

**FIGURE 4.** (A) Correlation of pre-Tx anti-ABO IgM peak titers with patient age and outcome. Patients were divided into four age groups (<1 year old, ≥1-8 years old, ≥8-16 years old, and ≥16 years old) and four outcomes (hepatic necrosis group, IHBC group, group with uneventful postoperative course, and group with death from causes other than hepatic necrosis or IHBC). (B) Correlation of post-Tx anti-ABO IgM peak titers with patient age and outcome. Patients were divided into four age groups and four outcomes.

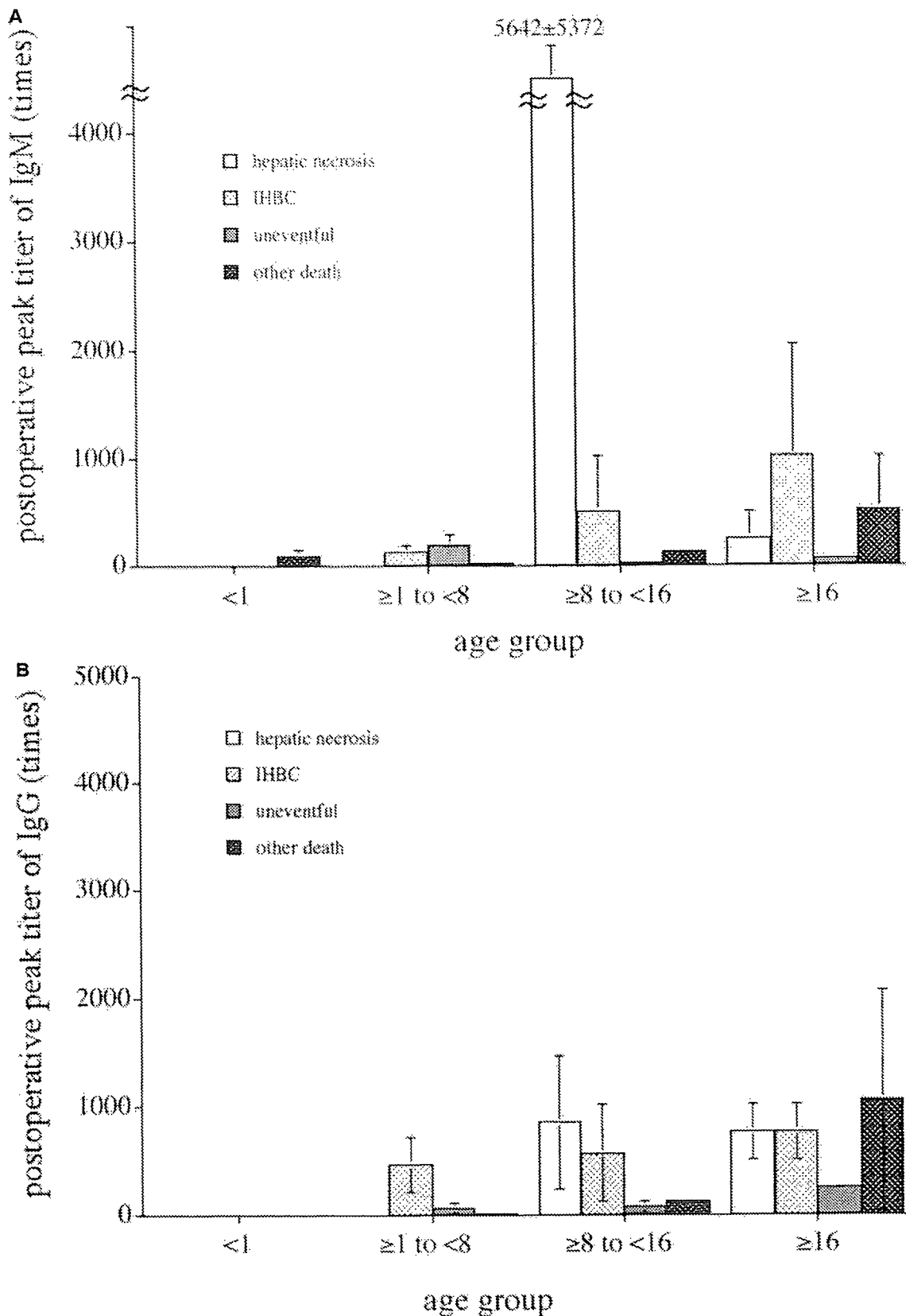


FIGURE 5. (A) Correlation of pre-Tx anti-ABO IgG peak titers with patient age and outcome. Patients were divided into four age groups and four outcomes, as in Figure 4(A). (B) Correlation of post-Tx anti-ABO IgG peak titers with patient age and outcome. Patients were divided into four age groups and four outcomes.

effective in decreasing pre-Tx Ab titers, it was ineffective in maintaining low post-Tx Ab titers, and once hepatic necrosis was established, no patients survived. Although the incidence of hepatic necrosis was lower for patients receiving cyclophosphamide induction and weekly steroid pulses, there currently is no therapy that is really changing the outcome in patients more than 1 year old.

Development of IHBC was correlated with recipient age greater than 1 and high anti-ABO IgM titers pre-Tx. IHBC usually developed within 3 months after Tx, and two types were observed radiologically: (1) multiple intrahepatic cysts and (2) a sclerosing cholangitis, with stenosis throughout the biliary tree. Both forms of IHBC were associated with acute or chronic cholangitis and progressive graft failure in 66% of cases. It should be noted that long-term graft survival was poor in this group. The cause of IHBC in ABO-I LTx remains unclear but is probably related to impaired arterial circulation secondary to Ab-mediated vasculitis. Our protocol including cyclophosphamide induction and weekly steroid pulses was effective in reducing the incidence of IHBC. Although patients with IHBC continued to suffer from cholangitis, two patients improved IHBC and three patients underwent retransplantation longer than 2 years after their first Tx, two patients died 5 and 6 years after Tx, and two patients survived with IHBC for 6 and 8 years. If we can avoid hepatic necrosis, ABO-I Tx can be acceptable for emergency cases. Furthermore, patients with IHBC can be salvaged further with a future ABO-identical or ABO-compatible cadaveric liver transplant in countries with an active cadaveric program.

Farges et al. (4, 24) have reported that hyperacute rejection is a complication in adult patients undergoing ABO-I cadaveric LTx. Histologic findings of hyperacute rejection were hemorrhagic infiltration of the portal tract and lobules and intense deposition of fibrinogen and IgM on sinusoidal and endothelial cells. Renard and Andrews (6) also reported hepatic necrosis with hemorrhagic and perivascular parenchymal collapse in pediatric cases, although there was no deposition of IgG, IgM, or C3.

A difference in outcome between adult and pediatric cadaveric LTx has been reported, with pediatric transplants being more successful (25, 26). The reasons for the more favorable outcome in children are not totally clear (27, 28), but they may be related to lower anti-ABO Ab levels (7) or to an immature complement system (29). Thus, the factors that initiate hyperacute rejection are absent during early infancy. In contrast, overimmunosuppression when undergoing splenectomy and additional immunosuppression also might contribute to poor outcome of adults, other than a high incidence of ABO-I-related complications. Patients 1 to 8 years old had worse long-term outcome than patients 8 years old, although there was no significant difference. It is possible that young children were immunologically mature enough to develop humoral responses to the donor; however, their general condition was unable to overcome biliary and septic complications.

Tanabe et al. (30) recently presented a case report showing the effect of portal infusion therapy on ABO-I LDLT. Their strategy targets endothelial injury as shown in our cases. We are currently following their protocol in a large series of high-risk patients and are preparing a long-term follow-up report.

## CONCLUSION

ABO-I LDLT may be carried out with relative safety in infants 1 year old using standard immunosuppression. Children 1 year old had a risk of long-term poor graft survival. Patients 1 to 8 years old and with high pre-Tx anti-ABO Ab titers had a risk of IHBC. Patients 8 years old or with high pre-Tx anti-ABO Ab titers remain at considerable risk of fatal outcome because of hepatic necrosis or the development of IHBC. Therefore, ABO-I LDLT should be restricted in these groups under current strategies. New strategies to prevent Ab-mediated rejection are required.

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## A SIMPLE SCORING SYSTEM TO EVALUATE THE EFFECTS OF COLD ISCHEMIA ON MARGINAL LIVER DONORS<sup>1</sup>

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**Background.** Exactly what constitutes a marginal donor remains ill defined. The authors set out to create a scoring system that objectively classifies a donor as marginal or nonmarginal and to define what the maximum acceptable preservation period is for the marginal liver to minimize early graft dysfunction.

**Methods.** The authors performed an analysis on data collected prospectively of 397 cadaveric liver transplants. Both univariate and multivariate analyses were performed on donor, recipient, and perioperative factors with relation to early allograft dysfunction. A score was developed that classified donors into marginal and nonmarginal populations, and the influence of cold ischemia was determined for each group.

**Results.** Multivariate analysis-determined donor age and steatosis (moderate to severe) were independent predictors of deranged function. This enabled the authors to produce a scoring system to differentiate marginal donors with respect to risk of early allograft dysfunction as follows: Formula (20.06 steatosis) (0.44 donor age), cutoff 23.1. In the marginal group, the cutoff value of cold ischemia time was 12.6 hr.

**Conclusions.** The authors developed a scoring sys-

tem that classified an organ as marginal or nonmarginal depending on the donor age and degree of steatosis. Marginal livers have a strong risk of developing early allograft dysfunction with increasing cold ischemia times and should be transplanted within 12 hr. Cold ischemia time was not found to be an important factor in the development of early allograft dysfunction in nonmarginal donors.

Those involved with liver transplantation are faced with the reality of an ever-increasing discrepancy between waiting lists and available organs. In 2001 alone, 1,978 potential liver recipients died on the U.S. list without receiving a graft (United Network for Organ Sharing database). Methods to overcome this problem have included the use of more marginal organs and those from non-heart-beating donors and split-liver and living-related transplantation. Each of these potential solutions has their own clinical and ethical drawbacks.

The use of livers from “marginal donors” has been shown in several studies to lead to an increased risk of primary graft dysfunction (1–4). What constitutes a marginal donor remains controversial, and different transplant units have developed their own arbitrary policies that differentiate whether a liver is used or discarded on the basis of broadly accepted guidelines. We aimed to clarify what donor parameters in our institution independently correlate with primary graft dysfunction (primary nonfunction [PNF] plus initial poor function [IPF]), and thereby develop a precise numeric formula by which any given donor can be prospectively classified as marginal or nonmarginal. We proceeded to examine the influence of cold ischemia on this susceptible subset of grafts, with the aim of developing a strict time threshold below which these organs could be safely used.

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## Living related liver donor transplantation: techniques and caution

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Despite the evolution and popularization of living donor liver transplantation, its surgical techniques are still somewhat controversial. Donor safety is of the utmost importance in any attempt to procure a high-quality graft of sufficient size for the recipient. Quantitative, qualitative, and anatomical assessment of the graft and adequate preparation are the first steps. During surgery, maximum care should be taken to preserve vascular, biliary, and hepatic parenchymal integrity. In addition, every step of the surgery should be planned and performed meticulously. Small errors or absences of coordination can lead to unexpected complications and only a small margin of error exists for both recipients and donors.

Living donor liver transplantation (LDLT) is entering its 16th year of clinical application [1]. Its indication has been extended from small children to adults and its graft selection repertoire has increased from the left lateral segment to the right lobe of the liver. Apart from the many ethical, socio-economic, and psychologic controversies that surround LDLT, controversy also surrounds the best approach to graft retrieval and implantation, despite the popularity of the procedure. Recent reports have disclosed the actual risk of partial liver retrieval to living donors [2,3]. The anatomic

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considerations and surgical techniques included in this procedure are final applications of the evolution of hepatobiliary surgery, and therefore require utmost care. An enormous breadth of experience goes into each step of donor selection, anatomic and medical evaluation, graft preparation, retrieval, and implantation. Specific criteria must be met before LDLT. This article summarizes current surgical approaches to LDLT and outlines some of the precautions that should be taken during LDLT.

### **Graft size and anatomic considerations in left-sided liver grafts**

Left lateral segment liver grafts are most commonly selected in small pediatric patients. Either extended left lateral segment grafts without the middle hepatic vein (MHV) or left lobe (left liver) grafts are often selected in larger children, and sometimes in small adults. A graft-to-recipient weight ratio (GRWR) of 1% to 40% of the standard liver volume of the recipient is generally sufficient to meet metabolic demands after implantation [4,5]. Recent experience suggests, however, that graft mass demand depends on the original disease and the clinical status of the recipient, as well as the quality of the grafted liver, along with other surgical and perioperative factors.

Conversely, a large-for-size graft can also pose a risk to small infants. It is preferable for the abdomen to be closed only with the skin, or with Gore-Tex or another type of artificial sheet that can be removed in a stepwise manner, to prevent graft compression after transplantation of a large-for-size graft. Reduced left lateral segment or monosegmental grafts are alternative choices to large-for-size grafts [6]. A criterion for graft reduction is not definite because it also depends on the shape of abdominal space. A graft weight greater than 4% to 5% of body weight can be used as a rough index. An extreme discrepancy in the distance from the hepatic vein to the portal vein between a graft and its recipient can pose a significant risk, however, even after graft reduction.

Left-sided grafts are rarely contraindicated as a result of variations in vascular anatomy. Separate portal branches to Couinaud liver segments II and III in the absence of the umbilical portion, combined with the supply of segment IV from the right branch of the portal vein, is a potential contraindication to left-sided grafts [7]. Duplicated portal venous branches, however, can be plastified into a single orifice in most cases. Absence of portal venous inflow to segment IV, with preserved arterial inflow and venous outflow, requires special consideration regarding regenerative capacity, although some bridging function can be expected.

The absence of a common trunk between the left hepatic vein (LHV) and MHV, or separate hepatic veins from segments II and III, are not contraindications because they can be unified either by close approach to the inferior vena cava (IVC) or by back-table venoplasty after retrieval.

Separate hepatic arteries to segments II and III can be dealt with by surgical microscope, and therefore is not a contraindication to donation. Intraoperative assessment enables identification of variations in vascular anatomy, and no benefit is gained by preoperative angiography, although recent advances in multislice CT or MRI provide a much clearer picture of arterial anatomy. Likewise, biliary anatomy can usually be assessed during surgery, and no variations are considered a contraindication. Preoperative CT or MRI cholangiography is indicated only in donors related to children with Alagille syndrome, who may have biliary hypoplasia despite normal liver and biliary enzymes.

### Left-sided liver retrieval

Living liver donors should be regarded as different from other patients in that they are not burdened by disease that can be an excuse for any surgery-related morbidity. The use of stockings and pneumatic boots is routine to reduce the risk of deep vein thrombosis. In addition, abduction of both arms should be controlled to minimize the incidence of median nerve injury. A central venous catheter is often helpful for beginners in controlling pressure during transection of the liver parenchyma. An upper median incision with bilateral extensions is the standard incision, with elongation of the right lateral extension for left lobe retrieval. Extending the incision to the xiphoid process is the key to obtaining a good view of the hepatic veins. Ringed-draping is helpful to reduce wound contamination during surgery.

After division of the round and falciform ligament, the LHV and MHV are exposed to their insertion to the IVC. Moderate mobilization of the right lobe is helpful in left lobe retrieval for later parenchymal transection. While taking care to protect the spleen, the left triangular and coronary ligaments are excised to reveal the left surface of the LHV and IVC. Division of the inferior phrenic vein, if present, is helpful to expose a long neck of the LHV. During excision of the gastrohepatic ligament, the Alantius ligament is transected close to the LHV and, if an aberrant left hepatic artery (LHA) of sufficient caliber is present, it is traced back to the left gastric artery for later possible reconstruction.

Hilar dissection is confined to the left side. The LHA is mobilized from the bifurcation and, if the middle hepatic artery (MHA) is included in the graft, it is also mobilized. Traction or pinching of the arteries should be avoided to prevent injury to the intima. Where it interferes with further dissection, a small MHA can be sacrificed. Attention should be paid to the caudate branches of the left portal venous branch (LPV) when the LPV is moved back to its origin. Caudate branches should be carefully divided and ligated. The left hepatic duct (LHD) can be roughly identified with minimal use of electrocautery. With a marking clip on the LHD, cholangiography is undertaken by directly puncturing the CBD using a 24-gauge needle in lateral segmentectomy, or by way of the cystic duct after cholecystectomy in

left lobectomy. The distal CBD and the cystic duct are temporarily clamped. To obtain a three-dimensional view, fluoroscopy is helpful. The marking clip is then replaced by a fine, marking suture after cholangiography. The parenchymal transection line is usually 1 cm to the right of the falciform ligament in lateral segment grafts, and 1 to 2 cm to the right of Cantrie's line in left lobe grafts. The transection line is extended posteriorly to the point of transection of the bile duct. Intraoperative ultrasonography may help to confirm the position of the MHV during left lobectomy.

Parenchymal transection may be performed by the procedure of the surgeon's choice. Our preference is to use a Cavitron Ultrasonic Aspirator (CUSA) and bipolar electrocautery equipped with a continuous irrigator. We also use blended spray high-power monopolar electrocautery. A straight plane of transection can be achieved by placing 3-0 Prolene traction sutures on both sides. Fine, flat scissors are also used for retraction. The operator handles the CUSA and monopolar electrocautery, the first assistant performs the bipolar electrocautery and places the retracting scissors, and the second and third assistants handle fine suction and traction. Small vessels are coagulated with or without small vascular clips. Large vessels are ligated with fixation using vascular clips. Large veins are oversewn with Prolene. Medium-sized drainage veins draining from segment IV into the LHV are usually sacrificed in lateral segmentectomy. In left lobectomy, the transection plane is angled to the left after identification of tributaries to the MHV.

During parenchymal transection, the LHD is cut sharply and the donor side is oversewn. It is important to establish a safety margin. Further transection of the parenchyma is then performed along the plane of the ligamentum venosus. Transection near the hepatic vein is done carefully to preserve a long segment of the LHV or the common trunk of the LHV and MHV. Once parenchymal transection is complete, hemostasis and absence of bile leak are confirmed on both surfaces. When a monosegmental graft is scheduled, the second stage of transection is performed in situ, along the right border of the hepatic vein coming from segment II [6]. We routinely give the donor 1000 U of heparin before vascular clamping. Non-crushing vascular clips are used to clamp the hepatic artery to prevent injury to the intima. Although obtaining a good length of portal vein is a major determinant of successful implantation, considerable care should be taken to avoid impingement of right-sided structures. After clamping and division of graft vasculature, the vascular stumps are oversewn with Prolene sutures.

The graft is taken promptly to the back table for cooling and perfusion. The graft is then perfused by way of the portal vein. We prefer histidine-tryptophan-ketoglutarate solution to University of Wisconsin solution and, unlike several other programs, we do not flush the artery or the bile duct because this might result in endothelial or epithelial injury [8]. The separate orifices of the hepatic vein are plastified into one with a U-shaped resection of the septum. After final hemostasis and vascular continuity is secured in



the donor, the omentum is placed on the transection plane to prevent adhesion with the stomach. When recipients with hypoplastic or sclerotic portal vein require interpositional vein graft because of biliary atresia, the left ovarian or inferior mesenteric vein is taken from the donor. A closed suction drain is then inserted and the incision closed.

### **Left-sided liver grafting**

The recipient native hepatectomy is performed in a standard fashion except for vascular and biliary management. The retrohepatic IVC is usually exposed from the right side, and division of the short hepatic veins is done in the same way as described in right lobe donors, with care not to induce IVC stenosis. The right hepatic vein (RHV) is clamped separately and divided near the liver. Hilar dissection is done with the goal of preserving adequate lengths of both vascular and biliary structures. If a previous Roux-Y limb is present, it is divided as near as possible to the biliary anastomosis, with care not to injure malnourished adherent bowel, especially in cases of post-Kasai biliary atresia. When duct-to-duct reconstruction is scheduled, the bile duct is dissected along with surrounding connective tissue, and is divided near its site of insertion into the liver. The hepatic artery is also divided near the liver to allow multiple anastomoses to be made. Care is taken to avoid intimal dissection at the stump. Even the use of a vessel loop can sometimes induce intimal injury.

After dissection of all other structures around the liver, the portal vein is divided above the bifurcation and the common trunk of the MHV and LHV is divided near the liver. Venovenous bypass is not necessary because complete cross-clamping of the IVC is avoided. In noncirrhotic cases, however, temporary porto-caval shunting, preferably using the right portal vein (RPV) stump, is recommended before hepatectomy.

After bleeding is controlled, vascular and biliary stumps are prepared for anastomosis. The common stump of the MHV and LHV is elongated, with removal of the diaphragmatic crus and the inferior phrenic vein. In contrast to several other proposals, we do not perform complex venoplasty for venous anastomosis [9]. The MHV/LHV common stump is typically used for anastomosis after size adjustment. When the graft LHV is larger, the RHV stump is clamped horizontally together with the MHV/LHV stump, and its border is cut open to make a large, common hole in line with the graft hepatic vein. A curved vascular clamp is helpful for this procedure. Temporary semitotal clamping of the IVC is usually tolerable. The portal vein is dissected back to the splenomesenteric junction to divide the collaterals and to obtain a good length for anastomosis. If the portal trunk is narrow and sclerotic because of repeated episodes of cholangitis in post-Kasai biliary atresia, it can be replaced by a vein graft at the splenomesenteric junction or, alternatively, an opened vein can be grafted along

the portal trunk to extend its diameter [10]. When portal flow is deemed insufficient by test declamping, division of small collaterals around the spleen is often effective in augmenting flow. The hepatic artery is also dissected back to the level of the gastroduodenal artery. In small infants, division of the gastroduodenal artery is often necessary to ensure adequate length and flow.

The graft is inserted into the abdominal cavity after being rinsed with cold albumin. The hepatic vein is anastomosed using running 5-0 vascular sutures. Attention should be paid to prevent inversion, especially of the posterior wall. There should be no tension on the suture. The IVC side-clamp is then replaced by a smaller clamp. Depending on its length and diameter, the graft portal vein is anastomosed with the LPV, the portal bifurcation, or the portal trunk of the recipient, using running 6-0 sutures. A large C-shaped reconstruction is intended. During anastomosis, both edges of the orifice are pulled and suture tension is minimized to allow for inflation after declamping. At this point, the hepatic vein and portal vein are declamped.

During the following procedure, a large gauze is placed into the right subphrenic space to prevent rotation of the graft to the right. Arterial anastomosis is performed using interrupted 8-0 sutures, usually under a surgical microscope [11]. Sharp edges, adequate removal of surrounding tissue, and absence of tension or kinks in the anastomosis contribute to the success of this procedure. When two significant arteries are present within the graft, a good back flow in the second one after the reperfusion of the major one can be a good reason to ligate the second one.

After revascularization is complete, flow velocity and signal patterns are checked by Doppler ultrasonography. Bile duct reconstruction is most commonly done by hepaticojejunostomy. A length of 30 to 40 cm is sufficient for Roux-Y limb, but tension of the anastomosis should be avoided. The anastomosis is made with running or interrupted 6-0 polydioxanone surgical sutures; we prefer the former with a minimal suture tension [12,13]. After completion of the posterior wall, a 4-gauge polyvinyl tube with side holes is inserted into the graft bile duct and lightly fixed to the anterior wall. The tube penetrates the distal wall of the Roux-Y limb with Witzel fixation. The tube is removed 8 weeks after surgery but can be omitted when the anastomosis is large. A short internal stent is used for extremely small biliary anastomoses. Where a duct-to-duct anastomosis is intended, the recipient bile duct can be dissected back to the upper margin of the pancreas to reduce anastomotic tension, if necessary. A running suture or the mixture with interrupted suture with an external stent for anastomotic decompression are the preferred methods. The biliary stent is also brought out either through the stump of the cystic duct by fixation with a rubber ring, or through the wall of the CBD using a light purse-string suture.

After hemostasis is confirmed, the graft falciform ligament is fully reconstructed to prevent graft rotation into the right subphrenic space.

Because venous outflow often depends strongly on graft position, the outflow pattern should be checked frequently by Doppler ultrasonography during both graft fixation and abdominal wall closure. Closed suction drains are placed in both subphrenic spaces and they and the biliary tube are brought out through separate orifices.

### **Graft size and anatomical considerations in right liver grafts**

Quantitative, qualitative, and anatomic evaluation of the graft and the remnant liver are the most crucial factors for successful right-lobe LDLT. A CT slice width of 7 mm or less is required to assess graft and remnant liver size accurately [14]. Our standard line for right lobe volumetry is approximately 1 cm to the right of the MHV, because transection is easier when the MHV is surrounded by parenchyma caused by a reduction of blood loss from small venous tributaries. This line can be shifted to some extent to either side during surgery.

Although the minimal graft volume required for successful transplantation might differ with right- and left-sided grafts because of differences in venous anatomy, the same criteria (GRWR or percentage of standard liver volume) are used to assess volume for left- and right-sided grafts. Assessment of minimal volume, however, also depends on a range of patient factors, as well as graft quality and surgical factors, although precise quantification based on these factors is difficult [15]. At the very least, noncirrhotic patients with metabolic disease, or patients with hepatocellular carcinoma and compensated cirrhosis, would be able to tolerate transplantation with smaller graft masses. It is also important to consider whether donors have an adequate liver volume to allow for donation. Although, on average, 40% of the initial liver volume is retained after right lobectomy, large variations in remaining liver volume are observed [16]. Leaving room for error with CT volumetry, retention of 35% of liver volume seems an appropriate cut-off point for donation. This percentage might be increased in aged donors or in those with steatosis.

Evaluation of steatosis in potential donors is also of great importance. We have not done preoperative liver biopsies for the evaluation of steatosis because of a potential risk of needle biopsy and potential presence of intrahepatic heterogeneity. Instead, we evaluate the liver-to-spleen CT-value ratio (L/S ratio) using plain CT [17]. The L/S ratio shows a strong negative correlation with the grade of macrovesicular steatosis as confirmed at surgery, and L/S ratios greater than 1.15 have been found to have a 100% negative predictive value for moderate (greater than 30%) macrovesicular steatosis. At lower values, candidates are encouraged to modify their diet and start physical conditioning, depending on the length of time remaining for the recipient. If significant macrovesicular steatosis cannot be excluded before transplantation, estimated graft and remnant liver volume should be modified according to steatosis. Although extracting a percentage of the

estimated liver volume according to the severity of steatosis has been suggested to give a "lean" volume, fully quantitative calculation is difficult. In addition, nonalcoholic steatohepatitis, which is observed in obese patients and may be resistant to dietary modification, poses a risk of chronic insufficiency after hepatectomy.

Greater variations in vascular and biliary anatomy are observed in right lobe grafts [12]. Multiple pedicles of the RPV are encountered in 8% of cases, most of which are safely managed in the recipient with either venoplasty or interpositional venous grafting. Multiple small RPV branches, which are often accompanied by a left-sided gall bladder and portal supply to segment IV from the RPV, commonly contraindicate retrieval. An evaluation of the relative size of the RHV, the MHV, and its tributaries (V5 and V8) is important to estimate congestion of the anterior segment (paramedian sector) following MHV deprivation. Significant accessory (right inferior) hepatic veins greater than 5 mm in diameter are observed in 30% of cases, and require reconstruction in the recipient. The right hepatic artery (RHA) is found to branch from the superior mesenteric artery in 13% of cases, which is advantageous because it provides a long arterial pedicle. It is not necessary to identify this before surgery, however. Although multiple biliary orifices are encountered within the graft in approximately 30% of cases, intraoperative cholangiography is sufficient to assess this situation because the problem can be managed by multiple duct-to-duct anastomosis or hepaticojejunostomy [12]. Although we need to ensure donor safety, we also need to make sure that we do not exclude too many suitable donors.

Right lobe grafts with the MHV may be indicated when grafts of limited quality (eg, steatotic or aged) or marginal anatomy (eg, small-for-size or a small RHV), are used in marginal recipients. In these cases, the size and quality of the liver parenchyma remaining in the donor should be assessed strictly. In particular, segment IV drainage veins should be evaluated to ensure preservation of the largest vein. A right posterior segment (right lateral sector) graft is sometimes selected in cases with a large right lobe or critically small remnant liver, but its indication is limited by portal venous, arterial, and biliary anatomic considerations.

### **Right liver retrieval**

Retrieval of the right lobe in living donors requires even greater meticulousness. Because blood loss averages approximately 300 g, preceding autologous blood collection is not necessary. Following a preparation protocol similar to that described for left-sided liver donors, the abdomen is entered through a right-sided subcostal incision, extending to the xiphoid process in the midline. Extension of the incision to the xiphoid process allows a good view of the hepatic veins. The use of three retractors, including one in the extreme right from downward, helps to ensure a good view of the retrohepatic space. Following division of the round ligament, the

falciform ligament is divided to reveal the border between the RHV and the MHV. It is important to avoid division of the left triangular ligament. It is also important that the falciform is later sutured to prevent torsion of the remaining left lobe.

The right coronary and triangular ligaments are divided from both sides of the liver. Once a bare area is dissected, the whole liver can be rotated into the left subphrenic space made by caudal retraction of the spleen. Separation of the right adrenal gland and the liver should be done with care because often they are adhered firmly. Sometimes a part of the adrenal gland remains attached to the liver, requiring careful management of bleeding. Rotating the liver and adequately retracting the right kidney safely exposes the retrohepatic cava, including the short and caudate veins, to the left of the midline even before hilar dissection. The tiny, short hepatic veins are meticulously divided with ligations or coagulation with vascular clips. If a short hepatic vein greater than 5 mm in diameter is present, it is preserved until the end of graft retrieval, or transected with a caval cuff. The caval side of the vein is oversewn, and the venous stump is temporarily clipped. The IVC ligament just below the RHV usually contains vessels of significant caliber and should be oversewn after transection. Finally, the RHV is fully exposed and encircled, and a flat silicon drain is passed between the RHV and the MHV as a guide for later parenchymal transection.

The liver is then returned to its original position. Placing a large piece of gauze behind the right lobe and retracting the duodenum facilitates hilar dissection. Cholecystectomy is performed and a tube for cholangiogram is inserted through the cystic duct. Cholangiogram can be postponed until the right hepatic duct (RHD) is roughly dissected and marked with a clip. Hilar dissection is started from the right side of the CBD with ventral retraction of the cystic duct. The RHA is identified first, followed by the portal vein. The RHA is dissected from its origin to the liver parenchyma. We do not pay much attention to the small arterial branches supplying the CBD or the common hepatic duct. All large branches to segment IV should be spared, however. Even the use of a vessel loop should be avoided to prevent injury to the intima. The posterior of the RPV is then exposed with division of caudate lobe branches, if necessary. Retraction of the CBD facilitates the exposure and encircling of the origin of the RPV. Early branching of RPV should be mobilized separately. The RHD is then divided sharply with or without encircling. The distance from the confluence with the left ductal system should be carefully measured to prevent serious biliary complications in the donor.

The RPV and RHA are temporarily clamped, the latter with a non-crushing vascular clip, to visualize the demarcation line of the liver. The line of transection, typically 1 cm to the right of the demarcation line, can be shifted to some extent toward either side, depending on the intended graft size. Shifting the line beyond Cantrick's line is useful to reduce congestion in the anterior segment, as long as the major anterior Glisson's capsule is not crossed. The transection line extends posteriorly to the point of bile duct

transection. Transection of the parenchyma is performed in a similar manner to that described for left-sided graft retrieval. We do not pay close attention to central venous pressure because it seldom affects our method of transection. A straight transection plane is maintained by placement of two traction sutures on both sides, and the flat silicon drain is passed beyond the RHA and RPV. Ventral traction of the drain helps to make a precise transection plane.

At the hilar plate, attention should be paid to the Glisson's capsule to the caudate lobe, which needs ligation. If reconstruction of the drainage veins from segments V or VIII is scheduled in the recipient, they are retained as long segments until graft retrieval. In our experience, temporary clamping of these hepatic veins does not allow prediction of future congestion. The indication for drainage reconstruction is determined preoperatively based on graft size, anatomic features, quality of the graft, and the recipient's condition. When drainage reconstruction is not indicated, these veins are divided and oversewn. The final steps of transection should be performed carefully because sometimes there are undivided short hepatic veins on the left side. In right lobe retrieval with the MHV, the transection plane is shifted 1 cm to the left of the demarcation line, and transection is performed with the left side of the MHV exposed. When the major drainage vein from segment IV is encountered, it is preserved and the MHV is divided before its confluence.

The procedure after parenchymal transection is similar to that in left-sided graft. Heparin is given to the donor. At vascular clamping and division, the graft RHV does not have to be very long, because redundancy can result in outflow disturbance. Smooth continuity of the portal vein from the trunk to the LPV should be confirmed, with mobilization of the trunk because a kink poses a risk of thrombosis in the remaining portal vein. The donor side of the bile duct is closed after the graft is removed and the vascular stumps are oversewn. After experiencing bile leakage from the ductal stump, we have made it routine to place a decompression biliary tube in right lobe donors. A 4-Fr tube is inserted through the cystic duct and upward beyond the site of ductal closure. The tube is lightly fixed to the cystic duct with an absorbable stitch and further fixed with a rubber ring. The ductal stump is oversewn after tube insertion and a completion cholangiogram is performed to confirm biliary integrity. Even if inserting the tubing through the cystic duct is difficult, decompression of the CBD is helpful. The tube is removed 3 weeks after the surgery. A closed suction drain is placed close to the cut surface of the liver before abdominal closure. Again, reconstruction of the falciform ligament is of vital importance.

### **Right liver grafting**

Hepatectomy is performed in much the same way as described for left-sided liver recipients. A long stump of the RHV is not necessary because redundancy of the RHV is a risk factor for outflow disturbance. Because

physiologic bilioenteric continuity and early oral intake are important for recipients of small-for-size grafts, we prefer biliary reconstruction by duct-to-duct anastomosis wherever possible [18]. Overexposure of the bile duct should be avoided. Although small arterial branches to the bile duct are often divided to elongate the bile duct or hepatic artery, the arteries at the 3-o'clock and 9-o'clock positions provide the main arterial supply of the bile duct [19]. Division of the bile duct should be high enough to meet the number of biliary orifices within the graft. The same principles applied to the dissection and division of the hepatic artery, portal vein, and hepatic veins in left-sided liver recipients should be applied to right-sided recipients. Venovenous bypass is not necessary, and the indication for temporary porto-caval shunting is the same as that in left liver recipients.

Stumps of the MHV and LHV are oversewn after hepatectomy if additional venous reconstruction is not scheduled. The portal vein is dissected back to the upper margin of the pancreas to obtain good mobilization for anastomosis. Test declamping is performed to confirm sufficient portal flow. In cases of portal venous thrombosis, thrombectomy is performed, and replacement with a venous graft or a jumping graft should be considered when significant extension of the thrombosis is observed. Sources of venous grafts include the external iliac vein, the intrahepatic LPV, or the jugular vein of the recipient. The hepatic artery is also dissected back to the gastroduodenal artery, but the latter is not divided. Just before an anastomosis is created, the vascular clamp on the RHV is replaced by a large Satinsky side-clamp, and the RHV cuff is extended downward to match the size of the graft RHV. The anterior wall is then cut to make an oval orifice.

The liver graft is placed in a natural position and the RHV is anastomosed with running 5-0 vascular sutures. After this, the big side-clamp is replaced by a regular clamp to release the IVC. The right inferior accessory veins with cuff are anastomosed to the IVC, followed by clamping with a small vascular clamp. The anastomotic orifice used for porto-caval shunting is often reused for anastomosis of accessory veins. Otherwise, it is oversewn after graft reperfusion. When the distance between the graft and recipient portal veins is long, gauze is placed behind the graft to reduce tension on the anastomosis. The graft portal vein is anastomosed using running 6-0 sutures to the RPV, portal bifurcation, or portal trunk of the recipient, depending on its diameter and distance. Suture tension is minimized. After completion of the portal venous anastomosis, the gauze is removed from behind the graft and the RHV, accessory veins, and then the portal vein are declamped.

When reconstruction of the anterior venous tributary is indicated, it is done after portal reperfusion. Sources of interpositional venous grafts include the LPV from the explant, the external iliac vein from the recipient, and the ovarian or inferior mesenteric veins from the recipient or donor, which are anastomosed to the graft on the back table. The opposite end of the venous graft is anastomosed either to the MHV stump or directly to the IVC. When a long segment of the MHV, or its tributary, is attached to the

liver graft, it can be anastomosed before graft reperfusion. Arterial anastomosis is performed as described in left-sided liver recipients, but usually under high-magnification surgical loupe. Positioning of the artery should be carefully planned before arterial anastomosis, considering the later requirement for duct-to-duct biliary anastomosis.

After confirming sufficient patency in all the vascular anastomoses by Doppler ultrasonography, biliary reconstruction is performed. Duct-to-duct anastomosis is most commonly selected. The technique used is principally the same as that described in left-sided liver transplantation. Because right lobe grafts often have multiple biliary orifices, these are anastomosed to the RHD, the LHD, or the cystic duct of the recipient. A biliary stent is inserted into each orifice with light fixation and exits either through the cystic duct or through the CBD. Very small (eg 1 mm) and distant biliary orifices are sometimes sacrificed and oversewn. Intraoperative cholangiography is not necessary after completion because the risk of bile leakage is low.

Because oral intake is often delayed in recipients of small-for-size grafts, resulting in prolonged cholestasis and poor synthetic function, we routinely insert a jejunostomy tube at the end of the operation. The insertion site of the jejunum should be firmly fixed to the abdominal wall. Two or three closed suction drains, one along the cut surface of the graft, are placed, and the abdominal wall is closed.

## Summary

LDLT is often performed under less than ideal circumstances, such as limited graft mass, aberrant vascular and biliary anatomy, limited sources of venous grafts, and a recipient in a state of deterioration. The margin for error is small in both recipients and donors. Every step of the surgery needs to be planned and performed in a meticulous and synchronized manner. Small errors or absences of coordination can lead to unexpected complications. In addition, use of a segmental graft requires the knowledge of the safety margin of hepatic adaptation to nonphysiologic situations for the safety of both recipient and donor. Scientific and clinical evidences for precise individualization of the tactics are still not sufficient. Further accumulation of knowledge and experience is awaited for the safest performance of this evolving surgery.

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# EFFICACY OF ANTERIOR SEGMENT DRAINAGE RECONSTRUCTION IN RIGHT-LOBE LIVER GRAFTS FROM LIVING DONORS<sup>1</sup>

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**Background.** The efficacy of additional venous reconstruction in the anterior segment has not been fully investigated for graft congestion in right-lobe liver grafts.

**Methods.** Posttransplant graft venous congestion in the anterior segment was evaluated using magnetic resonance imaging in right-lobe living-donor liver transplantation. Additional venous reconstruction was categorized into two types: reconstruction of tributaries from segment 5 or 8 (n = 11) and reconstruction of the middle hepatic vein (MHV) (n = 9). Forty-five grafts only with right-sided hepatic vein(s) including the right hepatic vein served as controls.

**Results.** No significant difference in congestion score of the anterior segment was observed between grafts with V5/8 and standard grafts 1 month after transplantation despite the patency of reconstruction. Only grafts with the MHV showed no congestion ( $P < 0.01$ ).

**Conclusions.** Drainage reconstruction of tributaries from the anterior segment produces only suboptimal benefits when evaluated radiologically. The addition of the main trunk of the MHV with its surrounding communication has the best effect on the congestion of the anterior segment.

In living-donor liver transplantation (LDLT), small-for-size grafts are often associated with a poor prognosis (1). LDLT using right-lobe grafts without the middle hepatic vein (MHV) has been established to mitigate the problem and is now widely accepted as a standard graft selection for adult patients. However, right-lobe grafts without the MHV potentially have the problem of tissue congestion in the anterior segment (right paramedian sector) (2, 3). To avoid congestion in the anterior segment, several technical modifications have been proposed and discussed in hepatic venous reconstruction (2, 4, 5). The present study aimed to evaluate their efficacy in the mitigation of graft congestion according to the methods of the additional reconstruction of drainage veins.

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## PATIENTS AND METHODS

During the period between October 2000 and December 2002, a total of 20 patients underwent right-lobe LDLT with additional reconstruction of drainage vein(s) in the anterior segment. All grafts were primary transplants and were categorized into two groups by the mode of venous reconstruction: 11 grafts received reconstruction of hepatic venous tributaries from segment 5 or segment 8 in addition to the right hepatic vein (RHV) (right-lobe graft V5/8), and nine grafts were retrieved with the MHV and underwent reconstruction of both the RHV and MHV (right-lobe graft with the MHV). Forty-five primary grafts with reconstruction of only the RHV (standard right-lobe graft) in the same period served as controls. Until September 2000, all right-lobe grafts were standard ones in our program because of the absence of apparent adverse events. Since October 2000, grafts with smaller RHV than MHV, small-for-size grafts less than 1.0% of recipient body weight, steatotic grafts, or grafts from donors older than 50 years received additional venous reconstruction with donor safety regarding remnant liver size and congestion assumed to be maintained. This protocol was started on the basis of the results of our previous study on graft tissue congestion (3).

Operations in donors were performed as described elsewhere (6). During mobilization of the liver, all of the right accessory hepatic veins with a significant size ( $> 5$  mm) were preserved with caval cuff and reconstructed in the recipient. In right-lobe grafts with V5/8 or the MHV, hepatic vein(s) from segment 5 or 8 or the MHV were preserved as long as possible during parenchymal transection. Interpositional venous grafts from the donor or recipient were used if needed for the reconstruction of V5, V8, and the MHV. Interpositional venous grafts were anastomosed with liver graft on the back table.

Posttransplant congestion was assessed using magnetic resonance imaging (MRI) as described previously (3, 7). Briefly, MRI was performed with a 1.5-T superconducting unit (Signa Horizon; General Electric Medical Systems, Milwaukee, WI). Graft parenchymal congestion was evaluated semiquantitatively in each segment on T2-weighted MRI using normal liver and spleen as negative and positive controls, respectively. Two abdominal radiologists evaluated graft congestion independently and found final consensus. The score of congestion was defined as described elsewhere (3): 0, isointensity relative to normal liver; 1, slightly higher intensity in a part of the parenchyma; 2, mildly higher intensity; and 3, moderately higher intensity. Values are shown as median and range. For statistical comparison, chi-square test or Fisher's exact probability test for categorical data and Mann-Whitney test or Kruskal-Wallis test for continuous data were used. Values of  $P < 0.05$  were regarded as statistically significant.

## RESULTS

Recipient, donor, and graft demographics are shown in Table 1. Recipients of right-lobe grafts with V5/8 were significantly younger than other groups with unknown reason. Donor-to-recipient weight ratio in right-lobe grafts with MHV and graft-to-recipient weight ratio in right-lobe grafts with V5/8 were significantly smaller than other groups. Warm ischemia time in standard right liver grafts was

TABLE 1. Recipient, donor, and graft demographics

	Standard right lobe	Right lobe with segments 5 and 8	Right lobe with MHV	P value
No.	45	11	9	
Recipient factor				
Gender (M/F)	22/23	8/3	8/1	0.0485
Age (yr)	19-69 (51)	16-58 (41)	38-64 (59)	0.0257
Cirrhosis (%)	77.8	81.8	66.6	NS
Child-Pugh-Turcotte score	6-12 (10)	6-12 (10)	5-13 (12)	NS
ABO combination <sup>a</sup>	29/8/8	7/4/0	6/2/1	NS
Donor-graft factor				
Gender (M/F)	28/17	5/6	3/6	NS
Age (yr)	19-64 (44)	25-61 (42)	22-58 (40)	NS
Donor-to-recipient weight ratio	0.73-1.58 (1.02)	0.69 -1.40 (0.91)	0.69-0.98 (0.82)	0.0185
Graft weight (g)	505-1,080 (670)	515-850 (650)	445-745 (675)	NS
GRWR <sup>b</sup> (%)	0.73-1.96 (1.09)	0.74 -1.44 (0.87)	0.79-1.15 (0.99)	0.0198
Accessory RHV reconstructed (%)	44.4	63.6	44.4	NS
Interpositional vein grafts	—	9	2	0.0077
Steatosis <sup>b</sup> (%)	20.0	36.4	0	NS
CIT <sup>c</sup> (min)	13-325 (55)	50-246 (89)	37-261 (66)	NS
WIT <sup>e</sup> (min)	23-68 (39)	42-81 (52)	27-60 (47)	0.0030

Numbers in parentheses are median values.

<sup>a</sup> Identical, compatible, or incompatible.

<sup>b</sup> Mild (< 30%) or moderate (> 60%) macrovesicular steatosis.

<sup>c</sup> GRWR, graft-to-recipient weight ratio; CIT, cold ischemia time; WIT, warm ischemia time.

shorter than in other groups. Seven of 11 additional reconstructions were performed before portal reperfusion.

Reconstruction of the MHV was performed by direct anastomosis with the inferior vena cava or MHV stump in seven of the nine grafts, and the other two grafts received interpositional vein grafts from the left portal venous branch of the native liver. In right-lobe grafts with V5/V8, interpositional vein grafts were left portal venous branch of the native liver in three grafts, inferior mesenteric vein from the recipient in two, left ovarian vein from the donor in one, inferior mesenteric vein and left portal venous branch from the recipient in two, and left ovarian vein and splenic artery from the recipient in one. Two of three cases using double venous grafts used longitudinal double grafts. V8 in the remaining two right-lobe grafts was reconstructed by direct anastomosis to the inferior vena cava. Good patency of V5 or V8 was confirmed on contrast-enhanced MRI in 7 of 11 grafts with additional V5/8 reconstruction. In three other grafts, patency of V5/8 was confirmed by Doppler ultrasonography. In one graft, blood flow in V5 could not be confirmed using both MRI and Doppler ultrasonography.

The total congestion score in the anterior segment in the first month of transplantation is shown in Figure 1. MRI scans of the grafts were obtained from 9 to 30 days (median, 22 days) after transplantation. Timing of MRI scans was similar among groups. Although right-lobe grafts with the MHV showed no congestion at all, congestion score in grafts with V5/8 showed no difference from standard grafts. There was no parenchymal congestion in segments 6 and 7 in right-lobe grafts with additional V5/V8 (Fig. 2). Despite the patency of reconstructed veins, mild parenchymal congestion remained in the anterior segment in most of the grafts. Patient survival at 12 months was similar among the groups:

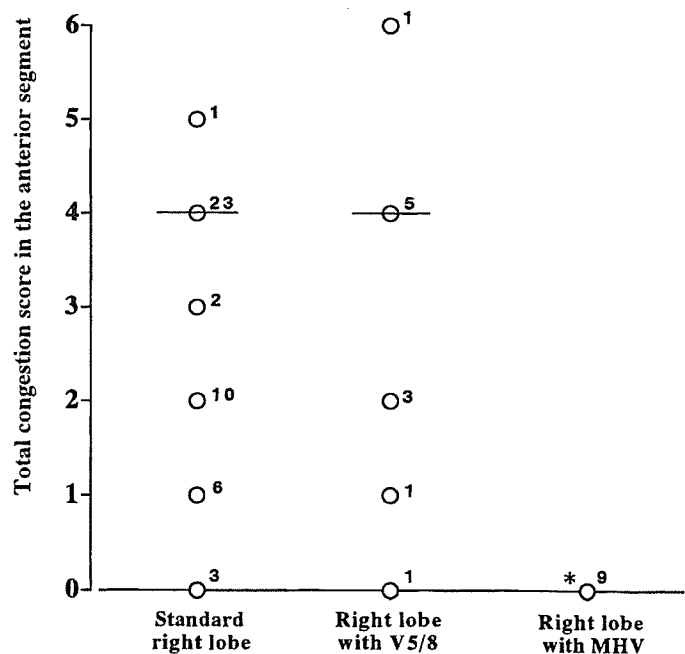


FIGURE 1. Total congestion score in the anterior segment in the first month after transplantation. (Bars) Median values. Numbers on the marks represent the number of grafts. \**P* 0.0006 and *P* < 0.0001, compared with standard right-lobe graft and right-lobe graft with segments 5 and 8, respectively.

90.8% for standard grafts, 100% for grafts with segments 5 and 8, and 100% for grafts with the MHV. One graft with segment 5 and 8 reconstruction showed no tissue congestion.

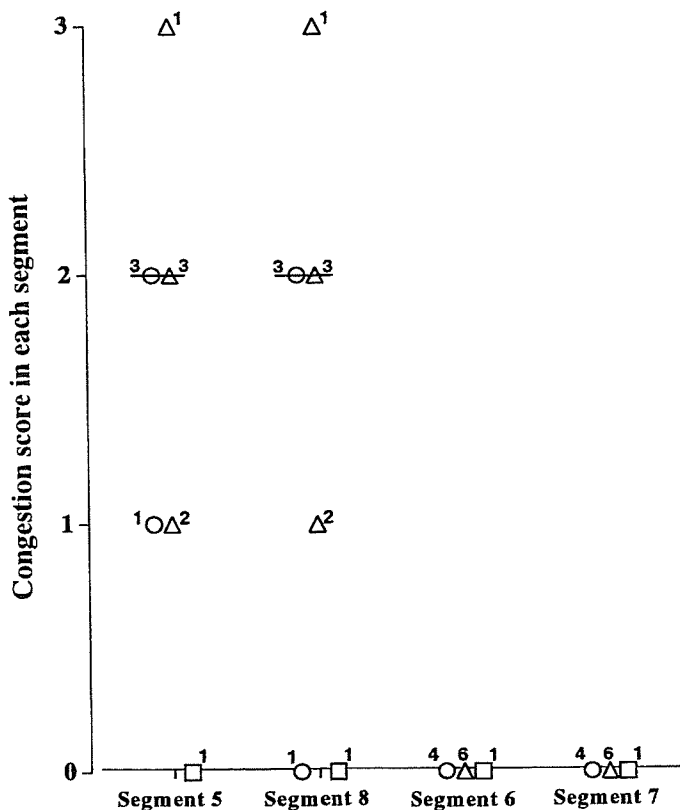


FIGURE 2. Congestion score in each segment of right-lobe grafts with segment 5 and segment 8 reconstruction. Grafts with segment 5 (circles), segment 8 (triangles), and both segment 5 and segment 8 (squares) reconstruction. (Bars) Median values. Numbers on the marks represent the number of grafts.

To evaluate the impact of the tissue congestion, postoperative liver function tests were analyzed in relation to additional vein reconstruction. Aspartate aminotransferase values from day 1 to day 4 in right-lobe grafts with the MHV were significantly lower than other groups. Also, alanine aminotransferase values from day 1 to day 7 in right-lobe grafts with the MHV were significantly lower than in other groups. However, there was no significant difference in serum bilirubin values and ascites production between the right lobe with V5/8 and the MHV (data not shown). Graft-to-recipient weight ratio was similar among groups.

DISCUSSION

Despite routine application of right-lobe grafts to adult recipients, deprivation of drainage veins from the anterior segment to the MHV may reduce graft quality and critically affect the functional capacity of the segment in small-for-size grafts. Lee et al. reported in their LDLT series using the right lobe that two grafts became congestive in the anterior segment, and one of them was lost by small functional capacity of the graft (2). So far in our series, we have not experienced graft loss directly attributable to graft congestion. However, our previous study suggested the latent occurrence of tissue congestion in the anterior segment and the possibility that such latent congestion may impair the functional

capacity of marginal grafts (3). In that study, morphologic changes consistent with graft congestion in the anterior segment occurred in 80% to 90% of the right liver grafts without the MHV. However, graft congestion improved gradually in most grafts after several months. Some salvage mechanisms may work, including intrahepatic anastomosis between the MHV and the RHV (8-10).

The present study clearly showed that right-lobe grafts with additional reconstruction of V5/8 do not significantly reduce tissue congestion defined on MRI despite the patency of reconstructed drainage. It is conjectured that venous drainage of parenchymal tissue adjacent to the MHV is still impaired even by the simple reconstruction of large tributaries to the MHV. Even if it is expected that reverse flow in the tributaries of the MHV later communicates with the RHV by means of small intraparenchymal routes and if the portal vein becomes a drainage route, graft congestion is not completely eradicated and reconstructed tributaries do not work as the MHV. However, interestingly, only one case of reconstruction of both V5 and V8 has no parenchymal congestion. It was assumed that the venous reconstruction of segments 5 and 8 is more potent for relieving parenchymal congestion. In contrast, right-lobe grafts with the MHV were free from any parenchymal congestion, which suggested that the presence of the MHV is necessary for the complete eradication of parenchymal congestion. In contrast, segments 6 and 7 of the right-lobe grafts showed no parenchymal congestion. This suggested that the major part of segments 6 and 7 drains into the RHV and the right accessory hepatic veins, if any. However, the present study investigated the efficacy of venous reconstruction of the marginal graft, and it is not a randomized study. Therefore, when the graft is not a marginal graft, the venous reconstructions are more potent for relieving parenchymal congestion.

CONCLUSION

Tissue congestion in grafts without the MHV is not completely eradicated by additional reconstruction of V5/8, as far as can be seen on MRI. Although the presence of the MHV is necessary for the complete eradication of parenchymal congestion, the venous reconstruction(s) itself may not be necessary when the graft was not a marginal graft. When marginal grafts are encountered in marginal recipients (e.g., small-for-size graft, older grafts, steatotic grafts, or grafts with a smaller RHV than MHV), effort should be made so that grafts are attached with the MHV rather than only tributaries, in the range where quantity and quality including venous drainage of the remnant liver is secured.

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