was useful for 2 weeks following whole liver transplantation.[19] The immune function of the recipients was not sufficiently restored at 2 weeks following LDLT; however, the immune function in patients who undergo whole liver transplantation may be restored within this period. Thus, assessments of immune function after LDLT would be required for at least 4 weeks. A representative case is presented in Figure 5(a).

Our study also demonstrated that IK value monitoring can be performed to effectively assess the risk of bacterial and fungal infections. The high rate of bacterial blood infections (18/42 episodes) suggests that the immunosuppressive state caused the infectious morbidity. However, the IK values of the recipients with infections improved to nearly the same values in the no infections group for 1 month following LDLT. Thus, infectious morbidity without severe infections did not substantially affect IK recovery after LDLT, although low IK values may cause infectious morbidity without severe infections. Notably, severe infection and low IK values may influence each other, and there were continuous low IK values prior to and after severe infectious events. In the previous study, severe sepsis caused low IK values and the proliferation of CD4 T cells; however, non-septic patients experienced non-substantial changes in immunological functions.[20–22] In the aforementioned case (presented in Fig. 5b), the post-LDLT patient developed postoperative pneumonia prior to the recovery of liver function, and the IK values remained low for 3 weeks. However, she recovered from the pneumonia, and the liver function and IK values also recovered.

It may be difficult to define a quantitative cut-off value to diagnose infection or rejection due to large inter- and intra-individual variations in the IK values, even among healthy individuals.[5,19] In our study, because the IK values in healthy volunteers were similar to those found by Kowalski *et al.*, we used the classification defined by Kowalski of low, moderate and strong immune function according to the IK values. Because of the possible variations caused by the procedure or different environments in each facility, IK values could be an index based on semi-quantitative or qualitative evaluations rather than quantitative evaluations. It is necessary to perform constant quality control checks and assess the IK values of healthy people at each facility.

Biopsy-proven acute rejection within 1 month following surgery was recognized in only three cases. As in previous reports, a high IK value was identified in the patient with ACR during the long-term observation period following liver transplantation.[8,10,23–25] This study evaluated a small number of patients and further investigations are needed.

The limitation of this study is that it is difficult to intervene in the immunosuppressive drug management of bacterial infections during the initial postoperative periods. However, this prospective study demonstrated that the immune function following transplantation in LDLT recipients improved during the first month and that the IK values of LDLT recipients were associated with bacterial infections during the early postoperative period following LDLT. The FK dose should be prospectively decided prior to infectious events according to the IK values. The IK values are another important parameter in determining the FK dose when reducing it in the treatment of severe sepsis.

In conclusion, the immune system of LDLT recipients dramatically improved following transplantation. The IK values of the LDLT recipients were associated with infectious event incidence during the perioperative period. Monitoring IK values was useful during both the acute and long-term postoperative periods. Thus, randomized controlled studies should be performed to assess the utility of IK-based intervention therapy employing individual doses of immunosuppressive drugs in an attempt to prevent bacterial infections during the perioperative period following LDLT.

ACKNOWLEDGMENTS

REFERENCES

1 Bonnel AR, Bunchorntavakul C, Reddy KR. Immune dysfunction and infections in patients with cirrhosis. *Clin Gastroenterol Hepatol* 2011; 9: 727–38.
2 Wieland E, Olbricht CJ, Susal C *et al.* Biomarkers as a tool for management of immunosuppression in transplant patients. *Ther Drug Monit* 2010; 32: 560–72.
3 Kaido T, Egawa H, Tsuji H, Ashihara E, Maekawa T, Uemoto S. In-hospital mortality in adult recipients of living donor liver transplantation: experience of 576 consecutive cases at a single center. *Liver Transpl* 2009; 15: 1420–5.
4 Kowalski RJ, Post DR, Mannon RB *et al.* Assessing relative risks of infection and rejection: a meta-analysis using an immune function assay. *Transplantation* 2006; 82: 663–8.
5 Hwang S, Kim KH, Song GW *et al.* Peritransplant monitoring of immune cell function in adult living donor liver transplantation. *Transplant Proc* 2010; 42: 2567–71.
6 Schulz-Juergensen S, Burdelski MM, Oellerich M, Brandhorst G. Intracellular ATP production in CD4+ T cells as a predictor for infection and allograft rejection in trough-level guided

pediatric liver transplant recipients under calcineurin-inhibitor therapy. *Ther Drug Monit* 2012; **34**: 4–10.

7 Te HS, Dasgupta KA, Cao D *et al.* Use of immune function test in monitoring immunosuppression in liver transplant recipients. *Clin Transplant* 2012; **26**: 826–32.

8 Mizuno S, Muraki Y, Nakatani K *et al.* Immunological Aspects in Late Phase of Living Donor Liver Transplant Patients: Usefulness of Monitoring Peripheral Blood CD4+ Adenosine Triphosphate Activity. *Clin Dev Immunol* 2013; **2013**: 982163.

9 Mizuno S, Nakatani K, Muraki Y *et al.* Combination assays for evaluation of immune function and CYP3A5 genotype to identify the risk of infectious complications and mortality in living donor liver transplant patients. *Ann Transplant* 2013; **18**: 349–57.

10 Cheng JW, Shi YH, Fan J *et al.* An immune function assay predicts post-transplant recurrence in patients with hepatocellular carcinoma. *J Cancer Res Clin Oncol* 2011; **137**: 1445–53.

11 Buttgereit F, Burmester GR, Brand MD. Bioenergetics of immune functions: fundamental and therapeutic aspects. *Immunol Today* 2000; **21**: 192–9.

12 Sottong PR, Rosebrock JA, Britz JA, Kramer TR. Measurement of T-lymphocyte responses in whole-blood cultures using newly synthesized DNA and ATP. *Clin Diagn Lab Immunol* 2000; **7**: 307–11.

13 Cao ZX, Chen XP, Wu ZD. Changes of immune function in patients with liver cirrhosis after splenectomy combined with resection of hepatocellular carcinoma. *Hepatobiliary Pancreat Dis Int* 2003; **2**: 562–5.

14 Xia XJ, Liu BC, Su JS *et al.* Preoperative CD4 count or CD4/CD8 ratio as a useful indicator for postoperative sepsis in HIV-infected patients undergoing abdominal operations. *J Surg Res* 2012; **174**: e25–30.

15 Deneve JL, Shantha JG, Page AJ, Wyrzykowski AD, Rozycki GS, Feliciano DV. CD4 count is predictive of outcome in HIV-positive patients undergoing abdominal operations. *Am J Surg* 2010; **200**: 694–9 discussion 9-700.

16 Hashimoto N, Shimoda S, Kawanaka H *et al.* Modulation of CD4(+) T cell responses following splenectomy in hepatitis C virus-related liver cirrhosis. *Clin Exp Immunol* 2011; **165**: 243–50.

17 Wang H, Ikegami T, Harada N *et al.* Optimal changes in portal hemodynamics induced by splenectomy during living donor liver transplantation. *Surg Today* 2015; **45**: 979–85.

18 Goralczyk AD, Abu-Ajaj W, Tsui TY *et al.* Liver transplantation in patients with liver cirrhosis and active pneumonia: an observational study. *Transpl Int* 2011; **24**: 1068–74.

19 Li RD, Sun Z, Dong JY *et al.* A quantitative assessment model of T-cell immune function for predicting risks of infection and rejection during the early stage after liver transplantation. *Clin Transplant* 2013; **27**: 666–72.

20 Hotchkiss RS, Osmon SB, Chang KC, Wagner TH, Coopersmith CM, Karl IE. Accelerated lymphocyte death in sepsis occurs by both the death receptor and mitochondrial pathways. *J Immunol* 2005; **174**: 5110–8.

21 Lawrence KL, White PH, Morris GP *et al.* CD4+ lymphocyte adenosine triphosphate determination in sepsis: a cohort study. *Crit Care* 2010; **14**: R110.

22 Sundar KM, Sires M. Sepsis induced immunosuppression: Implications for secondary infections and complications. *Indian J Crit Care Med* 2013; **17**: 162–9.

23 Cabrera R, Ararat M, Soldevila-Pico C *et al.* Using an immune functional assay to differentiate acute cellular rejection from recurrent hepatitis C in liver transplant patients. *Liver Transpl* 2009; **15**: 216–22.

24 Hashimoto K, Miller C, Hirose K *et al.* Measurement of CD4+ T-cell function in predicting allograft rejection and recurrent hepatitis C after liver transplantation. *Clin Transplant* 2010; **24**: 701–8.

25 Rodrigo E, Lopez-Hoyos M, Corral M *et al.* ImmuKnow as a diagnostic tool for predicting infection and acute rejection in adult liver transplant recipients: a systematic review and meta-analysis. *Liver Transpl* 2012; **18**: 1245–53.

Technical Refinement of Hepatic Vein Reconstruction in Living Donor Liver Transplantation Using Left Liver Graft

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Statistical Analysis C
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Background: In adult living donor liver transplantation (LDLT), left liver graft is generally safer for the donor. The aim of this study was to demonstrate a technical refinement for achieving sufficient outflow using left liver graft.

Material/Methods: Forty-seven cases using left liver were divided into 2 groups according to the procedures of hepatic vein reconstruction: the side-clamp group (21 cases), and the cross-clamp group (26 cases), to sufficiently enlarge the diameter of the hepatic vein with excising the inferior vena cava (IVC).

Results: The liver function tests at 7 days after LDLT were not significantly different between the 2 groups, but the median amount of ascites was significantly greater in the side-clamp group (1250 ml; range, 484–3690) than in the cross-clamp group (582 ml; 190–2785). When we selected the patients with the ratio of graft weight to recipient standard liver volume less than 30%, the 1-year patient survival after transplantation was significantly better in the cross-clamp group than in the side-clamp group (90% in cross-clamp group vs. 71% in side-clamp group, P<0.05).

Conclusions: In conclusion, hepatic vein reconstruction with cross-clamping of the IVC can secure a sufficient outflow in LDLT using left liver graft.

MeSH Keywords: Hepatic Veins • Liver Transplantation • Living Donors

Abbreviations: **LDLT** – living donor liver transplantation; **SFSS** – small-for-size syndrome; **MHV** – middle hepatic vein; **LHV** – left hepatic vein; **IVC** – inferior vena cava; **RHV** – right hepatic vein; **CECT** – contrast-enhanced computed tomography; **MELD** – model of end-stage liver disease; **GW/RSLV** – ratio of graft weight to recipient standard liver volume

Full-text PDF: http://www.annalsoftransplantation.com/abstract/index/idArt/893136

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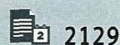
Background

In living donor liver transplantation (LDLT), the recipients sometimes encounter small-for-size syndrome (SFSS), with clinical manifestations of massive ascites and prolonged jaundice because of relatively excessive portal flow into insufficient graft liver volume [1]. SFSS can ultimately lead to graft failure, so several technical inventions have been introduced, mainly to decrease portal flow, such as porto-caval shunting [2], splenic artery ligation [3], or splenectomy [4]. However, as a matter of course, securing optimal outflow should be equally important to overcoming SFSS.

In regard to the donor selection in LDLT, several reports have introduced the possible advantages of left liver graft with the middle hepatic vein (MHV) (extended left lobe graft) over right liver graft, because although the actual volume is smaller in the left liver graft, the incidence of severe postoperative complications and mortality are greater in donors providing right liver graft than left liver graft [5] but the recipient outcome is not significantly different [6]. Accordingly, our current policy is to use the left liver graft as a first line because donor safety is the top priority in LDLT. Especially in LDLT using left liver graft, it is important to develop technical refinements to overcome SFSS.

The aim of this study was to show our new technique to achieve adequate outflow in LDLT using left liver graft.

Material and Methods

Patients

Of the 102 LDLT patients in Nagasaki University from April 2005 to May 2011, 47 adult LDLT cases using left liver graft with MHV were enrolled in this study. Initially, we preferred to use right liver graft in adult LDLT, but from April 2005 we changed our policy to use the left liver graft as the first-line. They were divided into 2 groups: a side-clamp group in which the hepatic vein was reconstructed with the conventional procedure of side-clamping the recipient MHV/left hepatic vein (LHV) (n=21, from April 2005 to May 2009), and a cross-clamp group in which our new and current procedure of cross-clamping the suprahepatic inferior vena cava (IVC) was performed (n=26, from June 2009 to May 2011).

Surgical techniques (Figure 1)

During the recipient operation, the right hepatic vein (RHV) was divided using a vascular stapling device [7]. After the portal triad was divided at the hepatic hilum, the whole liver was removed with dividing the MHV and LHV, which were clamped with vascular clamps. During the anhepatic phase, the tissue surrounding the MHV/LHV was carefully dissected, and the suprahepatic IVC just beyond the MHV/LHV was clamped last. After the infrahepatic IVC was also clamped, cavotomy was performed to make a large orifice for anastomosis, excising the right corner of the MHV longitudinally.

In the side-clamp group, the common trunk of the MHV/LHV was clamped, and hepatic vein reconstruction was performed after dividing the septum between the MHV/LHV.
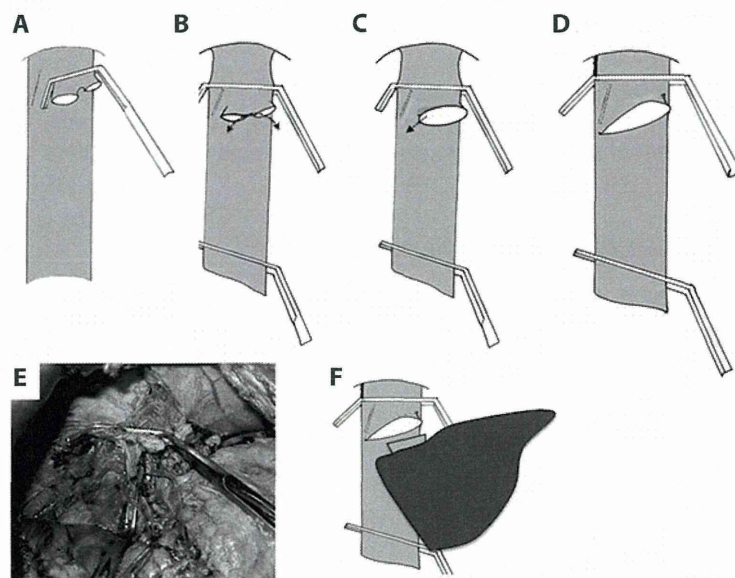
Figure 1. Procedure of hepatic vein reconstruction with IVC cross-clamping. At the final step of total hepatectomy of the recipient, the left hepatic vein (LHV) and middle hepatic vein (MHV) were divided with clamping of their common trunk (A). After the IVC was cross-clamped, the septum between the LHV and MHV was divided (B), and the right corner of MHV was excised horizontally (C) to create a larger orifice for anastomosis (D). Actual macroscopic finding of the procedure (E). The left liver graft was put in place, and HV reconstruction was performed with sufficient space for anastomosis (F).

In regard to the MHV/LHV of the graft, venoplasty was generally performed to make 1 orifice when the common trunk between MHV and LHV was short, or their orifices were independently divided [8]. Briefly, the septum between the MHV and LHV was divided longitudinally and sutured horizontally using 5-0 monofilament non-absorbable suture.

In both groups, hepatic vein anastomosis was performed using 4-0 non-absorbable monofilament suture.

Splenectomy was performed in the selected cases with platelet count less than or equal to 5000/µl or HCV-cirrhosis cases to collect platelets for subsequent interferon therapy after LDLT.

Postoperative care

Basic immunosuppression after transplantation consisted of tacrolimus and steroid.

Doppler ultrasound was performed daily to check the patency of vascular anastomosis in portal vein, hepatic vein, and hepatic artery until 7 days after LDLT and when indicated thereafter. Hepatic venous flow was considered as good when the wave form was biphasic or triphasic, and actual measurement of flow volume or velocity was not routinely performed. Contrast-enhanced computed tomography (CECT) of the liver was performed routinely at 7 days after LDLT, as long as the renal function was normal. We have digital data of imaging studies on computed medical charts from 2005, which made it possible for us to measure the diameter of the HV anastomosis accurately.

An abdominal drain was generally placed at the right subcostal space during surgery, and removed when the amount of ascites became less than 500 ml/day.

Analyses

The liver function tests, the amount of ascites before and after LDLT, the diameter of HV anastomosis on CECT, and patient/graft function after LDLT were compared between the 2 groups. The amount of ascites before LDLT was classified into 3 grades based on CT finding: none, minimal (visualized only at liver surface or pelvic space), and severe (visualized whole abdomen).

Statistical analyses were performed using the Mann-Whitney U test for continuous data, and the chi-square test for categorical data. Overall survival was calculated with the Kaplan-Meier method, and data were compared with the log-rank test. We considered P values <0.05 to be statistically significant.

Results

Patient characteristics and surgical outcome

The patient characteristics and surgical outcomes are summarized in Table 1. Recipient/donor ages, sex ratios, and preoperative model of end-stage liver disease (MELD) scores, Child-Pugh classification, total ischemia time (from vascular division in the donor to reperfusion in the recipient), the amount of ascites on CT before LDLT, and the degree of graft steatosis at time-zero biopsy were not significantly different between the groups. The surgery duration was shorter and intraoperative blood loss was less in the cross-clamp group compared to the side-clamp group, possibly because of the learning curve. Both groups each included 1 Child-Pugh grade A case of Caroli's disease, both of which underwent LDLT, not for decompensated cirrhosis, but for refractory cholangitis. In regard to the graft size, there was no significant difference between the groups for the median ratio of graft weight to recipient standard liver volume (GW/RSLV) – 35.3% (range, 24.8–48.0) in the side-clamp group vs. 33.7% (range, 22.5–46.6) in the cross-clamp group. The incidence of splenectomy was not significantly different between the groups – 12 cases (61.9%) in the side-clamp group vs. 20 cases (76.9%) in the cross-clamp group.

Postoperative liver functions, the amount of ascites, diameter of HV anastomosis, and graft survival

All patients in the cross-clamp group tolerated the procedure, without any significant hypotension during surgery or postoperative renal dysfunction. In most cases in the cross-clamp group, hepatic venous flow was excellent with triphasic wave form on Doppler ultrasound just after reperfusion (Figure 2).

Overall, the median prothrombin time and total bilirubin at 7 days after transplantation were not significantly different between the 2 groups, but the median amount of ascites was significantly less in the cross-clamp group (582 ml; range, 190–2785) than in the side-clamp group (1250 ml; range, 484–3690) (P<0.01, Mann-Whitney test) (Figure 3).

In an analysis of patients with extremely small graft size (GW/RSLV <30%; 7 in the side-clamp group, 10 in the cross-clamp group), the median prothrombin time was higher (P=0.106) in the cross-clamp group (49.0%; range, 28.0–66) than in the side-clamp group (39.0%; range, 25.0–53.0); the median total bilirubin was lower (P=0.079) in the cross-clamp group (3.8 mg/dl; range, 1.7–17.0) than in the side-clamp group (7.5 mg/dl; range, 1.7–14.5); and the median amount of ascites was less (P=0.184) in the cross-clamp group (628 ml/day; range, 209–2560) than in the side-clamp group (1060 ml/day; range, 484–3040), but these differences did not reach statistical significance (Figure 4).

Table 1. Patient characteristics and surgical outcomes.

	Side clamp (n=21)	Cross clamp (n=26)	
Recipient age	55 (25–68)	57 (27–72)	NS
Donor age	33 (19–64)	33(20–65)	NS
Gender	Male 11 Female 10	Male 12 Female 14	NS
MELD	16 (7–30)	15 (7–42)	NS
Child-Pugh			
A	1	1	
B	10	11	NS
C	10	14	
Preoperative ascites			
None	8	10	
Minimal	9	11	NS
Severe	4	5	
Duration of surgery (min)	915 (690–1,159)	746 (578–999)	P<0.01
Total ischemic time (min)	168 (84–219)	154 (107–282)	NS
Blood loss (g)	5 450 (1,350–26,876)	3 800 (980–17,600)	P<0.05
GW/RSLV (%)	35,3 (24.8–48.0)	33,7 (22.5–46.6)	NS
Graft stetatosis (%)	5 (0–50)	5 (0–50)	NS
Splenectomy	12	20	NS

Data are expressed as median (range); MELD – model of end-stage liver disease; GW – graft weight; RSLV – recipient standard liver volume; NS – not significant.
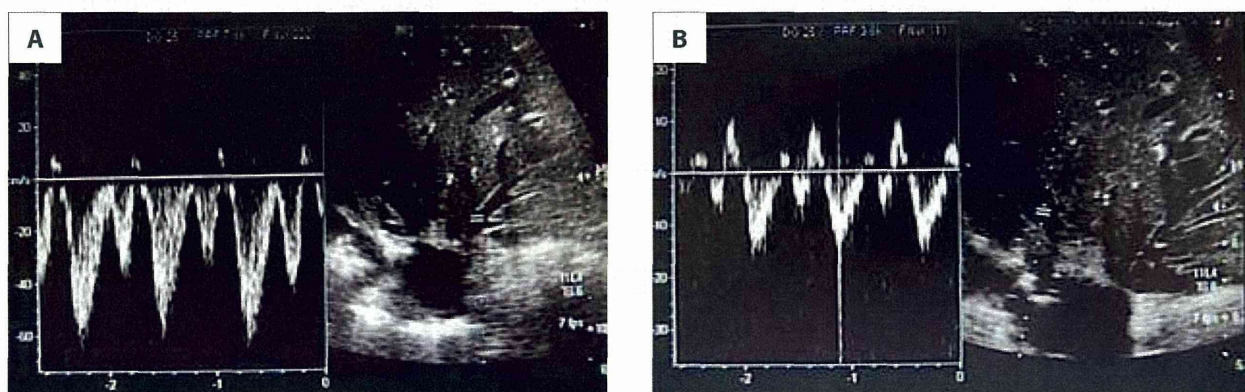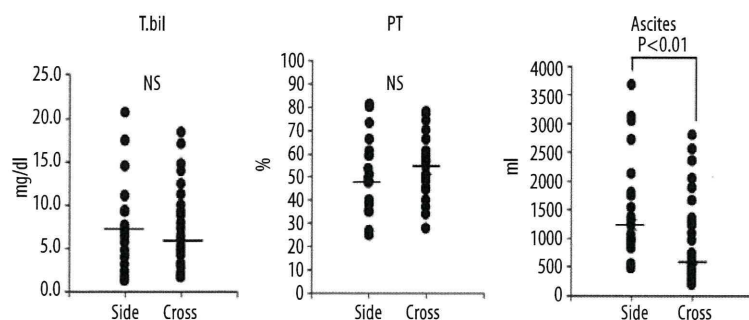
Figure 2. Doppler ultrasound just after reperfusion of the left liver graft. Hepatic venous flow was excellent with triphasic wave form both in LHV (**A**) and MHV (**B**).

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Figure 3. The level of total bilirubin, prothrombin time, and the amount of ascites 7 days after LDLT in the side-clamp group (n=21) and cross-clamp group (n=26). The amount of ascites was significantly less in the cross-clamp group.
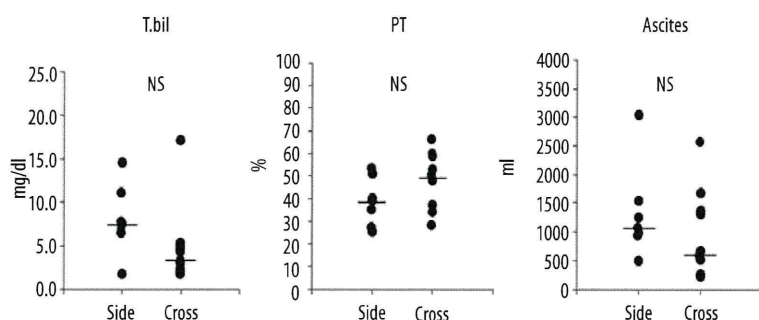
Figure 4. The level of total bilirubin, prothrombin time, and the amount of ascites 7 days after LDLT in the cases with extremely small graft size (GW/RSLV <30%; 7 in the side-clamp group and 10 in the cross-clamp group).
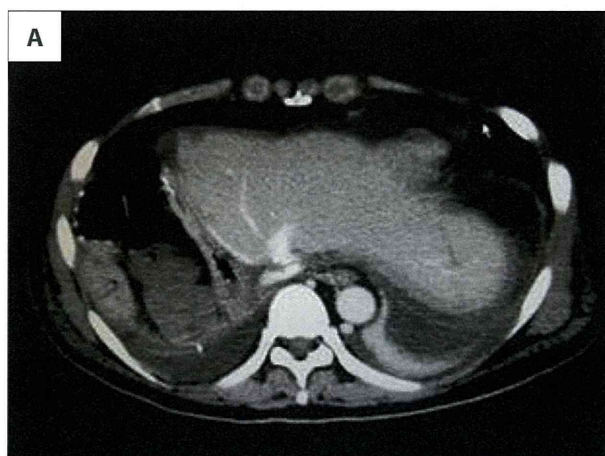
Figure 5. The diameter of HV anastomosis on CECT at 7 days after LDLT, in a case with side-clamp (A, 10.56 mm) and cross-clamp (B, 15.47 mm).

In the patients with extremely small graft size, the 1-year patient/graft survival was significantly better in the cross-clamp group than in the side-clamp group (90% vs. 71%; P<0.05, log rank test). Two patients died of graft failure 50 days and 38 days after LDLT in the side-clamp group, while 1 patient died of systemic candida infection 19 days after LDLT in the cross-clamp group. Of 2 patients who died of graft failure in the side-clamp group, 1 had bleeding of the esophageal varices without portal vein obstruction, and 1 had complicated sepsis; neither of these appeared to be directly related to SFSS.

CECT could be performed at 7 days after LDLT in 15 of 21 patients (71%) with side-clamp, and 19 of 26 (73%) with cross-clamp. The median diameter of HV anastomosis at 7 days after LDLT on CECT was significantly larger (P<0.05) in the cross-clamp group (14.8 mm; range, 6.9–19.5) than in the side-clamp group (10.9 mm; range, 5.5–14.6) (Figure 5).

Discussion

It is important to control the balance between the portal inflow and hepatic vein outflow of the liver to maintain hepatocyte

function. In general, portal circulation is hyper-dynamic in cirrhotic patients [9]; therefore, modulation of portal inflow is recognized as an effective procedure to overcome SFSS in LDLT. The balance of blood flow, as well as steatotic liver and older donor age, can affect SFSS, but blood flow is the only factor that can be controlled surgically. However, a few studies have demonstrated the importance of the outflow reconstruction from the point of view of avoiding SFSS. In LDLT cases using right liver graft, the reconstruction of MHV tributaries or right inferior hepatic vein have been well documented to avoid graft congestion [10,11]. As mentioned before, the outcome of LDLT recipients using a left liver graft is reported to be not different from that using a right liver graft in spite of the fact that left liver volume is generally smaller than right liver volume, possibly because the whole left liver is well drained via the middle and left hepatic veins. Accordingly, hepatic vein reconstruction is important to secure the sufficient outflow in LDLT using left liver graft. In this study, creating a larger orifice by cross-clamping the IVC proved to be an effective method to overcome SFSS with decreasing ascites, especially in cases of extremely small graft size (GW/RLSV <30%). Although differences in several factors, including total bilirubin, prothrombin time, and amount of ascites after LDLT, did not reach statistical significance (possibly because of small sample size), postoperative liver functions seemed better, and 1-year patient survival was significantly better in the cross-clamp group.

Actually, this procedure of HV reconstruction with cross-clamping is not novel. Tanaka et al. reported this procedure in selected pediatric LDLT cases more than 20 years ago [12], emphasizing that it is important to make a large orifice in IVC to avoid twisting at the HV anastomosis. In our study, the large diameter of the HV anastomosis was maintained better compared to the side-clamp group 7 days after LDLT. We believe that a large orifice with excising the IVC can produce long and short anastomosis of HV, and it contributes to sufficient venous outflow without twisting the anastomosis. Actually, measurement of portal and/or hepatic vein flow might be better to show the efficacy of the HV reconstruction with IVC cross-clamping, but unfortunately we did not routinely check the quantity of the portal/HV flows. As the objective analysis, we checked the diameter of HV anastomosis on CECT after LDLT.

Hypotension and/or postoperative renal dysfunction are potential concerns associated with cross-clamping IVC, but there were no cases that developed significant adverse effects, and all patients tolerated the procedure well, with sufficient fluid infusion.

Technically, because we used a vascular stapler to divide the right hepatic vein, the excision of the IVC was safely performed without any risk of cutting the continuous suture at the right hepatic vein, and sufficient space for anastomosis could be obtained by clamping the IVC, even in deep and small surgical spaces in adult cases.

This technique of cross-clamping the IVC can be adopted also in LDLT using a right lobe graft, especially in complex cases such as those requiring the reconstruction of multiple middle hepatic vein tributaries or right inferior hepatic veins. In our series, 2 cases of right lobe LDLT underwent multiple hepatic vein reconstruction successfully with cross-clamping of the IVC during the study period (data not shown).

Limitations of this study include its small sample size and the fact that it was a comparison study using historical control. Because the MELD score and Child-Pugh grade before LDLT were not different between the groups, the better outcome in the cross-clamp group might be related to just the learning curve, because the duration of surgery and blood loss were significantly less in the cross-clamp group. Also, in the cases of extremely small graft size, the liver functions and the amount of ascites did not reach statistically significant differences between the cross-clamp group and the side-clamp group. Although we believe a large orifice of HV anastomosis with IVC cross-clamping is theoretically feasible, the actual efficacy of cross-clamping needs to be demonstrated in a prospective randomized control study.

Conclusions

In conclusion, although a randomized study is needed to determine the actual advantage of this procedure, we have shown that creating a larger orifice with cross-clamping the IVC is a safe and effective procedure to overcome SFSS in LDLT using left liver graft.

References:

1. Hori T, Ogura Y, Ogawa K et al: How transplant surgeons can overcome the inevitable insufficiency of allograft size during adult living-donor liver transplantation: strategy for donor safety with a smaller-size graft and excellent recipient results. Clin Transplant, 2012; 26: E324–34

2. Boillot O, Delafosse B, Méchet I et al: Small-for-size partial liver graft in an adult recipient; a new transplant technique. Lancet, 2002; 359: 406–7

3. Graham JA, Samstein B, Emond JC, Kato T: Functional distal splenorenal shunt and splenic artery ligation as portal flow modulation in left lobe living donor transplantation. Liver Transpl, 2014; 20: 245–46

4. Yoshizumi T, Taketomi A, Soejima Y et al: The beneficial role of simultaneous splenectomy in living donor liver transplantation in patients with small-for-size graft. Transpl Int, 2008; 21: 833–42

5. Umeshita K, Fujiwara K, Kiyosawa K et al: Japanese Liver Transplantation Society. Operative morbidity of living liver donors in Japan. Lancet, 2003; 362: 687–90

6. Soejima Y, Shirabe K, Taketomi A et al: Left lobe living donor liver transplantation in adults. Am J Transplant, 2012; 12: 1877–85

7. Eguchi S, Kawashita Y, Takatsuki M, Kanematsu T: Application of endovascular stapler in living-donor liver transplantation. Am J Surg, 2007; 193: 258–59

8. Concejero A, Chen CL, Wang CC et al: Donor graft outflow venoplasty in living donor liver transplantation. Liver Transpl, 2006; 12: 264–68

9. Hori T, Yagi S, Iida T et al: Stability of cirrhotic systemic hemodynamics ensures sufficient splanchnic blood flow after living-donor liver transplantation in adult recipients with liver cirrhosis. World J Gastroenterol, 2007; 13: 5918–25

10. Yi NJ, Suh KS, Lee HW et al: An artificial vascular graft is a useful interpositional material for drainage of the right anterior section in living donor liver transplantation. Liver Transpl, 2007; 13: 1159–67

11. Hwang S, Ha TY, Ahn CS et al: Reconstruction of inferior right hepatic veins in living donor liver transplantation using right liver grafts. Liver Transpl, 2012; 18: 238–47

12. Tanaka K, Uemoto S, Tokunaga Y et al: Surgical techniques and innovations in living related liver transplantation. Ann Surg, 1993; 217: 82–91

Original Article

Prospective study of the safety and efficacy of intermittent inflow occlusion (Pringle maneuver) in living donor left hepatectomy

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Aim: The impact of intermittent inflow occlusion (Pringle maneuver) in living donor hepatectomy on the outcome of both the donor and the recipient is unknown. The aim of this study is to elucidate the safety and efficacy of Pringle maneuver in living donor hepatectomy.

Methods: Twenty consecutive cases of living donors who underwent left hepatectomy were prospectively divided into two groups, with (Group A, *n* = 10) or without (Group B, *n* = 10) the Pringle maneuver during hepatectomy. Intraoperative blood loss, postoperative liver functions in the donors and recipient outcome were reviewed.

Results: Median blood loss was significantly less in group A than in group B. Median alanine aminotransferase was signifi-

cantly higher on postoperative day 1 in group A than in group B, but the difference was not significant at 7 days after surgery. Eight of 10 recipients in each group survived with good graft function with a median follow-up period of 20 months in group A and 19 months in group B.

Conclusion: The Pringle maneuver was safely applied in living donor hepatectomy, but the only benefit was the reduction of blood loss during the donor surgery, and no positive impact on the recipient outcome.

Key words: hepatectomy, ischemic reperfusion injury, liver transplantation, living donor, Pringle maneuver

INTRODUCTION

R EDUCING BLOOD LOSS is essential to achieving good outcomes in hepatectomy, and intermittent inflow occlusion (the Pringle maneuver) has been widely adopted to control intraoperative bleeding during liver transection.[1–3] Although it has been proven that the Pringle maneuver does not cause remnant liver injury, the possibility of ischemia–reperfusion injury is of great concern in living donor hepatectomy, both in the graft and in the remnant liver. On the other hand, the Pringle maneuver is reported to protect the hepatocyte against ischemia–reperfusion injury by means of a

mechanism known as ischemic preconditioning, via heme oxygenase-1 (HO-1) upregulation in the liver.[4,5] Accordingly, Imamura *et al.* proposed that transplant physicians should not hesitate to use the Pringle maneuver in living donor hepatectomy.[6] However, the safety and feasibility of the Pringle maneuver in living donor liver transplantation (LDLT) have not been fully elucidated. The aim of this study is to elucidate the impact of the Pringle maneuver on the outcome of living donor hepatectomy and on graft function in the recipient.

METHODS

T HIS PROSPECTIVE STUDY was approved by the ethics committee of Nagasaki University Hospital (no. 09082890), and all patients were enrolled in this study after providing fully informed consent. Surgical procedures were the same in the groups as has been described in detail elsewhere.[7–9] Liver parenchymal transection was performed utilizing saline-linked electric

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