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Editorial Update

Living Donor Liver Transplantation with Special Reference to ABO-incompatible Grafts and Small-for-size Grafts

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Abstract. Living donor liver transplantation (LDLT) has developed on the basis of increased safety of conventional liver surgery and the need for expanding donor sources, especially in children. Indications for LDLT were soon extended to adult patients in Japan, where cadaveric donation was limited. The right liver is now routinely transplanted to adults to avoid small-for-size graft syndrome, even though the right liver graft has the disadvantages of less remaining donor liver and the question of donor safety. Assessing the suitable size or quality of the graft, as well as of the remnant donor liver, is one of the most important problems in adult LDLT. Although several tactics have been proposed to manage the small-for-size syndrome, their efficacy remains a question. We suggest that small-for-size syndrome is preventable by engaging in careful donor selection or using effective agents for hepatic microcirculatory disturbance control. Sometimes for LDLT only ABO-incompatible grafts are available from relatives, but they must be transplanted despite the expected poor outcome in adults and older children. To overcome the problems in this situation, we developed a novel protocol including intraportal infusion therapy with methylprednisolone, prostaglandin E_1, and gabexate mesylate. Two adult patients undergoing ABO- incompatible LDLT have now survived 53 and 35 months after transplantation with good liver function. However, the other two patients suffered thrombotic microangiopathy postoperatively and died owing to cerebral hemorrhage or multiple organ failure, respectively. Further investigation is needed to improve the outcome of liver transplantation across the ABO blood group barrier.

Living donor liver transplantation (LDLT) has developed on the basis of increased safety of conventional liver surgery and the need to expand donor sources, especially for children. The first LDLT was performed in 1988 in Brazil [1] and was immediately followed in 1989 by LDLTs in Australia, Japan, and the United States [2, 3]. Systematic institutional programs were started at Chicago, Kyoto, and Shinsyu and were further expanded with great success in Japan [4, 5], where cadaveric donation was limited owing to the legal difficulties, cultural factors, and unfavorable sociomedical systems. In this special situation in Japan, indications for LDLT were soon extended to adult patients, and the first adult-to-adult case was reported in 1993 from Shinsyu University [6].

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Although only the left liver was utilized as a graft at the beginning, the right liver is now routinely transplanted to adult patients to avoid small-for-size graft syndrome [7]. The right liver graft has the advantage for the recipient of a larger graft size but the disadvantage for the donor in that the remaining liver is diminished and may jeopardize donor safety. Assessing the suitable size and quality of the graft, as well as that of the remnant donor liver, is one of the most important problems associated with adult LDLT. The minimum requirements for graft size and remnant donor liver volume are currently being discussed, as are considerations of functional quality.

Another hurdle for LDLT is the need to achieve transplantation across the ABO blood group barrier, which generally results in low success rates. In Japan, where cadaveric donation is rare and donor selection is limited, when an ABO-matched donor cannot be found among the patient's relatives, end-stage liver disease sufferers have no choice but to submit to ABO-incompatible LDLT. ABO-mismatched liver transplantation seems to be a special issue only for LDLT, but its management would lead to an expansion of the donor pool and cadaveric transplantation. In this article, we describe the results of LDLT performed in our institution and discuss the problems associated with this approach, focusing on ABO-incompatible grafts and small-for size grafts.

LDLT in our Institution

Patients and Methods

Between April 1995 and April 2003, a total of 63 patients (32 children, 31 adults) underwent LDLT for various terminal liver diseases at Keio University Hospital. The major indications were biliary atresia in children and fulminant hepatic failure and primary biliary cirrhosis in adults (Table 1). The donor was one of the parents for all the pediatric patients and one of various relatives for the adults. A left-sided liver graft was applied in all the pediatric patients, whereas the right lobe was used in 13 adults, the left lobe in 11, the left plus caudate lobe in 6, and the extended right lobe in 1. The ABO blood type was matched in most of the cases, although three children and four adults received incompatible grafts.

Table 1. Indications, donors, grafts, and blood type matching.

Children (n = 32)[a]	Adults (n = 31)[b]
Indications	
Biliary atresia (n = 26)	Fulminant hepatitis (n = 9)
Fulminant hepatitis (n = 5)	PBC (n = 8)
Wilson's disease (n = 1)	Hepatitis B (± HCC) (n = 3:1)
	Hepatitis C (± HCC) (n = 1:1)
	Alcoholic LC (n = 2)
	PSC (n = 2)
	Caroli's disease (n =1)
	FAP (n = 1)
	Wilson's disease (n =1)
	Metastatic neoplasm (n = 1)
Donor	
Father (n = 15)	Father (n = 3)
Mother (n = 17)	Mother (n = 3)
	Offspring (n = 8)
	Sibling (n = 7)
	Spouse (n = 10)
Graft	
Lateral segment (n = 18)	Left lobe (n = 11)
Ext. lateral segment (n = 5)	Left lobe + S1 (n = 6)
Left lobe (n = 8)	Right lobe (n = 13)
Left lobe + S1 (n = 1)	Ext. right lobe (n = 16)
Blood type matching	
Identical (n = 23)	Identical (n = 1)
compatible (n = 6)	Compatible (n = 11)
Incompatible (n = 3)	Incompatible (n = 4)

PBC: primary biliary cirrhosis; HCC: hepatocellular carcinoma; LC: liver cirrhosis; PSC: primary sclerosing cholangitis; FAP: familiar amyloid polyneuropathy.

[a]Age range = 2 months ~17 years

[b]Age range = 22 ~60 years

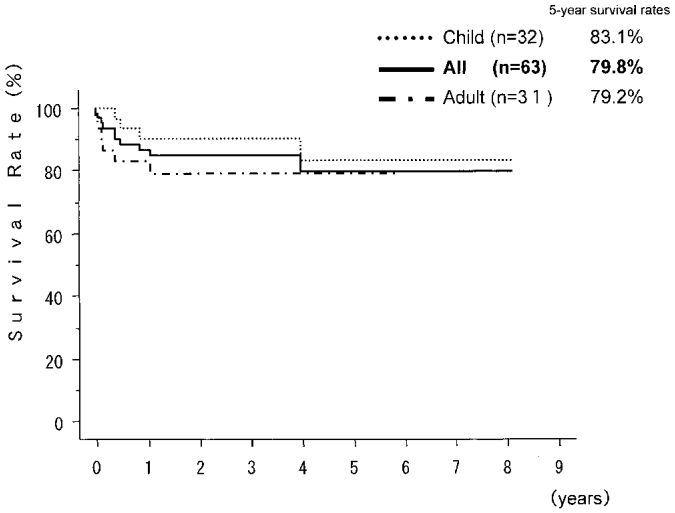

Fig. 1. Kaplan-Meier survival curves in the patients who underwent living donor liver transplantation in our institute. The 5-year cumulative survival rates were 79.8% in all, 83.1% in children, and 79.2% in adults. There were no statistically significant differences in the survival rates between the groups.

Mortality and Survival Rate

During the follow-up period of 1 month to 8 years (median 25.9 months), 55 patients remained alive, and 8 (3 children, 5 adults) are dead; thus the mortality rate was 12.7% for all recipients: 9.4% among children and 16.1% among adults. The causes of death included liver failure due to sepsis or probable immunologic responses, uncontrollable coagulopathy, brain death caused by fulminant hepatic encephalopathy, cardiac failure of unknown origin, brain hemorrhage due to mycotic *Aspergillus* aneurysm, or thrombotic microangiopathy. The 5-year cumulative survival rates were 79.8% in all, 79.2% in adults, and 83.1% in children (Fig. 1). There were no statistically significant differences between the groups. In general, adult patients had a worse prognosis than the pediatric patients after LDLT. According to the registry by the Japanese Liver Transplantation Society, the 5-year cumulative survival rates were 69.0% in adults ($\geq$ 18 years old) and 81.3% in children, which showed a statistically significant difference ($p < 0.001$).

Morbidity

A variety of complications occurred postoperatively: rejection, biliary or vascular complications, intraabdominal or intracranial hemorrhage, and infections. It would be expected that living-related donor transplantation would have some advantages in terms of histocompatibility matching and a low incidence of rejection compared with cadaveric transplantation. In our experience, acute cellular rejection proven by biopsy occurred in 26 patients (41.3%) under basic immune prophylaxis with tacrolimus (or cyclosporine A) and steroids. Severe rejection occurred in only seven patients (11.1%) including possible humoral rejection in an ABO-incompatible case, but no refractory rejection occurred. All episodes of rejection were controllable by steroid pulsing, except for a patient who had to be treated with OKT3 after abrupt noncompliant cessation of immunosuppression.

Biliary complications occurred in 20 of 61 patients with biliary reconstruction (32.8%); biliary leakage was seen in 8 patients (13.1%) and anastomotic stenosis in 9 (14.8%), especially in adults with a duct-to-duct anastomosis, who had the highest incidence of stenosis (5/15, 33.3%) [8]. Therefore we limited the use of duct-to-duct anastomosis to patients who had a sufficient blood supply to the anastomotic site, no tension at the anastomosis, a single orifice of the graft hepatic duct, and use of external stents.

Vascular complications developed in 10 patients (15.9%: 8 children and 2 adults), and 7 of them (11.1%: 5 children and 2 adults) required surgical intervention. These results are comparable to those reported in the Western literature. Complications in the five surgically treated children consisted of hepatic artery thrombosis (HAT) in three, portal vein thrombosis (PVT) in one, and portal compression by abdominal wall closure in one. The other three children who suffered HAT, PVT, or both were treated by interventional radiology. Complications in the two adults who needed surgery were portal obstruction due to drainage tube compression and splenic artery steal syndrome treated by splenic artery ligation. HAT and PVT occurred only in children and did not result in any fatal outcomes. Anticoagulants such as a serine protease inhibitor gabexate mesylate and antithrombin III were routinely used after transplantation, although heparin was administered according to coagulation data criteria: prothrombin time (PT)-INR < 2.0 and activated partial thromboplastin time (aPTT) < 45 in children; PT-INR < 1.5 and aPTT < 40 in adults.

Liver Transplantation across ABO Blood Group Barriers: Historical Review

Gordon and co-workers [9] have shown a significant advantage for ABO donor-recipient identity in liver transplantation, although the

Table 2. Keio University protocol for ABO-incompatible LDLT.

Systemic antirejection therapy
Perioperative plasma exchange: antidonor blood group IgG, IgM titer $\leq \times 16$
Splenectomy
Triple immunoprophylactic therapy: steroid, tacrolimus, cyclophosphamide or azathioprine
Intraportal infusion therapy: continuous infusion via a portal vein catheter for 21 days after transplantation
Methylprednisolone 125 mg/day for 7 days, then gradually tapered
Prostaglandin E_1 10 ng/kg/min
Gabexate mesylate 1 mg/kg/day

LDLT: living donor liver transplantation; Ig: immunoglobulin.

liver is resistant to hyperacute rejection from either type of antibody. They recommended that incompatible grafts be limited to small children or patients in urgent need of transplantation or retransplantation. Demetris et al. [10] drew attention to the phenomenon of antibody-mediated rejection in ABO-incompatible liver grafts. They documented a high rate of early graft failure and histologically widespread hemorrhagic necrosis with intraorgan thrombosis, as well as prominent arterial deposition of antibody and complement. Accordingly, they termed this syndrome "single-organ disseminated intravascular coagulation (DIC)."

Subsequently, the Paris group [11] demonstrated a high rate of graft failure (5-year graft survival was only 20%) and an increased frequency of severe rejection crises, arterial thrombosis, and biliary injury. Strong immunosuppression and plasmapheresis had little influence on poor outcome and were associated with a higher incidence of sepsis They therefore concluded that the use of ABO-incompatible liver grafts is justifiable only in emergencies, such as fulminant liver failure. In contrast, Cacciarelli et al. [12] demonstrated that ABO-incompatible liver transplantation could be accomplished successfully in infants with standard immunosuppressive protocols, and it resulted in a long-term outcome similar to that of ABO-compatible transplants.

ABO-incompatible LDLT: Keio University Protocol

Sometimes for LDLT, only ABO-incompatible grafts are available from relatives and must be transplanted despite the expected poor outcome in adults and older children. To overcome the hurdle in this situation, we developed a novel protocol that consists of two parts (Table 2).

The first part is a systemic antirejection therapy that basically follows the kidney protocol; that is, plasmapheresis is started preoperatively to reduce the level of antidonor blood group antibody to below 16×. Splenectomy is performed during transplantation to suppress antibody production. Triple immune prophylaxis based on a combination of steroids, tacrolimus, and antiproliferative agents is adopted. The target trough level of tacrolimus is set relatively high, at around 20 ng/ml for the first 3 weeks, and it is then rapidly reduced to below 10 ng/ml thereafter.

The second part of our protocol is intraportal infusion therapy [13]. Its main purpose is to control any local DIC arising in ABO-incompatible grafts. Three agents—methylprednisolone, prostaglandin E (PGE_1), and gabexate mesylate—are infused continuously for 3 weeks after transplantation through a catheter that had been placed in the portal vein during surgery. Methylprednisolone has a wide spectrum of antiinflammatory and immunosuppressive effects. PGE_1 improves hepatic blood flow and microcirculation through its vasodilating effects and inhibits platelet/leukocyte adhesion. Gabexate mesylate is a serine protease inhibitor that inhibits thrombin, Xa, and platelet aggregation. These agents seemed to us to be logically appropriate to control local DIC and immune responses. In pediatric patients, neither splenectomy nor intraportal infusion is indicated, but plasma exchange and triple immune prophylaxis are applied as routine antirejection therapy.

We have transplanted seven ABO-incompatible livers into three children and four adults. All the pediatric patients were infants less than 13 months old with biliary atresia. The four adults underwent transplantation for PBC, fulminant hepatic failure, and hepatitis B cirrhosis. The blood type combinations were B to O in three and one each of A to B, B to A, A to O, and AB to A. To date, all the pediatric patients are alive. Their postoperative courses were mostly uneventful, although HAT or bile leakage occurred. Late-onset HAT was successfully treated with interventional radiology, and bile leakage was cured by percutaneous drainage.

Among the adults, two patients have been doing well for 53 and 35 months, respectively, after transplantation despite temporary postoperative complications. The other two patients suffered from severe complications such as thrombotic microangiopathy (TMA), although their initial graft function was satisfactory. Antidonor blood group antibody titer in all cases remained low throughout the postoperative course. One patient had severe thrombocytopenia, hemolytic anemia with many fragmented red blood cells, and elevated lactate dehydrogenase (LDH) levels, suggesting a diagnosis of TMA; the patient died of a cerebral hemorrhage on day 16. It is unclear whether the cause of his death was related to the ABO-incompatible transplantation. However, high trough levels of tacrolimus and application of cyclophosphamide might influence such a complication. The other patient had postoperative complications such as biliary leakage, acute cellular rejection, and TMA and finally developed liver failure. She died of multiple organ failure 4 months after transplantation. The autopsy revealed severe intimal hyperplasia of the hepatic arterioles and portal venules, perivascular fibrosis of the central veins, degeneration of the hepatic ducts, and hemorrhagic necrosis in the grafted liver. TMA, which seemed to cause death or at least influence the prognosis in both patients, is not a condition commonly associated with liver transplantation, but it has been reported as a notable complication seen with bone marrow [14] and renal [15] transplantation. We had two patients with TMA among the four adults who underwent ABO-incompatible LDLT, and we failed to save them. It remains as a matter to be determined whether ABO-incompatible transplantation itself had any influence on the occurrence of TMA.

Recent advances in immunomodulatory therapy for ABO-mismatched grafts include the use of anti-CD20 monoclonal antibody or soluble complement receptor [16]. Further investigation is needed to improve the outcome of liver transplantation across the ABO blood group barrier.

Deciding on the Partial Liver Graft Type for Adults

A major concern for LDLT in adults is to determine the appropriate graft size, considering the balance between donor safety and the recipient's requirements. Among 806 LDLTs reported to the European Liver Transplant Registry by the end of 2001, 4 (0.5%) donor deaths were recorded. The first donor death among more than 2300 LDLT donors in Japan has occurred quite recently.

Donor safety is the top priority during LDLT. Resection of an excessive liver volume from the donor should therefore be strictly avoided. In general, if less than 30% of the whole liver remains in the donor, safe donation is not possible. As an aid to deciding on the volume of liver that can be safely removed for grafting, we calculate the donor's liver volume by computed tomography (CT); that is, the volumes of the left liver, right liver, and caudate lobe. If the left liver (segments 2, 3, and 4) or the left liver plus caudate lobe (segment 1) constitutes more than 35% of the standard liver volume (SLV) of the recipient, we use these portions as the graft. When the left-sided liver is less than 35% of the SLV of the recipient, we consider grafting the right liver. However, if the right liver volume of the donor makes up more than 65% of the donor's whole liver (i.e., the remaining liver volume of the donor is less than 35% of the whole liver), the donor is not acceptable.

Small-for-size Grafts for Adult Recipients: Brief Review

Even when following these general criteria to guide donor liver excision decisions, there are still cases in which the actual graft volume diverges from the estimated volume and constitutes less than 35% of the recipient's SLV. When the grafted liver is too small to meet the recipient's metabolic demands, various symptoms due to liver insufficiency can occur. This unfavorable condition, which includes such symptoms as persistent jaundice, massive ascites, coagulopathy, and renal failure, is termed "small-for-size syndrome." In an animal model, the minimum graft size for successful orthotopic partial liver transplantation is estimated to be about 25% to 30% of the recipient's original liver volume [17, 18]. In the clinical situation, Kiuchi et al. [19] demonstrated that the use of small-for-size grafts (less than 1% of the recipient's body weight or less than 50% of the SLV) leads to lower graft survival (61% at 1 year), and extra-small-for-size grafts (less than 0.8% of the recipient's body weight or less than 40% of the SLV) had an extremely low success rate (42% at 1 year). Lo et al. [20] and Sugawara et al. [21] also suggested that a graft weight / SLV ratio of 40% or less predicts a decreased chance of survival after LDLT. In contrast, Lo et al. [22] reported a successful case in which the patient received a small-for-size graft weighing only 25% of the recipient's standard liver mass during LDLT for fulminant hepatic failure. Nishizaki et al. [23] also showed that all five patients who received extra-small grafts with graft volume / SLV ratios of26% to 29% survived with no graft loss. Therefore, they concluded that small-for-size grafts of less than 30% of SLV could be employed together with careful intraoperative and postoperative management.

These findings together suggest that although small grafts of less than 40% of SLV do create a high risk for small-for-size syndrome it is also true that such small grafts do not always cause its development. Not only graft volume but also other factors such as graft quality, graft hemodynamics, ischemic time, and preoperative patient state seem to contribute to the development of this syndrome.

Several investigators have focused on graft hemodynamics, especially portal circulation, as a causative factor. Man et al. [24] reported that patients implanted with small-for-size grafts suffered from transient portal hypertension early after reperfusion and that the phenomenon was accompanied by intragraft endothelin-1 overexpression and plasma nitric oxide (NO) level reduction, leading to sinusoidal constriction together with down-regulation of heme oxygenase-1 and heat shock protein 70, which may account for the small-for-size graft injury. Smyrniotis et al. [25] also mentioned that small-for-size split liver transplantation might be associated with portal hypertension and diminished hepatic arterial flow. This impaired arterial flow appeared to be related to increased portal vein flow and intrahepatic portal hypertension. To avoid the small-for-size graft injury caused by portal overperfusion, several methods such as mesocaval shunting [26] and splenic artery ligation [27] have been applied to attenuate portal hypertension after reperfusion.

Several drugs are probably beneficial for the maintenance of hepatic microcirculation even in a small-for-size graft. ET-1 antagonists, NO donors, interleukin-1 receptor antagonists, and prostaglandin E_1 (PGE_1) have been shown to attenuate ischemia/reperfusion injury in the rat liver [28]. We demonstrated in the porcine liver transplantation model that intraportal infusion of PGE_1 improved hepatic allograft blood flow, predominantly through an effect on the hepatic arterial flow, and it might improve graft viability after orthotopic liver transplantation [29]. These drugs might have potential for attenuating small-for-size graft injury. Further basic and clinical investigations will clarify this issue.

Our Tactics and Results of LDLT Using Small-for-size Grafts

Based on the experimental data from porcine liver transplantation, we routinely use intraportal PGE_1 infusion at a dose of 5 to 10 ng/kg/min to maintain graft microcirculation and graft viability after adult LDLT. Currently, 25 of 31 adult LDLT cases have accepted intraportal infusion therapy for 1 to 3 weeks after surgery. As a technical issue, a temporary portosystemic bypass was created during the anhepatic phase in noncirrhotic patients or in patients with small-for-size grafts to prevent portal congestion and to attenuate any reperfusion injury. The portosystemic passive bypass was established using a heparin-bound bypass catheter between the inferior mesenteric vein and the left axillary vein, and the bypass flow was monitored by an ultrasonic transonic flowmeter.

For hepatic vein reconstruction, venoplasty was performed on both the graft and recipient vein to create a wide common anastomotic orifice. All significant (> 5 mm) short hepatic veins in the left liver plus caudate lobe graft or inferior right hepatic veins in the right liver graft were reimplanted directly into the cava. Anterior accessory veins were reconstructed in only one patient, who was given a small-for-size right liver graft without the middle hepatic vein (MHV) trunk because the graft had the great MHV tributaries (V5 was 11 mm, V8 was 8 mm).

Adult patients, excluding ABO-incompatible cases, were categorized into two groups by the graft volume (GV)/SLV ratio. For small-for-size grafts (SSGs), the GV/SLV was $\leq 35\%$ ($n = 5$) and for the relatively large size grafts (LSGs) it was $\geq 50\%$ ($n = 10$). All patients in the SSG group and 8 patients in the LSG group received an intraportal infusion of PGE_1.

Data on the grafts, donors, and recipients classified by graft size are shown in Table 3. There was a significant difference in donor age and graft size between the two groups. Concerning postoperative graft function, the serum total bilirubin and AST levels were similar for the two groups. The postoperative prothrombin times showed no statistically significant differences. Neither were there any significant differences in the amounts of postoperative ascites drainage between the groups (Fig. 2). The mortality rates were 0% in the SSG group and 10% in the LSG group (not significantly different). Our results demonstrate that the SSG in this particular situation survived with good postoperative function and did not lead to small-for-size syndrome.

Table 3. Graft, donor, and recipient data.

Parameter	LSG GW/SLV ≥ 50% (n = 10)	SSG GW/SLV ≤ 35% (n = 5)	p
Graft weight (g)	629 ± 93 (535–854)	393 ± 15 (384–414)	< 0.0001
GW/SLV (%)	59.4 ± 10.1 (51.7–84.4)	33.2 ± 2.1 (29.7–35.0)	< 0.0001
Right : left	7:3	0:5	
Donor age (years)	50 ± 10 (29–61)	25 ± 9 (20–41)	0.0001
Recipient age (years)	50 ± 9	37 ± 13	NS
Operating time (min)	721 ± 115		NS
CIT (min)	56 ± 25	50 ± 19	NS
WIT (min)	41 ± 6	649 ± 60	
		40 ± 9	NS

SSG: small-for-size grafts; LSG: relatively large size grafts; GW: graft weight; SLV: standard liver volume; CIT: cold ischemic time; WIT: warm ischemic time.

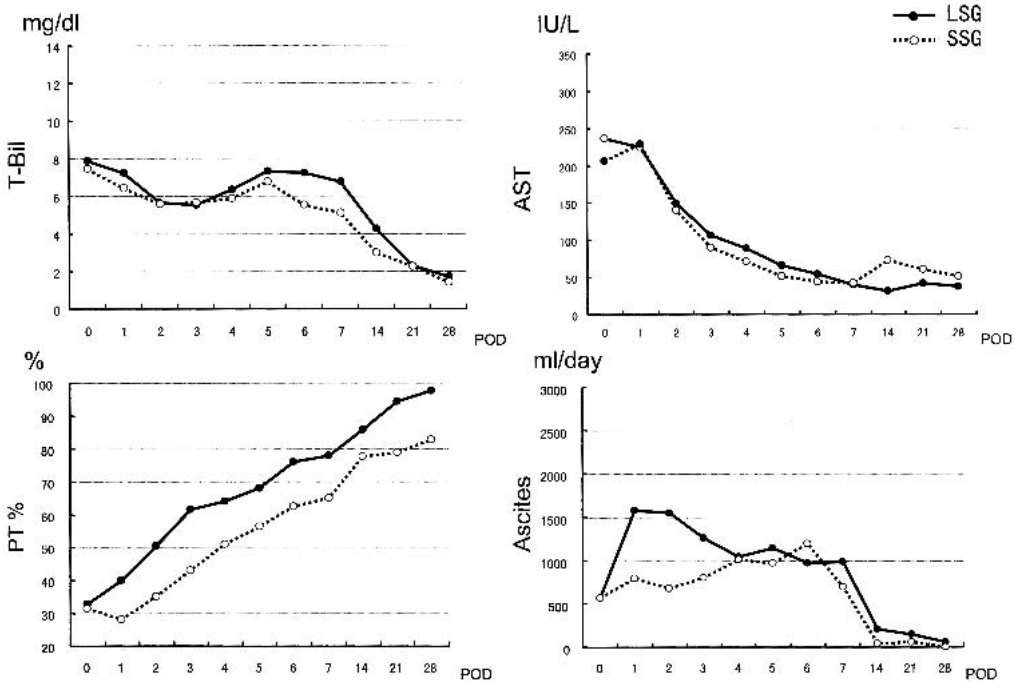

Fig. 2. Comparison of postoperative graft function between the small-for-size grafts group (SSG) and the relatively large size grafts group (LSG). The serum levels of total bilirubin (T-Bil) and aspartate aminotransferase (AST) were similar for the two groups. The postoperative prothrombin times (PT) and the postoperative ascites drainage amounts showed no statistically significant differences between the two groups.

Although the contributory factors for good results cannot be clearly determined here, it is speculated that the significantly younger age of donors of SSGs might have contributed. In general, old donor age (≥ 60 years) is a significant risk factor and is associated with decreased graft survival in cadaveric liver transplantation [30]. In our series, none of the four donors older than 60 years was assigned to the SSG group, and all the grafts from old donors had GV/SLV ratios of 42% to 54%.

The small-for-size syndrome developed only in a 38-year-old man with a minimum graft of 42% GV/SLV from a 65-year-old donor (his father). This patient underwent LDLT for primary sclerosing cholangitis in Child-Pugh C stage (scoring 13 points) and suffered persistent hyperbilirubinemia, ascites, and renal dysfunction for 2 months postoperatively, even though splenic artery ligation and intraportal PGE_1 infusion was performed to prevent the small-for-size syndrome. Thereafter, graft function gradually recovered with sufficient liver regeneration.

We cannot conclude that intraportal infusion of PGE_1 plays an important role in preventing the small-for-size syndrome because there have been no controlled studies. However, in view of our satisfactory LDLT results using SSGs, we believe that intraportal PGE_1 infusion is likely to have been beneficial for the maintenance of graft viability and function in SSGs.

Conclusions

It is concluded that small-for-size syndrome is caused not only by SSGs but also when medium-size grafts with functional or circulatory problems are employed (e.g., grafts from old donors or grafts with outflow block). We suggest that small-for-size syndrome may be preventable by careful donor selection or by using effective agents for hepatic microcirculatory disturbance control, such as PGE_1.

Résumé. L'idée de la transplantation hépatique dont le greffon provient d'un foie d'un donneur vivant (THDV) est basée sur une sécurité accrue de chirurgie conventionnelle et le besoin de trouver une source nouvelle de donneurs, surtout pour les enfants. Les indications de la THDV se sont très

vite étendues aux patients adultes au Japon, un pays où la disponibilité des cadavres est limitée. Le foie droit est actuellement transplanté aux adultes de façon routinière afin d'éviter le syndrome du petit greffon. Le prélèvement du foie droit présente deux inconvénients: la taille du foie donneur restant et la sécurité vitale du donneur. L'évaluation de la taille et de la qualité du greffon tout comme celles du foie restant du donneur est un des problèmes les plus importants en matière de THDV chez l'adulte. Bien qu'il existe plusieurs tactiques pour éviter le syndrome du petit greffon, leur efficacité reste un sujet de débat. Nous suggérons que le syndrome du petit greffon peut être évité par une sélection soigneuse des donneurs ou par l'utilisation d'agents efficaces pour contrôler les perturbations de la microcirculation hépatique. Quelquefois, en cas de THDV, seulement des greffons ABO incompatibles sont disponibles à partir des parents, et on est obligé de transplanter chez les adultes et les enfants plus âgés, malgré un pronostic plus mauvais. Pour surmonter l'obstacle dans cette situation, nous avons dévélopé un nouveau protocole qui comprends une infusion intra-portale de méthylprednisolone, de la prostaglandine E1 et de la gabexate mésilate. Deux patients adultes ayant eu une THDV avec un greffon ABO incompatible sont actuellement en survie 53 et 35 mois post-transplantation avec une fonction hépatique satisfaisante. Cependant, les deux autres patients ont eu une microangiopathie thrombotique en post-opératoire et sont décédés d'hémorragie cérébrale ou de défaillance polyviscérale. Il faut continuer les progrès pour améliorer l'évolution de la transplantation hépatique en dépit de la barrière ABO.

Resumen. El trasplante de hígado de donante vivo (THDV) se ha desarrollado con base en la creciente seguridad de la cirugía hepática convencional y la necesidad de ampliar las fuentes de donantes, especialmente en niños. Las indicaciones para THDV se extendieron prontamente a pacientes adultos en el Japón, donde la donación cadavérica es limitada. El hígado derecho actualmente es trasplantado rutinariamente en adultos con el fin de evitar el síndrome del injerto pequeño para el tamaño del receptor, pero tiene la desventaja en cuanto al tamaño residual del donante y a la seguridad del donante vivo. La evaluación de un volumen y una calidad adecuados del injerto, así como del remanente del hígado donante constituye uno de los más importantes problemas en el THDV. Aunque se han propuesto diversas tácticas para manejar el síndrome de injerto pequeño para el tamaño del receptor, su eficacia está aún por discutir. Sugerimos que el síndrome puede ser prevenido mediante una cuidadosa selección cuidadosa del donante o con el uso de agentes para el control de las alteraciones de la microcirculación hepática. En algunos casos de THDV, sólo se encuentran disponibles injertos ABO incompatibles de parientes, y se hace obligatorio el trasplante a pesar de la presumible asociación con resultados pobres en adultos y en niños mayores. Para sortear esta dificultad, hemos desarrollado un novel protocolo que incluye la infusión intra-portal de metilprednisolona, prostaglandina E-1 y mesilato gabexato. Dos pacientes adultos sometidos a THDV ABO- incompatible han sobrevivido 53 y 35 meses luego del trasplante con buena función hepática. Sin embargo, los otros dos pacientes desarrollaron microangiopatía trombótica postoperatoria y murieron por hemorragia cerebral o falla orgánica múltiple. Se requiere investigación adicional para mejorar los resultados del trasplante hígado a través de la barrera del grupo sanguíneo ABO.

References

1. Raia S, Nery JR, Mies S. Liver transplantation from live donors. Lancet 1989;2:497
2. Strong RW, Lynch SV, Ong TH, et al. Succesful liver transplantation from a living donor to her son. N. Engl. J. Med. 1990;322:1505–1507
3. Broelsch CE, Whitington PF, Emond JC, et al. Liver transplantation in children from living related donors: surgical techniques and results. Ann. Surg. 1991;214:428–437
4. Ozawa K, Uemoto S, Tanaka K, et al. An appraisal of pediatric liver transplantation from living relatives: initial clinical experiences in 20 pediatric liver transplantations from living relatives as donors. Ann. Surg. 1992;216:547–553
5. Hashikura Y, Makuuchi M, Kawasaki S, et al. Living-related liver transplantation: report of experiences at Shinsyu University Hospital. J. Hepatobiliary. Pancreat. Surg. 1995;2:52–57
6. Hashikura Y, Makuuchi M, Kawasaki S, et al. Successful living-related partial liver transplantation to an adult patient. Lancet 1994;343:1233–1234
7. Yamaoka Y, Washida M, Honda K, et al. Liver transplantation using a right lobe graft from a living related donor. Transplantation 1994;57: 1127–1130
8. Kawachi S, Shimazu M, Wakabayashi G, et al. Biliary complications in adult living donor liver transplantation with duct-to-duct hepaticocholedochostomy or Roux-en-Y hepaticojejunostomy biliary reconstruction. Surgery 2002;132:48–56
9. Gordon RD, Iwatsuki S, Esquivel CO, et al. Liver transplantation across ABO blood groups. Surgery 1986;100:342–348
10. Demetris AJ, Jaffe R, Tzakis A, et al. Antibody-mediated rejection of human orthotopic liver allografts. A study of liver transplantation across ABO blood group barriers. Am. J. Pathol. 1988;132:489–502
11. Farges O, Kalil AN, Samuel D, et al. The use of ABO-incompatible grafts in liver transplantation: a life-saving procedure in highly selected patients. Transplantation 1995;59:1124–1133
12. Cacciarelli TV, So SK, Lim J, et al. A reassessment of ABO incompatibility in pediatric liver transplantation. Transplantation 1995;60:757–760
13. Tanabe M, Shimazu M, Wakabayashi G, et al. Intraportal infusion therapy as a novel approach to adult ABO-incompatible liver transplantation. Transplantation 2002;73:1959–1961
14. Pettitt AR, Clark RE. Thrombotic microangiopathy following bone marrow transplantation. Bone Marrow Transplant. 1994;14:495–504
15. Chiurichiu C, Ruggenenti P, Rmuzzi G. Thrombotic microangiopathy in renal transplantation. Ann. Transplant. 2002;7:28–33
16. Pierson RN, Loyd JE, Goodwin A, et al. Successful management of an ABO-mismatched lung allograft using antigen-specific immunoadsorption, immunomodulatory therapy. Transplantation 2002;74:79–84
17. Shirakata Y, Terajima S, Mashima S, et al. The minimum graft size for successful orthotopic partial liver transplantation in the canine model. Transplant. Proc. 1995;27:545–546
18. Yanaga K, Kishikawa K, Suehiro T, et al. Partial hepatic grafting: porcine study on critical volume reduction. Surgery 1995;118:486–492
19. Kiuchi T, Kasahara M, Uryuhara K, et al. Impact of graft size mismatching on graft prognosis in liver transplantation from living donors. Transplantation 1999;67:321–327
20. Lo CM, Fan ST, Liu CL, et al. Minimum graft size for successful living donor liver transplantation. Transplantation 1999;68:1112–1116
21. Sugawara Y, Makuuchi M, Takayama T, et al. Small-for-size grafts in living-related liver transplantation. J. Am. Coll. Surg. 2001;192:510–513
22. Lo CM, Fan ST, Chan JK, et al. Minimum graft volume for successful adult-to-adult living donor liver transplantation for fulminant hepatic failure. Transplantation 1996;62:696–698
23. Nishizaki T, Ikegami T, Hiroshige S, et al. Small graft for living donor liver transplantation. Ann. Surg. 2001;233:575–580
24. Man K, Fan ST, Lo CM, et al. Graft injury in relation to graft size in right lobe live donor liver transplantation: a study of hepatic sinusoidal injury in correlation with portal hemodynamics and intragraft gene expression. Ann. Surg. 2003;237:256–264
25. Smyrniotis V, Kostopanagiotou G, Kondi A, et al. Hemodynamic interaction between portal vein and hepatic artery flow in small-for-size split liver transplantation. Transpl. Int. 2002;15:355–360
26. Boillot O, Delafosse B, Mechet I, et al. Small-for-size partial liver graft in an adult recipient; a new transplant technique. Lancet 2002;359:406–407
27. Troici R, Cammu G, Militerno G, et al. Modulation of portal graft inflow: a necessity in adult living-donor liver transplantation? Ann. Surg. 2003;237:429–436
28. Iwata K, Shimazu M, Wakabayashi G, et al. Intraportal perfusion of prostaglandin E1 attenuates hepatic postischemic microcirculatory impairments in rats. J. Gastroenterol. Hepatol. 1999;14:634–641
29. Kawachi S, Shimazu M, Wakabayashi G, et al. Efficacy of intraportal infusion of prostaglandin E1 to improve the hepatic blood flow and graft viability in porcine liver transplantation. Transplantation 1997;64: 205–209
30. Marino IR, Doyle HR, Aldrighetti L, et al. Effect of donor age and sex on the outcome of liver transplantation. Hepatology 1995;22:1754–1762