ANNALS OF SURGERY
Vol. 227, No. 4, 583–589

Biliary Atresia–Polysplenia Syndrome

Surgical and Clinical Relevance in Liver Transplantation

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Objective

To review a single center's 10-year experience with liver transplantation (LTx) for the biliary atresia–polysplenia syndrome (BA-PS) and to define surgical and clinical guidelines for its management.

Summary Background Data

BA is the most common indication for pediatric liver transplantation (LTx) and is associated with PS in 12% of cases. Only a few studies of LTx for BA-PS have been reported, and the optimal management of BA-PS patients undergoing LTx has yet to be determined.

Methods

From July 1985 to September 1995, 166 liver transplants were performed in 130 patients with BA and were included in the study. The malformations most commonly associated with BA-PS, surgical techniques used to overcome these anomalies, and surgical pitfalls that could have contributed to the outcome were characterized. Actuarial 10-year patient and graft survival for patients undergoing LTx for BA-PS were calculated and compared to those with isolated BA.

Results

Ten patients (7.8%) with BA had associated PS. An additional patient with PS without BA was included in the study. The diagnosis of PS was unknown before the transplantation in 72% of cases. Thirteen liver transplants were performed in these 11 patients. Modifications of the usual surgical technique were used to overcome the complex anatomy encountered. There was no association between the type of anomaly and the outcome, nor were there any significant differences in patient survival (72% *vs.* 73.5%, $p = 0.79$) or graft survival (56.4% *vs.* 54.6%, $p = 0.54$).

Conclusions

The association of BA with various anomalies should be considered a spectrum that may vary widely from patient to patient. The finding of two or more of these malformations in a patient awaiting transplantation should lead the surgeon to look systematically for other associated anomalies. With some special surgical considerations, the outcome in BA-PS patients should not differ from those with isolated BA.

Biliary atresia (BA) is the most common indication for liver transplantation (LTx) in infants and children.[1] It is associated with other congenital abnormalities in 9% to 37% of cases. The most common of these associations is the polysplenia syndrome (PS).[2–17] PS is a constellation of anomalies that can include polysplenia, midgut malrotation, situs inversus, preduodenal portal vein, interrupted or absent infrahepatic vena cava (IVC) with azygous or hemiazygous continuation, abnormal or atypical hepatic arterial supply, symmetric or isomeric liver, and bilobed right lung or pulmonary levoisomerism. Between 6% and 23% of BA patients have at least three components of this syndrome[2–5,7,9–11,13–17]; 31% to 50% of patients with polysplenia present with BA.[2,5]

With the advent of better surgical techniques and an increasing awareness of the vascular anomalies present in PS (*e.g.*, interrupted IVC, preduodenal portal vein, or atypical hepatic arterial supply), it is now possible to offer BA-PS patients the same therapeutic options used in the rest of the BA patients with comparable results.[9,12–15,17] Historically, the main cause of morbidity and mortality in BA-PS was related to the technical challenges encountered during surgery due to the complex surgical anatomy.

The purpose of this study is to present the 10-year expe-

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Table 1. ANATOMICAL FINDINGS IN 11 PATIENTS WITH BA-PS

Pt	Sex	Age	BA	P	AIVC	AHA	PDPV	MR	SI	SL	C	Other
1	F	2.8	+	−	+	+	−		−			
2	F	4.6	+	+	left	−	+	+	+			
3	F	2.2	−	−	+	+	+	+			−	Pancreatic mass
4	F	3.2	+	+	+	+	+	+			VSD	
5	F	0.5	+	?	+	+	+	+	+	+		Ileal atresia
6	M	8.1	+	+	+	+	+	+		+		Short bowell 80cm
7	M	9	+	+	+	+	+	+			VSD	Hepatic veins to atrium
8	F	0.5	+	+	−	+	+		−			
9	M	0.7	+	+	left	−	−	+	+			Lung levoisomerism
10	M	12	+	+	+	+	+		−	+	−	−
11	F	0.9	+	+	+	+	+		−			
Total			10	8	10	9	9	7	3	3	2	

BA-PS, bilary atresia polysplenia syndrome, F, female; M, male; age, in years; BA, biliary atresia; P, polysplenia; AIVA, absent inferior vena cava; AHA, anomalous hepatic artery; PDPV, preduodenal portal vein; MR, malrotation; SI, situs inversus; SL, symmetric liver; C, cardiac malformations; VSD, ventricular septal defect.

rience of the University of Nebraska Medical Center in transplanting BA-PS patients, to evaluate the effect of these anomalies on survival, and to suggest clinical and surgical guidelines for their management.

MATERIALS AND METHODS

Medical charts, operative notes, and pathology reports of 130 patients with BA who received 166 liver transplants at the University of Nebraska Medical Center from July 1985 to September 1995 were analyzed to determine the frequency and kinds of malformations most commonly associated with BA-PS. Surgical techniques used to overcome these problems and surgical pitfalls that could have contributed to the outcome were also characterized. Associations between the type of anomaly (BA-PS *vs.* BA) and the outcome (dead *vs.* alive) were evaluated using the Pearson chi square test. Actuarial 10-year patient and graft survival curves were calculated using the Kaplan-Meier method and compared between groups using the log-rank test.

RESULTS

Ten patients (7.8%) had at least three or more components of BA-PS. An additional patient transplanted for hepatic failure of unknown etiology had PS without BA and was included in the study. Thirteen transplants were performed in these 11 patients with PS, including 9 whole organs and 4 reduced-size allografts, of which 1 was from a living related donor. The diagnosis of BA-PS was not known before the transplant in eight patients; in the three others, not all the PS-associated anomalies had been discovered before that time. The anatomic findings of these patients are summarized in Table 1 and shown in Figures 1 to 3. The type of transplant and surgical complications are summarized in Table 2. The three patients with situs inversus in this series had a normally located heart (situs inversus abdominalis), allowing the grafts to be placed in the midepigastrium.

Ten patients had an anomalous IVC. In eight patients, the infrahepatic IVC was absent, with azygous or hemiazygous venous return continuation. In two patients with situs inversus, a left-sided IVC crossed the midline to join the hepatic veins and form the suprahepatic IVC, outside the substance of the liver. Seven of the eight patients with interrupted IVC had the hepatic veins draining into a short suprahepatic IVC; in the other, the hepatic veins drained directly into the heart, with no detectable IVC (Fig. 4).

The suprahepatic vena caval reconstruction was performed by anastomosing the donor suprahepatic IVC to a

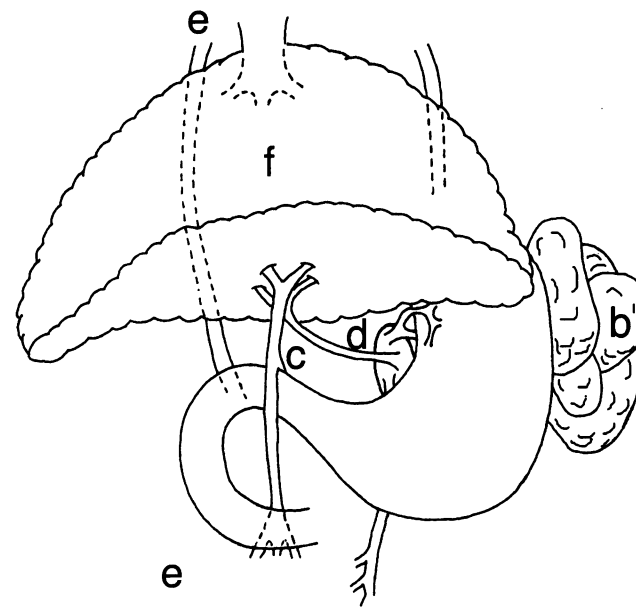

Figure 1. Anatomic malformations in patient No. 10. (a) Extrahepatic biliary atresia (not shown). (b) Polysplenia. (c) Preduodenal portal vein. (d) Anomalous hepatic artery arising directly from the aorta. (e) absent inferior vena cava with azygous continuation. (f) Symmetric liver.

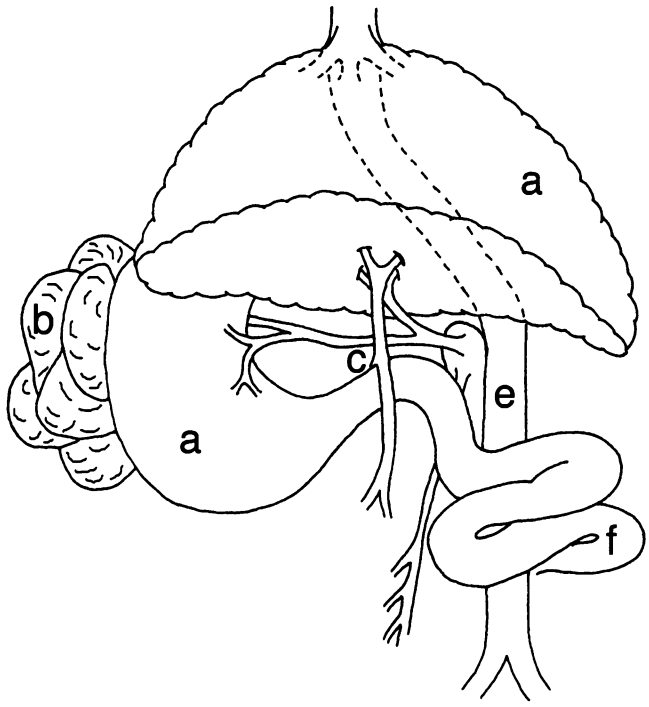

Figure 2. Anatomic malformations in patient No. 2. (a) Situs inversus. (b) Polysplenia. (c) Preduodenal portal vein. (d) Extrahepatic biliary atresia (not shown). (e) Left-sided inferior vena cava. (f) Malrotation.

cloaca of the recipient hepatic veins in 10 cases. In the one case in which the hepatic veins drained directly into the heart, the donor IVC was anastomosed to the most prominent hepatic vein, with ligature of the remaining hepatic vein branches. The distal IVC of the donor was ligated in nine cases and a lower caval anastomosis was performed in two instances, including one patient with a normal IVC and one patient with situs inversus. In the latter, the left-sided IVC was mobilized to allow a tension-free anastomosis (Fig. 5). In the other patient with situs inversus, the left-sided extrahepatic IVC was left *in situ* and the donor IVC anastomosis was performed using the piggy-back technique.

The hepatic artery (HA) was anomalous in 9 of 11 patients, originating directly from the aorta in 4 instances and in 1 case each in the following locations: common superior mesenteric-celiac trunk, superior mesenteric artery, left gastric artery with abnormally positioned celiac trunk, and nondefinable vessel coming from the midportion of the pancreas. A major hepatic artery could not be found in one case (see Figs. 1 to 3). In eight patients, the native HA was used for reconstruction; in three patients, a supraceliac graft was interposed between the donor celiac trunk and the recipient aorta. The donor iliac vessels were used for this purpose (Fig. 6). In four cases, the arterial anastomosis was performed immediately after completing the suprahepatic IVC anastomosis and before completing the abnormal anteriorly positioned preduodenal portal vein anastomosis. Two patients developed HA thrombosis; in both, the anastomosis had been performed to the distal recipient HA bifurcation. Both cases were detected during the first 24 hours after transplantation and were successfully thrombectomized, and the anastomosis was repeated more proximally toward the aorta. Both patients are alive and well with their original grafts.

A preduodenal portal vein (PV) was present in 9 of the 11 cases. The dissection of this vessel was not technically difficult, although it was susceptible to inadvertent damage during early dissection. An end-to-end anastomosis could be performed between the donor PV and that of the recipient in eight patients. In the other patient, the PV was too small, and a dilated coronary vein was anastomosed to the donor PV.

Of the 11 children, 9 are alive. The two deaths, one early and one late, were unrelated to the associated malformations. Patient No. 9 died on postoperative day 2 secondary to pulmonary edema, hypoxia, and severe respiratory acidosis. Patient No. 2 died 4 years after her transplant secondary to chronic rejection and biliary complications. Two patients were retransplanted as a result of rejection 3 and 14 months after their first transplant and are currently doing well with their second grafts.

The outcome of patients with BA-PS and those with isolated BA were compared, and no differences were found. The proportion of patients who died over the 10-year period was not significantly different between the BA-PS and BA groups (2/10 *vs.* 28/120), suggesting that there was no association between the type or number of anomalies and survival ($p = 0.81$, Pearson chi square test). Median survival times were similar between both groups (102 *vs.* 95 months), and the Kaplan-Meier 10-year actuarial patient and graft survival curves were not significantly different (72% *vs.* 73.5%, $p = 0.79$ and 56.4% *vs.* 54.6%, $p = 0.54$; log-rank test).

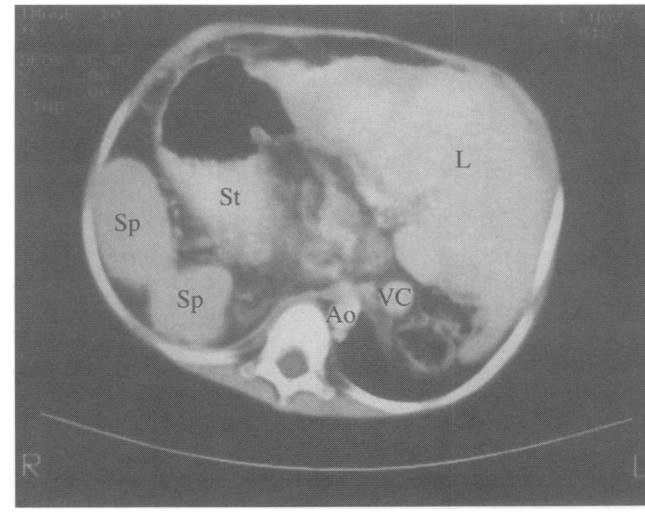

Figure 3. Abdominal computed tomography scan of patient No. 2 with situs inversus. The liver (L) is on the left, the vena cava (VC) is to the left of the aorta (Ao), and the spleens (Sp) and stomach (St) are on the right.

Table 2. TYPE OF TRANSPLANT, HEPATIC ARTERY ANATOMY AND RECONSTRUCTION, SURGICAL COMPLICATIONS AND OUTCOME IN 11 PATIENTS WITH BA-PS

Pt	Tx	HA Origin	Arterial Reconstruction (donor-recipient)	Complications	Status	Survival (*)
1	WL	SMA	CT-proximal HA		Home	3692 d
2	WL	Normal	CT-proximal HA		Dead	1997 d
3	WL	Half pancreas	Supraceliac graft	CCC	Home	3301 d
4	WL	Aorta	CT-proximal HA		Rjx 3mo	–
	Re Tx:RSL				Home	2800 d
5	WL	Common SMA-CT	HA-distal HA (bifurcation)	HAT	Home	2336 d
6	WL	LGA, abnormal CT	Supraceliac graft		Home	2098 d
7	WL	Aorta	CT-distal HA (bifurcation)	HAT	Home	2004 d
8	WL	Aorta	HA-proximal HA		Rjx 14 mo	–
	Re Tx:LR				Home	1390 d
9	RSL	Normal	CT-proximal HA		Dead	2 d
10	WL	Aorta	CT-proximal HA		Home	1011 d
11	RSL	Nonidentifiable	Supraceliac graft		Home	657 d

BA-PS, bilary atresia - polysplenia syndrome, WL, whole liver; Re Tx, retransplanted; RSL, reduced-size liver; LR, living related; HA, hepatic artery; CT, celiac trunk; SMA, superior mesenteric artery; LGA, left gastric artery; CCC, choledochocystocele; HAT, hepatic artery thrombosis; Rjx, rejection.
* as of October 6, 1995.

DISCUSSION

The reported incidence of extrahepatic abnormalities in patients with BA depends on the extent to which these patients are studied in the preoperative setting, during the surgical exploration at the time of the Kasai (if they are subject to LTx), and finally at necropsy. From a cumulative review of the cases reported in the literature,[2–17] one can estimate that 21% of patients with BA have some kind of associated malformation, and that the most common clinical picture is that of PS, which is present in about 12% of the cases.

Despite the increasing number of reports associating BA

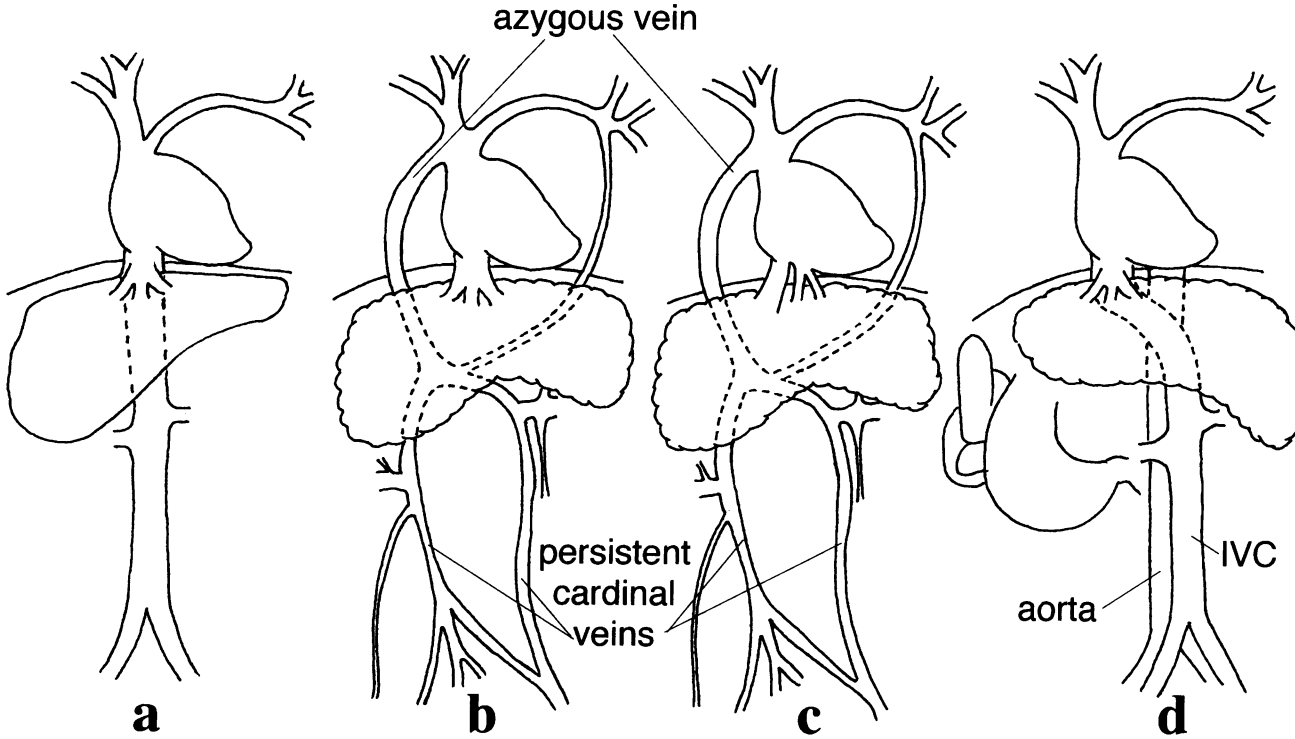

Figure 4. Different types of inferior vena cava (IVC) malformations present in this series. (a) Normal anatomy. (b) Absent IVC with azygous continuation and hepatic veins draining into a short suprahepatic IVC. (c) Absent IVC with azygous continuation and hepatic veins draining directly into the heart. (d) Left-sided IVC, crossing to the right over the aorta to join the hepatic veins.

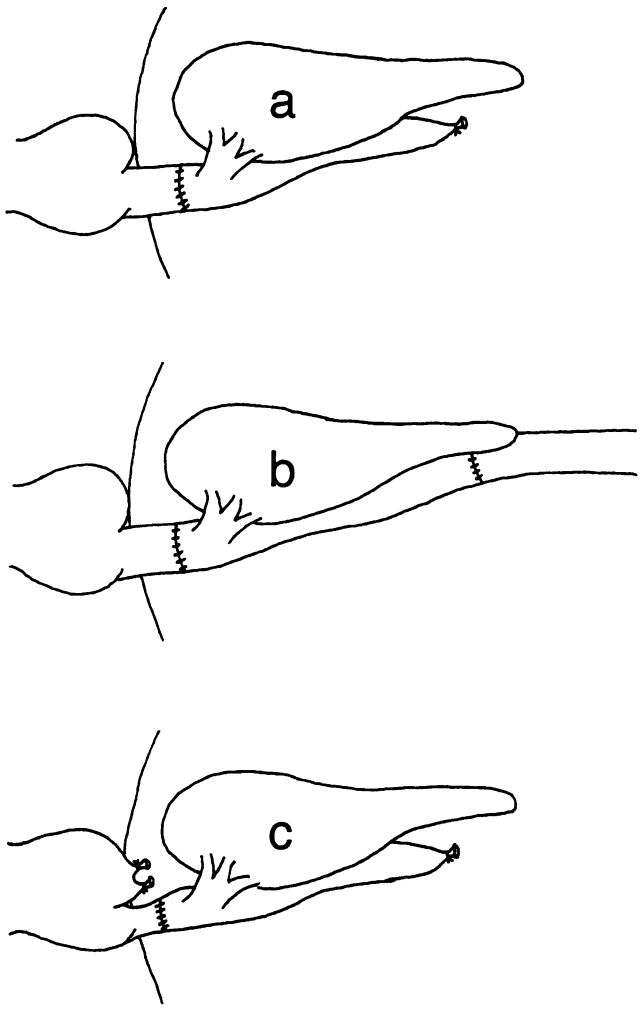

Figure 5. Types of inferior vena cava (IVC) reconstruction. (a) Donor suprahepatic IVC anastomosed to the confluence of the hepatic veins with ligature of the donor infrahepatic IVC. (b) Upper and lower caval anastomoses. (c) Donor suprahepatic IVC anastomosed to the most prominent hepatic vein with ligature of the other hepatic vein branches and of the donor infrahepatic IVC.

with PS over the last two decades.[2–5,7,9–11,13–17] no clear definition of this clinical entity has been stated. Several authors have reported patients with BA and more than three components of PS with a normal spleen[17–19] or asplenia.[6,13,16] However, the association of BA and polysplenia with no other anomaly has also been reported.[13,16] This has created some confusion about which patients should actually be included in this syndrome.[19] Karrer[19] has stated that "there is no compelling reason to arbitrarily require one of the components to be present more than another," and Davenport et al.[16] have suggested the term "biliary atresia splenic malformation syndrome" to encompass all variants.

It becomes more confusing when one analyzes the different reports in the literature, because the detection of a given anomaly depends on the thoroughness of the evaluation. Some components of the syndrome, such as polysplenia and preduodenal PV, can be easily identified during preoperative studies or the initial surgical exploration, but others, such as abnormal HA supply, absent IVC, or pulmonary levoisomerism, are not routinely identified during portoenterostomy and are evident only with wider dissection done at the time of the transplant or at necropsy.

In addition, it appears that there are different grades of expression of these anomalies. The PV has been reported as normal, preduodenal, or hypoplastic, and either in a normal or atypical location.[15,17,20] The IVC has similarly been reported as normal, interrupted with azygous or hemiazygous continuation, or located to the left and crossing to the right separate from the liver in patients with situs inversus abdominalis.[20] The origin of the common HA has also been reported to arise from almost anywhere.[4]

Initial attempts at LTx for patients with BA-PS were disappointing and tempered enthusiasm for this procedure. The first report of LTx in children with this spectrum of anomalies was published in 1974 by Lilly and Starzl.[4] Their three patients died secondary to vascular complications, and the authors stated that "children with this composite anomaly are highly questionable candidates for liver transplantation." The first long-term survivor with this anomaly after LTx was reported in 1986,[21] and a previous patient transplanted in 1985 is now being presented in this series. In 1989, Hoffman et al.[11] reported two cases, one of whom died of necrosis of the graft secondary to HA thrombosis and the other of rejection; however, the authors pointed out that LTx was a feasible undertaking and should not be denied to these patients. Since then, a steady increase in survival has been achieved by some groups, although the main cause of mortality and morbidity continues to be related to technical problems.[11,14,15,17,20,21]

During transplantation, the suprahepatic IVC anastomosis is of critical importance. It must be performed in a fashion that allows the liver to lie naturally in a position that does not cause obstruction of the vena cava or of the venous outflow from the liver. In patients with situs inversus, one should consider the position of the cardiac silhouette to determine the location of the suprahepatic IVC and diaphragmatic hiatus. This will determine the position of the graft in the abdomen. In patients with a normally positioned heart, the suprahepatic IVC enters the diaphragmatic hiatus

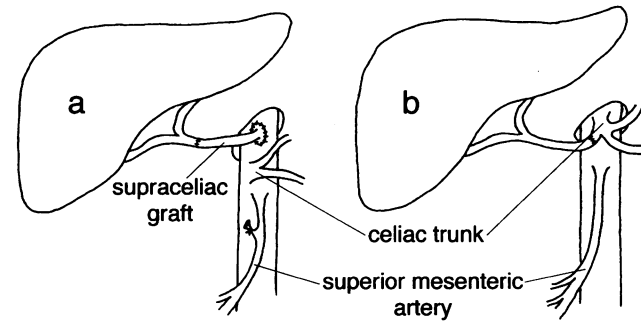

Figure 6. Types of arterial reconstruction. (a) Supraceliac graft interposed between donor celiac trunk and recipient aorta. (b) Donor celiac trunk anastomosed to proximal native hepatic artery.

on the right side or at least in the middle, allowing the surgeon to place the transplanted liver in the midepigastrium in a near-normal position. This would also depend on the feasibility of accommodating the right lobe of the graft, the spleen, and the stomach in the right upper quadrant of the abdomen. This is usually possible in patients with polysplenia, because the multiple small spleens are easily accommodated and are frequently located in a more caudal position.

When situs inversus is accompanied by dextrocardia (situs inversus totalis), the diaphragmatic hiatus of the IVC is displaced to the left, imposing a greater difficulty. If an anatomically normal liver is transplanted in such a patient, the right lobe will overlie the vertebral column and the orientation of the hilar vessels in the donor liver and the recipient portal triad will be opposite, making it necessary to undertake one or several of the following maneuvers: 1) use a smaller liver graft (smaller donor, segmental transplantation) so that the viscera can be accommodated and the abdominal wall closed; 2) use vascular grafts to overcome the discrepancy in orientation of the hilar vessels; and 3) delay abdominal wall closure (mesh). It has also been proposed that in this clinical situation the donor liver could be rotated 180° about its vertical axis so that it lies backward within the abdomen (anterior to posterior), allowing the right lobe to occupy the left subphrenic space and orienting the hilar structures of the donor liver with those in the native portal triad.[21] Fortunately, this clinical situation is rare.

When possible, the recipient infrahepatic IVC, either right- or left-sided, should be mobilized to allow a tension-free anastomosis with the donor liver or dissected free and left *in situ* for a piggy-back anastomosis of the donor suprahepatic IVC. In cases with absent IVC and azygous continuation, the donor infrahepatic IVC can be safely oversewn or simply ligated.

A preduodenal PV is usually more mobile and easier to dissect than a normally placed one. The main problem is the unperceived damage that could be inflicted to an unexpected, abnormally located vessel early in the dissection of the portal triad. When the PV is also hypoplastic, the dissection should be carried out more proximally, up to the confluence of the superior mesenteric and splenic veins, to get a vessel of appropriate size for the anastomosis. A vascular conduit or graft may be necessary to complete this anastomosis without tension.

In the earlier reports of LTx in patients with BA-PS, arterial complications were the main cause of death.[4] The anatomy of the HA is usually unknown at the time of the transplant; most frequently it is a small, tortuous vessel that abnormally originates from any branch of the celiac trunk, superior mesenteric artery, or aorta.[4] Also, the spatial orientation of the vessels at the porta hepatis is distorted, making the reconstruction more difficult. We have found it easier to do the arterial anastomosis before the portal in some cases in which the preduodenal PV is located just in front of the artery. An attempt should always be made to perform the HA anastomosis with a more proximal, large-caliber vessel or to place a supraceliac aortic graft. In this series, the two patients in whom the arterial anastomosis was done at the level of the proper HA bifurcation developed hepatic thrombosis artery (HAT) and required re-exploration and a new, more proximal anastomosis.

Although some series have reported a poorer prognosis in patients with BA and associated PS,[16] most have found no significant difference in outcome.[9,12–15,17] In the present study, no association between the type of anomaly and outcome could be demonstrated. The actuarial 10-year patient and graft survival rates were not significantly different between BA-PS and BA patients (72% *vs.* 73.5%, $p = 0.79$ and 56.4% *vs.* 54.6%, $p = 0.54$).

In summary, the association of BA with the anomalies described above should be consider a spectrum that may vary widely from patient to patient. The finding of two or more of these malformations in a patient awaiting LTx should lead the surgeon to look systematically for other associated anomalies. An early preoperative diagnosis may allow complications to be avoided. Caution should be exercised during early dissection, given that the common anatomic landmarks are not reliable in this clinical situation. With some special surgical considerations, the outcome in these patients should not differ from those with isolated BA.

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