Management of Congenital and Acquired Pulmonary Vein Stenosis

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Background. Pulmonary vein (PV) stenosis, whether congenital or after repair of total anomalous pulmonary venous connection (TAPVC), continues to carry a poor prognosis.

Methods. A retrospective review identified 36 patients who underwent repair of PV stenosis between December 1989 and June 2003. Fourteen with congenital PV stenosis underwent scar excision and primary repair (n = 2), intraoperative stent placement (n = 4), or sutureless pericardial marsupialization (n = 8). Twenty-two with acquired PV stenosis after TAPVC repair underwent anastomotic revision and/or vein repair (n = 11) or sutureless pericardial marsupialization (n = 11). Follow-up ranged from 1 month to 14 years (median, 30 months).

Results. Among the 14 patients with congenital PV stenosis, 8 died (3 early deaths, 4 late deaths with restenosis, and 1 late noncardiac death). Among the six survivors, five (4 after marsupialization) have not developed restenosis. Among 11 of 22 patients with acquired PV stenosis undergoing anastomotic revision or vein repair, there were 5 deaths (2 early, 2 late with restenosis, and 1 late noncardiac death) and 1 of the six survivors has developed restenosis. Of the remaining 11 undergoing marsupialization, there was one late death (with restenosis) and 10 survivors have no restenosis. Congenital etiology, use of marsupialization technique, presence of associated defect, and extent of disease were identified as risk factors for poor outcome.

Conclusions. Patients with pulmonary vein stenosis continue to have a guarded prognosis. Sutureless pericardial marsupialization was associated with satisfactory midterm results and appears superior to other conventional techniques.


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Follow-up for all patients ranged from 1 month to 14 years (median, 30 months).

Statistical Analyses
Statistical analyses were performed using Statview (Version 5.0.1, SAS Institute, Inc, Cary, NC) and MedCalc (Version 8.1.0.0, MedCalc Software, Mariakerke, Belgium) software. Actuarial survival was calculated using techniques of Kaplan and Meier, and differences in outcome were tested for significance using the Cox-Mantel log-rank test. Multiple risk factors were assessed using the Cox proportional hazards method. For all comparisons, differences were considered significant for \( p \) values less than 0.05.

Operative Procedures
All patients undergoing repair of pulmonary vein stenosis underwent cardiopulmonary bypass with bicaval cannulation. Deep hypothermia and either low-flow cardiopulmonary bypass or circulatory arrest were utilized in order to improve exposure of the pulmonary venous obstruction. Throughout the series, a variety of surgical techniques were applied, including anastomotic revision (for patients with acquired PV stenosis), intraoperative stent placement, patch venoplasty (using atrial tissue, pericardium, or polytetrafluoroethylene), dilatation, and scar excision with primary repair. The technique of sutureless pericardial marsupialization has been used frequently since 1998. For each patient, operative technique was selected based upon the specific anatomy of the stenosis.

Results

Congenital Pulmonary Vein Stenosis
Among the 14 patients undergoing repair of congenital pulmonary vein stenosis, two underwent scar excision and primary repair only, four patients had stents placed, and eight patients underwent SPM. Two patients underwent multiple interventions for PV stenosis. One underwent placement of stents on three occasions, and the other underwent initial pericardial patch venoplasty and then a stent. Outcomes are illustrated in Figure 1. Both patients undergoing excision and repair died late (one with restenosis and one noncardiac death). One of the four stented patients died early, two died late with restenosis, and the fourth patient is alive at 10 years with no restenosis; this patient had unilateral disease with a small lung but a patent stent at follow-up. In the group of eight undergoing marsupialization, there were two early deaths and one late death (with associated restenosis). Five SPM patients are alive at a median follow-up of 25 months, although one patient with unilateral disease has developed severe restenosis. Overall, for the 14 patients with congenital PV stenosis, good outcomes occurred in only five patients (four of whom underwent marsupialization).

Acquired Pulmonary Vein Stenosis
Twenty-two patients presented with acquired pulmonary vein stenosis (Fig 1). Thirteen patients underwent initial anastomotic revision. Six of these patients required reoperation due to recurrent stenosis. Four patients requiring reoperation underwent a nonmarsupialization type of repair, while two proceeded to marsupialization. This left 11 patients in the "repair only" group. Nine patients with acquired PV stenosis underwent initial sutureless pericardial marsupialization. Including the two patients who underwent an unsuccessful initial repair, a total of 11 patients ultimately underwent marsupialization. After
marsupialization, no patients have undergone reoperation for pulmonary vein restenosis. Outcomes for the patient groups are shown in Figure 1. Among the patients undergoing repair alone, there were five deaths. Two deaths were early and three were late. Two late deaths occurred in association with severe restenosis, and the other was noncardiac in etiology. Six patients in the repair group are alive at a median follow-up of 31 months, but one has developed restenosis. Among the 11 patients undergoing SPM, there was one late death, which was secondary to restenosis. The remaining 10 patients are alive at a median follow-up of 18 months and none has developed restenosis.

**Risk Factor Analysis**

Actuarial survival was performed using the Kaplan-Meier technique. Survival for all patients undergoing repair for PV stenosis is shown in Figure 2. A trend suggesting an improved outcome was seen in patients with acquired PV stenosis (Fig 3). Patients undergoing sutureless marsupialization demonstrated significantly improved survival (Fig 4). Using Cox proportional hazards analysis, several potential risk factors, including single ventricle anatomy, bilateral disease, heterotaxy syndrome, surgical technique, and etiology, were assessed for significance. The presence of an associated defect \( (p = 0.02) \), bilateral disease \( (p = 0.03) \), and use of a nonmarsupialization technique \( (p = 0.04) \) were found to be independent significant risk factors for poor outcome (Table 3).

**Comment**

Congenital PV stenosis is a very rare lesion, which has been noted to occur in about 0.4% of congenital heart defects [5]. One or multiple veins may be affected. Histologically, the lesion is characterized by fibrous intimal thickening in most cases and medial hypertrophy in many [6]. Congenital PV stenosis can be fatal even when it is unilateral. The first surgical repair of congenital PV stenosis was reported by Kawashima and colleagues in 1971 [7]. Surgical approaches have evolved over the years, with techniques such as suture and sutureless methods gaining popularity. The outcomes of repair, as shown in Figure 2, indicate that sutureless marsupialization has a significant advantage in survival compared to other methods.

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**Table 3. Risk Factors for Poor Outcome (Cox Proportional Hazards)**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>p Value</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated defect</td>
<td>0.02</td>
<td>1.36</td>
<td>0.27–2.5</td>
</tr>
<tr>
<td>Nonmarsupialization procedure</td>
<td>0.04</td>
<td>1.13</td>
<td>0.07–2.2</td>
</tr>
<tr>
<td>Bilateral (diffuse) disease</td>
<td>0.03</td>
<td>1.14</td>
<td>0.10–2.2</td>
</tr>
</tbody>
</table>

CI = confidence interval.
years, but results have been generally disappointing. Diffuse restenosis has been documented as a significant cause of late mortality after repair [8].

Acquired PV stenosis may be anatomically localized to the anastomosis, in which case the natural history is more favorable, or the stenosis may extend diffusely into the branch pulmonary veins. The latter behaves in a fashion similar to the congenital form of the disease. Unfortunately, in practice it can sometimes be difficult to distinguish these forms of acquired PV stenosis at the time of presentation. Acquired PV stenosis occurs in approximately 7% to 11% of early survivors after total anomalous pulmonary venous connection repair [6, 9, 10]. Results of repair of acquired PV stenosis have also been less than optimal due to the problem of restenosis [11, 12].

All conventional surgical approaches have created potential injury to the pulmonary vein wall either by direct suturing or stent placement. Early in our series, stenting was attempted in several patients. The results obtained at our center and others have been poor, and we have abandoned this technique for this application [13]. It is possible that, in the future, drug-eluting stents such as those used to treat coronary artery disease might play a role in the treatment of recurrent PV stenosis. The technique of pericardial marsupialization was introduced to minimize injury to the pulmonary vein wall by avoiding direct suturing of the vein. Reports from other centers using SPM have shown promising results [2, 4].

Some centers have offered lung or combined heart-lung transplantation for the treatment of pulmonary vein stenosis [14]. This approach has been less than optimal due to the high mortality incurred while on the waiting list and due to poor long-term graft survival.

In this report, we have reviewed the results of surgical repair of congenital and acquired PV stenosis using several techniques. Restenosis remains a significant problem for this patient population. In most cases, late deaths were secondary to restenosis. The data presented here suggest that congenital etiology, presence of associated defects, and bilateral (diffuse) disease are significant risk factors for mortality and restenosis. The technique of sutureless marsupialization was found to be a statistically significant protective factor by Kaplan-Meier techniques and Cox proportional hazards. Since the technique was not adopted at our center until 1998, follow-up in these patients is more limited. At our center, SPM has become the preferred initial approach for patients with either congenital or acquired PV stenosis. In some cases of acquired PV stenosis, anastomotic revision alone may still be appropriate. However, if additional risk factors are present, a better approach may involve a revision in conjunction with SPM.

Limitations of this study include its retrospective nature, small patient numbers, and limited follow-up. It remains clear that PV stenosis remains a difficult clinical problem, but sutureless pericardial marsupialization appears to offer improved outcomes. Longer follow-up will be required to confirm its efficacy.

**References**


**DISCUSSION**

DR CHRIS CALDARONE (Toronto, ON, Canada): I would like to congratulate Dr Devaney on a lucid presentation and commend the Ann Arbor group for employing a novel surgical repair to deal with a challenging problem of pulmonary vein stenosis. The authors use a surgical technique, “sutureless pericardial marsu-
At the Hospital for Sick Children in Toronto we have maintained a great interest in the underlying pathophysiology of pulmonary vein stenosis and this procedure’s potential applications. At recent count, we have performed over 40 of these procedures, but because of the small numbers involved complex statistical analyses are difficult to perform. Which raises one small point: I noticed that in the manuscript you lumped death and restenosis together in your multivariable analysis. Although that does increase statistical power, certainly from the point of view of patients, it is not an identical outcome. I hope the following questions will be of interest to the Society.

First, it has been our observation that post-repair pulmonary vein stenosis appears to have three basic subtypes. The most minimal form of the disease is limited to the anastomotic area with sparing of the pulmonary veins and confluence, suggesting a technical error or imperfection at the time of initial repair. The intermediate form is limited to the pulmonary venous confluence in addition to the anastomotic area. And the most extensive form of the disease includes a fibrous reaction extending retrograde deep into the lung parenchyma. In this subset I am somewhat skeptical that any surgical procedure will reverse this process.

With these observations in mind, my first question is whether in your series the success or failure of this procedure was linked to the extent of pathology, and are there specific anatomic subsets in which the technique is of greater benefit?

My second question is related to the pathophysiologic basis behind the apparent success of the sutureless technique for post-repair pulmonary vein stenosis. Would you please share with us your thoughts on why the procedure may be efficacious at all? Does it simply limit imperfections by avoiding suture-induced geometric distortion of the cut edges of the pulmonary veins? Does lack of suture material or handling actually reduce local inflammation? Or, by widely opening the pulmonary veins, does it simply delay but not alter the inevitable progression of the disease?

Finally, my third question is related to expanding the indications for the procedure. Because of favorable results similar to yours and a favorable safety profile, we have expanded our indications for this procedure to patients felt to be at risk for future pulmonary vein stenosis. This indication includes primary repair of total anomalous pulmonary venous connection in patients with a small pulmonary venous confluence or some other anatomic feature suggesting future obstruction, and in some patients with single ventricle physiology and pulmonary vein distortion in whom an increase in pulmonary blood flow can be expected at a palliative procedure.

Because our ability to predict future pulmonary vein stenosis is limited, however, testing the hypothesis that prophylactic use of this sutureless technique will be difficult without better predictive models or some type of prospective trial. With this in mind, would you please comment on the appropriateness of expanding the indications for the sutureless technique to the primary procedure designed to prevent pulmonary vein stenosis.

Once again, I enjoyed your presentation and enjoyed the opportunity to review this paper.

And to the last question of the discussant, is it appropriate to use the sutureless procedure to prevent pulmonary vein stenosis beforehand in any TAPVD (total anomalous pulmonary venous drainage) patients primary operation? The Schumacker modification of the old Senning procedure, which nobody does any more, was something like the sutureless procedure for pulmonary vein stenosis, because you just incise the right-sided veins and put the pericardium around to get the pulmonary veins Senning tunnel.

DR DEVANEY: First of all, I would like to acknowledge the pioneering work of Dr Caldaroni and Dr Coles in Toronto with their great work and really reintroducing this technique. I first will address some of his questions and try to answer them as best I can.

The first question, I think, involved a question regarding the extreme heterogeneity of this clinical problem. Clearly, patients present with a wide variety of stenosis, and certainly there is no question that patients with localized disease, such as those that may occur after repair of total veins, are going to fare better than those who have the real more severe form of the disease with stenosis extending into the hilum of each lung. Clearing, there is not much surgically that can be done for those patients. However, certainly we did evaluate this in the manuscript by looking at the extent of disease based on bilaterality. Patients that had bilateral disease tended, on the whole, to have the more severe diffuse form of the disease.

The second question involved why does the procedure work? Well, I really don’t know. We haven’t done any laboratory investigation studying this disease process, but I think you touched on the main principles that I think are important, which is really a no-touch technique.

As you may know, the histology of the pulmonary vein stenosis involves severe intimal fibrosis and thickening, and the concern is that any injury to the intima might stimulate progression of this fibrosis. Therefore, using a sutureless technique and really minimizing any injury to the wall of the vein I think is an important factor in the success of this procedure. You may be right that perhaps just making a wide open communication may just be delaying the inevitable, but even given our relatively limited follow-up time, I think the technique has certainly showed quite a bit of promise.

Your next question regarded whether we should be expanding the indications of this technique, and you use as an example whether we should be doing it for all patients with total veins, or at least some subset of patients. Well, just looking at all patients that undergo repair of total anomalous pulmonary venous connection, the incidence of acquired pulmonary vein stenosis is about 10%, looking at a number of different series, which means that 90% of patients actually do pretty well, and I think it may be difficult to decide which patients are going to do poorly. But you may be right; patients that have a very small left atrium may be good candidates for this technique, and I think it would be interesting to apply it to this subset of patients with total veins.

And the final discussant’s question regarded the technique of left-sided marsupialization. Our technique is really quite similar. We do on occasion incorporate the left atrial appendage, but it really can be done in a very analogous fashion. And I think the discussant hit it right on the head. This is really old technology or an old technique that has been rejuvenated recently. I believe it was originally described by Dr Senning and was revived by Drs Lacour-Gayet, Coles, and colleagues in applying this technique to this clinical problem.

Again, I thank everyone for your attention and I appreciate the opportunity to present the data today. Thanks.