Midterm Outcomes in Supravalvular Aortic Stenosis Demonstrate the Superiority of Multisinus Aortoplasty

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Background. Surgical techniques for repair of supravalvular aortic stenosis (SVAS) include McGoon’s one-patch, Doty’s two-patch, and Brom’s three-patch method. In this review we evaluated mid-term clinical outcomes of these techniques at our institution.

Methods. Our cardiac surgery database identified patients with SVAS repair from 1990 to 2008. Follow-up records, reintervention and reoperation data, and most recent echocardiograms were obtained.

Results. From 1990 to 2008, 20 patients (70% male) underwent surgery for SVAS. Mean age was 3.6 ± 5.6 years. In chronological sequence, 8 patients had single-patch aortoplasty, 4 had the Doty procedure, and 8 received Brom’s symmetric three-patch aortoplasty. Of the Brom patients, 6 had Williams syndrome. Aortic cross-clamp times were 40.1 ± 13.6 minutes (one-patch), 60.3 ± 38.8 minutes (Doty), and 104 ± 20.5 minutes (Brom). Perioperative mortality was 5.0% (1 patient in one-patch group). Mean postoperative length of stay was 10 ± 10.6 days. Follow-up data were available for all survivors (mean follow-up, 6.3 ± 6.0 years; range, 6 months to 16 years). There were no late deaths. Follow-up echocardiograms revealed a peak Doppler gradient across the aortic outflow tract of 33 ± 18.0 mm Hg (one-patch), 10 ± 1 mm Hg (Doty), and 18 ± 12 mm Hg (Brom). All patients in the Doty and Brom groups had less than moderate aortic insufficiency. Reoperations were required in 5 of 8 one-patch patients (62%) for residual aortic stenosis (n = 3), aortic insufficiency (n = 1), and subvalvar stenosis (n = 1). No Doty or Brom patient has required aortic reoperations, which was nearly statistically associated with freedom from reoperation (p = 0.06). Subvalvar stenosis was the only risk factor associated with reoperation (p = 0.0028).

Conclusions. Despite a longer cross-clamp time, SVAS repair by Doty or Brom aortoplasty restores normal hemodynamics and reduces the need for reoperation when compared with the classic one-patch technique. Our current preference for SVAS repair is the Brom three-patch symmetric aortoplasty.

ing sinus incisions, termed the slide aortoplasty. The purpose of this study is to evaluate our surgical experience using the three different patch aortoplasty surgical techniques because we have not adopted the slide aortoplasty technique. We evaluated the risk factors for adverse outcomes with each of the surgical techniques, particularly regarding aortic insufficiency, aortic stenosis, and the need for reoperation.

Material and Methods

Patients and Procedures

The Institutional Review Board at Children’s Memorial Hospital, Chicago, IL, approved this review as a retrospective study and granted a waiver of informed consent. A retrospective review of the Children’s Memorial Hospital cardiothoracic surgical database identified all patients who underwent surgery for SVAS from 1990 to 2008. Chart review and the database were used to determine demographics, operative details, perioperative events, and complications. Mid-term follow-up was obtained from a combination of the cardiovascular surgery database, the Children’s Memorial Hospital electronic medical record, the cardiology charts, and the echocardiogram database.

Surgical Technique

Supravalvular aortic stenosis was repaired using one of several techniques. Our technique of Brom aortoplasty has been previously described [9]. The main technical issue pertains to restoring the symmetry of the aorta by making separate incisions into each of the three sinuses of Valsalva to allow for placement of equal augmenting patches. After the initial antegrade cardioplegia dose, the aorta is completely transected just at the level of maximal stenosis. A longitudinal incision is made into each sinus to maximally augment the aortic root by carrying the incision into the midportion of the respective sinuses. The first incision is into the noncoronary artery sinus. The incision into the right coronary artery sinus is to the left of the coronary orifice, and a similar incision into the left coronary artery sinus is to the right of the coronary orifice. Three pulmonary homograft patches are appropriately equally and symmetrically sized to augment each of the sinuses. The reconstructed aorta is then anastomosed to the distal ascending aorta that has been augmented with an additional shield; a diamond-shaped anterior patch. For the one-patch repair patients are similarly placed on cardiopulmonary bypass, and after antegrade cardioplegia, a single incision is made across the supravalvular aortic stenosis into the noncoronary sinus. A diamond-shaped Gore-Tex (W.L. Gore & Assoc, Flagstaff, AZ) patch is inserted [5]. For the Doty repair, an inverted Y-shaped incision is extended past the supraaortic stenosis into the noncoronary sinus and into the right coronary sinus to the left of the right coronary ostium [6]. A “pantaloon” Gore-Tex patch is then inserted into this region.

Statistical Analysis

Statistical analysis was performed with a commercially available statistical program using the χ² test and Student’s t test as appropriate. Risk factors (sex, Williams syndrome, anatomic aortic stenosis substrate, bicuspid aortic valve, aortic valvotomy, pulmonary arterioplasty, and subaortic myectomy) were examined for association with time to reintervention using the log-rank test. Kaplan-Meier curves are presented for time to reintervention by type of repair (one-patch or Brom) and by whether or not the patient had subaortic myectomy. We could not perform the analysis with the Doty group because of the small number of patients (n = 4). Significance was set as a probability value of less than 0.05. Analyses were conducted using SAS 9.1 (SAS Institute, Cary, NC), and graphs were prepared using Microsoft Excel (Microsoft Corp, Redmond, WA).

Results

Patient Characteristics and Intraoperative Factors

A total of 20 patients underwent repair for SVAS at our institution from 1990 to 2008. The mean age of the patients was 3.6 ± 5.6 years; 70% were male and 30% were female. The mean weight was 15 ± 16 kg. Eight patients had repair using a one-patch aortoplasty (McGoon technique), 4 had repair with the two-patch aortoplasty (Doty technique), and 8 patients underwent repair using Brom’s symmetric three-patch aortoplasty (Table 1). One patient who underwent the one-patch technique had fusion of the left coronary ostium to the supravalvular aortic ring, which occluded the left coronary ostium, and subsequently had a single patch placed into the left sinus of Valsalva to relieve the coronary obstruction. Three patients who were repaired with the one-patch method had previous surgical procedures, including an interrupted aortic arch repair, aortic valvotomy, and coarctation of the aorta. Ten patients had Williams syndrome of whom 6 had a Brom repair. In addition to the SVAS surgical repair, concomitant surgical procedures were 7 pulmonary arterioplasties, 3 subaortic myectomies, and 1 aortic valvotomy. The means for

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LOS = length of stay; XC = cross-clamp.
aortic cross-clamp times were as follows: the entire group, 69.7 ± 36 minutes; McGoon’s one-patch, 40.1 ± 13.6 minutes; Doty’s two-patch, 60.3 ± 38.8 minutes; and Brom’s three-patch, 104 ± 20.5 minutes.

Early Results
There was 1 early death resulting in an early mortality rate of 5%. This occurred in a patient who underwent a one-patch repair, and there were no deaths in the other two groups. The single death occurred in a high-risk infant (10 months) with supravalvular narrowing of both the aorta and pulmonary artery with small branch pulmonary arteries and suprasystemic right ventricular pressure. After successful single-patch insertion into the sinus of Valsalva of the aorta and patch augmentation of the main, right, and left pulmonary arteries, the patient was unable to separate from cardiopulmonary bypass because of suprasystemic right ventricle pressures and died in the operating room. For the remaining patients, there were no major complications or mediastinitis in the postoperative period. The mean length of stay was 10 ± 10.6 days for the entire group, 10 ± 5.8 days for the one-patch repair, 13 ± 7 days for the Doty repair, and 10 ± 6 days for the Brom repair (Table 1).

The peak aortic systolic gradient seen on echocardiogram at hospital discharge was 24 ± 13 mm Hg. This was significantly reduced from the preoperative peak gradient of 82 ± 17 mm Hg (Fig 1). The peak gradient at hospital discharge was 31 ± 12 mm Hg after one-patch repair, 17 ± 9.7 mm Hg after Doty operation, and 22 ± 15 mm Hg after Brom operation. Three patients had early obstruction as defined by a peak gradient equal to or greater than 40 mm Hg: 2 patients repaired by the one-patch technique and 1 patient repaired by the Brom technique. Both of the patients who were repaired with the one-patch technique had a bicuspid aortic valve with valvular obstruction despite a concomitant aortic valvotomy repair. The patient repaired by the Brom technique also had Williams syndrome with extensive multilevel obstruction of the right and left outflow tracts that required extensive relief with a Brom aortoplasty, subaortic myectomy, right and left pulmonary arterioplasty, main pulmonary arterioplasty, and right ventricular subvalvular outflow tract resection with Gore-Tex patch augmentation. The early obstruction in the left ventricular outflow tract of this patient was at the subaortic level with a peak gradient of 40 mm Hg, which preoperatively was a peak gradient of 100 mm Hg. At hospital discharge, all 8 patients who had a Brom repair had no more than a mild aortic regurgitation.

Late Outcomes
Follow-up data were obtained from the cardiovascular surgery database, cardiology charts, hospital electronic medical record, and the echocardiogram database. Follow-up data were obtained in all 19 patients who survived to discharge. Mean duration of follow-up was 6.3 ± 6.0 years (range, 6 months to 16.2 years), and for each of the respective surgical groups, follow-up was 10 ± 6.9 years for the single-patch repaired group, 4.0 ± 6 years for the Doty repaired group, and 3.8 ± 3.2 years for the Brom repaired group. There was no late mortality. Of the 8 patients in the single-patch group, 5 had reoperations, which included 4 aortic root operations (2 Ross procedures, 1 aortic homograft, and 1 modified Konno), and 1 subaortic membrane resection at a mean time to reinter- vention of 3.1 ± 1.4 years. The peak gradient increased to 67 ± 73 mm Hg for these patients requiring a reoperation, but subsequently returned to 33 ± 18 mm Hg after the reoperation (Fig 1).

At last follow-up, the mean peak gradient for the entire group was 22 ± 6 mm Hg, and for each of the repaired groups, the mean peak gradient was 33 ± 18 mm Hg (one-patch), 10 ± 1 mm Hg (Doty), and 18 ± 12 mm Hg (Brom). Four patients had late residual gradients equal to or greater than 40 mm Hg, which included 3 patients in the one-patch repaired group and 1 patient in the Brom repaired group. This 1 patient in the Brom repaired group was the same patient we previously described requiring extensive bilateral outflow tract reconstructions and who continued to have obstruction at the aortic subvalvular level. Postoperatively this patient had a peak gradient of 40 mm Hg and rose to 47 mm Hg at 1-year follow-up, all at the aortic subvalvular level. Univariate analysis indicated that concomitant subaortic myectomy surgery was the only associated risk factor with a recurrent gradient requiring a reoperation (p = 0.028, log-rank test). None of the other factors examined, including
Williams syndrome, sex, concomitant valvotomy, diffuse or discrete aortic type, and concomitant pulmonary plasty were associated with reoperations ($p > 0.15$; Table 2, Fig 2).

The Kaplan-Meier curve estimated the median time to reintervention for those with subaortic myectomy was 2.8 years (95% confidence interval, 1.3 to 4.3). Patients without subaortic membrane resection had a median time to reintervention of more than 7.0 years. There was a trend toward an increased need for reoperation in the patients who were in the one-patch group as compared with the patients in the Brom group ($p = 0.06$; Fig 3). We were unable to perform the analysis with the Doty technique because of inadequate patient numbers ($n = 4$). The Kaplan-Meier curve estimated the median time to reintervention for the patients in the one-patch repaired group was 5.7 years (95% confidence interval, 2.8 to 9.1). Patients who had the Brom repair had a median time to reintervention that was not estimated owing to no reinterventions seen in this group. At last follow-up, aortic regurgitation was graded as trivial in 4 patients (2 in one-patch and 2 in Brom), mild in 10 patients (3 in one-patch, 2 in Doty, and 5 in Brom), and moderate in 5 patients (4 one-patch and 1 Brom; Fig 4). All but 1 of the patients with the Brom repair had less than moderate aortic regurgitation.

### Comment

Many different surgical techniques have evolved during the last 40 years for the correction of SVAS. Because of higher residual aortic peak gradients and reoperations of the one-patch repaired patients, we adopted the Brom aortoplasty technique to correct SVAS in 1997. We believe that the Brom aortoplasty is a complete, encompassing technique to restore the geometry of the aortic root, even more than the Doty repair. We have now adopted this technique for all our patients regardless of associated lesions in the left ventricular outflow tract. The advantages of this technique include complete augmentation of the supravalvular narrowing, restoring the physical and symmetrical geometry of the aortic root, and preventing growth limitations by patch augmentation of all the sinuses of Valsalva. In our series at follow-up, the patients who had the Brom repair had less aortic regurgitation, aortic stenosis, and reoperations.

The initial description of SVAS pertained to the nar-
occur more proximally in the ascending aorta or may narrow the supravalvular aorta as a result of hyperplasia and thickening of the media immediately above the sinuses of Valsalva, creating the typical hourglass appearance (Fig 5). Despite this simple and discretely narrowed ring of aorta, many secondary effects may occur more proximally in the ascending aorta or may involve the ascending aorta [10]. The sinuses of Valsalva may become thinned and hypoplastic. The components of the aortic root may change owing to the stenotic ring that may alter the relationship of the commissures and, subsequently, the free edge of the aortic valve leaflets. In extreme instances, fusion of the edges of the aortic wall leaflet to the supravalvular ridge may compromise the coronary artery ostium and thus coronary artery flow [1]. In addition, as a result of the high proximal pressures from the supravalvular ridge, the coronary arteries may be injured in extreme conditions and myocardial infarction may occur. Also, associated lesions may be present, including bicuspid aortic valve, subvalvular stenosis, coarctation of the aorta, and pulmonary artery stenosis [1].

The sinotubular junction plays a critical role in creating a flexible aorta that dynamically changes with systole and diastole. This critical component of the left ventricular outflow tract is altered in the SVAS aorta because of a rigid narrowing ring near the sinotubular junction. This constriction subsequently alters the elastic properties of the aorta and thus may restrict the flattening and straightening of the aortic valve leaflets occurring in systole [11]. In this way, the aortic valve leaflets may degenerate with time and may be accelerated in situations in which a bicuspid valve is present. A recent study by Metton and colleagues [12] reported that despite the surgical technique used in the SVAS repair, bicuspid aortic valve was a risk factor associated with late residual obstruction, which further supports this dynamic interaction of the left ventricular outflow tract in the SVAS patients. However, our series did not show that the bicuspid valve was a risk factor for reintervention. Interestingly, subvalvular stenosis, another associated lesion with SVAS, was a risk factor for reintervention in our series. The subvalvular region is also a major contributor to the efficiency of the left ventricular outflow tract and is most likely affected by a rigid supravalvular ring.

The primary goal of the surgical repair of SVAS is to relieve the left ventricular obstruction created by the supravalvular ring. The initial surgical techniques relieved only the SVAS narrowing by manual dilation of the ring [13], resecting the ring with direct reanastomosis of the aorta [14, 15], and in extreme situations, apical-aortic conduits [16]. The surgical repair then progressed with a focus on restoring the geometry of the aortic root through various iterations of patch aortoplasty. Both the one-patch repair and Doty repair have been shown to have good early results but have limited long-term results owing to increasing aortic stenosis and regurgitation [17–19]. There are few mid-term studies with the Brom reconstruction and even fewer comparing all three SVAS operative types. One report by Hazekamp and colleagues [19] reported no significant differences with the aortic gradient or aortic regurgitation among all three groups. Another study reported by Stamm and colleagues [20] had no difference in survival rate and freedom from reoperations among all three surgically repaired groups. Only a recent report by Metton and colleagues [12] demonstrated that patients who were repaired with the Brom technique had statistically significant lower aortic gradients and regurgitation in comparison to the other two types of repaired groups. The recent review by Scott and associates [21] showed no advantage to all-autologous slide aortoplasty. Although our results did not reach statistical significance, there was a trend indicating that the Brom repaired group had improved surgical outcomes. Our surgical series are similar to those reported by others that involved the three-sinus aortoplasty technique either by Brom aortoplasty or sliding aortoplasty (Table 3).

In our series, the majority of the patients had Williams syndrome, which is an underlying elastin arteriopathy involving the aorta and pulmonary arteries [1]. The elastin disorder results from a microdeletion of the elastin gene on chromosome 7q11.23. Because of the reduction in elastin production, shear stress in the aorta may result in smooth muscle hypertrophy and increased collagen deposition, causing medial thickening. Furthermore, intimal thickening may occur as a result of fibrous growth. The elastin arteriopathy may range from the discrete type narrowing the supravalvular area to the diffuse type that extends the narrowing throughout...
the aortic arch and branch vessels [1]. In addition, the elastin arteriopathy may also involve other large arteries, such as the pulmonary arteries either at the central or branching level. The natural history of the pulmonary arterial stenosis may decrease spontaneously with time, which makes surgical indications limited in these patients. A recent report also indicates that the systemic arterial lesions may also regress and that only patients with the most severe and symptomatic lesions should have an operation [18].

Our study has several limitations. The study population is limited because of the rarity of the lesion, and the subgroups are therefore further limited in size, which makes statistical analysis difficult. The progressive evolution of the surgical procedure resulted in different timings for each of the surgical repairs, thus limiting the follow-up duration for each of the surgical types. The mean follow-up was 6.3 ± 6.0 years, and the mean time to reintervention was 3.1 ± 1.4 years. Even though we do not have more follow-up time in the Brom repaired patients (mean, 3.8 ± 3.2 years) and thus may have now seen the potential failure in this group, this may be mitigated by the fact that most of the reinterventions occurred in the first 3 years postoperatively, which has also been reported by others [12]. Although the current results appear promising, it will be important to continue examining the endurance of the Brom repair for a longer duration.

Our current study demonstrates a low operative mortality and complication rate for repair of SVAS, regardless of surgical technique. Of the examined associated lesions in the left ventricular outflow tract, subvalvular stenosis was an associated risk factor for reoperation and should be aggressively addressed during the initial surgical repair. Mid-term follow-up demonstrates that the Brom aortoplasty is associated with a low reoperation rate and incidence of aortic regurgitation, and makes this operation our procedure of choice for SVAS in all patients.

We would like to thank our statistician, Christine Sullivan, MS.


DISCUSSION

DR JOHN H. CALHOON (San Antonio, TX): Congratulations, Dr John H. Calhoon and your colleagues, on a very nicely presented series of supravalvular AS (aortic stenosis) patients treated with three different techniques. Thanks to the Society for the opportunity to discuss it. Thank you also for forwarding me your slides as well as your manuscript in advance.

This study was not randomized and, in my mind, really illustrates the evolution of your own surgical approach over the last nearly 20 years. There are a few things I would like to maybe understand more. One is there is still a not insignificant gradient in a number of your patients when you get through, whether it is the Brom or the others. Have you learned over time, and it wasn’t really illustrated in your manuscript or during your talk, what you can do to decrease that gradient further? Second, you continue to see what I would call not insignificant aortic insufficiency, and have you learned, similarly, anything that would diminish that in your orientation or construct of your patches? Finally, you demonstrated nicely your technique; the illustrations were great. You chose to use homograft patches. In those patients that you reoperated on, have you thought of a different material? In my own mind, sometimes the homograft patches when you have to go back in can be very brittle and bad, at other times they are fine. Are you happy with that tissue or are you thinking of using a different tissue or have you thought of it, and, if so, what is it?

I enjoyed your paper very much and thanks for the opportunity to discuss it.

DR KAUSHAL: Thank you very much for your comments. To begin with, I will answer the first and second questions because they are related. If you make your incision into the noncoronary sinus and extend it too far into the sinus, this will create unequal augmentation of the sinuses. I think that this plays a critical role in restoring the geometry of the aortic root. In addition, when you insert your shield-shaped homograft and they are not symmetrical, a little bit bigger than what you expect, then you can potentially change the geometry of the sinuses.

We determined the etiology of the aortic valve stenosis or regurgitation in follow-up, in particular, looking at other associated lesions and how they are related. In our series, subaortic stenosis was associated with reoperations. In other published series, bicuspid valve was associated with critical restenosis. Thus, other associated LVOT (left ventricular outflow tract) lesions with supravalvular aortic stenosis are underappreciated and may cause complications in the future.

Concerning your last question, we have been successful with pulmonary homograft and have had good long-term outcomes with homograft.

DR GEORGE DAICOFF (St. Petersburg, FL): Consistent with the idea of innovators, I would like to just indicate that Dr Brom was a professor at Leiden University, The Netherlands, and I went to visit him when I was on sabbatical from Chicago, and, unfortunately, he wasn’t doing any of these operations, but he was doing a coarctation of the aorta, and he had such a great clamp that held his clamps that I bought one. But, anyway, he was one of the innovators from the Netherlands that you never hear about.

DR KAUSHAL: I was looking back at the original Brom’s arterioplasty technique, which was only described in a surgical chapter. He never published any series about his technique.

DR KIRK R. KANTER (Atlanta, GA): Of the five reoperations in your series, four of them had aortic valve replacements. With this in mind, was the reoperation recurrence really for supravalvar stenosis, which you implied? Or was it actually for patients with multilevel left ventricular outflow tract obstruction in whom you had successfully dealt with the supravalvar aortic stenosis? I am unsure if you really demonstrated an inferiority of the one-patch technique with your patients.

You did not mention anything about coronary arteries. These patients, as you well know, have coronary artery anomalies. Early on in our experience, we had terrible problems with cardiac arrest with induction of anesthesia or cardiac arrest in the cath lab because of the coronary artery anomalies. None of your patients had opening of the coronary arteries as concomitant procedures. Also, I found particularly in the younger patients that you have to deal with the entire ascending aorta up to the base of the innominate artery and not just to the supravalvar area.

DR KAUSHAL: Due to the low number of patients in each surgical group, we could not perform propensity matching to determine the best surgical technique. But what I can comment about is that of the patients that required reoperations, the supravalvar region had no stenosis but other areas of the LVOT were problematic. Three out of the four patients who required aortic root surgery had bicuspid valves.

As to your question about the coronary ischemia, we had one patient who had a left coronary ostial ridge but didn’t have ischemia. In this patient, we resected the ridge and patched the sinus. We have had no patients who have had coronary ischemia.