Midterm and Long-term Results of Percutaneous Endovascular Treatment of Venous Outflow Obstruction after Pediatric Liver Transplantation

Francisco C. Carnevale, MD, PhD, Alexandre T. Machado, MD, Airton M. Moreira, MD, PhD, Miguel A. De Gregorio, MD, PhD, Lisa Suzuki, MD, PhD, Uenis Tannuri, MD, PhD, Nelson Gibelli, MD, Joao G. Maksoud, MD, PhD, and Giovanni G. Cerri, MD, PhD

PURPOSE: To evaluate retrospectively the midterm and long-term results of percutaneous endovascular treatment of venous outflow obstruction after pediatric liver transplantation.

MATERIALS AND METHODS: During a 9-year period, 18 children with obstruction of a hepatic vein (HV) or inferior vena cava (IVC) anastomosis underwent percutaneous transluminal angioplasty (PTA) with balloon dilation or stent placement in case of PTA failure after liver transplantation. Patients’ body weights ranged from 7.7 kg to 42.6 kg (mean, 18.8 kg ± 9). Potential predictors of patency were compared between balloon dilation and stent placement groups.

RESULTS: Forty-two procedures were performed (range, 1–11 per patient; mean, 2). Technical and initial clinical success were achieved in all cases. Major complications included one case of pulmonary artery stent embolization and one case of hemothorax. Three children (25%) with HV obstruction were treated with PTA and nine (75%) were treated with stent placement. Three children with IVC obstruction (75%) were treated with PTA and one (25%) was treated with a stent. There were two children with simultaneous obstruction at the HV and IVC; one was treated with PTA and the other with a stent. Cases of isolated HV stenosis have a higher probability of patency with balloon-expandable stent treatment compared with balloon dilation (P < .05). Follow-up time ranged from 7 days to 9 years (mean, 42 months ± 31), and the primary assisted patency rate was 100% when stent placement was performed among the first three procedures.

CONCLUSIONS: In cases of venous outflow obstruction resulting from HV and/or IVC lesions after pediatric liver transplantation, percutaneous endovascular treatment with balloon dilation or stent placement is a safe and effective alternative treatment that results in long-term patency.


Abbreviations: HV = hepatic vein, IVC = inferior vena cava, PTA = percutaneous transluminal angioplasty

ONE of the main factors for success in liver transplantation is the patency of vascular reconstructions, which allows efficient perfusion and drainage of the transplanted organ. In pediatric patients, factors such as donor and recipient differences in hepatic vein (HV) and inferior vena cava (IVC) diameters, neo-intimal hyperplasia, graft growth, children’s growth rates, and the possibility of graft torsion in the anastomosis line all increase the risk of vascular complications and may negatively impact outcomes (1–4).

The development of new techniques such as living-donor, split-liver, and reduced-size liver transplantation has increased the number of grafts available for transplantation and consequently reduced the mortality rates and time spent on transplant waiting lists (5–9).

Despite the great progress achieved in the management and control of immune and infectious complications associated with transplantation, there has been a relative increase in vascular complications following anastomoses involving small structures in trans-
plant recipients (10–14). According to the literature, the incidence of stenosis in the HV anastomosis after liver transplantation in children is approximately 2% (2,5,10,15,16).

Percutaneous angioplasty with or without stent placement is a safe and effective method for the treatment of vascular lesions (17–20). PTA with balloon dilation has become the first therapeutic option for the management of vascular complications following liver transplantation (10,14,18,21–23).

The use of endovascular techniques is relatively new in the pediatric population, and there is no agreement on the best therapeutic approach to be used in these patients. One of the issues relevant in pediatric transplant recipients is the influence of interval growth of the child on the site of endovascular therapy. Few reports have been published to address the use of angioplasty in pediatric liver transplant recipients, and these have included small numbers of patients and limited follow-up times (17–19). In the present work, we aimed to investigate midterm and long-term outcomes in pediatric liver transplant recipients with HV and/or IVC stenosis undergoing percutaneous endovascular treatment.

**MATERIALS AND METHODS**

Eighteen children who underwent PTA with balloon dilation and/or stent placement in case of PTA failure for the treatment of venous outflow obstruction after liver transplantation were referred to our pediatric interventional radiology center over a 9-year period (March 1998 to June 2007). This retrospective study was approved by our institutional review board. We performed a chart review of all children sent to our institution who had undergone liver transplantation and angioplasty with or without stent placement for HV and/or IVC venous outflow obstruction (Tables 1, 2). Patients included 10 girls and eight boys whose ages ranged from 10 months to 14.5 years (mean, 4.7 y) and whose body weights ranged from 7.7 kg to 42.6 kg (mean, 18.8 kg ± 9). Indications for liver transplantation in these patients were biliary atresia, Alagille syndrome, primary sclerosing cholangitis, autoimmune hepatitis, fulminant hepatic failure, congenital hepatic fibrosis, and Caroli disease. Ten patients (55.5%) received a hepatic graft from a living donor and eight (44.5%) received a graft from a cadaver donor. HV-to-IVC reconstruction (ie, “piggyback technique”) was performed in 13 children and IVC-to-HV reconstruction was performed in five children with use of 4–0 or 5–0 Prolene running suture.

The graft was reperfused after completion of the portal vein anastomosis, and surgical reconstruction of the artery was then performed. Finally, the bile duct reconstruction was performed with use of a Roux-en-Y limb of the jejunum.

The diagnosis of venous outflow system obstruction or patency was based on clinical and laboratory data, Doppler ultrasound (US) findings, and liver biopsy. Ascites, pleural effusion, persistent hyponatremia, lower-extremity edema, and hepatomegaly were seen in most patients. Abnormal liver biopsy findings showed moderate to severe venous congestion in zone 3 with central vein and sinusoidal dilation. The most prevalent Doppler US findings were increased blood flow velocity, abnormality of the waveform, and increased resistance index blood flow.

Doppler US examinations were performed by one pediatric radiologist with use of an SSD-2000 Multi-view (Aloka, Tokyo, Japan) or Logic 500 or Logic 7 scanner (GE Medical Systems, Milwaukee, Wisconsin) with a 5.0-MHz or 2.0–5.0-MHz convex probe. All examinations were performed with the patient in the supine or left lateral decubitus positions, without breath-holding or sedation. Patients had usually fasted for 2–3 hours before the examination. Images of the spectral Doppler waveform of the HV were obtained at least twice in each examination. The angle-corrected highest peak velocity was measured in two segments of the vein: at the anastomosis or narrowest portion of the HV/IVC and in the main HV trunk 1–2 cm proximal to the HV/IVC anastomosis. Because it is not always possible to define the exact location of the HV anastomosis, many times the narrow-segment measurement was taken in the narrowest segment between the HV and IVC, guided by the flow (usually aliasing is present in the narrowest portion). The ratio between the two velocity rates was calculated. Spectral Doppler waveform of the HV was classified as monophasic (ie, flat or minimal oscillation flow), multiphasic (ie, oscillation of >50% of the distance between the baseline and peak diastolic flow), or triphasic (ie, flow with a reversed phase).

After the diagnosis of venous outflow obstruction was confirmed, children underwent angiographic evalua-
tion with endovascular treatment under general anesthesia. Vascular access was performed through the right internal jugular vein in all children, followed by IVC angiography with a 5-F pigtail catheter (Boston Scientific, Natick, Massachusetts) and selective catheterization of the HV with a 5–6-F diagnostic 3.5 right Judkins catheter (Boston Scientific). In patients in whom simultaneous dilation of the HV and IVC was needed, additional vascular access was performed through the right common femoral vein. An angulated 0.035-inch hydrophilic Glidewire (Terumo, Somerset, New Jersey) was used to traverse the vascular system.

Angiography was performed to identify the site of stenosis and measure the diameter of the involved vessels. Materials were chosen based on the vascular diameter measurements performed by angiography with a centimeter-sizing pigtail catheter (Cook, Bloomington, Indiana) and/or with the stenosis measurement program of the Integris Allura angiography equipment (Philips, Best, The Netherlands). Pressure gradients were measured proximal and distal to the lesion, in the right atrium, and in the IVC (inferior and superior to anastomosis lines) with the diagnostic catheter. Gradient values greater than 5 mm Hg were considered hemodynamically significant.

Before dilation, patients received 50–100 IU of heparin based on body weight. Then, two extended dilations (2 minutes each) were performed with use of angioplasty balloons (Ultra-thin; Boston Scientific). We overdilated strictures with balloons by 10%–30% compared with normal-diameter veins. Balloon sizes used were 8–14 mm in diameter by 20–40 mm in length for HV stenoses and 10–20 mm in diameter by 20–40 mm in length for IVC stenoses. After the procedure, a control angiogram was obtained and diagnostic catheter, obstruction dilation with full expansion of the balloon and diagnostic catheter, obstruction dilation with full expansion of the balloon or stent, a gradient less than 5 mm Hg across the lesion, and less than 30% residual stenosis on follow-up venography. Whenever any finding suggested stenosis recurrence, patients underwent a new diagnostic angiography examination.

Technical success was defined by successful traversal of the venous outflow obstruction. Whenever any finding suggested stenosis recurrence, patients underwent a new diagnostic angiography examination.

Technical success was defined by successful traversal of the venous outflow obstruction. Whenever any finding suggested stenosis recurrence, patients underwent a new diagnostic angiography examination.

Technical success was defined by successful traversal of the venous outflow obstruction. Whenever any finding suggested stenosis recurrence, patients underwent a new diagnostic angiography examination.

Technical success was defined by successful traversal of the venous outflow obstruction. Whenever any finding suggested stenosis recurrence, patients underwent a new diagnostic angiography examination.

Technical success was defined by successful traversal of the venous outflow obstruction. Whenever any finding suggested stenosis recurrence, patients underwent a new diagnostic angiography examination.

Technical success was defined by successful traversal of the venous outflow obstruction. Whenever any finding suggested stenosis recurrence, patients underwent a new diagnostic angiography examination.

Technical success was defined by successful traversal of the venous outflow obstruction. Whenever any finding suggested stenosis recurrence, patients underwent a new diagnostic angiography examination.

**Table 2 Patient and Liver Transplantation Data**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Birth Date</th>
<th>Weight (kg)</th>
<th>Indication for Transplantation</th>
<th>Transplantation Date</th>
<th>Venous Reconstruction*</th>
<th>Diagnostic Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>10/1/90</td>
<td>27.0</td>
<td>Primary sclerosing cholangitis</td>
<td>9/25/00; living donor</td>
<td>Left and middle HV–left and middle HV</td>
<td>Biopsy</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>8/4/87</td>
<td>33.9</td>
<td>Autoimmune hepatitis</td>
<td>6/8/98; living donor</td>
<td>Left HV–IVC</td>
<td>Duplex US</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>7/12/99</td>
<td>14.0</td>
<td>Fulminant hepatic failure</td>
<td>10/9/00; living donor</td>
<td>Left HV–IVC</td>
<td>Biopsy</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>10/14/98</td>
<td>14.3</td>
<td>Biliary atresia</td>
<td>8/4/02; living donor</td>
<td>Left HV–IVC</td>
<td>Duplex US</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>6/14/90</td>
<td>42.6</td>
<td>Congenital hepatic fibrosis</td>
<td>11/27/00; living donor</td>
<td>Left HV–IVC</td>
<td>Biopsy</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>10/27/97</td>
<td>16.5</td>
<td>Biliary atresia</td>
<td>1/25/01; cadaveric donor</td>
<td>Left HV–IVC</td>
<td>Biopsy</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>7/1/99</td>
<td>15.1</td>
<td>Biliary atresia</td>
<td>1/22/03; cadaveric donor</td>
<td>Left HV–IVC</td>
<td>Biopsy</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>8/12/93</td>
<td>28.0</td>
<td>Biliary atresia</td>
<td>8/26/00; living donor</td>
<td>Left HV–IVC</td>
<td>Biopsy</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>8/5/98</td>
<td>15.0</td>
<td>Alagille syndrome</td>
<td>2/10/03; living donor</td>
<td>Left and middle HV–left and middle HV</td>
<td>Biopsy</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>10/9/98</td>
<td>11.0</td>
<td>Biliary atresia</td>
<td>4/2/01; living donor</td>
<td>Left and middle HV–left and middle HV</td>
<td>Biopsy</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>10/7/96</td>
<td>18.2</td>
<td>Alagille syndrome</td>
<td>6/26/00; living donor</td>
<td>Left and middle HV–IVC</td>
<td>Biopsy</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>3/20/04</td>
<td>7.7</td>
<td>Caroli disease</td>
<td>3/28/05; living donor</td>
<td>Left HV–IVC</td>
<td>Duplex US</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>10/16/99</td>
<td>14.0</td>
<td>Alagille syndrome</td>
<td>12/27/04; cadaveric donor</td>
<td>Cava interposition</td>
<td>Duplex US</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>7/11/99</td>
<td>15.0</td>
<td>Alagille syndrome</td>
<td>3/9/04; cadaveric donor</td>
<td>Cava interposition</td>
<td>Biopsy</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>2/10/98</td>
<td>26.5</td>
<td>Biliary atresia</td>
<td>3/23/04; cadaveric donor</td>
<td>Cava interposition</td>
<td>Duplex US</td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>4/5/98</td>
<td>17.2</td>
<td>Biliary atresia</td>
<td>8/13/03; cadaveric donor</td>
<td>Cava interposition</td>
<td>Duplex US</td>
</tr>
<tr>
<td>17</td>
<td>F</td>
<td>5/22/99</td>
<td>16.0</td>
<td>Biliary atresia</td>
<td>10/1/02; cadaveric donor</td>
<td>Cava interposition</td>
<td>Duplex US</td>
</tr>
<tr>
<td>18</td>
<td>M</td>
<td>5/22/97</td>
<td>8.0</td>
<td>Biliary atresia</td>
<td>12/29/97; living donor</td>
<td>Cava interposition</td>
<td>Biopsy</td>
</tr>
</tbody>
</table>

* Displayed as donor–recipient where applicable.
patients with sufficient follow-up. Primary patency was defined as the interval between initial dilation (with balloon or stent placement) and first presentation for outflow obstruction requiring percutaneous venography. Primary assisted patency was defined as patency after initial dilation until treatment with repeated percutaneous dilation or stent placement.

Initial univariate analysis of potential predictors of patency was performed with Cox analysis (Medcalc Software, Mariakerke, Belgium). These factors were patency comparing HV angioplasty with a balloon versus HV stent placement. P values less than .05 were considered to indicate a significant difference.

RESULTS

From March 1998 to June 2007, a total of 18 children with venous outflow obstruction (ie, HV lesion, IVC lesion, or both) underwent endovascular treatment with PTA or stent placement. The technical success rate in dilating or placing a stent in the lesion was 100%. Children's weights ranged from 7.7 kg to 42.6 kg (mean, 18.9 kg), and the youngest patient treated was 10 months of age.

Indications for an endovascular approach to treatment were based on clinical data and laboratory abnormalities compatible with venous efflux obstruction confirmed by a combination of liver biopsy and US in eight children (44.4%) and by US in 10 children (55.6%). Follow-up time ranged from 7 days to 9 years (mean, 42 months ± 31).

Loss of follow-up occurred in five treated children (27.8%), all of whom had patent venous outflow anastomoses at the time of last follow-up. One of these children (patient 16) had acute obstruction of the IVC and HV anastomoses on the first day after liver transplantation as a result of graft twisting at the suture line. This patient had primary stents placed simultaneously in the HV and IVC on the second postoperative day, with significant clinical and laboratory improvement after the procedure. However, the patient died 9 days after transplantation as a result of massive central nervous system bleeding.

Another patient (patient 5) was initially treated with PTA in the HV and needed another PTA procedure in the HV and IVC as a result of recurrence of the stenosis, which was performed with the “kissing balloon” technique 3 months after the first procedure. The patient remained asymptomatic for 6 months, after which a stent was implanted in the HV for recurrence of the HV anastomosis stenosis. Six months later, the patient underwent placement of a new stent in the HV as a result of recurrence of the stenosis at the proximal edge of the stent near the IVC. At this time, a balloon was placed in the IVC to protect against stent migration during deployment. Despite significant clinical and laboratory improvement, the patient died 30 days after the last procedure as a result of lymphoproliferative disease. The overall patency time was 16 months. Two other children (patients 7 and 9) underwent PTA in the HV and IVC, respectively, with good results until death as a result of hepatic chronic rejection 6 months and 1 month after the procedure, respectively. Patient 13 had IVC stenosis and underwent PTA 1 month after transplantation. The patient died of sepsis secondary to subphrenic abscess 3 months after PTA.

A total of 42 endovascular proce-
dures were performed (range, 1–11 per patient; mean, 2). Nine children (50%) with an isolated lesion at the HV and four (22.2%) with an isolated lesion at the IVC were treated with balloon dilation or stent placement. Three children (16.7%) had initial HV stenoses that progressed to IVC impairment and had to be treated with multiple interventions. Two (11.1%) had simultaneous initial lesions at the HV and IVC. One of these with stenosis after liver transplantation was treated with balloon dilation, and the other was treated with two stents in the HV and IVC with the kissing stent technique the day after liver transplantation (Tables 3, 4).

Regarding the patients with obstruction at the HV \((n = 12)\), the obstruction resolved in three children (25%) with PTA and in nine (75%) with stent placement after failure of balloon dilation. Figure 4 shows that isolated HV stenoses are associated with a higher probability of patency with stent placement than balloon dilation alone at follow-up \((P < .05)\). Among children with an initial lesion at the HV, three cases (25%) progressed to involve the IVC. Two of these cases were those with the worst results in the present study (patients 1 and 5).

Concerning the children with an isolated lesion at the IVC \((n = 4)\), three lesions (75%) resolved with PTA balloon dilation and one (25%) resolved with primary stent placement as a result of early stenosis at posttransplantation day 11.

In the patients with simultaneous obstructive lesions at the HV and IVC \((n = 2)\), resolution was achieved with PTA in one case and primary stent placement in the other.

All treated veins were patent at the day of last follow-up or at the time of death unrelated to the procedure or the venous outflow blockage. All patients with an isolated lesion at the IVC \((n = 4)\) were treated successfully with only one intervention, and three patients with an isolated HV lesion did well with PTA balloon dilation.

Table 3

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Total Procedures</th>
<th>Procedure Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>2</td>
<td>Procedure 1: HV PTA Procedure 2: HV stent</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>Procedure 1: HV PTA, IVC PTA Procedure 2: HV PTA, IVC PTA</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>Procedure 1: HV PTA Procedure 2: HV stent Procedure 3: IVC PTA</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>Procedure 1: HV PTA Procedure 2: IVC PTA Procedure 3: HV stent</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>Procedure 1: HV PTA Procedure 2: IVC PTA</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>Procedure 1: HV PTA</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>Procedure 1: HV PTA</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>Procedure 1: IVC PTA</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>Procedures 1–3: HV PTA</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
<td>Procedure 2: HV PTA, IVC PTA</td>
</tr>
<tr>
<td>12</td>
<td>2</td>
<td>Procedure 1: HV PTA Procedure 2: IVC PTA</td>
</tr>
<tr>
<td>13</td>
<td>1</td>
<td>Procedure 1: IVC PTA</td>
</tr>
<tr>
<td>14</td>
<td>1</td>
<td>Procedure 1: IVC PTA</td>
</tr>
<tr>
<td>15</td>
<td>1</td>
<td>Procedure 1: IVC stent</td>
</tr>
<tr>
<td>16</td>
<td>1</td>
<td>Procedure 1: IVC stent</td>
</tr>
<tr>
<td>17</td>
<td>2</td>
<td>Procedure 1: HV PTA</td>
</tr>
<tr>
<td>18</td>
<td>1</td>
<td>Procedure 1: HV PTA</td>
</tr>
</tbody>
</table>

Table 4

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No. of Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>HV PTA</td>
<td>18</td>
</tr>
<tr>
<td>HV stent</td>
<td>9</td>
</tr>
<tr>
<td>HV PTA, IVC PTA</td>
<td>7</td>
</tr>
<tr>
<td>IVC PTA</td>
<td>4</td>
</tr>
<tr>
<td>IVC stent</td>
<td>1</td>
</tr>
<tr>
<td>HV PTA, IVC stent</td>
<td>1</td>
</tr>
<tr>
<td>HV stent, IVC stent</td>
<td>1</td>
</tr>
<tr>
<td>HV stent, IVC PTA</td>
<td>1</td>
</tr>
</tbody>
</table>
alone. More than one intervention was needed in 10 patients (55.5%). In six patients (60%), there was an isolated restenosis of the HV, and all were treated successfully with stent placement. Another child (patient 11) had HV stenosis that progressed to the IVC and was treated successfully with IVC balloon dilation and HV stent implantation. The patient with simultaneous HV and IVC lesions (patient 3) showed a good response to simultaneous PTA with the kissing balloon technique, and the two other patients had HV restenosis that progressed to the IVC and required multiple interventions (one and three additional interventions, respectively).

Three children in whom venous outflow obstruction developed had undergone repeat liver transplantation as a result of graft problems. All patients received a second transplant with use of the piggyback technique, and two developed stenosis of the HV and the other IVC stenosis.

Table 5 shows the characteristics of balloons and stents and the numbers of procedures required to treat all the lesions. The time interval between liver transplantation and the first endovascular procedure ranged from 2 days to 32 months (mean, 8 months).

Regarding the technical success and primary patency associated with the type of procedure, PTA alone was performed in seven children (three with HV stenosis, three with IVC stenosis, and one with simultaneous stenosis of the HV and IVC). All patients were asymptomatic and the treated lesions were patent at the time of last follow-up when stents were used. In the patients with an isolated HV stenosis, better results were observed when stent placement was performed. The patency rate was 100% in the stenotic lesions when stents were placed in as many as three PTA procedures (range, 7 d–9 y; mean, 42 months).

Two major complications associated with the procedure were observed in our group of patients (two of 43 procedures; 4.6%). The first was a hemothorax during right internal jugular vein catheterization that was successfully treated with pleural drainage and the second was a stent displacement with consequent left pulmonary embolization retrieved with endovascular techniques. This child developed a stenotic lesion at the HV anastomosis that was initially treated with four consecutive balloon dilations. Because of the stenosis recurrence, a stent (Jostent P-17; Abbott, North Chicago, Illinois) was placed at the HV during the fifth procedure. An undesirable shortening of the stent was observed after its deployment, but nothing was done because of the satisfactory angiographic and pressure findings at the end of the procedure. The child was discharged the day after the procedure but returned with sudden chest pain, dyspnea, and hemoptysis 3 days after stent placement. Chest radiography confirmed stent embolization to the left pulmonary artery. The stent was taken out through the right common femoral vein with an Amplatz Goose Neck snare (Microvena, White Bear Lake, Minnesota). Phlebotomy was performed to facilitate stent withdrawal and reduce the risk of vascular lesion.

DISCUSSION

The development of new liver transplantation techniques such as living-donor, split-liver, and reduced-size transplantation has led to a significant increase in the number of organs available for transplantation and a consequent reduction in morbidity and mortality related to prolonged time waiting for a suitable organ. Conversely, the numbers of vascular and nonvascular complications have also increased significantly (18–20,24).

Hepatic venous outflow obstruction is an uncommon complication after liver transplantation, the reported incidence of which ranges from 1% to 7% (5,25–27). In children, the incidence of stenosis in the HV anastomosis after

![Figure 4. Long-term follow-up comparing the probability of patency of HV angioplasty with balloon dilation and HV angioplasty with balloon-expandable stent placement. Isolated HV stenoses have a greater probability of patency with stent treatment than with balloon treatment alone at late-term follow-up ($P < .05$).](image)
liver transplantation is approximately 2% (2,5,10,15,16). For piggyback orthotopic whole-liver transplantation, the incidence of HV outflow obstruction ranges from 1.5% to 2.5% (26,27) and the mortality rate has been reported to be as high as 24% (26). Different possible reasons have been suggested for venous outflow occlusion after liver transplantation. Possible causes in the immediate posttransplantation period include direct compression of the vein by a graft that is too large, twisting of the venous Anastomosis when a graft that is too small slides out of place, excessively tight sutures, and venous congestion of the graft with resultant extrinsic compression of the venous Anastomosis. Posttransplantation HV outflow obstruction is likely secondary to intimal hyperplasia and fibrotic change at the site of the anastomosis (20,26,27). Parrilla et al (27) reported that the incidence of HV outflow obstruction was significantly lower (0.28% vs 1.6%) when the patch of supraportal veins was composed of three vessels (ie, right, middle, and left) instead of the traditional two (ie, middle and left).

The incidence of venous outflow obstruction in living-donor and split-liver cadaveric grafts in pediatric patients suggests a higher incidence (2%–9%) than with whole-liver transplantation (1,5,28,29). This is a result of the shorter vascular pedicles, smaller anastomosis diameters, and potential for a size mismatch in children (20). The incidence of venous outflow obstruction in living-donor liver transplantation is higher when left-lobe grafts are used rather than right-lobe grafts (5.8% vs 0.8%) (21). This might be a result of increased anatomic variation of the left HV and the technical challenges presented by the angle and size of the reconstruction (20,29–31). Many complications were observed at the beginning of the pediatric liver transplantation program and in other patients referred to our group.

In the pediatric population undergoing liver transplantation, the same risk factors associated with vascular complications have been identified (17,18,28,31). Technique difficulties related to the reconstruction of the organ involving small structures, as well as to the disproportion between the graft and the receptor, are implied as significant risk factors for vascular complications after liver transplantation in children. Disproportion between the graft and receptor and graft growth can lead to twisting of the vascular structures and torsion of the graft at the anastomoses lines. Special care with the surgical technique, use of fixation points anchoring the graft to the abdominal wall, and the type of vascular reconstruction may all reduce the risk of complications in this set of patients (18,20,28).

Different vascular reconstruction techniques involving the HV have been described, particularly the piggyback type, as well as terminal–lateral reconstruction in the IVC, union of the left and middle HV of the donor, and union of the right, middle, and left HV of the receptor (31). Each transplantation center appears to have special preference and experience with certain techniques. Knowing the technique used in the transplantation procedure is then critical before starting angiographic evaluation and percutaneous interventional procedures. Some authors (31) have reduced the complication rate in the hepatic drainage venous system with use of a broad triangular technique with the receiver’s IVC, also including the HV orifice.

Clinical findings in venous outflow obstruction depend on the type of transplantation and reconstruction technique used. Abdominal pain, ascites, lower-extremity edema, pleural effusion, and hepatosplenomegaly are the most commonly found abnormalities. Hepatic enzymes elevation and persistent hyponatremia can also occur. Differential diagnosis with HV and/or IVC occlusion is crucial for better patient management.

The diagnosis of venous outflow obstruction is suggested by clinical and laboratory abnormalities and is confirmed by US and liver biopsy findings (21). Histopathologic findings correspond to moderate fibrosis in zone 3 as a result of sinusoidal dilation and necrosis areas around the central lobular vein. After treatment of the obstruction, hepatic architecture appeared normal with total reversion of the fibrosis process (Fig 5).

US is considered the best imaging technique to follow patients after endovascular treatment of venous outflow obstruction (32). The noninvasive technique is very effective in the detection of venous flow abnormalities. However, the technique is highly operator-dependent, and better accuracy is observed only for very experienced professionals. High-velocity blood flow and abnormalities in the waveform are suggestive of stenosis (Fig 6). Cavography and HV angiography can then be used to confirm the diagnosis.

At our center, diagnostic and therapeutic angiographic studies in pediatric patients are always performed under general anesthesia and by the same group of interventional radiologists. Vascular access is preferentially performed through the right internal jugular vein for technical reasons. In patients in whom there is a need for double access, the right femoral access is used. In the beginning of our experience, we were not using Doppler US guidance during vascular punctures. This certainly contributed to the hemotherax observed in one patient.

In our opinion, the right Judkins diagnostic catheter seems to be best for selective catheterization of the HV in children after liver transplantation. The catheter is relatively rigid, can be applied with torque, and has a slight angle in its extremity that makes selective HV catheterization easier without opposition against the vein wall and consequent obstruction when placed along the HV anatomic curve.

The type of venous reconstruction between the donor and receptor seems, at least partially, to determine the type of lesion in the transplanted organ. IVC stenosis is related to caval Anastomosis. In the present series of children, the only child with IVC stenosis associated with piggyback reconstruction was a patient who required repeat transplantation and had received a first graft with caval reconstruction (patient 9). We believe an endothelial lesion occurred in the first transplant and its venous reconstruction was the main factor determining the development of stenosis in this patient. Conversely, no association was observed between HV stenosis and the type of venous reconstruction of the graft.

IVC lesions were successfully treated with PTA in three children. Another child (patient 15) was treated with primary stent placement. This patient had reduced-size liver transplantation from a cadaver donor with caval anastomosis. The child had impressive ascites, lower-extremity edema, and right pleu-
ral effusion at day 11 after liver transplantation and had an acute episode of high gastrointestinal hemorrhage that necessitated the use of a Sengstaken-Blakemore balloon. Angiographic study revealed severe stenosis at the superior IVC anastomosis with reduced blood flow. As a result of the case severity and the fact that it occurred in the early postoperative period, primary stent placement was chosen as the preferential therapy. This patient also had hemothorax after jugular vascular access that was successfully treated with chest drainage. The child had a good clinical course after these complications and remains alive with primary patency at 36 months. We believe PTA with a balloon is the best treatment option in patients with IVC obstruction because of the vessel’s anatomic characteristics and because the IVC is more subject to increase in diameter with the child’s growth after this treatment.

Patients with less favorable results were those treated with three or more HV balloon dilations and subsequent stent placement in the HV and IVC. These cases are similar to the initial cases in our experience in which we performed multiple balloon dilations and did not use metallic stent placement. At that time, pediatric surgeons were afraid to use stents in children. Our results have demonstrated that balloon-expandable stents can be safely used even in small children. It is important to note that most pediatric transplant recipients receive adult cadaveric or living-donor graft livers, and that vascular anatomy is big enough to place a stent without problems related to the growth of the child.

As also observed in adult patients (20), stent placement in the pediatric population was associated with very good results when indicated soon after initial PTA failure (11,32–34). We believe that the use of a metallic stainless-steel balloon-expandable stent (10–12 mm in diameter) at the suture line between the HV and the IVC is compatible with the diameter of the HV of a healthy adult. Moreover, the physical characteristics of this kind of stent allows for repeat or additional dilation if needed in the future. Good patency rates seen with the use of metallic stainless-steel balloon-expandable stents have been reported recently (20).

In the present series, the best results were seen in patients with early indications for stent placement (ie, a maximum of three dilations), with a 100% patency rate in this group. After failure of treatment with balloon PTA, we believe angioplasty with stent placement should be performed mainly when the
obstruction is in the HV, and in children with IVC lesions progressing from an HV stenosis. In this population, cases of an isolated HV stenosis are associated with a higher probability of patency at follow-up when treated with balloon-expandable stents versus balloons alone (P < .05; Fig 4). Compared with children who underwent early stent placement, worse results were seen in children with an initial lesion at the HV who were treated with multiple balloon dilations before stent placement.

Sometimes we observed an elastic recoil lesion during balloon angioplasty, which suggested an external force on the suture line resulting from torsion, kinking, compression, or hypertrophy of the graft with consequent obstruction of the HV. This aspect reinforces the idea of using a metallic stent to treat it (20).

Besides the inherent risks associated with vascular access (eg, hematoma, pseudoaneurysm, pneumothorax, hemotherax, thrombosis, and fistulas) and the use of contrast agents (eg, renal failure, allergic reactions), PTA and stent placement are associated with other complications such as dissection, thrombosis, vascular rupture, stent misplacement, and intravascular embolism. One of the major complications was a hemothorax during right internal jugular vein catheterization in a child with an acute episode of high gastrointestinal hemorrhage in whom a Sengstaken–Blake more balloon had been placed to control it. The hemothorax was successfully treated with pleural drainage. The use of Doppler US imaging could have assisted vascular access catheterization and reduce the risk of complications, but it was not used in this procedure. The other complication was a case of stent displacement with consequent pulmonary embolism that was caused by an undesirable shortening and incorrect positioning of the stent. The stent was retrieved with endovascular techniques and femoral phlebotomy was performed to facilitate stent withdrawal and reduce the risk of vascular lesion. The patient developed venous thrombosis in the right femoral vein that was treated during a period of 6 months with oral anticoagulation therapy. Femoral vein recanalization was observed on Doppler imaging examination, and the patient was asymptomatic at follow-up. This is a rare complication that has recently been described in the treatment of HV stricture after liver transplantation (20).

We observed rupture of the angioplasty balloon during IVC dilation in one child. A restenosis developed at the proximal edge of the HV stent that was successfully treated with a new stent protruding into the IVC. Perforation of the balloon was attributed to the stent mesh. No clinical or hemodynamic consequences were seen. This child had significant clinical and laboratory improvement after the second stent placement but died 30 days after the last procedure as a result of lymphoproliferative disease.

The other patient who underwent multiple interventions and stent placement procedures was a 27-kg girl who received a living related donor liver transplant with piggyback technique for primary sclerosing cholangitis. A stenotic lesion developed at the HV anastomosis that was treated with multiple balloon dilations before stent placement and an accidental HV stent embolization treated with placement of another stent. The child was treated with HV and IVC stents placed during different procedures and developed four intrastent restenoses at the HV during follow-up, which were successfully treated with balloon dilations. Because bare stents were used to treat the HV and IVC lesions and there was some difficulty in crossing the HV stent from the jugular approach, recanalization of the HV was performed through a percutaneous transhepatic approach with transposition and dilation of the lesion with the kissing balloon technique. We believe multiple interventions at the endothelium of the IVC and HV transition before stent placement were the cause of restenosis in this child. Despite these procedures, the patient is doing well and exhibited good cumulative venous outflow patency 6 years after liver transplantation.

In our patients, endovascular treatment rescued all the grafts with venous efflux block and kept them functional. In none of the patients was there progression to vascular anastomosis obstruction.

A total of five deaths occurred in the present series, none of which were directly related to the endovascular procedures reported. Causes of death included lymphoproliferative disease, brain hemorrhage, sepsis, and chronic liver rejection in two children.

The use of anticoagulant drugs and antiplatelet aggregation in venous stenosis is still controversial (17). We have systematically recommended 50–100 IU/kg of heparin based on body weight before crossing the obstruction and full-dose heparin for the following 30 days. These transplant recipients also receive aspirin 100 mg/d continuously as hepatic arterial thrombosis prophylaxis. There is also no agreement on the use of antibiotics in these procedures, and we routinely use intravenous first-genera tion cephalosporin prophylactically.

Treatment of venous outflow obstruction after liver transplantation has been reported by different groups who performed venoplasty with balloon or stent placement in adults and children (5,17–20,23,25,28,35,36). The use of metallic stents seems to be more acceptable in light of the good results shown during follow-up (20).

Some experimental studies have investigated the use of retrievable stents, drug-releasing stents, and 1-23brachythrombolytherapy for the treatment of arterial stenosis (37,38). These investigational protocols have been tested in other diseases and scenarios and have demonstrated promising results. It is possible that such approaches will be used in the future for the management of venous outflow restenosis.

Venoplasty with balloon angioplasty alone or with metallic stent placement to treat venous outflow obstruction after liver transplantation remains controversial. The discussion is much more controversial regarding the pediatric population. In all of our children who were treated with stent placement, the stent diameter was compatible with the diameter of a healthy adult HV after vessel analysis. As such, the final diameter of the treated stenosis will not be affected or influenced by the graft or the patient’s growth.

Despite the excellent technical and initial clinical success rates in this group of children, the present study is limited by its retrospective nature and its inclusion of a limited number of patients.

Based on our initial experience, we strongly recommend the use of balloon-expandable stents after recurrence of stenosis after an initial dilation procedure. Balloon-expandable stents have are easily and precisely deployed, and their use seems to reduce the intimal wall injury caused by repeated balloon dilations. In addition, a long duration of patency was observed in this series after stent treatment. Short- and long-term re-
In our patients demonstrate that endovascular treatment of obstruction of venous outflow after liver transplantation in pediatric patients is safe and effective. PTA should be the first choice in the management of these patients. Unsuccessful response to PTA requires metallic stent placement. Even with good results of PTA and stent placement in children, longer follow-up in a study of a greater number of patients is needed to support this idea.

References