 cm beneath it. In one patient it was difficult to clearly separate the membrane from the right aortic valve cusp, and in six it attached to the middle third of the aortic leaflet of the mitral valve. The aortic valve appeared to be normal angiographically in 19 patients, and thickened in nine. Of the nine preoperative patients evaluated for aortic insufficiency, eight had mild and one had moderate aortic insufficiency, judged by rapidity and extent of LV opacification following aortic root angiography. Two patients had mild mitral insufficiency on both preoperative physical examination and LV angiography. One patient, also, had a small subaortic ventricular septal defect, one had mild coartation of the aorta, and two had valvular aortic stenosis. Left ventricular angiography revealed a normal-sized LV cavity in all patients; however, in 11 there was systolic obliteration of the apex. The LV appeared to be thickened angiographically in ten patients and normal in the remaining 18. Four patients appeared to have asymmetric ventricular septal thickening on LV angiography; however, simultaneous biventricular angiography was not performed. Three patients had abnormal anterior mitral valve movement impinging on the ventricular septum. With postextra-

<table>
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<th>Table 1. Age Distribution of Patients with DMSS</th>
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<tbody>
<tr>
<td>Age (yr)</td>
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</tr>
<tr>
<td>less than 5</td>
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<td>5 - 9</td>
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<td>10 - 19</td>
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<tr>
<td>20 - 29</td>
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<tr>
<td>30 - 39</td>
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<tr>
<td>&gt;40 (age 54)</td>
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<tr>
<td>Total</td>
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<tr>
<th>Table 2. Correlation between Symptoms, Electrocardiogram and Peak Systolic Gradient in Patients with DMSS</th>
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<tbody>
<tr>
<td>History</td>
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<tr>
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</tr>
<tr>
<td>Asymptomatic</td>
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<tr>
<td>Symptomatic</td>
</tr>
<tr>
<td>Chest pain</td>
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<tr>
<td>Dyspnea</td>
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<tr>
<td>Syncope</td>
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<td>Increased LV voltage</td>
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<td>LVH and strain</td>
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<tr>
<th>Electrocardiogram</th>
<th>Number (%)</th>
<th>Age (yr) Mean (Range)</th>
<th>PSG (mm Hg) Mean (Range)</th>
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<tr>
<td>Normal</td>
<td>11</td>
<td>36</td>
<td>3-35</td>
</tr>
<tr>
<td>Increased LV voltage</td>
<td>11</td>
<td>36</td>
<td>6-14</td>
</tr>
<tr>
<td>LVH and strain</td>
<td>9</td>
<td>29</td>
<td>9-54</td>
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<tr>
<th>History and electrocardiogram</th>
<th>Number (%)</th>
<th>Age (yr) Mean (Range)</th>
<th>PSG (mm Hg) Mean (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic without LVH and strain</td>
<td>8</td>
<td>26</td>
<td>4-35</td>
</tr>
<tr>
<td>Symptomatic with LVH and strain</td>
<td>8</td>
<td>26</td>
<td>9-32</td>
</tr>
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*P < 0.005. 
Abbreviations: PSG = peak systolic gradient; LVH = left ventricular hypertrophy.
systolic contractions, these three patients also had increased LV outflow gradients with decreased peripheral arterial pulse pressure. Left ventricular wall motion was normal or hyperkinetic in all patients.

Unoperated Patients

Six patients did not have surgical resection of their subaortic membranes. These patients were asymptomatic at the time of catheterization diagnosis (ages 5, 11, 14, 19, 20, and 35 years), and had PSG of 25, 25, 25, 60, 60, and 60 mm Hg, respectively. Five of these patients have remained asymptomatic with no evidence on examination or electrocardiogram of progressive obstruction — follow-up one to five years, mean three years. One patient (age 20 years) developed chest pain and left ventricular hypertrophy and strain over a two-year interval with PSG increased from 60 to 120 mm Hg, which led to surgical resection.

Surgical Findings and Follow-up

Twenty-six patients had surgical resection, and in all, cardiopulmonary bypass and a transaortic approach was employed. There was a wide spectrum of operative findings. The obstructing membranes varied from fibrous webs of less than one millimeter to broad bands several millimeters thick; they were positioned from just beneath, to several centimeters beneath the aortic valve. The membranes attached to varying degrees of the LV outflow tract, and in some patients, were circumferential. The membranes attached medially to the upper interventricular septum in all patients; however, in one it also adhered to the right aortic valve cusp. The lateral attachment of these membranes was onto the proximal segment of the anterior leaflet of the mitral valve, although in four patients this attachment was onto the medial third of the mitral valve leaflet.

In 22 of the 26 patients, resection of the discrete membrane alone, or with a rim of fibromuscular tissue at its site of insertion, was required to relieve LV outflow tract obstruction; and in four patients, submembranous fibromuscular tissue in the LV outflow tract was also excised. Concomitant aortic valvulotomy for associated valvular aortic stenosis was performed in two patients — interestingly both had tricuspid aortic valves with normal-sized anuli.

Twenty patients have been asymptomatic after membrane resection (follow-up two months to 15 years, mean six years). Six patients have had significant problems since the operation. These were related in two to residual subaortic fibromuscular obstruction, and in four, to new diffuse subaortic obstruction which developed after from one to six years. One of the former patients died three weeks following membrane resection with severe low cardiac output. (The patient, previously reported by Block et al.,11 was 57 years old.) The other with residual obstruction (age 4 years) required extensive resection of subaortic musculature, as well as mitral valve replacement because of severe iatrogenic mitral insufficiency related to membrane resection. The latter patient has returned to full activity with no residual LV obstruction based on a follow-up of 18 months. In the four patients who developed new LV obstruction, initial PSG measured in the operating room following mem-

brane resection were less than 20 mm Hg. One of these patients (age 9 years, at membrane resection) developed chest pain and electrocardiographic findings of LVH and strain after 15 months, and also acquired bacterial endocarditis. After his antibiotic course, repeat cardiac catheterization in this patient demonstrated new, severe, diffuse subaortic obstruction. At surgery, resection of this diffuse, fibromuscular obstruction was performed with relief of the LV gradient. Postoperatively his chest pain was no longer present, although he continued to have electrocardiographic evidence for LVH and strain. Three years following his repeat resection, however, he died suddenly. At autopsy severe LVH with extensive LV fibrosis and diffuse fibromuscular outflow narrowing was found. The remaining three patients in whom new outflow tract gradients evolved, in spite of early absence of significant obstruction, were recatheterized because of symptoms or electrocardiographic LVH and strain, after from one to six years. Their PSGs were between 60 and 100 mm Hg. Two of these patients had septal thickening, abnormal systolic movement of the anterior mitral valve leaflet, and accentuation of the LV gradient with decrease of the peripheral pulse in postextrasystolic contractions. These three patients are presently being treated with propranolol.

Although preoperative diastolic decrescendo murmurs were heard in 17 patients, only eight had residual postoperative murmurs, two patients had not had a murmur preoperatively. The one patient in whom the membrane adhered to the right aortic valve cusp has moderate residual postoperative aortic insufficiency by physical examination, and no significant LV enlargement by echocardiogram or gated cardiac blood pool scan. Two of the remaining patients with murmurs of mild aortic insufficiency had bacterial endocarditis involving their aortic valves, and the remaining had thickened but tricuspid aortic valves visualized at surgery.

Evidence of healed, bacterial endocarditis was found on the aortic valve in two patients, and on the excised subvalvular membrane in a third. Postoperatively, one patient developed new, complete left bundle branch block. No patient developed complete heart block. One patient had a small, hemodynamically insignificant, postoperative ventricular septal defect.

Discussion

Despite the fact that DMSS was initially described in 1942,19 and has been reported in more than 200 patients,1–10 a number of aspects concerning its incidence among patients with LV obstruction, its natural history, its clinical course and presentation, and its peri- and late postoperative management still warrant attention.

In our experience with 185 patients with congenital LV outflow tract obstruction under age 40 years, 30 (16%) had DMSS, an incidence within the range described by others.1–10 Our review includes the largest number of adults (12 over age 20 years). It is noteworthy that nearly all of the previously reported patients with this lesion have been young (less than 40 years). Our oldest patient was 57 years and is both the oldest we could find in the literature as well as one of only three reported patients with DMSS over age 40 years. (The others were aged 41, 44 and 44 years9, 12.) The
rarity of older patients with DMSS in the face of its relatively high incidence among young patients with congenital LV obstruction (8% to 30%11-14) has not previously been commented on. We cannot readily account for this difference. However, knowledge of the fate of older patients with DMSS is extremely important as it may significantly affect the management of all patients.

There are several possible explanations for the apparent age-related disparity in the incidence of DMSS. One possibility is that DMSS leads to early death. While early death is conceivable in view of the severity of obstruction in many of these patients, there have been few reported early DMSS deaths either in hospital or out of the hospital.44-46 Therefore, early death alone seems an unlikely explanation. It would also seem unlikely that clinical or autopsy misdiagnosis or oversight could explain the rarity of DMSS in older patients. Another possible explanation for the age-related disparity in incidence of DMSS is that this lesion itself changes with age. A conceivable, but certainly a rare and fortuitous loss of obstruction might occur secondary to erosion of the obstructing membrane itself by endocarditis.

As has been postulated by others,8 in some patients DMSS may merge with more diffuse types of muscular LV obstruction including idiopathic hypertrophic subaortic stenosis.11-14 In such patients, the pathophysiology of the latter then dominates both the clinical and autopsy presentation. Our finding of residual or new onset subaortic fibromuscular obstruction in 24% of our patients supports the existence of such an interrelationship. Others have observed this connection.11, 15, 21-23 Both the coincidence that idiopathic hypertrophic subaortic stenosis is relatively less common in the young while DMSS is rare in older patients, as well as the presence of a related family history of LV obstruction in both entities lend support to this hypothesis.

A relationship between discrete and diffuse LV outflow obstruction is also suggested by occasional patients who have coexisting discrete as well as diffuse (type II) obstruction.22 It seems likely that the variants of subaortic LV obstruction are interrelated, with DMSS generally being on the mild end of the spectrum, type II22 obstruction possibly being intermediate in extent and severity of outflow obstruction, and tunnel or tubular narrowing being most severe and extensive, and also being most intractable to management.12, 22-25 Although we have raised the question that DMSS may evolve with age into more extensive variants of subaortic obstruction by citing the age-related disparity in the incidence of DMSS, additional documentation and studies to clarify this are clearly needed. Such clarification has particular practical importance, however, because if such a transformation does occur, a broader diagnostic and therapeutic approach to DMSS is needed.

A number of other clinically important findings in these patients warrant emphasis. The impressive incidence (13%) of LV obstructive lesions found in immediate family members of patients with DMSS has also been reported by others.17, 21, 36-38 and makes careful screening of families of these patients an essential part of their evaluation. In addition, the high incidence of bacterial endocarditis in patients with DMSS (13%), which has been noted by others,2, 6, 12, 21, 27, 31 makes meticulous bacterial endocarditis prophylaxis essential. Particularly because significant LV obstruction frequently recurs in these patients, but also because of the frequent association of other congenital heart lesions with DMSS and aortic valve deformity, we feel that postoperative endocarditis prophylaxis is warranted.

The clinical presentation of patients with DMSS has been well described.1-3, 4, 6-7, 9-24 In our patients, at least one cardiac symptom, either chest pain, dyspnea, or syncope, was present in the majority (73%), and the appearance of symptoms correlated well with the LV outflow obstruction (table 2). Only 27% of our patients were asymptomatic. In these latter patients, as in patients with valvular aortic stenosis,26 there was a wide range in severity of PSG (25-140 mm Hg); therefore, absence of symptoms does not rule out severe obstruction. Chest pain correlated best with severe PSG (60-180 mm Hg, mean 109 mm), even in younger patients in whom it is often difficult to assess. As in patients with valvular aortic stenosis, sudden death is a concern in DMSS and has been reported by others.2, 21 While none of our unoperated patients died suddenly, 16% described syncope, which has also been reported by others,21-23 and we did have one late postoperative sudden death. There was an excellent correlation between the electrocardiographic findings of left ventricular hypertrophy and strain, and the severity of PSG, and only rarely did we find a patient who did not have a strain pattern but had severe obstruction (table 2). Furthermore, the absence of both symptoms and a strain pattern separated approximately one-quarter who had PSG less than 90 mm Hg (mean 65 mm) from one-quarter who had severe obstruction, PSG greater than 85 mm Hg (mean 119 mm) in whom both symptoms and strain were present (table 2) (P < 0.005).

The diagnostic features of DMSS have also been well described,1-3, 4, 6-7, 21-24 and our findings parallel those of others. The following findings are of particular help in differentiating patients with DMSS from those with valvular aortic stenosis: the frequency in the former of aortic insufficiency (57%), found far less often in patients with valvular lesions; the absence of ejection clicks (no patient), a frequent accompaniment of valve lesions in the young; and the rarity of post-stenotic dilatation of the ascending aorta (2 patients), a frequent finding in valvar stenosis. No patient in our study had fluoroscopic evidence of calcification (probably related to their relatively young age). The echocardiogram is helpful in the evaluation of patients with DMSS, as has recently been reviewed.31-34 We presently use echocardiography in both our pre- and postoperative evaluation, particularly in follow-up for new or residual LV obstruction. However, because only our more recent patients have had such evaluation, we excluded this data in this review.

Proposed guidelines for surgical resection of DMSS have been more liberal than those suggested for valvular aortic stenosis, and include patients with PSG between 40 and 60 mm Hg.19, 21, 24 In view of our low peri-operative mortality (one patient), and the benign, postoperative course in the majority of our patients (76%), we concur with these guidelines. However, as we have shown, there is a significant postoperative morbidity in these patients (24%); therefore, close and long-term postoperative evaluation to identify those with persisting or recurrent symptoms or left ventricular hypertrophy and strain is essential. Muscular obstruction in these patients can be severe, and can cause late sudden death.
as found in our study and as reported by others,\textsuperscript{12, 21, 23} in spite of the early postoperative absence of significant outflow obstruction. These patients may require repeat outflow resection, or beta blockade. In addition, close follow-up of those patients who have not had surgery is warranted, as one of our patients developed severe obstruction over a two-year period of observation. Finally, in rare patients, iatrogenically-produced aortic or mitral valve insufficiency may complicate membrane resection.

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