Table 5: Prognostic factors for infectious complications: univariate analysis of 259 patients given rituximab prophylaxis

			Bacterial infection				Fungal infection				CMV disease			
Characteristics	Category	N	Odds ratio	95% CI	p-Value	p-Value (global association)	Odds ratio	95% CI	p-Value	p-Value (global association)	Odds ratio	95% CI	p-Value	p-Value (global association)
			Logistic regression analysis				Logistic regression analysis				Logistic regression analysis			
Local infusion	No	40	1.000	–	–	–	1.000	–	–	–	1.000	–	–	–
	Yes	218	1.449	0.671–3.128	0.345		0.830	0.173–3.993	0.816		2.945	1.373–6.319	0.006*	
	Unknown	1	–	–	–		–	–	–		–	–	–	
Splenectomy	No	90	1.000	–	–	–	1.000	–	–	–	1.000	–	–	–
	Yes	169	0.588	0.342–1.011	0.055		0.913	0.260–3.208	0.887		1.071	0.641–1.791	0.793	
Anti-lymphocyte antibodies	No	244	1.000	–	–	–	1.000	–	–	–	1.000	–	–	–
	Yes	15	2.010	0.703–5.747	0.193		1.650	0.197–13.82	0.644		1.049	0.369–2.982	0.929	
Prophylactic IVIG after transplantation	No	214	1.000	–	–	–	1.000	–	–	–	1.000	–	–	–
	Yes	45	1.792	0.925–3.471	0.084		1.922	0.489–7.559	0.350		1.626	0.851–3.106	0.141	
Timing of rituximab administration before transplantation	≤ 6 days	22	1.000	0.383–2.501	0.964	–	1.000	–	–	–	1.000	–	–	–
	>7 days	236	0.979	–	–		0.402	0.081–1.988	0.264		1.012	0.421–2.435	0.978	
	Unknown	1	–	–	–		–	–	–		–	–	–	
Number of doses of rituximab	1	225	1.000	–	–	0.513	1.000	–	–	0.010*	1.000	–	–	0.004*
	2	22	0.638	0.227–1.798	0.396		1.543	0.181–13.17	0.692		3.038	1.256–7.980	0.019*	
	3	12	1.549	0.475–5.050	0.468		10.288	2.278–46.47	0.002*		36.742	4.737–999.9	0.017*	
Dose of rituximab	Regular	162	1.000	–	–	–	1.000	–	–	–	1.000	–	–	–
	Small	66	1.742	0.948–3.203	0.074		0.122	0.000–0.984	0.152		0.455	0.249–0.832	0.011*	
	Unknown	31	–	–	–		–	–	–		–	–	–	
Dose and number of doses of rituximab	Regular × 1	134	1.000	–	–	0.283	1.000	–	–	0.040*	1.000	–	–	0.001*
	Regular × 2	16	0.679	0.182–2.526	0.563		2.243	0.220–12.32	0.412		14.802	3.517–137.3	0.003*	
	Regular × 3	12	2.101	0.625–7.058	0.230		8.542	1.756–37.86	0.006*		35.805	4.548–999.9	0.018*	
	Small × 1	60	1.828	0.955–3.501	0.069		0.192	0.001–1.734	0.270		0.780	0.412–1.451	0.440	
	Small × 2	6	1.471	0.258–8.390	0.664		2.108	0.015–23.08	0.657		0.110	0.000–0.964	0.167	
	Unknown	31	–	–	–		–	–	–		–	–	–	
Regimen	RS	30	1.000	–	–	0.266	1.000	–	–	0.685	1.000	–	–	0.034*
	R	10	2.611	0.574–11.71	0.221		3.105	0.232–41.87	0.366		2.609	0.574–11.71	0.221	
	RI	81	2.351	0.929–6.670	0.089		0.900	0.141–9.567	0.917		3.176	1.264–8.982	0.021*	
	RIS	137	1.566	0.642–4.318	0.357		0.980	0.195–9.654	0.983		4.053	1.688–11.07	0.004*	
	Unknown	1	–	–	–		–	–	–		–	–	–	

IVIG, intravenous immunoglobulin; R, only rituximab; regular dose, 500 mg/body or 375 mg/m^2; RI, rituximab and infusion; RIS, rituximab and infusion and splenectomy; RS, rituximab and splenectomy; small dose, 300 mg/body or less.
*$p < 0.05$.

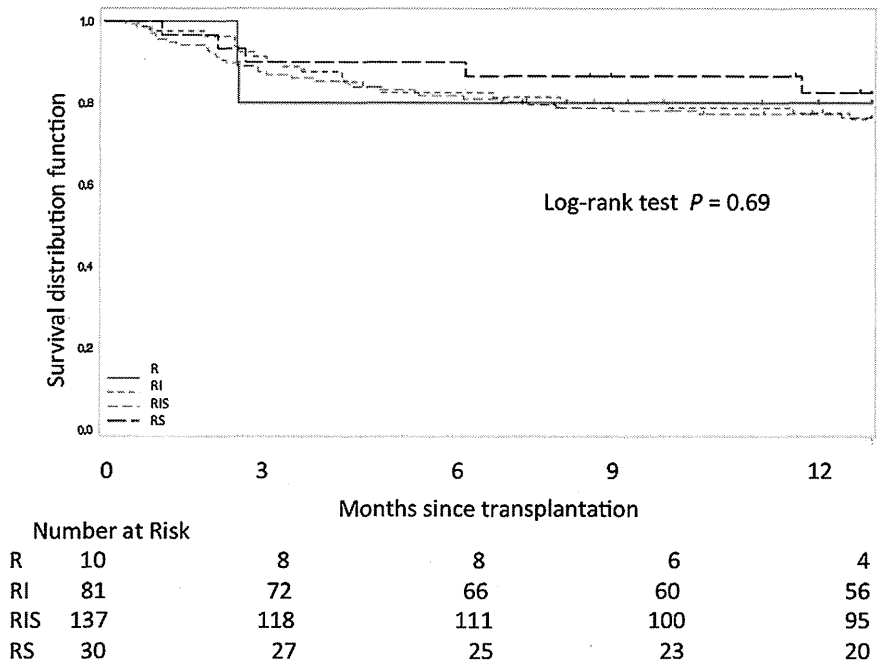

Figure 5: One-year survival of patients in the rituximab group. R, rituximab without splenectomy or local infusion (n = 10); RI, rituximab with infusion but without splenectomy (n = 81); RIS, rituximab with both infusion and splenectomy (n = 137); RS, rituximab with splenectomy but without infusion (n = 30). There were no significant differences among regimens with additional desensitization in patients with rituximab prophylaxis.

is performed, the greater the potential for an increase in DSA titer. However, we observed no significant relationship between the number of plasmapheresis procedures and clinical outcomes (Table 1).

IVIG is also a standard procedure, especially for human leukocyte antigen-related DSA in kidney transplantation, and the IVIG dose often ranged from 0.1 to 2 g/kg (18,19). In liver transplantation, Ikegami et al (4) reported a small series with desensitization by rituximab and IVIG (0.8 g/kg), and their cases were included here. We found no significant effect of IVIG on overall survival or AMR in the entire adult cohort (Table 1) and no additional effects in the rituximab group (Table 5). We analyzed the AMR incidence in each regimen with IVIG versus without IVIG (Figure 6). The AMR incidence was reduced from 26% to 9% in the local infusion and splenectomy (IS; no rituximab) regimen when IVIG was added, but this difference was not significant (p = 0.19). Among regimens with rituximab (R, RI, RIS and RS), the incidences were similar between with IVIG and without IVIG. IVIG is not approved in Japan and is not covered by insurance. IVIG costs 1.5–2.0 million yen per injection, whereas 500 mg of rituximab costs 0.3 million yen. A prospective study is required to elucidate the effects of IVIG in patients after rituximab prophylaxis.

The incidence of adverse effects of rituximab was 1.6% (4/258), and all patients recovered and underwent LDLT. Rituximab prophylaxis could be tolerated by patients with end-stage liver diseases. The incidences of bacterial

Table 6: Comparison of antibody titers between patients with and without AMR under rituximab prophylaxis

		AMR+			AMR−			
		N	Median	Mean ± SD	N	Median	Mean ± SD	p-Value
IgM	Peak before transplantation	15	64	158 ± 255	211	64	147 ± 199	0.881
	At transplantation	16	4	7 ± 8	213	4	16 ± 48	0.700
	Peak posttransplantation	16	64	593 ± 1091	223	8	49 ± 181	<0.001*
IgG	Peak before transplantation	14	128	408 ± 584	215	64	319 ± 771	0.221
	At transplantation	13	16	27 ± 35	210	8	34 ± 96	0.265
	Peak posttransplantation	13	256	1002 ± 2196	212	16	68 ± 187	<0.001*

AMR, antibody-mediated rejection. p-values are derived from Wilcoxon sum-rank test.
*$p < 0.05$ for AMR+ versus AMR−.

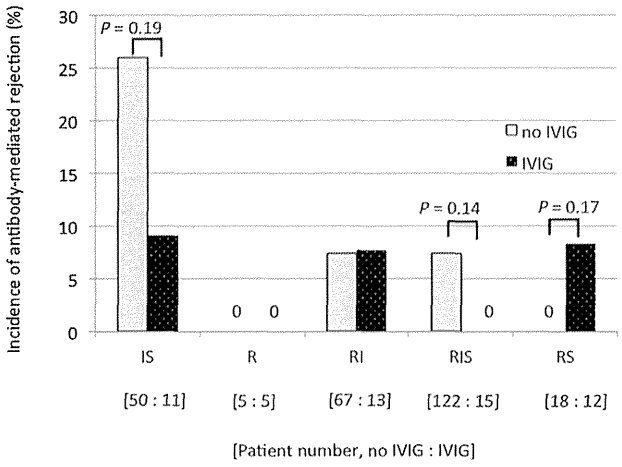

Figure 6: Comparison of the incidences of antibody-mediated rejection (AMR) with and without intravenous immunoglobulin (IVIG) in each regimen. IS, local infusion with splenectomy without rituximab; R, rituximab without splenectomy or local infusion; RI, rituximab with infusion but without splenectomy; RIS, rituximab with both infusion and splenectomy; RS, rituximab with splenectomy but without infusion. There were no significant differences in the incidence of AMR.

infections and CMV disease after transplantation were similar between the nonrituximab and rituximab groups, but the incidence of fungal infection was significantly lower in the rituximab group. Although data for the amount of steroid and trough levels of calcineurine inhibitors were not collected here, the total amount of conventional immunosuppressant might be reduced in light of the expected beneficial effects of rituximab. Lower amounts of conventional immunosuppressants might be a reason for the lower fungal infections.

In this study, half the patients were given 500 mg/body, a quarter were given 300 mg/body and a quarter were given 375 mg/m^2 (corresponding to 430–762 mg/body; median, 600 mg/body). One reason for dose reduction could be concern about potential adverse effects in patients with end-stage liver diseases. In kidney transplantation, Shirakawa et al (20) reported a successful trial to reduce rituximab from 500 to 200 mg/body. Here, there was a tendency toward a higher incidence of AMR in patients treated with ≤300 mg/body compared with 500 mg/body or 375 mg/m^2; however, three patients treated with 130 mg/body or 200 mg/body belonged to the same center, and one of them died from severe AMR. More evidence is needed before we can recommend reducing the rituximab dose below 300 mg/body in liver transplantation.

Multiple administrations of rituximab are standard in the treatment of B cell lymphoma. However, because the amount of targeted B cells is expected to be much smaller in transplant patients, a single dose is usually applied. A single dose is standard in kidney transplantation. Here, there were patients with two administrations in six centers and with three administrations in three centers, but the majority of these patients underwent transplantations in 2010 or earlier. All three centers changed their policy to one dose in 2012 on the basis of our data. The current study clearly demonstrates that multiple doses provide no significant benefit in terms of AMR incidence or survival, whereas they increase the incidences of fungal and CMV infections.

The Kyoto group recommended early administration of rituximab to deplete B cells, although the incidence of clinical AMR did not increase significantly in patients with late administration (2). Here, the timing of rituximab administration had no significant effect on AMR incidence on patient survival. Furthermore, 6 of 22 patients with FHF were given rituximab within 6 days before transplantation and survived without AMR. Hence, administration of rituximab immediately before transplantation is a promising therapeutic strategy.

The titers decrease after desensitization before transplantation and increase or do not change immediately after transplantation, and they usually decrease thereafter when patients survive (1). Hence, the optimum cut-off values vary among time points, between IgM and IgG. In rituximab-treated patients, peak IgG and IgM DSA titers posttransplantation were significantly greater in those with AMR, and the AMR incidence was significantly higher in patients with peak titers posttransplantation above optimum cut-off values calculated from ROC curves (i.e. IgM, ≥64; IgG, ≥128). Theoretically, it is an option to treat patients preemptively by using other desensitization methods such as IVIG and plasmapheresis when antibody titers are above the cut-off values; however, the decision is still difficult.

This study had limitations. It was an uncontrolled retrospective observational study with many confounders, some of which may have been nonrandom and unaccounted for, and thus despite the use of appropriate multivariate statistics unknown bias was possible. Because of the extent of co-linearity between rituximab and era, estimates of regression coefficients still might be unstable, although we tried to adjust era effects as much as possible. Prospective studies are required to examine the causality of the relationships found.

In conclusion, outcomes in adult ABO-I LDLT have significantly improved in the latest era coincident with the introduction of rituximab.

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Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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ORIGINAL ARTICLE

Selection of a Right Posterior Sector Graft for Living Donor Liver Transplantation

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Right posterior sector (RPS) grafts have been used to overcome graft size discrepancies, the major concern of living donor liver transplantation. Previous studies have reported the volumetry-based selection of RPS grafts without anatomical exclusion. We reviewed our data and established selection criteria for RPS grafts. The procurement of RPS grafts [conventional (n = 3) and extended (n = 5)] was performed for 8 of 429 recipients at our center. Extended RPS grafts contained the drainage area of the right hepatic vein. The mean graft weight (GW) according to 3-dimensional computed tomography volumetry was 488 g, and the GW/standard liver weight (SLW) ratio was 42.6%. The mean actual GW was 437 g, and the GW/SLW ratio was 38.4%. One donor exhibited standard bifurcation of the right portal vein (PV) and the left PV, and 2 donors exhibited trifurcation of the left PV, the right anterior portal vein (APV), and the posterior PV. The remaining 5 donors exhibited APV branching from the left PV, which is the most suitable anatomy for RPS grafts. Two recipients died of sepsis or small-for-size graft syndrome. One underwent retransplantation because of an intractable bile leak and fibrosing cholestatic hepatitis. Intractable bile duct (BD) stenosis developed in 4 of the 6 survivors. In conclusion, with the significant complications and potential concerns associated with RPS grafts, these grafts should be used very rarely and with extreme caution. Donors with the standard bifurcation of the PV and the posterior BD running through the dorsal side of the posterior PV are not suitable candidates for RPS grafts. Extended RPS graft procurement is recommended for easier parenchymal transection. ***Liver Transpl 20:1089-1096, 2014.*** **© 2014 AASLD.**

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See Editorial on Page 1019

Since a 1994 report demonstrating successful living donor liver transplantation (LDLT) between adults,[1] living donors have been increasingly used because of the disparity between the demand and the supply. Right lobe (RL) grafts, which account for >60% of the total liver mass, are the allografts most commonly used for LDLT. Although our previous reports have indicated an average hospital stay of <14 days and the performance of living donation without the need for nonautologous blood transfusions,[2,3] serious donor complications and death are possible. In the

Abbreviations: ACR, acute cellular rejection; AD, anterior duct; AIH, autoimmune hepatitis; APV, anterior portal vein; BD, bile duct; CT, computed tomography; D-D, duct-to-duct anastomosis; FCH, fibrosing cholestatic hepatitis; GW, graft weight; HA, hepatic artery; H-J, Roux-en-Y hepaticojejunostomy; LC-B, liver cirrhosis due to hepatitis B; LC-C, liver cirrhosis due to hepatitis C; LDLT, living donor liver transplantation; LHD, left hepatic duct; LL, left lobe; LL+C, left lobe with caudate lobe; MELD, Model for End-Stage Liver Disease; PBC, primary biliary cirrhosis; PD, posterior duct; PHA, posterior hepatic artery; PHD, posterior hepatic duct; PSC, primary sclerosing cholangitis; PV, portal vein; RHV, right hepatic vein; RL, right lobe; RPS, right posterior sector; RW, recipient body weight; SFSG, small-for-size graft; SLW, standard liver weight.

Tomoharu Yoshizumi designed the study. Tomoharu Yoshizumi, Toru Ikegami, Koichi Kimura, Tetsuo Ikeda, Hideaki Uchiyama, and Ken Shirabe performed the study. Tomoharu Yoshizumi and Koichi Kimura collected the data. Tomoharu Yoshizumi and Toru Ikegami analyzed the data. Ken Shirabe and Yoshihiko Maehara provided critical comments. Tomoharu Yoshizumi wrote the article.

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meantime, the initial experiences with left lobe (LL) grafts demonstrated a higher incidence of small-for-size graft (SFSG) syndrome, graft failure, and recipient complications.[4,5] Consequently, LL grafts have been virtually abandoned, and RL grafts have replaced them for routine use at many centers. Nonetheless, we must consider donor safety and should avoid performing excessive surgery on healthy living donors.[3] The right posterior sector (RPS) graft is an alternative to RL and LL grafts. The RPS graft ensures the acquisition of a graft larger than the LL graft, and it is associated with improved donor safety in comparison with the RL graft.[6] Kokudo et al.[7] simply selected the graft type to harvest 40% of the recipient's standard liver weight (SLW). Recently, similar volumetry-based selection of RPS grafts has been reported.[8] In both cases, RPS grafts were not excluded on the basis of anatomical variations.

Our institute is a high-volume center for LDLT and liver surgery[9-11] and has used RPS grafts for LDLT since 2006. Previous reports have indicated that 6% to 18% of donors have sufficient volume to provide an RPS graft.[12,13] Sugawara et al.[13] stated that they had no exclusion criteria for RPS graft procurement from an anatomical point of view. We have been faced with great difficulties in the performance of accurate donor hepatectomy and in the management of recipients of RPS grafts even though experienced transplant surgeons have performed both the donor and recipient surgeries. Therefore, we have thought that mere volume-based selection of RPS grafts should not be performed.

The aim of this study was to establish selection criteria for RPS grafts with a focus on the vascular and bile duct (BD) anatomy of the RL.

PATIENTS AND METHODS

Recipients

Between May 1997 and December 2013, 429 recipients underwent adult LDLT for end-stage liver disease at Kyushu University Hospital. RPS grafts were used for 8 of these recipients. The etiologies of liver cirrhosis included hepatitis C with hepatocellular carcinoma (n = 4), hepatitis B with hepatocellular carcinoma (n = 1), autoimmune hepatitis (AIH; n = 1), primary biliary cirrhosis (PBC; n = 1), and primary sclerosing cholangitis (PSC; n = 1; Table 1). This study protocol was approved by the institutional review board of Kyushu University Hospital.

Donor and Graft Selection

Donors were selected from candidates who volunteered to be living donors.[3,9] They were required to be within a third degree of consanguinity with the recipients or spouses, and they were 20 to 65 years old. For donors without a third degree of consanguinity with the recipient, individual approval was obtained from the ethics committee of Kyushu University Hospital. Three-dimensional computed tomography (CT) was introduced for the volumetric analysis and delineation of the vascular anatomy. The SLW of recipients was calculated according to Urata's formula.[14] The graft weight (GW) was predicted with CT volumetric analysis. We determined the graft type for each recipient on the basis of the preoperatively predicted GW/SLW ratio. A left lobe with caudate lobe (LL+C) graft was used when the preoperatively predicted GW/SLW ratio was ≥35%. When the GW/SLW ratio with an LL+C graft was <35% and the remnant donor liver volume after right lobectomy was ≥35%, an RL graft was used. When the remnant liver volume after right hepatectomy was <35%, an RPS graft was considered.

Graft Retrieval Technique

After removal of the gallbladder, vessel tape was used to encircle the root of the right Glissonian pedicle, the anterior and posterior Glissonian pedicles, and the right hepatic vein (RHV). The right hepatic artery (HA) was controlled as well. For conventional RPS graft retrieval (cases 1, 4, and 5), the posterior Glissonian pedicle was clamped, and the objective area was recognized from the surface of the liver. For cases 2, 3, and 6 to 8, the drainage area of the RHV was harvested as an extended RPS graft.[15] The drainage area of the RHV was included in the graft and was recognized by the discoloration of the liver surface when the right HA and the RHV were clamped simultaneously. The right liver was mobilized by the division of each short hepatic vein. For a conventional RPS graft, parenchymal transection was performed toward the root of the posterior Glissonian pedicle and the RHV. For an extended RPS graft, the anterior fissure was opened, and the cutting line was directed straight to the root of the RHV by the division of the dorsal branches originating from the anterior portal vein (APV) trunk. Real-time C-arm cholangiography was performed to determine the cutting line of the posterior BD. After the division of the posterior BD and the administration of a bolus infusion of 5000 U of heparin, the posterior hepatic artery (PHA), the posterior branch of the portal vein (PV), and the RHV were divided.

Recipient Surgery and Postoperative Management

The recipient surgery and the perioperative management of the recipients, including immunosuppression regimens, have been described elsewhere.[16] For BD reconstruction, we preferred duct-to-duct anastomosis (D-D) to Roux-en-Y hepaticojejunostomy (H-J). D-D or H-J was performed over a 2.0-mm C-tube with intermittent 6-0 PDS-II sutures.[17] Immunosuppression was initiated with a protocol based on either tacrolimus (Prograf, Astellas Pharma, Inc., Tokyo, Japan) or cyclosporine A (Neoral, Novartis Pharma K.K., Tokyo, Japan) with a steroid and/or mycophenolate mofetil (Chugai Pharmaceutical Co., Ltd., Tokyo, Japan). Tacrolimus was used in 4 recipients, and cyclosporine was used in 3 recipients. One

TABLE 1. Characteristics of the Recipients of RPS Grafts and Their Donors

Variable	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Recipients								
Sex	Female	Male	Male	Female	Female	Male	Female	Female
Age (years)	50	61	25	53	46	51	60	61
Etiology	PBC	LC-C	PSC	LC-C	LC-C	LC-B	LC-C	AIH
Status	Hospitalized	Home	Home	Home	Home	Home	Home	Hospitalized
MELD score	29	12	19	10	21	13	17	26
Body weight (kg)	57.2	61.3	54.4	73.0	63.8	63.9	50.0	54.5
SLW (g)	1114	1232	1123	1219	1148	1163	1062	1092
BD reconstruction	H-J	D-D	H-J	D-D	D-D	D-D	H-J	D-D
Follow-up (days)	54	1617	1437	14	1284	765	115	212
Complication	Sepsis	BD stenosis ACR	None	SFSG syndrome	BD stenosis	BD stenosis	Bile leak FCH	BD stenosis
Outcome	Dead	Alive	Alive	Dead	Alive	Alive	Retransplant	Alive
Donors								
Sex	Male	Male	Female	Male	Male	Male	Male	Male
Age (years)	43	36	28	52	43	36	63	41
Variation of PV	APV from left PV	APV from left PV	APV from left PV	Bifurcation	Trifurcation	APV from left PV	APV from left PV	Trifurcation
Variation of HA	PHA from proper HA	Long PHA	Short PHA	Short PHA	Long PHA	Long PHA	Short PHA	Short PHA
Variation of BD	Standard bifurcation	PHD from LHD	PHD from LHD	Standard bifurcation	Standard bifurcation	PHD from LHD	Standard bifurcation	Standard bifurcation
Operative time (minutes)	572	404	540	607	367	290	412	343
Blood loss (mL)	800	241	399	396	383	150	600	250
Grafts								
Estimated GW (g)	496	543	474	594	448	429	441	482
Actual GW (g)	430	441	404	325	467	433	474	518
Estimated GW/SLW ratio (%)	44.5	44.1	42.2	48.7	39.0	36.9	41.6	44.1
Actual GW/SLW ratio (%)	38.6	35.8	36.0	26.7	40.7	37.2	44.6	47.4
Estimated GW/RW (%)	0.87	0.89	0.87	0.81	0.70	0.67	0.88	0.88
Actual GW/RW (%)	0.75	0.72	0.74	0.45	0.73	0.68	0.95	0.95

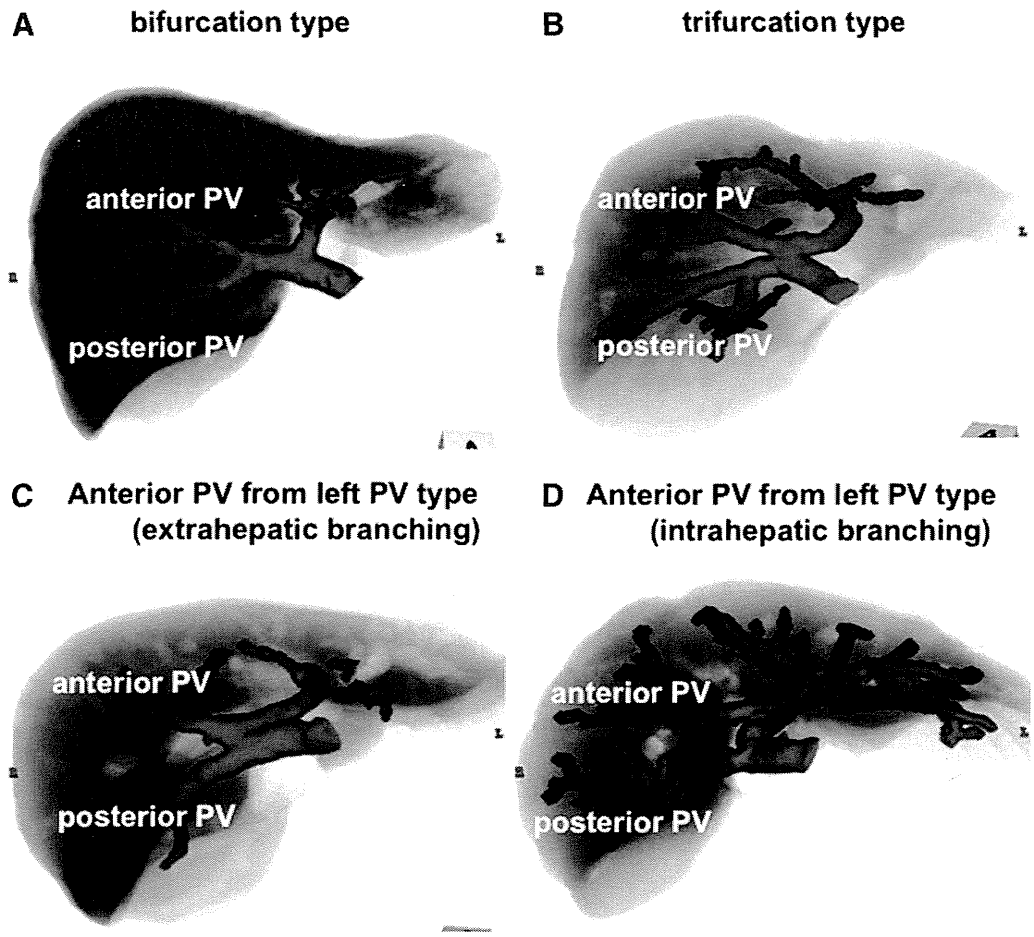

Figure 1. Anatomical PV variations according to preoperative 3-dimensional CT. (A) Bifurcation: the right posterior PV and the right APV were branching from the right PV (case 4). (B) Trifurcation: the left PV, the right APV, and the right posterior PV were branching from the main PV (cases 5 and 8). (C) APV from the left PV: the APV was extrahepatically branching from the left PV (cases 1-3 and 7). (D) APV from the left PV: the APV was intrahepatically branching from the left PV (case 6).

recipient did not receive a calcineurin inhibitor because of a poor postoperative disease course.

Statistical Analysis

Data are expressed as means. All statistical analyses were performed with JMP 9.0 software (SAS Institute, Inc., Cary, NC). A P value < 0.05 was considered significant.

RESULTS

Anatomical PV and HA variations determined with preoperative 3-dimensional CT for 8 donors are shown in Figs. 1 and 2. One donor (case 4; Fig. 1A) had bifurcation of the right PV and the left PV, and this meant that the right posterior PV and the right APV were branching from the right PV; this is considered to be the standard anatomy.[18] Two other donors (cases 5 and 8; Fig. 1B) had trifurcation of the left PV, the right APV, and the right posterior PV. Four donors had extrahepatic branching of the APV from the left PV (cases 1-3 and 7; Fig. 1C). The remaining donor had intrahepatic branching of the APV from the left PV (case 6; Fig. 1D).

As for the HA, the right PHA and the right anterior HA were branching from the right HA in 7 donors (cases 2-8; Fig. 2A). The right PHA was branching from the proper HA in 1 donor (case 1; Fig. 2B). Therefore, all RPS grafts had a single HA in our cases. The length of the extrahepatic PHA was dependent on the length of the right HA. When the liver had a short right HA, the extrahepatic PHA was long (Fig. 2A1). When the liver had a long right HA, the extrahepatic PHA was short (Fig. 2A2), and this made arterial reconstruction very difficult.

Figure 3 shows a representative optimal cutting line of the extended RPS graft (case 6). Figure 3A is the frontal view, and Fig. 3B is the right lateral view. The cutting line, which can be confirmed in the right lateral view, is between the RHV and the APV. The RHV branches that extend toward the right anterior sector are preserved.

Intraoperative cholangiography showed that 5 donors had the usual bifurcation of the hilar hepatic duct. The posterior duct (PD) was joining the right hepatic duct from the cranial side of the right anterior

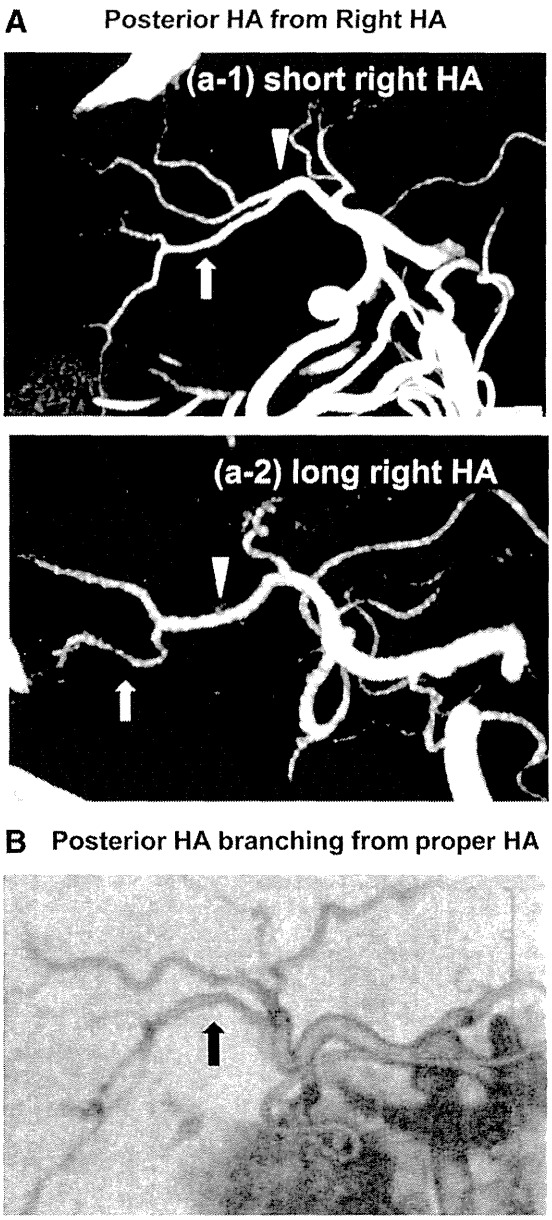

Figure 2. Anatomical HA variations according to preoperative 3-dimensional CT. (A) The right PHA and the right anterior HA were branching from the right HA (arrowhead; cases 2-8). The length of the extrahepatic PHA (arrow) was dependent on the length of the right HA. (a1) The liver had a long extrahepatic PHA (cases 2 and 6). (a2) The liver had a short extrahepatic PHA due to a long right HA (cases 3-5, 7, and 8). (B) The right PHA was branching from the proper HA (case 1). The extrahepatic PHA (arrow) was relatively long in this variation.

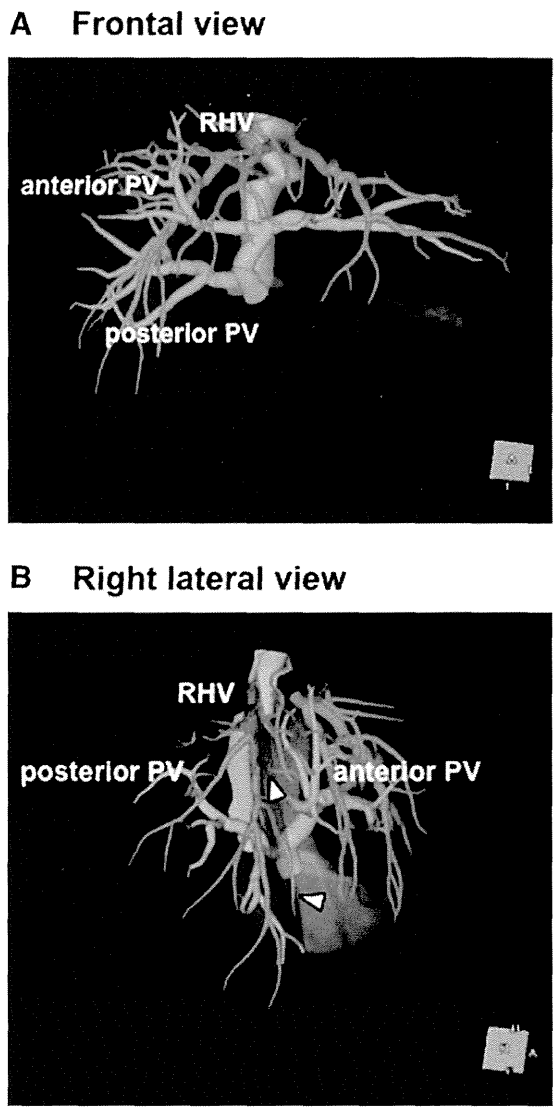

Figure 3. Representative cutting line on preoperative 3-dimensional CT. (A) Frontal view. (B) Right lateral view. The cutting line, which can be confirmed in panel B, lies between the RHV and the APV. The RHV branches that extend toward the right anterior sector (arrowheads) are preserved.

duct (AD) in 5 donors (cases 1, 4, 5, 7 and 8; Fig. 4A). The PD in the posterior Glissonian sheath was turning toward the dorsal-cranial side of the right AD and was joining the left hepatic duct (LHD) in 3 donors (cases 2, 3, and 6; Fig. 4B). All 8 PDs were running on the cranial side of the right posterior PV; therefore, the reconstruction of these ducts in the recipients was possible.

Table 1 shows the characteristics of the recipients of RPS grafts and their donors. The mean estimated GW according to 3-dimensional CT volumetry was 488 g, and the GW/SLW ratio was 42.6%. The mean actual GW was 437 g, and the GW/SLW ratio was 38.4%. There was no statistical difference between the actual data and the estimated data. The mean estimated remnant liver weight was >50% of the donor whole liver weight (data not shown).

Figure 5 shows representative enhanced CT scans of donors 7 days after hepatectomy. Figure 5A shows a CT scan of case 4, from whom an RPS graft was taken. The remnant liver had an unevenly cut surface. Figure 5B presents a CT scan of case 2, from whom an extended RPS graft was taken. Because the procedure for extended RPS graft procurement enabled the transection line to connect the root of the posterior Glissonian sheath and the root of the RHV in a straight line, the cut surface of the remnant liver was

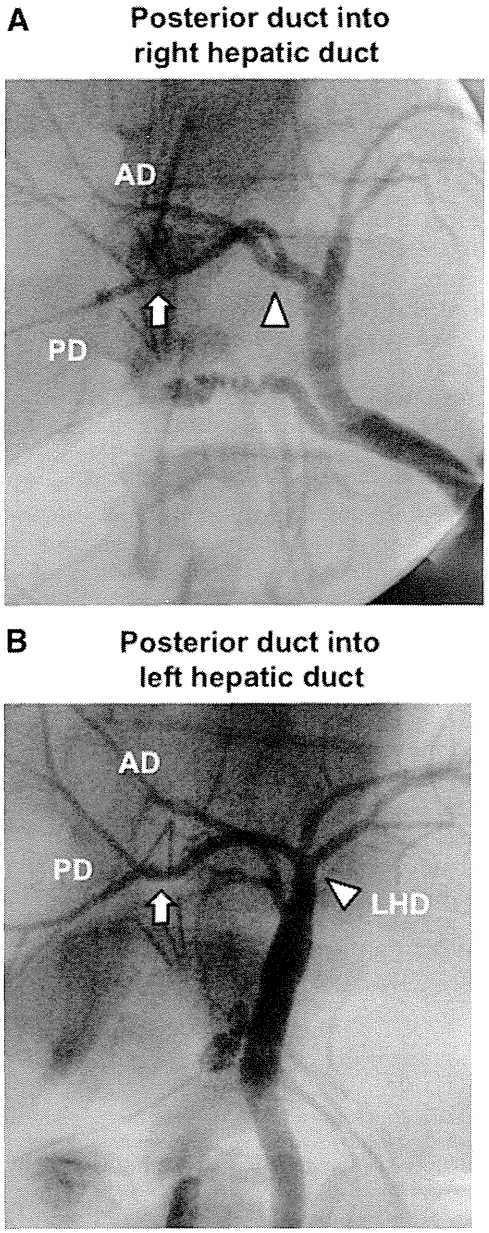

Figure 4. Anatomical variations of the hepatic duct according to intraoperative cholangiography. (A) The PD (the arrow indicates the actual cutting line of the duct) joined the right hepatic duct from the cranial side of the right AD (arrowhead) in 5 donors (cases 1, 4, 5, 7, and 8). (B) The PD (the arrow indicates the actual cutting line of the duct) in the posterior Glissonian sheath turned toward the dorsal-cranial side of the right AD and joined the LHD (arrowhead) in 3 donors (cases 2, 3, and 6).

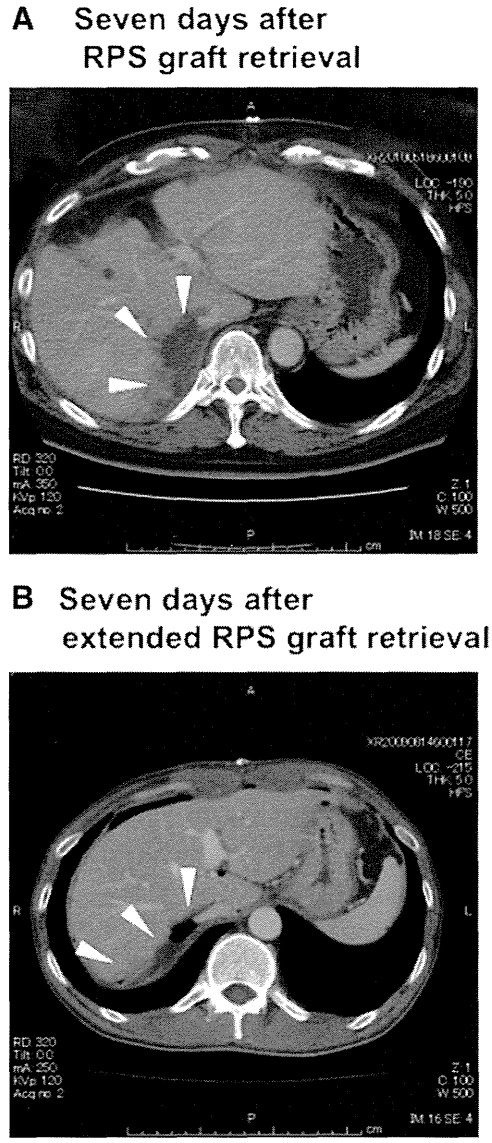

Figure 5. Representative enhanced CT 7 days after donor hepatectomy. (A) From this donor, an RPS graft was retrieved (case 4). The remnant liver had an unevenly cut surface (arrowheads). (B) From this donor, an extended RPS graft was retrieved (case 2). The cut surface of the remnant liver was straight (arrowheads).

straight. Furthermore, CT revealed no congestion in the patients with extended RPS grafts.

Two recipients died of sepsis or SFSG syndrome. One underwent retransplantation with a cadaveric whole liver for intractable bile leakage and fibrosing cholestatic hepatitis (FCH) and was doing well after the retransplantation. Intractable BD stenosis developed in 4 of the 6 survivors. BD stenosis developed 120, 85, 225, and 134 days after LDLT in cases 2, 5, 6, and 8, respectively. For cases 2, 5, and 6, the endoscopic transpapillary approach was tried several times, but it failed. Therefore, a BD stent was finally placed with a rendezvous technique.[19] A BD stent was thereafter placed for all cases. For case 8, a BD stent was placed by an endoscopic transpapillary approach.

DISCUSSION

The development of the RPS graft was intended to overcome the disproportionate distribution of right and left liver volumes. However, many transplant surgeons have not been comfortable with RPS graft procurement.[12] One reason is that the parenchymal transection plane is wide, and a slight dislocation of

the transection plane easily creates a large difference between the actual graft volume and the estimated graft volume (as in case 4 of this study). Therefore, we performed extended RPS graft procurement, which added the RHV drainage area in the right anterior sector to the RPS graft. This procurement procedure enabled the transection line to connect the root of the posterior Glissonian sheath and the root of the RHV in a straight line, as in Fig. 5B. Some may complain that such an extended RPS graft includes the ischemic area of the right anterior sector because the portal and arterial inflows are divided during the procurement. We usually include the caudate lobe after the division of the caudate PV and HA branch with an extended LL graft because this inclusion enables us to make the transection line straight and to more easily harvest the extended LL+C graft.[3] No complication due to the ischemic area developed during the postoperative course of the donor.

Another reason that many transplant surgeons have not been comfortable with RPS graft procurement is that it is often not feasible in living donors with a standard liver anatomy. Very short and small stumps of the HA and the PV, which make reconstruction very difficult, are present with a standard anatomy. Previous studies revealed that 79.7% to 92.5% of the donors had standard anatomical variance of the PV.[12,18] Livers with the APV branching from the left PV (eg, cases 1-3, 6, and 7 in this study), which account for 4.2% to 7.6% of donor livers,[12,18] must be the most suitable livers for RPS graft procurement in terms of the PV. Conversely, RPS graft procurement is the best way to maintain donor safety with such anatomical variance; this was especially true for case 6, in which the APV was branching from the intrahepatic umbilical portion of the left PV. As for the HA, the estimated extrahepatic length of the arterial stump should be checked preoperatively because a short stump makes arterial reconstruction difficult. We have not used jump grafts for arterial reconstruction.

Concern about the BD is a third factor discouraging the harvesting and use of RPS grafts. Recently, Yoshida et al.[20] reported detailed anatomical variations of the BD for the RPS with 3-dimensional CT. Biliary trees were divided into 7 types in that report. Three of 52 livers (5.8%) had dual BDs coming from the RPS, and this would make BD reconstruction very difficult in the recipient. Furthermore, they studied the running pattern of the posterior PV, HA, and BD. The posterior BD was running through the dorsal side of the posterior PV in 3 livers (5.8%), for which BD reconstruction seemed impossible. They also reported that 10.2% of the PDs were running ventrally and inferiorly to the right PV. This biliary anatomy seems to be the most favorable for the RPS graft, although we did not find this anatomy among our 8 patients. A Tokyo group reported a 35% incidence of BD stenosis in recipients.[21] They concluded that the incidence of stenosis after LDLT using RPS grafts was within an acceptable range. However, BD stenosis developed in 67% of the surviving recipients in our small cohort. We used a minimal hilar dissection technique to keep vascular networks around the recipient BD. This technique decreased the incidence of BD stenosis to 14.6% in 214 LDLT cases.[22] Moreover, the average BD orifice in our 8 cases was 2.6 mm. BD complications were not related to procurement (duct injury due to devascularization). BD stenosis was still due to technical difficulties with the anastomosis of the small BD of the RPS graft. Furthermore, the endoscopic approach to BD stenosis was intractable because of the relatively sharp angle of the BD even though experienced endoscopists performed the procedure.

We previously proposed the feasibility of LL+C grafts for LDLT.[2,23] The selection criterion for LL+C grafts at our center is a predicted GW/SLW ratio $\geq$ 35%. However, LL+C grafts with a GW/SLW ratio $<$ 35% were sometimes used when the donor was young and the recipient status was not poor.[5,10] Therefore, mere volume-based selection of an RPS graft should be avoided before the possibility of using an LL+C graft is seriously examined.

In conclusion, with the significant complications and potential concerns associated with the use of RPS grafts, these grafts should be used very rarely and with extreme caution. A thorough understanding of the anatomical variations of the PV, HA, and BD via imaging is necessary for the use of RPS grafts, even for experienced transplant surgeons, because the standard bifurcation of the PV and the posterior BD running through the dorsal side of the posterior PV are not suitable for the harvesting of RPS grafts. Extended RPS graft procurement is recommended for easier parenchymal transection.

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ORIGINAL ARTICLE

Re-Evaluation of the Predictive Score for 6-Month Graft Survival in Living Donor Liver Transplantation in the Modern Era

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The limitations of donor age, graft size, and the Model for End-Stage Liver Disease (MELD) score have not been apparent in living donor liver transplantation (LDLT). Our team developed a formula for predicting graft survival after LDLT; the formula includes the graft weight, donor age, MELD score, and portosystemic shunt status. The aims of this study were to re-evaluate the reliability of our formula and to assess whether our modified treatment strategy has improved 6-month graft survival. Two hundred seventeen patients were allocated into 2 groups: patients with predictive scores ≥ 1.30 (n = 162) and patients with predictive scores < 1.30 (n = 55). The latter group was also divided into subgroups of patients with scores of 1.15 to 1.30 (n = 37) and patients with scores < 1.15 (n = 18). Survival rates for patients with scores < 1.30 were significantly worse than rates for patients with scores ≥ 1.30 ($P = 0.006$). Survival rates for patients with scores < 1.15 were significantly worse than rates for patients with scores of 1.15 to <1.30 ($P < 0.001$). A multivariate analysis showed that a predictive score < 1.15 (odds ratio = 7.87, $P = 0.006$) and a body mass index ≥ 30 kg/m^2 (odds ratio = 13.3, $P < 0.001$) were independent risk factors for 6-month graft mortality. In conclusion, predictive scores reliably predict 6-month graft survival and could allow a widening of the safe ranges for donor ages and graft sizes. ***Liver Transpl 20:323-332, 2014.*** **© 2013 AASLD.**

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Variables such as the Model for End-Stage Liver Disease (MELD) score, donor/recipient age, recipient body mass index (BMI), and pretransplant diagnosis reportedly allow the prediction of short-term mortality after liver transplantation.[1,2] Recently, D-MELD, the product of the donor age and the preoperative MELD score, has been proposed as a highly accurate tool for predicting outcomes after liver transplantation.[3] However, in the field of living donor liver transplantation (LDLT), the use of partial hepatic grafts can complicate prediction.[4] Since the introduction of adult LDLT, graft size has become a concern, particularly for patients with Child C cirrhosis and/or portal hypertension. Small-for-size graft (SFSG) syndrome after LDLT remains a major complication of this procedure.[5,6] Because the occurrence of SFSG syndrome appears to depend on multiple factors related to both donors and recipients,[7] the ability to predict this complication before LDLT remains limited. Thus, left lobe grafts have been virtually abandoned and are

Abbreviations: BMI, body mass index; BW, body weight; FHF, fulminant hepatic failure; GW, graft weight; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; LDLT, living donor liver transplantation; MELD, Model for End-Stage Liver Disease; NS, not significant; SFSG, small-for-size graft; SLW, standard liver weight.

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Tomoharu Yoshizumi designed the study. Tomoharu Yoshizumi, Toru Ikegami, Mizuki Ninomiya, Hideaki Uchiyama, Tomohiro Iguchi, and Yo-Ichi Yamashita performed the study. Tomoharu Yoshizumi, Yuki Bekki, and Hirofumi Kawanaka collected data. Tomoharu Yoshizumi, Ken Shirabe, and Yoshihiko Maehara analyzed data. Tomoharu Yoshizumi wrote the article.

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routinely replaced with right lobe grafts at many LDLT centers.[8,9] It is important to consider donor safety and to avoid performing excessive surgery on healthy living donors.[10-12] More donors of right lobes reportedly experience complications from the procedure in comparison with donors of left lobes.[13]

To avoid excessive surgery in living donors, we developed a formula for predicting early graft function after LDLT.[4] This formula includes the graft size, the donor age, the MELD score, and the portosystemic shunt status and correlates well with graft function and 6-month graft survival. It allows the calculation of the minimum graft size required for a given patient and thus permits transplant surgeons to use living donor left lobe grafts with greater confidence.

Since we reported the formula, we have changed some treatment strategies to improve the prognosis of LDLT. First, because splenectomy is an independent factor for the prevention of SFSG syndrome after LDLT, especially when smaller grafts are used, splenectomy is performed in most patients with chronic liver disease.[5] Second, enteral nutrition is introduced within 48 hours of LDLT to prevent bacterial sepsis.[14]

The aims of this study were to re-evaluate the reliability of our formula in a validation set and to assess whether our modified treatment strategy has improved the 6-month graft prognosis after LDLT.

PATIENTS AND METHODS

Patients

We previously developed and reported our formula with our database of patients up to March 2006. Therefore, patients for the current study were drawn from the period of April 2006 to June 2013. Two hundred twenty-five patients underwent adult LDLT at Kyushu University Hospital during this time. Because their graft function after LDLT could not be accurately ascertained, cases with irreversible brain damage due to fulminant hepatic failure (FHF; n = 2), apparent technical failure (n = 2), graft-versus-host disease (n = 1), or a dual graft (n = 1) were excluded from the study. Data for 2 patients were not available from the database. Consequently, 217 cases were reviewed retrospectively. The study protocol received a priori approval by the institutional review board of Kyushu University Hospital. Our selection criteria for performing LDLT for patients without hepatocellular carcinoma (HCC) were as follows: (1) no other potentially curative modality available and (2) no other organ dysfunction present. There was no restriction on recipient age.[15] Our selection criteria for performing LDLT in HCC patients were as follows: (1) no other potentially curative modality available, (2) no extrahepatic metastasis, and (3) no major vascular infiltration.[16,17] The predictive score alone was not a contraindication to LDLT.

Donor and Graft Selection

Donors were selected from candidates who had volunteered to be living donors.[18,19] They were required to be within 3 degrees of consanguinity or the spouse of the recipient and to be between 20 and 65 years of age. For donors not within 3 degrees of consanguinity with the recipient, individual approval was obtained from the ethics committee of Kyushu University Hospital. Good Samaritan donations were not used. Three-dimensional computed tomography was performed for volumetric analysis and delineation of the vascular anatomy. Decisions about graft types were based on the ratio of the preoperatively predicted graft weight (GW) to the standard liver weight (SLW). Left lobe grafts were used when the preoperatively predicted GW/SLW ratio was ≥35%.

Postoperative Management

The graft procurement technique, recipient surgery, and perioperative management of recipients, including immunosuppression regimens, have been described previously.[18,19] Simultaneous splenectomy was performed in 171 recipients to decrease portal vein pressure or improve pancytopenia.[5] Twelve recipients underwent splenectomy before LDLT. Immunosuppression was initiated with a protocol based on either tacrolimus (Prograf, Astellas Pharma, Tokyo, Japan) or cyclosporine A (Neoral, Novartis Pharma K.K., Tokyo, Japan) with steroids. Tacrolimus was used in 120 patients, and cyclosporine was used in 93 recipients. Four recipients did not receive calcineurin inhibitors because of their poor postoperative courses. The target trough concentration of tacrolimus was set at 10 ng/mL for 3 months after LDLT, and this was followed by 5 to 10 ng/mL thereafter. The target trough concentration of cyclosporine A was set at 250 ng/mL for 3 months after LDLT, and this was followed by 150 to 200 ng/mL thereafter. Methylprednisolone was initiated on the day of LDLT, after which the dosage was tapered; prednisolone was substituted 7 days after LDLT. Prednisolone treatment was tapered and discontinued 6 months after LDLT. Mycophenolate mofetil was used in 208 recipients and was begun at 1 g/day on the day after LDLT; the dosage was tapered and discontinued 6 months after LDLT. The trough concentration of mycophenolate mofetil was not measured.

Predictive Scores

Predictive scores were calculated from the following clinical data: donor age, GW (expressed as a percentage of the recipient SLW), MELD score, and portosystemic shunt status (eg, gastrorenal or splenorenal shunts). SLW was calculated with a formula developed by Urata et al.[20] The MELD score was calculated with a formula reported by Kamath et al.[21] A portosystemic shunt was defined as a shunt that was shown by preoperative computed tomography to be ≥1 cm in diameter and that was ligated during the LDLT procedure to maintain portal flow and prevent stealing of this flow.[4] In our formula, the portosystemic shunt factor value was set at 1.0 for patients who

TABLE 1. Comparison of Variables Between the Major Groups Based on Predictive Scores

Variable	Predictive Score ≥1.30 (n = 162)	Predictive Score <1.30 (n = 55)	*P* Value
Recipients			
Age (years)*	55 (18-73)	50 (19-64)	<0.001
Sex: male [n (%)]	75 (46.3)	21 (38.2)	NS
Primary diagnosis (n)			0.007
Liver cirrhosis			
HCV	81	13	
HBV	15	8	
Cryptogenic	8	2	
Alcohol	4	5	
Nonalcoholic steatohepatitis	2	3	
Autoimmune hepatitis	5	0	
FHF	13	9	
Primary biliary cirrhosis	21	7	
Primary sclerosing cholangitis	6	3	
Other	7	5	
BMI (kg/m^2)†	23.4 ± 3.3	23.3 ± 3.7	NS
MELD score†	15.9 ± 7.4	18.1 ± 8.4	0.07
Portosystemic shunt [n (%)]	53 (32.7)	28 (50.9)	0.02
Pretransplant diabetes mellitus [n (%)]	22 (13.6)	7 (12.7)	NS
Splenectomy [n (%)]	135 (83.3)	48 (87.3)	NS
Portal pressure at closure (mm Hg)†	15.6 ± 3.7	16.1 ± 3.4	NS
Operation time (minutes)†	790 ± 153	821 ± 195	NS
Blood loss (mL)†	4674 ± 4527	4634 ± 4503	NS
Enteral nutrition [n (%)]	151 (93.2)	52 (94.5)	NS
Calcineurin inhibitor: tacrolimus [n (%)]	86 (53.1)	34 (61.8)	NS
Donors/grafts			
Graft: left and caudate lobes [n (%)]	94 (58.0)	32 (58.2)	NS
GW/SLW ratio (%)†‡	40.7 ± 8.1	38.7 ± 7.2	0.12
GW/BW ratio (%)†	0.79 ± 0.17	0.75 ± 0.14	0.18
ABO: identical/compatible/incompatible (n)	113/36/13	36/15/4	NS
Consanguinity [n (%)]	143 (88.3)	29 (52.7)	<0.001
Age (years)*	33 (20-56)	48 (28-63)	<0.001
Sex: male [n (%)]	104 (64.2)	34 (61.8)	NS
BMI (kg/m^2)†	21.9 ± 2.4	22.2 ± 2.6	NS
Operation time (minutes)†	408 ± 79	398 ± 78	NS
Cold ischemia time (minutes)†	103 ± 58	121 ± 79	0.09
Warm ischemia time (minutes)†	42 ± 13	43 ± 15	NS
Blood loss (mL)†	406 ± 395	569 ± 384	<0.001

*Ranges are shown in parentheses.
†The data are presented as means and standard deviations.
‡SLW = 706.2 × Body surface area + 2.4.

underwent shunt ligation during the surgery and at 0 for patients who did not undergo shunt ligation.

The formula that we developed is as follows:

$$\text{Predictive score} = 0.011 \times \text{GW (\%)} - 0.016 \times \text{Donor age (years)} - 0.008 \times \text{MELD score} - 0.15 \times \text{Shunt (if present)} + 1.757$$

According to this formula, the 217 patients were divided into 2 groups according to their calculated predictive scores: ≥1.30 (n = 162) and <1.30 (n = 55). The probabilities of graft survival 6 months after the operation were compared for the 2 groups.

Patients with predictive scores < 1.30 were further subdivided into 2 groups: those with predictive scores of 1.15 to <1.30 (n = 37) and those with predictive scores < 1.15 (n = 18). The probabilities of graft survival 6 months after the operation were compared for these 2 subgroups.

Surgical complications and causes of death within 6 months were compared for the 3 groups.

Statistical Analysis

Significant differences between the groups were determined with the χ^2 test, Student *t* test, or Mann-

TABLE 2. Detailed Data for Patients With Predictive Scores < 1.30 Who Died Within 6 Months

	Patient Number						
Variable	1	2	3	4	5	6	7
Recipients							
Age (years)/sex	62/female	60/female	66/female	63/male	53/female	51/male	37/female
Primary diagnosis	HCV, HCC	HCV, HCC	FHF	HBV, HCC	HCV, HCC	Alcohol	Chronic rejection
MELD score	16	17	31	13	10	24	13
BMI (kg/m^2)	33.9	19.5	25.0	26.5	30.4	18.7	15.8
Portosystemic shunt	No	No	No	Yes	No	Yes	No
Splenectomy	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Portal pressure (mm Hg)*	24	18	16	14	22	18	17
Operation time (minutes)	777	1091	626	825	959	715	1298
Blood loss (mL)	38,000	10,200	745	7000	4350	1200	35,388
Enteral nutrition	Yes	Yes	Yes	Yes	Yes	Yes	No
Donors/grafts							
Graft type	Left and caudate lobes	Posterior	Left and caudate lobes	Right lobe	Posterior	Left and caudate lobes	Left and caudate lobes
GW/SLW ratio (%)†	35.4	44.6	39.3	35.1	26.7	30.1	29.7
GW/BW ratio (%)	0.56	0.95	0.74	0.62	0.45	0.64	0.72
ABO status	Compatible	Identical	Identical	Identical	Compatible	Identical	Identical
Relationship	Husband	Husband	Son	Wife	Husband	Son	Father
Age (years)	61	63	42	62	52	28	62
BMI (kg/m^2)	25.1	23.1	25.0	19.6	26.0	19.3	25.0
Operation time (minutes)	459	412	287	338	607	357	570
Cold ischemia time (minutes)	51	194	50	153	76	72	140
Warm ischemia time (minutes)	31	52	36	32	48	40	54
Blood loss (mL)	850	600	430	230	396	300	550
Predictive score	1.042	1.104	1.269	0.897	1.138	1.298	0.987
Cause of death	Graft failure	Graft failure	Acute cellular rejection	Graft failure	Graft failure	Sepsis	Enteral bleeding

*The portal pressure was measured just before closure.
†SLW = 706.2 × Body surface area + 2.4.

TABLE 3. Comparison of Variables Between the Subgroups Based on Predictive Scores

Variable	Predictive Score: 1.15 to <1.30 (n = 37)	Predictive Score: <1.15 (n = 18)	*P* Value
Recipients			
Age (years)*	49 (18-69)	52 (19-64)	NS
Sex: male [n (%)]	15 (40.5)	6 (33.3)	NS
Primary diagnosis (n)			NS
Liver cirrhosis			
HCV	8	5	
HBV	5	3	
Cryptogenic	2	0	
Alcohol	3	2	
Nonalcoholic steatohepatitis	3	0	
FHF	7	2	
Primary biliary cirrhosis	4	3	
Primary sclerosing cholangitis	3	0	
Other	2	3	
BMI (kg/m^2)†	23.3 ± 3.5	23.5 ± 4.2	NS
MELD score†	17.7 ± 8.2	18.9 ± 8.9	NS
Portosystemic shunt [n (%)]	17 (45.9)	11 (61.1)	NS
Pretransplant diabetes mellitus [n (%)]	6 (16.2)	1 (5.6)	NS
Splenectomy [n (%)]	31 (83.8)	17 (94.4)	NS
Portal pressure at closure (mm Hg)†	15.7 ± 3.5	17.0 ± 3.1	NS
Operation time (minutes)†	819 ± 207	824 ± 173	NS
Blood loss (mL)†	4709 ± 5209	4471 ± 2453	NS
Enteral nutrition [n (%)]	35 (94.6)	17 (94.4)	NS
Calcineurin inhibitor: tacrolimus [n (%)]	25 (67.6)	9 (50.0)	NS
Donors/grafts			
Graft: left and caudate lobes [n (%)]	21 (56.8)	11 (61.1)	NS
GW/SLW ratio (%)†‡	38.7 ± 7.8	38.8 ± 5.9	NS
GW/BW ratio (%)†	0.75 ± 0.14	0.76 ± 0.15	NS
ABO: identical/compatible/incompatible (n)	22/11/4	14/4/0	NS
Consanguinity [n (%)]	23 (62.2)	6 (33.3)	0.045
Age (years)*	46 (28-62)	54 (38-63)	<0.001
Sex: male [n (%)]	21 (56.8)	13 (72.2)	NS
BMI (kg/m^2)†	22.0 ± 2.7	22.8 ± 2.3	NS
Operation time (minutes)†	390 ± 70	415 ± 92	NS
Cold ischemia time (minutes)†	127 ± 91	110 ± 50	NS
Warm ischemia time (minutes)†	44 ± 15	41 ± 14	NS
Blood loss (mL)†	505 ± 335	700 ± 449	0.08

*Ranges are shown in parentheses.
†The data are presented as means and standard deviations.
‡SLW = 706.2 × Body surface area + 2.4.

Whitney test. The Kaplan-Meier method was used to calculate the survival probability for up to 6 months after LDLT. Survival between the groups was compared with a log-rank test. A multivariate analysis (Cox stepwise regression) was performed to identify risk factors associated with graft loss at <6 months. Variables that were used for this analysis included recipient age, recipient sex, primary diagnosis, admission on foot, recipient BMI, presence of pretransplant diabetes mellitus, splenectomy, portal pressure at closure, enteral nutrition, presence of consanguinity between the donor and the recipient, graft type, blood type, donor sex, and predictive score. Because they were used to calculate predictive scores, the donor age, the MELD score, the GW/SLW ratio, and the portosystemic shunt status were not used as variables. A P value < 0.05 was considered significant. Data are expressed as means and standard deviations. All statistical analyses were performed with JMP 9.0 software (SAS Institute, Cary, NC)

RESULTS

Table 1 shows a comparison of variables for the 2 major groups classified by predictive scores. Recipients with scores ≥ 1.30 were older than those with scores < 1.30, whereas donors for patients with scores ≥ 1.30 were younger than those for patients with scores < 1.30. The distribution of the primary diagnoses was skewed because of the presence of diseases such as hepatitis C virus (HCV) and FHF. The scores for the variables that were used in the formula

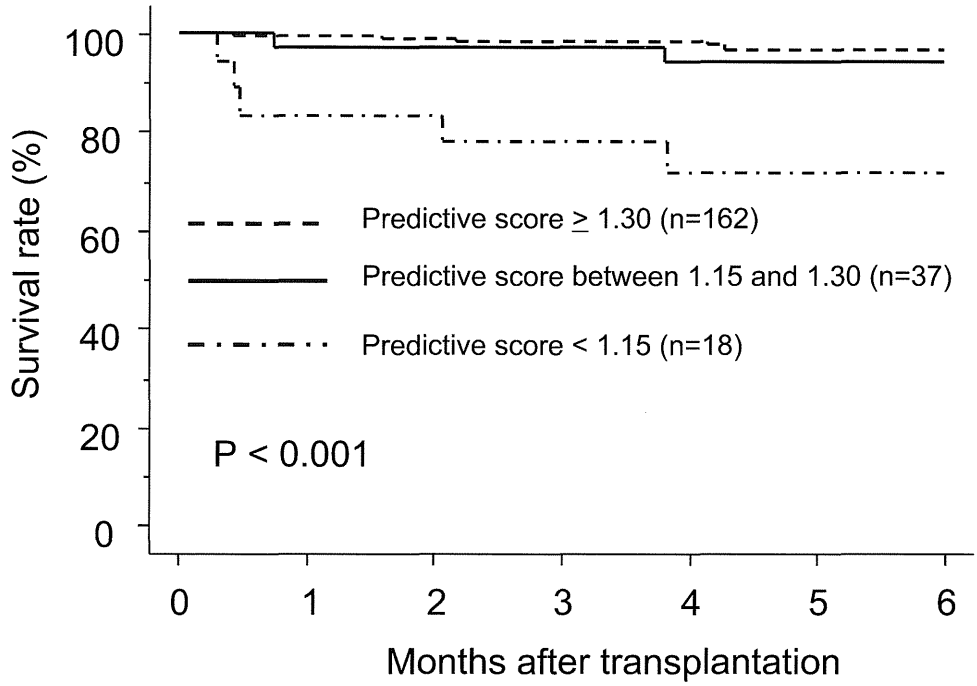

Figure 1. Six-month graft survival according to predictive scores. The graft survival for patients with scores ≥ 1.30 (n = 162) and patients with scores ranging from 1.15 to <1.30 (n = 37) was significantly better than the graft survival for patients with scores < 1.15 (n = 18, $P < 0.001$). The 6-month graft survival probabilities were 96.8%, 94.4%, and 71.8%, respectively.

for calculating the predictive scores, such as the porto-systemic shunt status and the donor age, were different for the groups; however, the MELD scores and the GW/SLW ratios did not differ significantly between the groups. More donors for patients with scores ≥ 1.30 were consanguineous in comparison with donors for patients with scores < 1.30. Donor operative blood loss was less for those with scores ≥ 1.30 versus those with scores < 1.30.

The surgical complications for patients with scores ≥ 1.30 were pancreatic leakage after splenectomy (n = 13 or 8.0%), SFSG syndrome (n = 7 or 4.3%), bile leakage (n = 7 or 4.3%), infections (including pneumonia and intra-abdominal abscesses; n = 6 or 3.7%), acute cellular rejection (n = 5 or 3.1%), sepsis (n = 4 or 2.5%), intra-abdominal bleeding requiring relaparotomy (n = 3 or 1.9%), and multiorgan failure (n = 1 or 0.6%). The surgical complications for patients with scores < 1.30 were pancreatic leakage after splenectomy (n = 2 or 3.6%), SFSG syndrome (n = 4 or 7.3%), infections (including pneumonia and intra-abdominal abscesses; n = 2 or 3.6%), sepsis (n = 3 or 5.5%), intra-abdominal or enteral bleeding requiring relaparotomy (n = 4 or 7.3%), and acute cellular rejection (n = 1 or 1.8%).

The causes of death of patients with scores ≥ 1.30 were sepsis (n = 4 or 2.5%), pneumonia (n = 1 or 0.6%), and multiorgan failure (n = 1 or 0.6%). The surgical complications for patients with scores < 1.30 were graft failure (n = 4 or 7.3%), pneumonia (n = 1 or 1.8%), sepsis (n = 1 or 1.8%), and enteral bleeding due to uncontrollable portal hypertension (n = 1 or 1.8%).

Graft survival rates for patients with scores < 1.30 were significantly worse than rates for patients with scores ≥ 1.30 ($P = 0.006$). Although the graft survival rates were significantly worse for patients with scores < 1.30, their 6-month graft survival rate was 87.0%. Thus, the previously established cutoff value of 1.30 did not distinguish high-risk patients from low-risk patients in this study.

Table 2 shows detailed data for 7 patients with predictive scores < 1.30 who died within 6 months. The predictive scores for 5 of these 7 patients were <1.15. Therefore, patients with predictive scores < 1.30 were divided into the following 2 subgroups: those with predictive scores of 1.15 to <1.30 (n = 37) and those with predictive scores < 1.15 (n = 18).

Table 3 shows a comparison of variables for the 2 subgroups classified by predictive scores. Donors with scores 1.15 to <1.30 were younger than those with scores <1.15. More donors for patients with scores 1.15 to <1.30 were consanguineous in comparison with donors for patients with scores < 1.15.

Figure 1 shows 6-month graft survival after LDLT according to the predictive score. The graft survival rates of patients with scores ≥ 1.30 and patients with scores of 1.15 to <1.30 were significantly better than the rates of patients with scores < 1.15 ($P < 0.0001$). The 6-month graft survival probabilities were 96.8%, 94.4%, and 71.8%, respectively.

A univariate analysis produced the following risk factors for 6-month graft survival after LDLT: a BMI ≥ 30 kg/m^2 and a predictive score < 1.15

TABLE 4. Risk Factors for 6-Month Graft Mortality After LDLT: A Univariate Analysis

Variable	Graft Survival (%) 1 Month	3 Months	6 Months	*P* Value
Recipients				
Age				NS
≥60 years (n = 70)	95.7	95.7	92.5	
<60 years (n = 147)	98.6	96.6	95.1	
Sex				NS
Male (n = 96)	99.0	97.9	94.6	
Female (n = 121)	96.7	94.9	94.1	
Etiology				NS
FHF (n = 22)	95.2	95.2	95.2	
Other (n = 195)	97.9	96.4	94.2	
Admission on foot				NS
Yes (n = 29)	96.6	93.0	88.9	
No (n = 188)	97.9	96.8	95.1	
BMI				<0.001
≥30 kg/m^2 (n = 7)	57.1	57.1	57.1	
<30 kg/m^2 (n = 210)	99.0	97.6	95.5	
Diabetes mellitus				NS
Yes (n = 29)	96.6	93.0	88.9	
No (n = 188)	97.9	96.8	95.1	
Splenectomy				NS
No (n = 34)	97.1	94.0	94.0	
Yes (n = 183)	97.8	96.1	94.4	
Portal pressure				NS
≥20 mm Hg (n = 27)	92.6	88.9	88.9	
<20 mm Hg (n = 190)	98.4	97.3	95.0	
Enteral nutrition				NS
No (n = 14)	100	92.9	92.9	
Yes (n = 203)	97.5	96.5	94.4	
Donors/grafts				
Sex				NS
Male (n = 138)	97.1	94.9	92.6	
Female (n = 79)	98.7	98.7	97.4	
Graft type				NS
Left and caudate lobes (n = 126)	98.4	95.9	94.2	
Other (n = 91)	96.7	96.7	94.4	
Donor-recipient matching				
ABO-incompatible				NS
Yes (n = 17)	100	100	100	
No (n = 200)	97.5	96.0	93.8	
Consanguinity				0.066
No (n = 45)	93.3	91.1	88.8	
Yes (n = 172)	98.8	97.6	95.7	
Predictive score				<0.001
<1.15 (n = 18)	83.3	77.8	71.8	
≥1.15 (n = 199)	99.0	97.9	96.3	

(Table 4). An absence of consanguinity had a *P* value 0.066 according to the univariate analysis. A multivariate analysis that included these variables showed that a predictive score < 1.15 (odds ratio = 7.87, *P* = 0.006) and a BMI ≥ 30 kg/m^2 (odds ratio = 13.3, *P* = 0.0003) were independent risk factors for 6-month graft mortality after LDLT (Table 5).

DISCUSSION

Predictive scores calculated with our proposed formula have proved to be extremely useful for predicting the probability of 6-month graft survival. A crucial feature of this formula is that it uses variables that can be obtained before LDLT. Using data from technetium-99m galactosyl human serum albumin liver scintigraphy, we previously set the cutoff value at 1.30.[4] When the preoperatively calculated score was ≥1.15, the 6-month graft survival rate was 96.3% in this study. This rate was better than our previously reported rate,[4] probably because of the introduction of simultaneous splenectomy[5] and early enteral nutrition[14] and because of changes attributable to the greater experience that we have amassed since our

TABLE 5. Risk Factors for Graft Mortality After LDLT: A Multivariate Analysis

Variable	Odds Ratio	95% Confidence Interval	*P* Value
Predictive score < 1.15: yes versus no	7.87	1.81-34.5	0.006
BMI ≥ 30 kg/m^2: yes versus no	13.3	3.32-55.6	<0.001
Consanguinity: no versus yes	1.25	0.29-5.40	0.76

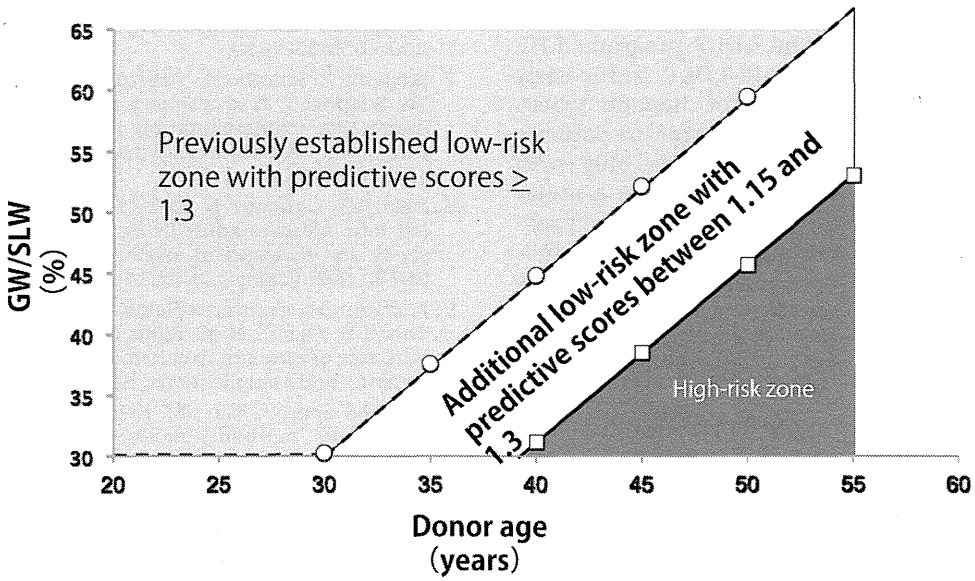

Figure 2. Representative scheme for selecting grafts. For a patient with a MELD score of 20 and a huge portosystemic shunt, a partial hepatic graft with a 45% GW/SLW ratio from a ≤40-year-old donor is needed to achieve a predictive score ≥ 1.30 (light gray space). A 35% GW/SLW ratio with a 40-year-old donor is enough to achieve a score ≥ 1.15 (white space). Our present treatment strategy, which includes simultaneous splenectomy and enteral nutrition, has widened the safety range for donor ages and graft sizes.

previous report. Splenectomy is routinely performed at our center for patients undergoing LDLT, but this is not standard in most of the world; this practice has a potential influence on our outcomes and predictive scores. Some hold the reservation that splenectomy during liver transplantation is closely associated with septic complications and a poorer prognosis.[22,23] However, the incidence of septic complications in the present study did not differ significantly from the incidence in our previous study (data not shown). We have previously speculated that because whole grafts have a greater liver mass than partial liver grafts, the former may not lead to excessive portal vein flow into the graft. It has been suggested that splenectomy during whole liver graft transplantation may lead to insufficient portal flow, which would induce hepatic atrophy and liver failure.[5] Such inadequate portal flow might lead to septic complications. Improvements in posttransplant care, such as enteral nutrition, may also have contributed to a decrease in the occurrence of sepsis in our study.

A predictive score < 1.15 is an independent risk factor for 6-month graft mortality. MELD scores and/or the presence of a huge portosystemic shunt cannot be easily changed, whereas the graft size (ie, graft type; particularly left lobe versus right lobe) is modifiable and can be selected on the basis of the patient's condition. For example, when a patient's MELD score is 20 and the patient has a huge portosystemic shunt, a partial hepatic graft with a 45% GW/SLW ratio from a ≤40-year-old donor is needed to achieve a predictive score ≥ 1.30 (Fig. 2). Indeed, a 35% GW/SLW ratio from a 40-year-old donor is enough to achieve a score ≥ 1.15. Furthermore, we should consider that the risk of using an older donor is ameliorated by a larger graft, which is likely to leave the donor with a small remnant; this is not the best for an older patient.

Some may object that according to the formula, the presence of a shunt negatively affects the prognosis. The presence of shunts may be very protective against the occurrence of SFSG syndrome. Furthermore, several published reports have described the salvage of small grafts with portosystemic shunts.[24,25] Another report recommends not touching already existent portosystemic shunts.[26] Our basic strategy when we perform LDLT is to close any shunts whenever possible to obtain adequate portal flow.[27] Huge patent shunts