Surgical Repair of Pulmonary Venous Stenosis: A Word of Caution

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Background. Pulmonary vein stenosis (PVS), both congenital and acquired, is challenging to treat surgically with uncertain long-term results. We reviewed an 11-year surgical experience in 52 children.

Methods. From 2002 to 2012, 52 children age 0 days to 13 years (mean 1.9 years, median 11.7 months) weighing 2.2 to 32.5 kg (mean 9.3 kg, median 7.6 kg) had surgical relief of PVS. Based on clinical characteristics or complexity, 33 (63%) had a sutureless pericardial well repair and 19 (37%) had a more standard patch repair. There were no significant differences in clinical characteristics between the 2 techniques. Twenty children (38%) had prior anomalous pulmonary vein repair and 8 had primary pulmonary vein stenosis; 26 (50%) had other operations at the time of PVS relief.

Results. There were 2 hospital deaths (10.5%) in the “standard” group and 5 (15.2%) in the sutureless group (p > 0.99). Despite postoperative evidence of PVS relief by echocardiogram or cardiac cath in all patients, at 5 years, actuarial freedom from PVS recurrence or death in the hospital survivors was 67% in the standard group and 58% in the sutureless group. Most recurrences or deaths occurred within 6 months of operation. Heterotaxy, single ventricle anatomy, bilateral disease, and previous anomalous pulmonary vein repair were not predictors of failure.

Conclusions. Surgical treatment of pulmonary vein stenosis remains a challenging problem with nontrivial early mortality and ongoing risk for recurrence or death regardless of surgical technique employed. Clearly, development of methods for earlier intervention or detection and improved surgical techniques are warranted.

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Patient Population

From January, 2002 to December, 2012, 52 children had surgical relief of pulmonary vein stenosis at Children’s Healthcare of Atlanta at Egleston, the pediatric hospital affiliated with Emory University School of Medicine. Based on the clinical characteristics of the patient and the preference of the surgeon, the repair was with a more traditional technique (standard technique) or a sutureless technique (also referred to as a pericardial well technique). The distribution of standard repairs compared with sutureless repairs by year of operation is shown in Figure 1. Although standard repairs were more common early in the series and sutureless repairs later in our experience, both techniques were employed throughout the 11 years of the study. Table 1 shows the patient characteristics at the time of operation. The clinical characteristics at initial operation were similar between the standard technique patients and the sutureless technique patients with no statistically significant differences. Interestingly, 16 of the 52 patients (31%) had clinical evidence of aspiration preoperatively.

Twenty children (38%) had previous repair of total or partial anomalous pulmonary venous connection. Eight children had a previous Norwood procedure, 4 with a restrictive or intact atrial septum or with TAPVC. Forty-two patients (81%) had previous cardiac operations (mean 1.8 ± 0.99 operations per patient in those with a prior operation); only 8 patients had primary pulmonary vein stenosis in isolation or in combination with an atrial
septal defect, ventricular septal defect, or patent ductus arteriosus.

Operative Technique

All patients had repair utilizing cardiopulmonary bypass. For the standard repair patients, a variety of techniques were employed alone or in combination [8] including resection of scar tissue, patch augmentation of the stenosed vein(s), reimplantation of the affected pulmonary vein, or use of a flap of left atrial appendage across the narrowed area [9]. For those with the sutureless technique, the affected veins were opened widely back to normal tissue and an autologous in situ pericardial flap was sewn around the opening to the left atrium (or common atrium) as described by Lacour-Gayet [3, 6] and the Toronto group [7, 10], although, in general, all scar tissue was not excised as recommended by Lacour-Gayet, the stenosed veins were simply opened out to a normal appearing pulmonary vein. Ten of the sutureless technique patients (30%) had bilateral relief of pulmonary vein stenosis and 23 (70%) had unilateral repair; 6 of 10 on the right and 17 of 22 on the left (Table 1). Twenty-six patients (50%) had a variety of other operations performed at the time of the pulmonary vein repair, the most common of which was a Fontan or Glenn procedure in 7.

Statistics

Continuous variables were compared by analysis of variance and are presented as the mean ± standard deviation. Nominal variables were compared by χ² analysis with the Fisher exact test. Life table analysis was done by the Kaplan-Meier survival method with significance determined by log-rank analysis. Significance was defined as a p value of 0.05 or less.

Results

Early Results

Operative mortality, defined as death within 30 days of operation or before hospital discharge, whichever was longer, was 2 patients (10.5%) in the standard technique group and 5 patients (15.2%) in the sutureless group (p > 0.99). The details are shown in Table 2. Two of the 7 early deaths were in infants with hypoplastic left heart syndrome and intact or restrictive atrial septum. The remaining hospital survivors had confirmation of satisfactory relief of pulmonary vein stenosis documented by postoperative echocardiography or cardiac catheterization.

Follow-Up

On average, follow-up of 3.6 ± 3.2 years, there have been 7 deaths; all but 1 within 6 months of pulmonary vein stenosis repair. Four of the late deaths were in the sutureless surgical group and 3 were in the standard surgical group. All 7 patients had documented recurrence of pulmonary vein stenosis prior to death. Eight other children have developed evidence of recurrent pulmonary vein stenosis 6 weeks to 5 years after the original pulmonary vein relief; 6 in the sutureless group and 2 in the standard group. The actuarial freedom from death or pulmonary vein restenosis in the hospital survivors is shown in Figure 2, stratified by surgical strategy. There was no statistically significant difference between the 2 operative strategies as well as the presence of heterotaxy, previous TAPVC repair, single ventricle anatomy,
Table 1. Patient Characteristics at the Time of Pulmonary Venous Stenosis Repair

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>&quot;Standard&quot; Technique (n = 19)</th>
<th>Sutureless Technique (n = 33)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at pulmonary vein repair (years)</td>
<td>2.2 ± 3.1</td>
<td>1.8 ± 2.0</td>
<td>0.62</td>
</tr>
<tr>
<td>Weight at pulmonary vein repair (kg)</td>
<td>10.0 ± 7.9</td>
<td>8.8 ± 1.0</td>
<td>0.53</td>
</tr>
<tr>
<td>Number previous operations</td>
<td>1.5 ± 1.2</td>
<td>1.5 ± 1.1</td>
<td>0.97</td>
</tr>
<tr>
<td>Heterotaxy, n (%)</td>
<td>2 (11%)</td>
<td>7 (21%)</td>
<td>0.97</td>
</tr>
<tr>
<td>Previous TAPVC/PAPVC repair, n (%)</td>
<td>8 (42%)</td>
<td>12 (58%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Bilateral vein involvement, n (%)</td>
<td>10 (53%)</td>
<td>10 (30%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Single ventricle, n (%)</td>
<td>5 (26%)</td>
<td>12 (36%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Hospital mortality, n (%)</td>
<td>2 (10.5%)</td>
<td>5 (15.2%)</td>
<td>&gt;0.99</td>
</tr>
</tbody>
</table>

PAPVC = partial anomalous pulmonary venous connection; TAPVC = total anomalous pulmonary venous connection.

There were 16 children who had operation for pulmonary vein stenosis after repair of TAPVC. Excluding 2 patients who were early mortalities (1 in the standard group and 1 in the sutureless group), 5 had a standard repair and 9 had a sutureless repair. The actuarial 5-year freedom from recurrence or death for the TAPVC patients was 50% compared with 65% for the non-TAPVC patients (p = 0.097). The actuarial freedom from recurrence or death was not statistically different for the standard repair or a sutureless pericardial wall repair. Although the clinical characteristics of the patients assigned to either surgical strategy were not statistically different (Table 1), almost certainly there was some selection bias in the choice of operation with the more challenging patients probably more likely having a sutureless approach. As shown in Figure 1, although both techniques were employed throughout the 11 years of this series, the use of the sutureless technique appeared to be more frequent recently.

Pulmonary venous obstruction after repair of TAPVC is particularly challenging with reported 5-year recurrence-free survival around 50% [1, 2, 5] and an operative mortality of 27% [4]. The introduction of the sutureless technique for relief of pulmonary vein stenosis by Lacour-Gayet [6] and Coles [7] described improved surgical results for this vexing problem. Using the sutureless technique, several groups have reported improved survival with this strategy [1, 5, 10, 11]. However, the reported results have not been as favorable with the sutureless technique in children with primary pulmonary vein stenosis [2, 12] or even in those with single ventricle anatomy [1].

In our series we showed a 5-year actuarial freedom from recurrent pulmonary vein stenosis or death in hospital survivors of about 60%, with no significant differences between the standard and sutureless techniques (Fig 2; Table 3). As mentioned above, the apparent equivalence of the techniques may have been confounded by selection bias of operative strategy with the more difficult patients undergoing a sutureless operation. Prediction of post-repair recurrence or death by a preoperative pulmonary vein score as proposed by Yun and colleagues from Toronto [11], and later validated by Viola [12], was not performed in this series.

Unlike others, we did not demonstrate a recurrence-free survival disadvantage in children with heterotaxy syndrome, single ventricle anatomy, bilateral pulmonary vein involvement, or primary pulmonary vein stenosis (Table 3), although the numbers in each group were small.

Table 2. Operative or Hospital Deaths

<table>
<thead>
<tr>
<th>Age at Operation</th>
<th>Number Previous Operations</th>
<th>Diagnosis</th>
<th>UniV/BiV</th>
<th>Operative Repair</th>
<th>Unilateral/Bilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 days</td>
<td>0</td>
<td>HLHS/Intact atrial septum</td>
<td>UniV</td>
<td>Standard</td>
<td>Unilateral</td>
</tr>
<tr>
<td>11 days</td>
<td>1</td>
<td>TAPVC</td>
<td>BiV</td>
<td>Standard</td>
<td>Bilateral</td>
</tr>
<tr>
<td>4.5 months</td>
<td>0</td>
<td>Primary pulmonary vein stenosis</td>
<td>BiV</td>
<td>Sutureless</td>
<td>Bilateral</td>
</tr>
<tr>
<td>3.7 years</td>
<td>4</td>
<td>Unbalanced CAVSD</td>
<td>UniV</td>
<td>Sutureless</td>
<td>Bilateral</td>
</tr>
<tr>
<td>10 months</td>
<td>1</td>
<td>Shone’s syndrome</td>
<td>BiV</td>
<td>Sutureless</td>
<td>Unilateral</td>
</tr>
<tr>
<td>2 months</td>
<td>1</td>
<td>TAPVC</td>
<td>BiV</td>
<td>Sutureless</td>
<td>Bilateral</td>
</tr>
<tr>
<td>9 days</td>
<td>1</td>
<td>HLHS/restrictive atrial septum</td>
<td>UniV</td>
<td>Sutureless</td>
<td>Unilateral</td>
</tr>
</tbody>
</table>

BiV = biventricular; CAVSD = complete atriocentric septal defect; HLHS = hypoplastic left heart syndrome; TAPVC = total anomalous pulmonary venous connection; UniV = univentricular.

Comment

This series presents a heterogeneous group of patients undergoing surgical relief of pulmonary vein stenosis, both primary and acquired. The type of repair employed was broadly categorized as a standard repair or a sutureless pericardial wall repair. Although the clinical characteristics of the patients assigned to either surgical strategy were not statistically different (Table 1), almost certainly there was some selection bias in the choice of operation with the more challenging patients probably more likely having a sutureless approach. As shown in Figure 1, although both techniques were employed throughout the 11 years of this series, the use of the sutureless technique appeared to be more frequent recently.

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In our series we showed a 5-year actuarial freedom from recurrent pulmonary vein stenosis or death in hospital survivors of about 60%, with no significant differences between the standard and sutureless techniques (Fig 2; Table 3). As mentioned above, the apparent equivalence of the techniques may have been confounded by selection bias of operative strategy with the more difficult patients undergoing a sutureless operation. Prediction of post-repair recurrence or death by a preoperative pulmonary vein score as proposed by Yun and colleagues from Toronto [11], and later validated by Viola [12], was not performed in this series.

Unlike others, we did not demonstrate a recurrence-free survival disadvantage in children with heterotaxy syndrome, single ventricle anatomy, bilateral pulmonary vein involvement, or primary pulmonary vein stenosis (Table 3), although the numbers in each group were small.
so a true difference may not have been apparent. It is interesting that 24 patients in this series (46%) had neither primary pulmonary vein stenosis nor a prior repair of anomalous pulmonary venous connection. It is unclear why such a large number of children with previous heart operations unrelated to the pulmonary veins should develop pulmonary vein stenosis. The failure of the sutureless technique in our experience to drastically reduce postoperative recurrence or death was particularly disappointing. It is noteworthy that the majority of adverse events occurred within 6 months of operation although there were occasional recurrences out to 5 years (Fig 2). Nonetheless, over half the patients remain alive and recurrence free after 5 years (Fig 2).

In summary, surgical treatment of pulmonary vein stenosis remains a challenging problem, with nontrivial early mortality and ongoing risk for recurrence or death regardless of surgical technique employed. The heterogeneous nature of this disease makes it difficult for a single center to have sufficient numbers to make substantive conclusions about optimal surgical strategies. In our experience many previously described risk factors were not confirmed. Clearly, development of methods for earlier intervention and detection as well as improved surgical techniques are warranted.

### References

6. Lacour-Gayet F, Ray C, Planche C. Pulmonary vein stenosis. Description of a sutureless surgical procedure using the

### Table 3. Risk Factors for Recurrent Pulmonary Vein Stenosis or Death

<table>
<thead>
<tr>
<th>Variable</th>
<th>Free From Recurrence/Death (n = 30)</th>
<th>Recurrence/Death (n = 22)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary pulmonary vein stenosis, 8 pts; n (%)</td>
<td>6 (75%)</td>
<td>2 (25%)</td>
<td>0.44</td>
</tr>
<tr>
<td>Heterotaxy, 9 pts (n, %)</td>
<td>5 (56%)</td>
<td>4 (44%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Previous TAPVC/PAPVC repair, 20 pts; n (%)</td>
<td>8 (40%)</td>
<td>12 (60%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Bilateral vein involvement, 20 pts; n (%)</td>
<td>10 (50%)</td>
<td>10 (50%)</td>
<td>0.40</td>
</tr>
<tr>
<td>Single ventricle, 17 pts; n (%)</td>
<td>8 (47%)</td>
<td>9 (53%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Sutureless technique, 33 pts; n (%)</td>
<td>18 (55%)</td>
<td>15 (45%)</td>
<td>0.57</td>
</tr>
</tbody>
</table>

PAPVC = partial anomalous pulmonary venous connection; pts = patients; TAPVC = total anomalous pulmonary venous connection.

DISCUSSION

DR CARL LEWIS BACKER (Chicago, IL): Kirk, I am curious as to what these patients actually died of. We had a recent patient who underwent pulmonary vein stenosis repair. Follow-up CT [computed tomographic] scan showed a widely patent sutureless technique, but the child had unrelenting pulmonary hypertension. We consulted Dr Caldarone, who has come to the microtechnique, but the child had unrelenting pulmonary hypertension. We had a recent patient who underwent pulmonary vein stenosis repair. Follow-up CT scan showed a widely patent sutureless repair, but the child had pulmonary hypertension with what appeared to be wide open pulmonary veins.

So what did the patients who had repair of pulmonary vein stenosis die of?

DR KANTER: Most of the deaths were early. Unrelenting pulmonary hypertension was unusual as a cause of death in our series. Certainly a lot of them had persistent pulmonary artery hypertension, but that did not seem to be the problem. The early deaths were almost all multisystem organ failure, probably related to a combination of low cardiac output and ongoing problems with other problems in a cascade of events that occurs with pulmonary problems, pulmonary hypertension, renal failure, that sort of thing.

But two of the patients in this series were children with hypoplastic left heart syndrome and restrictive atrial septum that the zero-day one was the one that was born and had the pulmonary vein stenosis repaired at the time of the Norwood operation, and one of them is a long-term survivor.

But the causes of death were multifactorial, and definitely persistent lethal pulmonary hypertension was not the common mode.

DR CHRISTOPHER A. CALDARONE (Toronto, Ontario, Canada): Kirk, thanks for that presentation. In our experience, the sutureless repair has been pretty useful for post repair pulmonary vein stenosis and in contrast has been largely ineffective in the patients with primary pulmonary vein stenosis or congenital pulmonary vein stenosis. So it was a little bit hard to tell from your presentation how those may have differed in terms of restenosis.

When you take out the perioperative deaths as you described that probably really are not related to either procedure, and you just look at the patients who after hospital discharge went on to have progressive pulmonary vein stenosis, was there a difference in those two populations? Because in our experience they behave quite differently.

DR KANTER: Because of the numbers, there were only six late deaths, three in each group, and they were not as hard to tease that out. But we certainly had restenosis and deaths in patients who had a pericardial well repair for recurrent stenosis after a total veins repair, one of the three patients in that group.

As I was writing the paper, I was interested. One thing that we have not done that you guys have written about is that if you have a recurrence, our philosophy has been we have done all we can do. There is nothing more to do other than a transplant. But the Toronto group, you write that you go back and do some more, and I wonder if we have not been aggressive enough in these late recurrences.

DR CALDARONE: Well, it is hard to know because, like you said, it is a vexing problem, and this particular procedure is not a panacea. I agree.

There are two things which we may be doing different. I don’t know. One is we do some pretty rigorous intraoperative assessment of the pulmonary veins with the belief that any residual stenosis at the time of repair is just going to progress with time. And we look for any turbulence at the site of the repair, and we will aggressively revise a repair at that point. Whether we start it off with a conventional repair or a sutureless type repair, that is one thing that we do.

With regard to patients who come back with a current stenosis who have had a sutureless repair, yes, we have actually redone sutureless repairs. But that is limited to the situations where there is obvious upstream pulmonary vein dilation.

When it is the upstream pulmonary vein string sign as you described, we say the same thing as you did. We have done all we can do, and we do not feel that any surgical intervention is going to help in that situation.

DR KANTER: I think you are bringing up a good point; is that you can almost predict the ones that are not going to do well because they do not have that nice plump upstream pulmonary vein, and you know that they are going to be back in six months to a year with recurrent stenosis.

DR CALDARONE: Yes, absolutely. That preoperative MRI [magnetic resonance image] or CT is really, really useful in deciding which patients are worth having a go at. Thank you.

DR BACKER: Chris, before you leave the microphone, I would like to ask both you and Kirk about de novo isolated pulmonary vein stenosis. For example, you encounter a patient who has had a Fontan operation and they are not doing well. Then you reevaluate them and find there is an isolated left pulmonary vein stenosis. It occurs despite the fact that the patient never had instrumentation of that area, and no surgery there. What do you think causes this de novo isolated left pulmonary vein stenosis?

DR KANTER: It seems to me that it is the left lower pulmonary vein that is the most typical.
DR BACKER: Correct, it is most frequently the left lower pulmonary vein.

DR KANTER: And I wonder if it is either during the original operation you have distorted the pericardium so that the heart is sitting in a funny fashion or if you have got cardiomegaly that is pressing on the vein.

But when you get in there, there is no obvious anatomic reason for it. But we are pretty aggressive at going after those patients, and we call that primary.

DR CALDARONE: Yes, I think that is an unnamed syndrome, and it is typically the left lower pulmonary vein. In our experience, it is associated with a volume-loaded heart, often a postoperative mediastinum which makes me suspect that things are relatively fixed in the mediastinum and possibly an anterior located descending aorta. The combination of those factors I think leads to kind of a flattening of the left lower pulmonary vein, and we find that stenosis as well.

Yasuhiro Kotani, who is going to make the next presentation, actually is probably the world expert on that syndrome; although it has not been published yet.

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Sixty-First Annual Meeting

The Sixty-First Annual Meeting of the Southern Thoracic Surgical Association (STSA) will be held November 5-8, 2014 at the JW Marriott Tucson Starr Pass Resort & Spa in Tucson, Arizona.

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