Transpl Int (2000) 13: 333–339

ORIGINAL ARTICLE

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Hepatic grafts from live donors: donor morbidity for 470 cases of live donation

Received: 24 November 1999
Accepted: 13 March 2000

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Abstract Living donor-morbidity was evaluated in 470 consecutive cases of living donor liver transplantation carried out from June 1990 to May 1999 at Kyoto University. Grafting was categorized into 4 groups according to the resection lines; left lateral segmentectomy (S2 + 3, $n = 282$, R1), extended left lateral segmentectomy without middle hepatic vein (MHV) (S2 + 3 + part4, $n = 45$, R2), left lobectomy with MHV (S2 + 3 + 4, $n = 99$, R3) and right lobectomy without MHV (S5 + 6 + 7 + 8, $n = 43$, R4). Intraoperative blood loss and operation duration were less for left lateral segmentectomy, but no significant difference was observed between left lobectomy and right lobectomy. The length of postoperative hospital stays was comparable among all groups except for the group with right lobe grafting. The AST values at the peak and at POD 7 were significantly elevated for right lobectomy, but the AST value normalized within one month in the majority of the cases. The close follow-up of donors with more than 1000 ml intraoperative bleeding, and of those donors who stayed in hospital for more than 30 days, the close follow-up, furthermore, of those donors with AST values higher than 100 IU/L AST after one month, revealed complete recovery. Biliary leakage was the most common and annoying complication after donor operations, especially in for right lobe grafting, but all donors recovered completely with conservative or minimal invasive therapy. The two cases of re-operation due to adhesive mechanical ileus we encountered were resolved completely. Finally, no donor-operation related death was noted. In conclusion, the morbidity of living donors is low or minimal even for right lobectomy, the most extended procedure, and complete recovery can be expected in all cases.

Key words Living donor liver transplantation · Living related liver transplantation · Donor safety · Donor morbidity

Introduction

Living donor liver transplantation has been accepted in Japan since 1990. Though it was initially introduced to save pediatric patients, we have been expanding its indication to older children, even to adolescents and adults. Grafts that were small, compared to the size of the donor, significantly correlated with poor post-transplant survival results, especially when the graft was under 0.8% of the recipient's body weight [5]. To solve this problem, auxiliary partial orthotopic liver transplantation (APOLT) has been introduced since 1995, which was successful in some but not in all cases [4]. In February 1998, after a long discussion among the staff and the ethical committee of Kyoto University regarding donor safety, we embarked on the new strategy of

Table 1 Donor demographics

	R1	R2	R3	R4
	S2 + 3	S2 + 3 + part4 MHV (−)	S2 + 2 + 4 MHV (+)	S5 + 6 + 7 + 8 MHV (−)
Donor age	31.8 ± 6.0	37.6 ± 6.8	42.2 ± 8.7	42.8 ± 10.6
Graft weight	253 ± 48	303 ± 97	373 ± 71	653 ± 125
Recipient age	2.4 ± 2.3	11.1 ± 11.4	21.4 ± 13.8	34.4 ± 12.9
Recipient weight	10.3 ± 4.8	26.2 ± 13.6	44.7 ± 12.9	58.8 ± 10.6
Graft Wt/recipient Wt ratio	2.9 ± 1.3	1.3 ± 0.6	0.9 ± 0.3	1.1 ± 0.3

using the right lobe from the living donor (which had been abandoned due to bitter experience in our early case # 3) to obtain the larger grafts. In this paper, we summarize our experience with 470 living donor liver transplantations (LDLT) with special regards to the safety, morbidity, and feasibility of grafting from the living donor.

Table 2 Relationship to the recipients

	R1	R2	R3	R4
Parents	280	42	74	13
Grand parents	2			
Siblings		1	14	18
Children		2	4	5
Spouse			6	7
Step parent			1	

Patients and methods

Four hundreds seventy consecutive LDLTs that were carried out from June 1990 to May 1999 were analyzed. They are categorized to four groups according to their resection lines; left lateral segmentectomy (S2 + 3, $n = 282$, R1), extended left lateral segmentectomy without middle hepatic vein (S2 + 3 + part4, $n = 45$, R2), left lobectomy with MHV (S2 + 3 + 4, $n = 99$, R3) and right lobectomy without MHV (S5 + 6 + 7 + 8, $n = 43$, R4). One case of right lobectomy (case # 3) was excluded from the analysis, but it is referred to in the discussion.

Donors were selected from parents, grandparents, siblings, offspring, and spouses of the recipients. Donors were fully informed of the risks and benefits of LDLTs, and their consent was obtained. Resection lines were selected according to the estimated CT volumetry [3], aiming to obtain 0.8% or more graft weight compared to the recipient body weight.

Preoperative evaluation and operative procedure of the donor have been published in elsewhere [8]. Briefly, the donors underwent doppler ultrasonography and CAT scan of the abdomen as well as the usual preoperative assessment including blood chemistry, CBC, serological testing for possible contagious/transmissible disease as well as respiratory and cardiovascular profiles. Intraoperative ultrasonography and cholangiography were routinely carried out for the final identification of the anatomy of hepatic veins, portal vein, and biliary trees. After mobilization of the lobe (right or left) and dissection of the vessels at the hepatic hilum, parenchyma transection were performed using CUSA and bipolar electrocautery along the previously determined resection line without clamping of inflow or outflow. The graft core cooling with preservation solution (HTK or UW solution) was performed via portal vein only. Vascular stumps of hepatic vein(s), portal vein, and hepatic artery(s) were closed using Prolene suture or simply double tied with silk sutures. The biliary stump was closed with running or interrupted suture, using PDS or Prolene threads.

Postoperative management was carried out with the usual general surgical care, including drain care and oral intake processing. An epidural line which would remain in place for a couple of days and greatly reduce the patient's postoperative pain was placed on initiation of the donor operation. Intraoperative blood loss, operation duration, postoperative hospital stay, liver function tests, complications/morbidity/mortality were evaluated. As right lobe grafting is a relatively newly introduced procedure, the above results after Feb. 1998 were also analyzed.

Statistical analyses were based on Scheffe's F test and Fisher's test, and statistical significance was defined as $P < 0.05$.

Results

Demographics of the donors

Table 1 shows donor- and graft characteristics including donor- and recipient age, recipient body weight, graft weight, and the graft weight/recipient body weight ratio. The donors of larger grafts were older than those of smaller grafts and reflected the major parent-child combination in donor-recipient relationship. Of 469 donors, 280 were parents of the recipient (126 fathers: 154 mothers) as shown in Table 2. There were 14 cases of non-related combinations such as spouse to spouse (13 cases) or step parent to the recipient (1 case).

Intraoperative blood loss

Blood loss during the operation in all cases was shown in Fig. 1 a. That of recent cases was shown in Fig. 1 b. In the current series, blood loss for right lobectomy (347 ± 192 cc) was higher than that for left lateral segmentectomy (196 ± 135 cc), which was comparable to that in left lobectomy (297 ± 211 cc). In 97.65% of the cases (459 out of 469), intraoperative blood loss was less than 1000 ml. No donor, except for one case of right lobe grafting, (case # 3, exceptional right lobectomy case in our early experience) received heterologous

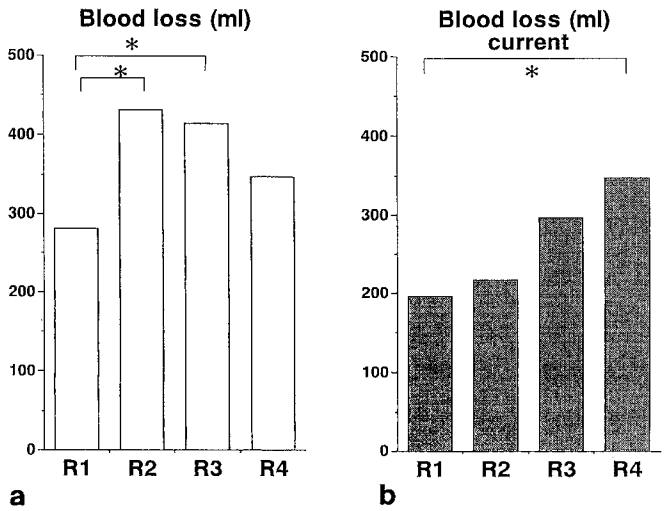

Fig. 1 **a** Blood loss of total series, **b** blood loss of current series after right lobectomy was introduced. * $P < 0.05$

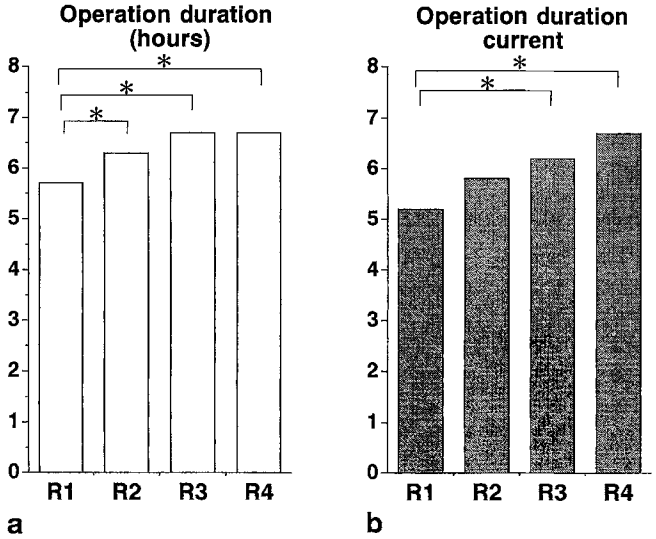

Fig. 2 **a** Operation (duration (hours) of total series, **b** operation duration of current series after right lobectomy was introduced. * $P < 0.05$

Table 3 Cases of intraoperative blood loss. more than 1000 cc

Case no.	R	Blood loss (ml)	Minimal Hb
65	R1	1150	11.4
142	R1	1050	10.3
155	R1	1760	10.4
1	R2	1310	9
7	R2	1200	7.9
165	R2	1070	13.1
279	R2	1120	9.1
33	R3	1040	11.4
59	R3	1200	8.6
79	R3	1220	11.7

blood transfusion. Ten donors experienced more than 1000 ml intraoperative bleeding, and the minimal hemoglobin level after operation of those donors were shown in Table 3. The lowest Hb level after operation was 7.9 in case # 7 (preoperative Hb; 11.5), which returned to the preoperative level within 3 weeks.

Operation time

Operation time in all cases is shown in Fig. 2 a. That of recent cases is shown in Fig. 2 b. The average operation time of left lateral segmentectomy was shorter than that of other procedures. The longest operation time was 12 h in our early cases, when the donor operation was sustained for several hours to accommodate recipient hepatectomy.

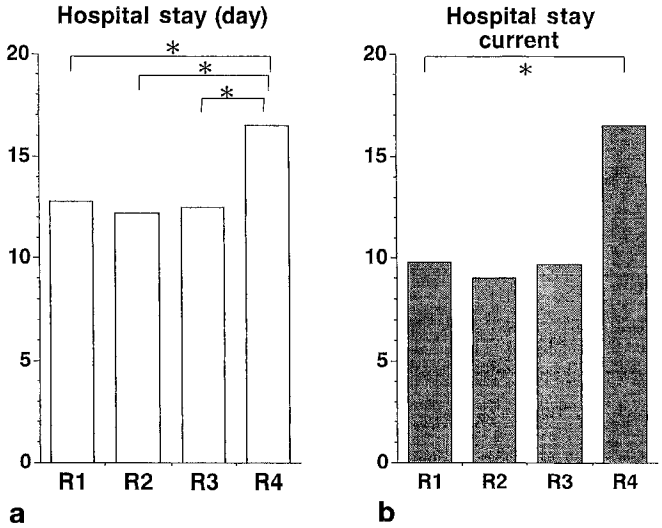

Fig. 3 **a** Hospital stay after operation (days) of total series, **b** hospital stay of current series after right lobectomy was introduced. * $P < 0.05$

Hospital stay after operation

Hospital stay after operation in all cases are shown in Fig. 3 a. That of recent cases are shown in Fig. 3 b. The average hospital stay for right lobectomy (16.5 ± 13.4 days) was longer than that of other procedures.

The donors who stayed for more than 30 days are summarized in Table 4. Most cases were due to biliary leakage especially in right lobectomy cases. Follow-up of these donors resulted in complete recovery without

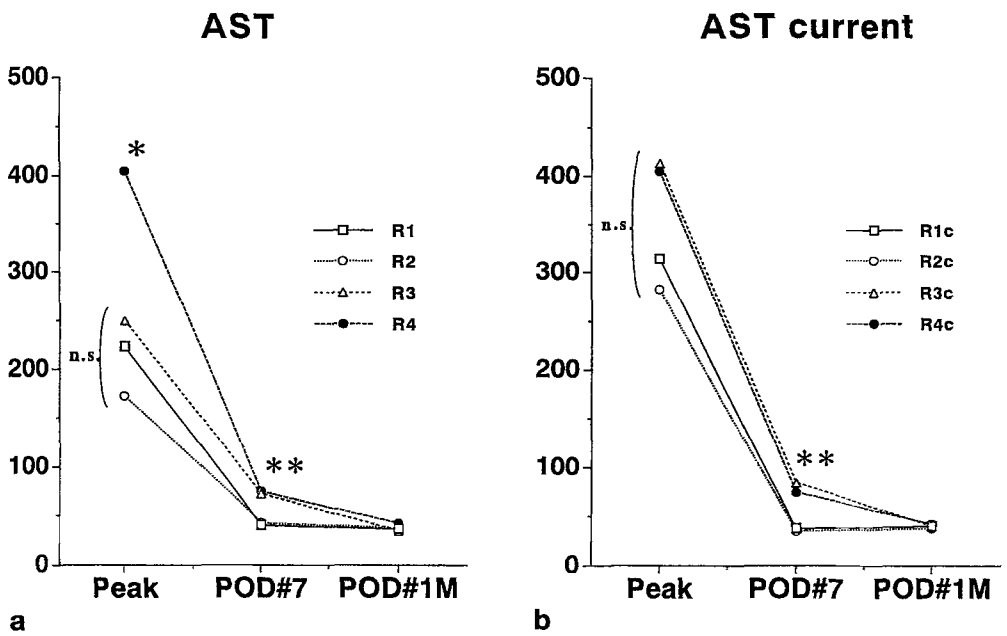

Fig. 4 **a** AST values at the peak, postoperative day (POD) 7 and postoperative day 1 month of total series, **b** AST values at the peak, postoperative day (POD) 7 and postoperative day 1 month of current series after right lobectomy was introduced. * $P < 0.05$

Table 4 Donors who stayed in the hospital more than 30 days

Case no.	Hospital stay (days)	Resection	Reason
87	32	R1	MRSA peritonitis
200	35	R1	BIIe leakage (POD5)
458	38	R4	BIIe leakage (POD5)
430	47	R4	BIIe leakage (POD11)
449	82	R4	BIIe leakage (POD13)

Table 5 Donors with more than 1000 IU/L peak AST value

Case no.	R	Age	Peak AST	AST at 1 M
195	R1	29	1000	76
447	R1	58	1849	39
259	R3	51	1090	31
389	R3	38	2405	17
461	R4	47	1304	30

Table 6 Donors with AST values more than 100 at 1 month post op

Case no.	R	1 Month	Latest
262	R1	157	25
361	R1	109	16
386	R3	110	31
396	R3	118	37

persistent morbidity, as we were informed by the donor's family physician or in the course of telephone interviews.

Peak AST and total bilirubin values

Aspartate aminotransferase (AST) and total bilirubin (T.B.) levels after operation are shown in Fig. 4 a/4 b and 5 a/5 b, respectively. The peak values were obtained within 6 days after operation. The peak AST values of the total series are significantly higher for right lobectomy (405 ± 211 IU/L), but this is not obvious for the current series. At day seven, there still was a significant increase of AST values for right and left lobectomy in comparison to other minor procedures in both series, but there was no significant difference among any procedures one month after the operation. The peak total bilirubin values were significantly high in right lobectomy (3.2 ± 1.6 mg/dl) in both the total and the current series, as well as the day 7 values, but they all dropped to the normal range within one month.

Peak values of AST according to the donor age are shown in Fig. 6. No significant relationship between donor age and peak AST values was seen. The analysis was also performed for peak ALT, TB, hospital stay against donor age, but no significant difference was obtained (data not shown here). Peak values of AST according to the remnant volume of the donor for right lobectomy is shown in Fig. 7. No significant relationship between remnant hepatic volume (%) of the donor for right lobectomy and peak AST was seen. The peak

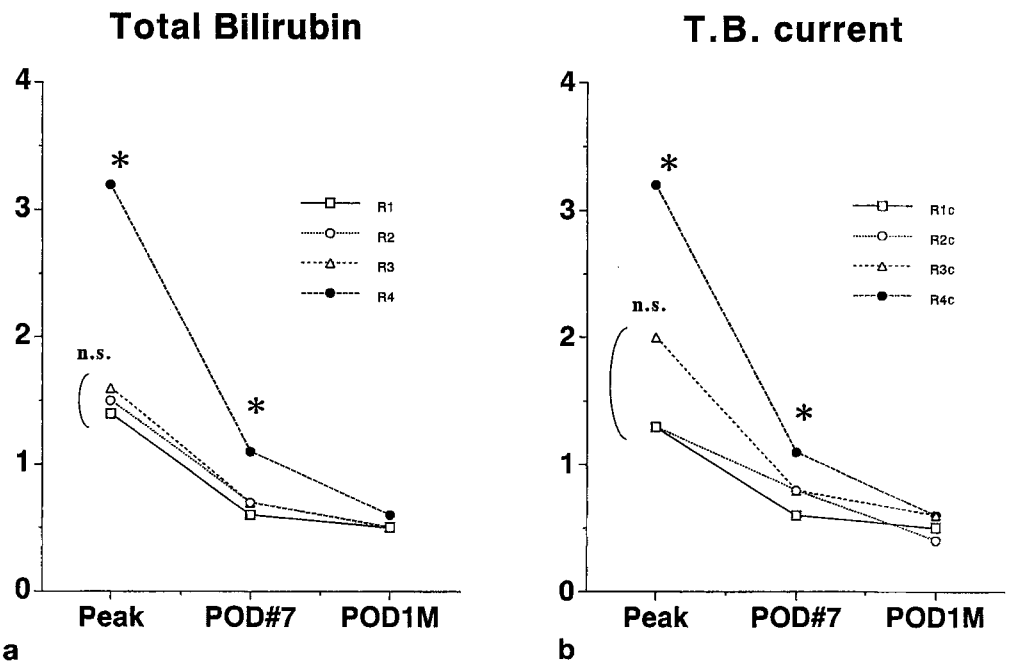

Fig. 5 **a** Total bilirubin (T.B.) values at the peak, postoperative day (POD) 7 and postoperative day 1 month of total series, **b** total bilirubin (T.B.) values at the peak, postoperative day (POD) 7 and postoperative day 1 month of current series after right lobectomy was introduced. * $P < 0.05$

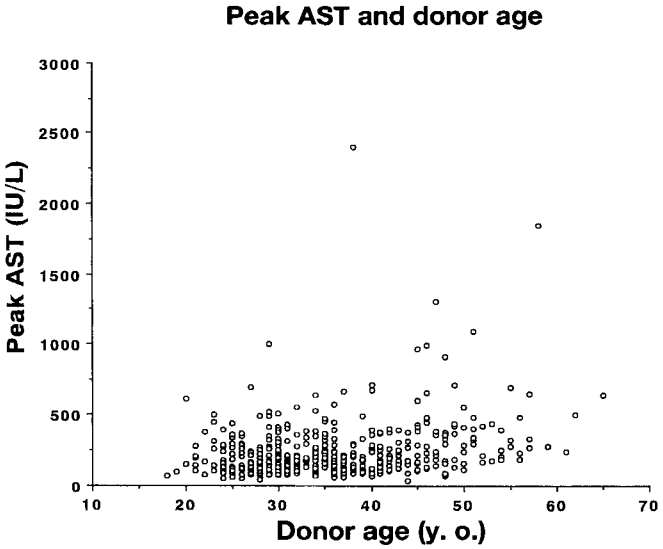

Fig. 6 Peak AST values were plotted according to the donor age

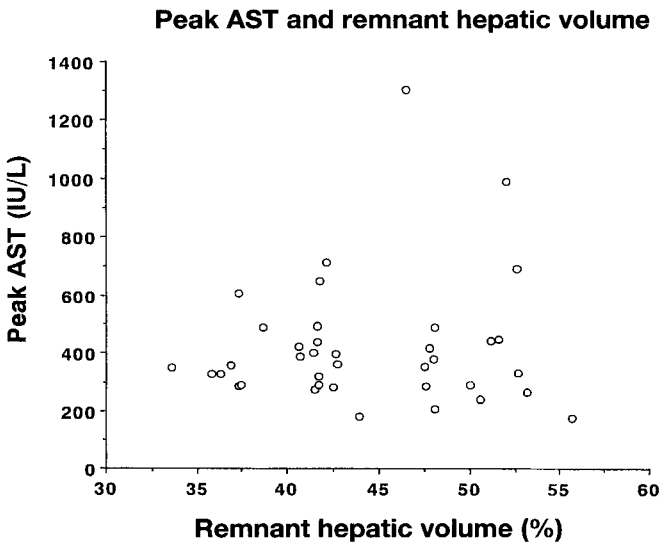

Fig. 7 Peak AST values were plotted according to the remnant hepatic volume (%)

AST, peak T.B., hospital stay were also not related to the remnant hepatic volume (%), data not shown here. Although five donors showed more than 1000 IU/l peak AST values, as shown in Table 5, all dropped to less than 100 within one month. Four donors showed continuous abnormal AST values (> 100 IU/l) one month after graft procurement. Table 6 shows the follow up of those donors. All showed AST values of normal range in the latest examination and are enjoying normal life without any persistent liver dysfunction, as we were informed by the donor's family physician or in the course of telephone interviews.

The demographics of old donors, 56 years old or more, are summarized in Table 7. The oldest donor, a 65-year-old, underwent lateral segmentectomy and was discharged after 12 days without any complications. Right lobe grafts were taken from two 56-year-old donors. They were discharged after 11 and 16 days without

Table 7 Old donors. *R* Resection, *BW* donor body weight, *Compl.* complications, *WI* wound infection, *GW* graft weight, *HS* hospital stay (day)

Case no.	R	Age	BW (Kg)	Blood loss (ml)	Operation time	Compl.	AST peak	T.B. peak	AST 1 M	T.B. 1 M	GW (g)	HS (day)
274	R3	56	79.6	680	10.40	WI	187	3.8	32	0.7	440	22
429	R4	56	50.0	390	6.18		490	3.3	34	0.3	575	11
468	R4	56	64.5	540	7.03		233	4.2			660	16
183	R3	57	58.2	640	6.20		271	0.9			420	17
328	R3	57	75.0	240	6.08		333	1.7	37	0.5	446	8
397	R4	57	80.8	495	8.42		648	3.3	81	1	790	11
447	R1	58	51.0	30	5.48	WI	1849	1.4	39	0.5	220	11
203	R3	59	77.4	530	7.30		279	1.8			420	15
359	R3	61	57.0	120	5.99		245	1.3	47	0.5	295	12
386	R3	62	51.0	200	5.00		506	1.3	110	0.3	430	7
369	R1	65	47.5	118	4.01		636	1.1	43	0.5	270	12

Table 8 Postoperative Complications

	R1	R2	R3	R4
n	282	45	99	43
Bile leak	28 (9.9%)	2 (4.4%)	3 (3.0%)	8 (18.6%)
Wound infection	9 (3.2%)	1 (2.2%)	6 (6.1%)	
Ileus	5 (1.8%)		1 (1.0%)	
Gastritis/peptic ulcer	4 (1.4%)	1 (2.2%)	1 (1.0%)	
Cholecystitis	1 (0.4%)			
Burn	1 (0.4%)			
MRSA peritonitis	1 (0.4%)			
Granulocytopenia	1 (0.4%)		1 (1.0%)	
Athelectasis			1 (1.0%)	
Pulmonary embolism			1 (1.0%)	
Pancreatitis	1 (0.4%)			1 (2.3%)
Depression			1 (1.0%)	
Bleeding				1 (2.3%)

any complication. A 62-year-old donor (case # 386) still had increased AST levels after one month, but the latest examination showed a normal AST level (31 IU/l).

Postoperative complications in all cases are shown in Table 8. In our program, we had no donor operation-related mortality. Biliary leakage was the major cause for morbidity in this study. The number of biliary leakages was significantly higher for right lobectomy than that of other procedures. Donors with biliary leakage were treated by postponed removal of the abdominal drainage tube or, in cases when it had been removed, by reinsertion of the drainage tube under ultrasound guidance (5 cases). This complication also contributed to longer hospital stays, as mentioned above, but all patients recovered completely without persistent morbidity. There were two cases of re-operation, both being due to mechanical ileus, one after 1 year, the other after 6 years and 10 months after the initial donation.

Discussion

Donor safety is the primary concern of living donor liver transplantation [2, 6]. With the expansion of the recipient population from pediatric patients to adolescents and even to adults, we were forced to expand the resection mass from the donor, from the left lateral segment to the right lobe, possibly a more risky procedure for the donor [8].

We performed the world's first right lobe grafting in our early series (case # 3), which has been reported in detail elsewhere. In summary, the donor had aberrant hepatic arterial anatomies, small arteries to segment 2 and 3 originating separately from the proper hepatic artery. Intraoperative blood loss was 2300 ml, and the donor received heterologous blood transfusion in addition to 800 ml autologous blood. AST increased to 192 IU/l with maximum T.B. value of 5.2 mg/dl. The hospital stay of this donor was 18 days. All these morbidity and problems were an exception in our early series of living donor liver transplants starting June 1990. We decided not to use the right lobe for grafting after case # 3.

The survival rate of the recipients who received grafts of less than 0.8% of their body weight was poor in comparison to those who received a graft weighing 0.8% or more of their body weight. APOLT procedure with/without second look remnant native liver hepatectomy was introduced to overcome this problem. Yet it is not satisfactory, the survival rate being 60%. Finally, right lobectomy from the healthy donor was reconsidered and reintroduced in February 1998, which enabled us to provide full strategies to fight against hepatic failure in adults [10]. The average weight of the right lobe graft was 644 g, which allowed us to provide enough liver volume for recipients to 80 kg, (if 0.8% of the recipient weight was considered to be the safe margin) which covers most of the Japanese population.

Right lobectomy in donor operation is still controversial, even in Japan, because of morbidity/mortality of the donor [1, 9]. Miyagawa recommended enlarging the left lobe with the caudate lobe (segment 1) to increase graft volume [7]. It increases the graft volume from 29% to 32% of the standard liver volume (SLV), which would in our experience, still not be enough for some adults.

On average, blood loss and operative time of right lobe grafting were not significantly different from those of left lobectomy. With increased experience in graft procurement from the living donor, our current average blood loss has dropped to around 200–350 ml. Although ten donors had lost more than 1000 ml due to intraoperative bleeding, the minimum Hb level after operation was 7.9 for the lowest donor. He was discharged from the hospital at day 11 without event with an Hb level of 9.0 without having received any heterologous blood. Currently we are eliminating autologous blood transfusion protocol in all procedures including right lobectomy.

The AST values at peak and on POD 7 were significantly higher for right lobectomy than for other modalities, but, on average, no difference was observed one month after operation. Thus, the recovery from grafting was slightly slow for right lobectomy, but final results were satisfactory. The follow up of those cases which showed abnormal values after one month confirm final recovery of all cases.

No donor operation-related death occurred. Biliary leakage after donor operation annoyed some patients, who had to stay longer in hospital than usual. Although in five donors, an intraabdominal drainage tube had to be re-inserted under ultrasound guidance, no persistent complications were noted in the long run. Re-operation of the donor happened twice in our series, both being due to adhesive mechanical ileus years after the initial operation. No other surgical procedure were required postoperatively.

In conclusion, the morbidity of the donors of partial hepatic grafts to their loves ones is minimal even in the most extended procedure of right lobectomy, and complete recovery can be expected in all cases.

Acknowledgements This work was supported in part by grants from the Scientific Research fund of the Ministry of Education, and a Research Grant for Immunology, Allergy and Organ Transplant, Ministry of Health and Welfare, Japan.

References

1. Emond JC, Renz JF, Ferrell LD, Rosenthal P, Lim RC, Roberts JP, Lake JR, Ascher NL (1996) Functional analysis of grafts from living donors. Ann Surg 224: 544–554
2. Greval HP, Thistlethwaite JR, Loss GE, Fisher JS, Cronin DC, Siegel CT, Newell KA, Bruce DS, Woodle ES, Brady L, Kelly S, Boone P, Oswald K, Millis M (1998) Complications in 100 living-liver donors. Ann Surg 228: 214–219
3. Higashiyama T, Yamaguchi T, Mori K, Nakano Y, Yokoyama T, Takeuchi T, Yamamoto N, Yamaoka Y, Tanaka K, Kumada K, Ozawa K (1993) Graft size assessment by preoperative computed tomography in living related partial liver transplantation. Br J Surg 80: 489–492
4. Inomata Y, Kiuchi T, Kim ID, Uemoto S, Egawa H, Asonuma K, Fujita S, Hayashi M, Tanaka K (1999) Auxiliary partial orthotopic living donor liver transplantation as an aid for small-for-size grafts in larger recipients. Transplantation 67: 1314–1319
5. Kiuchi T, Kasahara M, Uryuhara K, Inomata Y, Uemoto S, Asonuma K, Egawa H, Fujita S, Hayashi M, Tanaka K (1999) Impact of graft size mismatching on graft prognosis in liver transplantation from living donors. Transplantation 67: 321–327
6. Malago M, Rogiers X, Burdelski M, Broelsch CE (1994) Living related liver transplantation: 36 cases at the University of Hamburg. Transplant Proc 26: 3620–3621
7. Miyagawa S, Hashikura Y, Miwa S, Ikegami T, Urata K, Terada M, Kubota T, Nakata T, Kawasaki S (1998) Concomitant caudate resection as an option for donor hepatectomy in adult living related liver transplantation. Transplantation 66: 661–663
8. Tanaka K, Uemoto S, Tokunaga Y, Fujita S, Sano K, Nishizawa T, Sawada H, Shirahase I, Kim HJ, Yamaoka Y, Ozawa K (1993) Surgical techniques and innovations in living related liver transplantation. Ann Surg 217: 82–91
9. Urata K, Kawasaki S, Matsunami H, Hashikura Y, Ikegami T, Ishizone S, Momose Y, Komiyama A, Makuuchi M (1995) Calculation of child and adult standard liver volume for liver transplantation. Hepatology 21: 1317–1321
10. Wachs ME, Bak TE, Karrer FM, Everson GT, Shrestha R, Trouillot TE, Mandell MS, Steinberg TG, Kam I (1998) Adult living donor liver transplantation using a right hepatic lobe. Transplantation 66: 1313–1316