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SEMINAR ON BALLOON AORTIC VALVULOPLASTY—V

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Follow-Up Recatheterization After Balloon Aortic Valvuloplasty

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The results of recatheterization were assessed in a select group of 95 patients enrolled in the Mansfield Scientific Aortic Valvuloplasty Registry to determine whether any procedural or patient-related variables at baseline predicted either initial immediate or follow-up (6.2 ± 3.3 months) results. At the follow-up catheterization, 39 (41%) of the patients were in improved condition and 56 patients (59%) had recurrence of symptoms, allowing for analysis of the effect of the procedure in two symptomatic patient subsets.

In the total group the aortic valve area increased initially from 0.56 ± 0.16 to 0.87 ± 0.27 cm^2 but partial return to the baseline valve area was evident at follow-up (0.63 ± 0.25 cm^2). Similarly, the mean aortic gradient initially decreased from 72 ± 30 to 35 ± 16 mm Hg but then increased to 55 ± 25 mm Hg at follow-up. Neither the initial nor the late hemodynamic results appeared affected by any definable procedural variable at the time of valvuloplasty, including the maximal diameter of balloons, number of balloons simultaneously used, mean inflation time or total number of inflations.

Such technical concerns also did not seem to affect short- or long-term outcome. Similarly, no baseline hemodynamic variable clearly separated those who became increasingly symptomatic from those whose condition was improved at the 6 month interval. At recatheterization, a reduction in the aortic valve area toward baseline was observed in 24 (62%) of the 39 improved patients and in 45 (80%) of the 56 who were symptomatic. At follow-up the less symptomatic group did have a greater aortic valve area (0.70 ± 0.32 versus 0.58 ± 0.18 cm^2; p = 0.02) and a slightly higher ejection fraction (59 ± 19% versus 48 ± 20%; p = 0.07) than the symptomatic group.

Thus, in this select group of patients, differences in procedural techniques at the time of aortic valvuloplasty did not appear to influence the return toward the baseline aortic valve gradient at follow-up. Fewer symptoms at follow-up were observed in those patients achieving the greatest aortic valve area after the procedure and in those with maintenance of left ventricular contractile performance.

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Percutaneous balloon aortic valvuloplasty has emerged as a therapeutic option in selected patients with severe aortic stenosis who are poor candidates for surgery (1–5). However, clinical studies (2,6,7) have revealed that evidence for restenosis, with or without return of clinical symptoms, occurs frequently. The acute relief of aortic obstruction observed using balloon catheter techniques appears to result from fracture of valvular calcium, tearing of commissural scar and perhaps stretching of the cusps or the aortic anulus (8–13). In the early days after the procedure, partial return of a pressure gradient occurs because of both remodeling of the aortic valve and an improvement in stroke volume (14,15). Restenosis may be an inevitable consequence at some point, after the procedure, although the mechanism of restenosis has yet to be well defined and its definition is controversial especially in light of the vagaries in the measurement of aortic valve area. It remains unclear, for example, which factors, such as valve architecture (12), underlying ventricular function (16–18) or variations in the procedure itself (19–23), might be most important in delaying restenosis or the return of symptoms. Preliminary studies (3) have suggested that the final aortic valve area probably best predicts early restenosis, and it has been advocated that a final aortic valve area >1.0 cm^2 after valvuloplasty should always be sought.

To date, follow-up data in patients after aortic valvuloplasty have primarily used noninvasive methods, such as Doppler echocardiography, to estimate the severity of the valvular gradient or to measure aortic valve area. Although Doppler gradients correlate reasonably well with invasive measures, substantial standard errors for the measurement of the mean aortic gradient and of the aortic valve area using the continuity equation have been described (24). For these

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reasons, follow-up invasive data are important to allow for comparison of serial hemodynamic changes with use of similar techniques.

Analysis of data in the Mansfield Scientific Aortic Valvuloplasty Registry from December 1, 1986 to September 1, 1988 reveals that 95 patients underwent repeat catheterization after aortic valvuloplasty. This time interval is greater than that reported elsewhere in this seminar. Both patient characteristics and details of the technique at the time of the initial procedure were available for review. This presentation is an assessment of the effect of these variables on the subsequent follow-up invasive hemodynamic outcome in these patients.

Methods

The Mansfield Scientific Aortic Valvuloplasty Registry. The Registry is a corporate-sponsored data base established through Mansfield Scientific and conducted under Food and Drug Administration-approved investigation device exemption. Clinical sites were required to complete a questionnaire regarding a series of procedural events, hemodynamic results and complications in all patients undergoing aortic valvuloplasty using balloon valvuloplasty catheters designed by the parent company. In addition to clinical follow-up, data from repeat catheterization were also sought.

During this time, 785 patients were enrolled in the Registry. At the time of this report, 525 patients were both alive and eligible for a 6 month follow-up catheterization. Follow-up catheterization was not a routine requirement; therefore, many patients underwent recatheterization because of recurrence of symptoms. In some centers recatheterization was incorporated into an institutionally approved protocol for the evaluation of the aortic valvuloplasty procedure. Therefore, the Registry included a mixed group of patients who had undergone repeat catheterization. Of the 525 eligible patients, 95 (18%) underwent recatheterization and these patients form the basis of this report.

An aortic valvuloplasty data base form allowed recording of information regarding the valvuloplasty procedure, as well as pertinent hemodynamic data and clinical symptoms. The procedural data base included the number of balloons used, the maximal diameter of each balloon, the balloon length, the number of inflations, the duration of each inflation and information on whether balloon rupture occurred and whether any complications ensued.

A baseline data base was also derived regarding the symptomatic status of each patient. This included documentation of fatigue, shortness of breath, angina, syncope, congestive heart failure class (New York Heart Association) and angina class (Canadian Cardiovascular Society). The overall clinical status was also recorded as stable, improving or worsening.

Recatheterization data were tabulated in a manner similar to that recorded at baseline. Recatheterization was performed at an average of 6.2 ± 3.3 months after the baseline procedure. At recatheterization 42 patients (44%) underwent repeat aortic valvuloplasty. Another five patients had repeat valvuloplasty during the same readmission. Thirteen patients (14%) underwent aortic valve replacement during the follow-up hospital admission and seven patients (7%) died during that hospital stay.

Patient characteristics. Table 1 outlines pertinent baseline clinical descriptors before valvuloplasty in the 95 patients who underwent recatheterization and contrasts them with descriptors in the subgroup of patients who did not undergo repeat catheterization. The two groups had similar baseline characteristics except for slightly more coronary artery disease and slightly less congestive heart failure in the study cohort. At 6 months more symptoms were present in the recatheterization group. Because 30% of patients died before they were eligible for recatheterization, the significance of this observation is unclear except that it confirms the view that many patients were restudied because symptoms were present. Because all descriptors were not recorded for all data items, Table 1 includes the actual number of patients from whom the data were derived for each variable. Overall, the patient group is elderly with mild to moderate coronary artery disease, moderately well preserved ventricular function and a modest degree of aortic regurgitation.

Table 2 outlines the symptomatic status of the 95 patients at baseline and at the time of the repeat study. Symptomatic improvement at recatheterization was evident in regard to heart failure classification, syncope and angina. However, the overall number of patients with any symptom of fatigue or dyspnea was unchanged. At the time of recatheterization, the condition of 39 (41%) was considered improved, whereas 56 (59%) had either similar or worse symptoms compared with baseline.

Statistical analysis. Data were expressed as the mean values ± SD or as mean values and the 95% confidence limits for the mean. Statistical analysis between groups was performed using either a paired or unpaired t test for continuous data and Fisher's exact test for dichotomous variables. A p value < 0.05 was considered significant.

Results

Initial and follow-up hemodynamic changes observed. Table 3 outlines the initial hemodynamic changes observed in the patients at the time of their original aortic valvuloplasty procedure and contrasts the data with data observed at follow-up catheterization. Ejection fraction values obtained immediately after the procedure were not recorded on the data sheets and were not available for review.

Figure 1 displays the immediate effects of aortic valvuloplasty on the aortic valve area and contrasts these initial measurements with values observed at follow-up catheterization. It is obvious that a return toward the baseline gradient and aortic valve area was common. When patients with fewer symptoms were compared with those whose

Table 1. Comparison of Patients Undergoing Recatheterization With Patients Who Had No Recatheterization Performed

	Recatheterization		No Recatheterization		
	No. (%)	n	No (%)	n	p Value
Baseline characteristic					
Male (%)	47 (49%)	95	310 (45%)	690	NS
Age (yr)	75 ± 10	95	78 ± 5	690	<0.001
CHF	51 (54%)	95	296 (68%)	435	<0.01
NYHA I or II	23 (24%)	91	84 (19%)	444	NS
NYHA III or IV	68 (71%)	91	360 (81%)	444	NS
Fatigue	56 (59%)	95	317 (71%)	445	<0.05
Dyspnea	83 (87%)	95	431 (91%)	472	NS
Angina	53 (56%)	95	239 (51%)	469	NS
Syncope	22 (23%)	95	113 (25%)	455	NS
Aortic regurgitation					
0 to mild	57 (85%)	67	380 (88%)	433	NS
Moderate to severe	10 (15%)	67	53 (12%)	433	NS
CAD					
None or 1VD	70 (74%)	89	424 (76%)	560	NS
2VD or 3VD	19 (26%)	89	136 (24%)	560	NS
Prevalvuloplasty Hemodynamics					
AVA (cm^2)	0.56 ± 0.16	95	0.50 ± 0.18	684	<0.01
Peak to peak aortic gradient (mm Hg)	72 ± 30	95	60 ± 23	690	<0.001
LVEDP (mm Hg)	19 ± 11	95	19 ± 14	670	NS
LVEF (%)	49 ± 20	65	49 ± 19	316	NS
Postvalvuloplasty Hemodynamics					
AVA (cm^2)	0.87 ± 0.27	95	0.82 ± 0.31	673	NS
Mean aortic pressure gradient (mm Hg)	35 ± 16	95	30 ± 13	678	<0.001
Follow-up symptoms					
Mean F/U time (mo.)	6.2	95	6.7	443	NS
CHF	47 (49%)	95	102 (34%)	298	<0.01
NYHA I or II	35 (37%)	95	241 (62%)	386	<0.0005
NYHA III or IV	54 (57%)	95	145 (38%)	386	<0.005
Fatigue	58 (61%)	95	147 (49%)	303	<0.05
Dyspnea	68 (71%)	95	185 (60%)	307	<0.05
Angina	31 (33%)	95	63 (21%)	303	<0.025
Syncope	11 (12%)	95	20 (7%)	293	NS
Improved (%)	39 (41%)	95	211 (65%)	325	<0.0005

The baseline characteristics, hemodynamic values before and immediately after valvuloplasty and the symptoms at the follow-up (F/U) interval are displayed for those who had, compared with those who had not, undergone recatheterization. There are no differences noted in any baseline characteristic except for a slight increase in fatigue and congestive heart failure (CHF) in the subsets not undergoing recatheterization. No hemodynamic measurement differed between the two groups. At follow-up the recatheterization group of patients had more symptoms in all categories and were generally less improved. This suggests that in the majority of patients recatheterization was performed because of symptoms. AVA = aortic valve area; CAD = coronary artery disease; LVEDP = left ventricular end-diastolic pressure; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; VD = vessel disease.

symptoms had returned to baseline severity, there was no difference in any measurable baseline hemodynamic variables. Similarly, when the immediate results of the valvuloplasty were assessed, there was no acute postprocedural hemodynamic variable seen more commonly in the patients with improved status than in those with recurrent symptoms (Table 4).

At follow-up catheterization, many patients with improvement demonstrated evidence for a return of the valve gradient. The follow-up aortic valve area was larger in patients who were clinically improved at 6 months. These patients also had a higher ejection fraction and had experienced a greater change in the ejection fraction from baseline (from 50 ± 21% to 59 ± 19%) compared with that in patients whose symptoms had worsened or returned to baseline

Table 2. Symptomatic Status of Patients Undergoing Recatheterization

	At Baseline	At 6 Month Recatheterization	p Value
Congestive heart failure	51 (54%)	47 (49%)	NS
Fatigue	56 (59%)	58 (61%)	NS
Dyspnea	83 (87%)	68 (71%)	NS
NYHA I or II	23 (24%)	35 (37%)	<0.05
NYHA III or IV	68 (71%)	54 (57%)	<0.05
Angina	53 (53%)	31 (33%)	<0.05
Syncope	22 (23%)	11 (12%)	<0.05

The change in symptomatic status in patients undergoing recatheterization is redisplayed from Table 1. At recatheterization a reduction in anginal and syncopal symptoms was noted but there was no change in overall symptoms of heart failure in this select subset. More patients reported functional class I or II symptoms at follow-up than at baseline.

Table 3. Hemodynamic Data

	Baseline Before BAV	n	Immediately After BAV	n	At Follow-Up Catheterization	n
Aortic valve area (cm^2)	0.56 ± 0.18	95	0.87 ± 0.27	95	0.63 ± 0.25	92
Mean aortic gradient (mm Hg)	72 ± 30	95	35 ± 16	95	55 ± 25	94
Peak to peak aortic gradient (mm Hg)	59 ± 21	95	32 ± 12	95	51 ± 21	94
LVEF (%)	49 ± 20	65	NA	—	53 ± 21	48
LVEDP (mm Hg)	19 ± 11	95	16 ± 9	94	19 ± 10	95

Baseline, immediate postvalvuloplasty and follow-up catheterization hemodynamic data in 95 patients. The initially improved hemodynamic values observed after balloon aortic valvuloplasty (BAV) have returned toward baseline in many patients. Abbreviations as in Table 1.

levels. This finding may have clinical relevance because it appears symptoms may not recur despite evidence for a return toward baseline of the aortic valve area and gradient in some patients.

Analysis of the procedural events and their impact on outcome. Several valvuloplasty technique variables were assessed to determine their relation to either the immediate or at 6 month follow-up catheterization outcome. Figure 2 displays the effect of maximal balloon size (diameter) on the change in aorta valve area observed, the aortic valve area after the valvuloplasty procedure and the aortic valve area at recatheterization. Although there is a slight trend toward a larger resultant aortic valve area at recatheterization when larger balloons were used initially, in general the use of a larger balloon size did not seem to correlate with a better valve area at restudy. The number of patients for whom each balloon size was used is recorded at the bottom of the figure and it is important to note that the overwhelming majority of patients had either a single 20 mm balloon (63%) or a combination of balloons with a total summed diameter of 30 mm (11%). Because of the small number of patients with balloons of other sizes, it is difficult to discern the true effect of balloon size, other than that of the two most commonly used.

The effect of the total number of balloon inflations on aortic valve area either immediately after the procedure or at recatheterization is shown in Figure 3. Again, the number of inflations appears to be unrelated to outcome; from two to six inflations were performed in most instances. On the assumption that the duration of each inflation may play a role, the hemodynamic status immediately after the procedure was assessed relative to inflation time. However, Figure 4 reveals no obvious relation between inflation time and aortic valve area. Similar findings were obtained for all hemodynamic variables. The majority of inflations lasted ≤30 s.

When these same technical variables were reassessed in the symptomatic subsets at 6 month follow-up study, no relation between any technical event and symptomatic outcome was found. For instance, the largest diameter balloon or balloons in the patients with symptomatic improvement

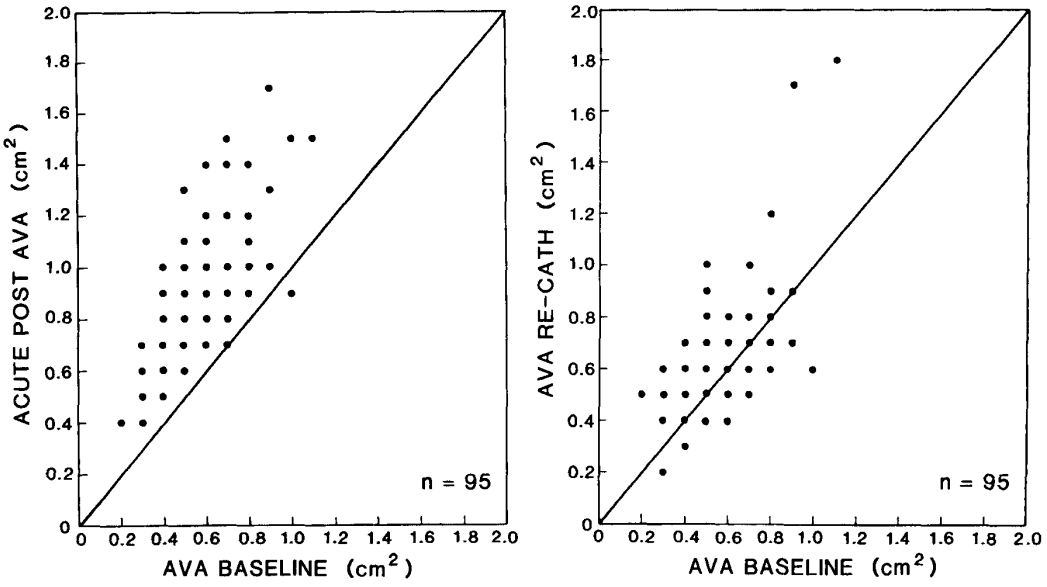


Figure 1. Aortic valve area data in 95 patients. **Left panel,** the effect of balloon aortic valvuloplasty on the aortic valve area (AVA) immediately after the procedure. Note the upward shift in data points. **Right panel,** at recatheterization the aortic valve area has returned to baseline in many patients, although there are still more patients above the line of identity than below it. Individual **dots** often represent more than one patient.

Table 4. Comparative Analysis of 39 Patients Symptomatically Improved Versus Those 56 With Similar or Worse Symptoms at the 6 Month Follow-up Catheterization

	Improved Compared With Baseline (n = 39)	Similar or Worse Compared With Baseline (n = 56)	P
AVA (cm^2)			
Baseline	0.57 ± 0.19	0.56 ± 0.18	0.71
Acute post	0.91 ± 0.29	0.85 ± 0.24	0.32
Follow-up	0.70 ± 0.32	0.58 ± 0.18	0.02
Mean aortic gradient (mm Hg)			
Baseline	62 ± 21	57 ± 20	0.20
Acute post	32 ± 11	31 ± 18	0.47
Follow-up	50 ± 20	52 ± 22	0.72
Ejection fraction (%)			
Baseline	50 ± 21	47 ± 20	0.58
Follow-up	59 ± 19	48 ± 20	0.07
LVEDP (mm Hg)			
Baseline	21 ± 14	19 ± 12	0.42
Acute post	16 ± 9	17 ± 8	0.76
Follow-up	20 ± 11	18 ± 9	0.44

At follow-up catheterization, the aortic valve area (AVA) was greater and the ejection fraction marginally higher in the group of patients with clinical improvement. No other identifiable variable was found that was more common in the improved subset. Abbreviations as in Table 1.

was 23 ± 6 mm versus 23 ± 6 mm in those with recurrent symptoms. Likewise, the average inflation time in the improved group was 32 ± 19 s versus 29 ± 27 s in the group with recurrent symptoms (p = 0.56).

Seventy patients (74%) had a single balloon procedure; the double balloon technique was used in 25 (26%). After the use of two balloons, the postvalvuloplasty area was 0.85 ± 0.09 cm^2 and the mean gradient was 38.5 ± 4.7 mm Hg. With use of a single balloon, the postprocedure aortic valve area was 0.88 ± 0.06 cm^2 and the mean gradient was 29.6 ± 2.7 mm Hg. However, this study was not designed to determine if the final aortic valve area is improved by the use of two balloons rather than one. Most patients underwent double balloon valvuloplasty when a single balloon procedure was deemed inadequate.

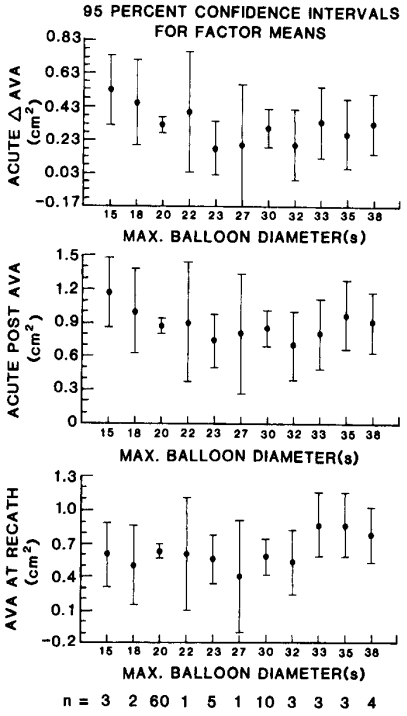
Discussion

Aortic valvuloplasty results in initial improvement in the measured outflow gradient in most patients. However, the final aortic valve area that results is frequently less than that observed after aortic valve replacement (24). A return of the aortic valve area toward baseline is probably a certainty at some time after the procedure.

Mechanisms of Restenosis

Why restenosis occurs has not been completely elucidated. Our study suggests that there is no measurable technique-related variable that predicts a rapid return of the aortic gradient by 6 months. It is more likely that restenosis is an inherent property of the architecture of the stenotic aortic valve itself. It may also be a function of the status of

Figure 2. Effect of maximal balloon sizes. Maximal balloon diameter was determined by using maximal balloon size derived from the maximal diameter of a single inflated balloon or the simple summation of the maximal diameter of two balloons. The relation between this diameter and the acute change (Δ) in the aortic valve area (**top panel**), the acute post valvuloplasty aortic valve area (**middle panel**) and the aortic valve area at recatheterization (RECATH) (**bottom panel**) is shown. The number of patients at each maximal balloon diameter size is shown at the bottom of the figure. No clear pattern is evident, although most patients had either a 20 or 30 mm maximal diameter used. Data are expressed as mean ± 95% confidence interval.



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