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ORIGINAL ARTICLE

Ligation of left renal vein for large spontaneous splenorenal shunt to prevent portal flow steal in adult living donor liver transplantation

Sung-Gyu Lee,[1] Deok-Bog Moon,[1] Chul-Soo Ahn,[1] Ki-Hun Kim,[1] Shin Hwang,[1] Kwang-Min Park,[1] Tae-Yong Ha,[1] Gi-Young Ko,[2] Kyu-Bo Sung,[2] Gi-Won Song,[1] Dong-Hwan Jung,[1] Ki-Myung Moon,[1] Bum-Soo Kim[1] and Yong-Pil Cho[3]

1 Division of Hepatobiliary Surgery and Liver Transplantation, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
2 Department of Radiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
3 Division of Vascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

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Correspondence
Sung-Gyu Lee MD, FACS, Division of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, 388-1 Pungnap-dong, Songpa-gu, Seoul 138-736, Korea. Tel.: +82 2 3010 3485; fax: +82 2 474 9027; e-mail: sglee2@amc.seoul.kr

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Summary

Persistance of a large spontaneous splenorenal shunt (SRS) may result in graft failure in adult living donor liver transplantation (LDLT) because it reduces the effective portal perfusion to the partial liver graft by diversion of hepatotrophic portal flow into this hepatofugal pathway. We performed a prospective study to evaluate the efficacy of ligation of left renal vein (LRV) to prevent portal flow steal and the safety of this procedure to the renal function in adult LDLT patients with SRS. Between October 2001 and January 2005, 44 cirrhotic patients with large SRS underwent LDLT with ligation of LRV. Each patient received pre- and postoperative computed tomography and Doppler USG to assess the changes of collaterals and portal flow, as well as serial renal and liver function tests. Portal flow after ligation of LRV was statistically and significantly increased when compared with pre-operative value ($P = 0.001$). Whereas four patients (9.1%) demonstrated sustained, elevated serum creatinine levels after operation, the renal function tests returned to normal in 40 patients. All patients recovered with satisfactory regeneration of the partial liver graft and there was no procedure-related permanent renal dysfunction. In conclusion, ligation of LRV to prevent a 'portal steal phenomenon' seems to be a safe and effective graft salvage procedure for large spontaneous SRS (>10-mm diameter) in adult LDLT.

Introduction

Spontaneous diversion of portal flow through a wide variety of collateral vessels into systemic circulation is commonly found in portal hypertensive cirrhotic patients. In advanced stages, portal flow becomes hepatofugal and may determine a 'portal steal phenomenon' with a dramatic decrease in hepatic perfusion [1–5]. After deceased donor whole-liver transplantation, the significant reduction in portal pressure with obliteration of collateral vessels is the usual consequence after interposing an adequate-sized graft with normal intrahepatic vascular resistance between the splanchnic and systemic circulations [6].

In contrast, persistence of portal hypertension may be more or less continuous after adult partial living donor liver transplantation (LDLT) frequently having an inadequate-sized graft with increased intrahepatic vascular resistance [2].

Adequate portal inflow is essential to the rapid regeneration of small partial liver graft after adult LDLT to meet the metabolic demands of the recipients.

Persistance of large spontaneous splenorenal shunts (SRS) can draw portal flow away from the liver graft and

thus predispose to the impaired graft regeneration and the subsequent small-for-size graft failure after LDLT.

To treat SRS, direct division of SRS and/or splenectomy may be technically difficult and even more dangerous [7,8].

As an alternative therapeutic modality, we have used the left renal vein (LRV) ligation that is simple and safe procedure.

The aim of this study was to evaluate the safety and efficacy of ligation of the LRV to prevent portal flow steal and its detrimental effect to renal function in adult LDLT patients with large spontaneous SRS.

Patients and methods

From October 2001 to January 2005, adult LDLTs were performed in 665 patients with end-stage liver disease. Of these, 44 patients (6.6%) with a large spontaneous SRS (>10-mm diameter at the level of transition into LRV) who received ligation of LRV during the transplant procedure were included in this study. Permission to perform the present study was given by the Asan Medical Center Institutional Review Board, University Ulsan College of Medicine. Informed consent was obtained from all patients included in this study.

The male-to-female ratio was 31:13, and the average age was 51 years (range: 26–64 years). Indications for LDLT included hepatitis B viral cirrhosis and/or hepatocellular carcinoma (40 cases, 91.0%), hepatitis C viral cirrhosis (two cases, 4.5%), and primary biliary cirrhosis (two cases, 4.5%). The median CTP and MELD score of patients was 11 (range: 6–14) and 20 (range: 6–40). There were six acute-on-chronic liver failure patients.

Each patient received 3-dimensional computed tomography (CT) scan (Sensation 16 channel, Siemens, Germany) and colour Doppler ultrasound (DUS) (Sequoia, Siemens, Germany) before and after surgery, to assess the changes of collaterals and portal blood flow, as well as renal function tests, including urine output, serum creatinine, urinalysis and DTPA (diethylene triame pentaacetic acid) – renal scan to evaluate the functional changes of the kidney after ligation of the LRV.

Living donor liver transplantations were performed by using 19 right lobe grafts (43.2%), 18 dual grafts (40.9%), and seven left lobe grafts (15.9%). Mean graft-recipient weight ratio (GRWR) was 0.97 ± 0.19% (range: 0.49–1.45%). Six patients (13.6%) received small-for-size grafts <0.8% of GRWR. During recipient operation, we conducted an isolation of LRV easily just left to the inferior vena cava after Kocher maneuver before total hepatectomy. After total hepatectomy, we compared the amount of portal flow from the divided end of portal vein (PV) during declamping and clamping of LRV with vascular clamp in order to appraise the degree of shunting flow through SRS. When marked augmentation of portal flow was noted by the clamping of LRV, ligation of LRV was performed before arterial anastomosis of liver graft.

Simultaneously, we also had examined Doppler USG at the time of preligation and postligation of LRV in the first 20 patients, but did not perform it recently because the visual inspection of portal flow from the divided end of PV was ample evaluation.

Results were expressed as mean ± SD. Quantitative assays were compared with the unpaired Student *t*-test or one-way ANOVA, and categoric data were compared with χ^2-test. Correlation between parameters was evaluated by the Pearson or Spearman correlation coefficient. Statistical calculations were performed with SPSS for windows (release 12.5; SPSS Inc, Chicago, IL, USA). *P*-value <0.05 was considered statistically significant.

Results

On pre-operative 3-dimensional CT scan, the diameter of SRS at the point of transition into LRV was 17.3 ± 5.9 mm (range: 10–30 mm), and the diameter of main PV was 9.2 ± 3.3 mm (range: 3.7–16.0 mm), which was inversely related with the size of SRS. Pre-operative DUS showed that flow velocity was reduced in most of the patients in comparison with the healthy subjects (mean: 10.2 ± 10.1 cm/s; range: 16–27 cm/s): PV stenosis (<10-mm-calibered main trunk) in 24 patients (54.5%), absence of the intraluminal Doppler signal and Doppler waveform in seven patients (15.9%), and reversed portal flow in three patients (6.8%). Intra-operative DUS examination showed a significant increment of portal flow between pre- and postligation of LRV after engraftment, corresponding to the result of visual estimation of portal flow through the divided end of PV on clamping and declamping of LRV after total hepatectomy (Fig. 1).

On postoperative DUS examination, the velocity of main PV was a peak (mean, 85.4 ± 39.5 cm/s, range: 35–238 cm/s) on the first postoperative day, and decreased to 53.4 ± 25.0 cm/s (range: 21–120 cm/s) on the 7th day according to the graft regeneration. However, there was adequate hepatopetal flow to the graft. Implanted grafts functioned well. Total bilirubin values also decreased in all patients on 3rd postoperative day when compared with pre-operative values.

Table 1 demonstrated the changes of renal function before, 1 day, and 3 months after transplantation. Preoperative urinalysis showed proteinuria in seven patients (15.9%) and hematuria in 11 patients (25.0%). Whereas 1 day after LDLT with ligation of the LRV, urinalysis showed proteinuria in 22 patients (50.0%) and hematuria in 43 patients (97.7%), proteinuria and hematuria were

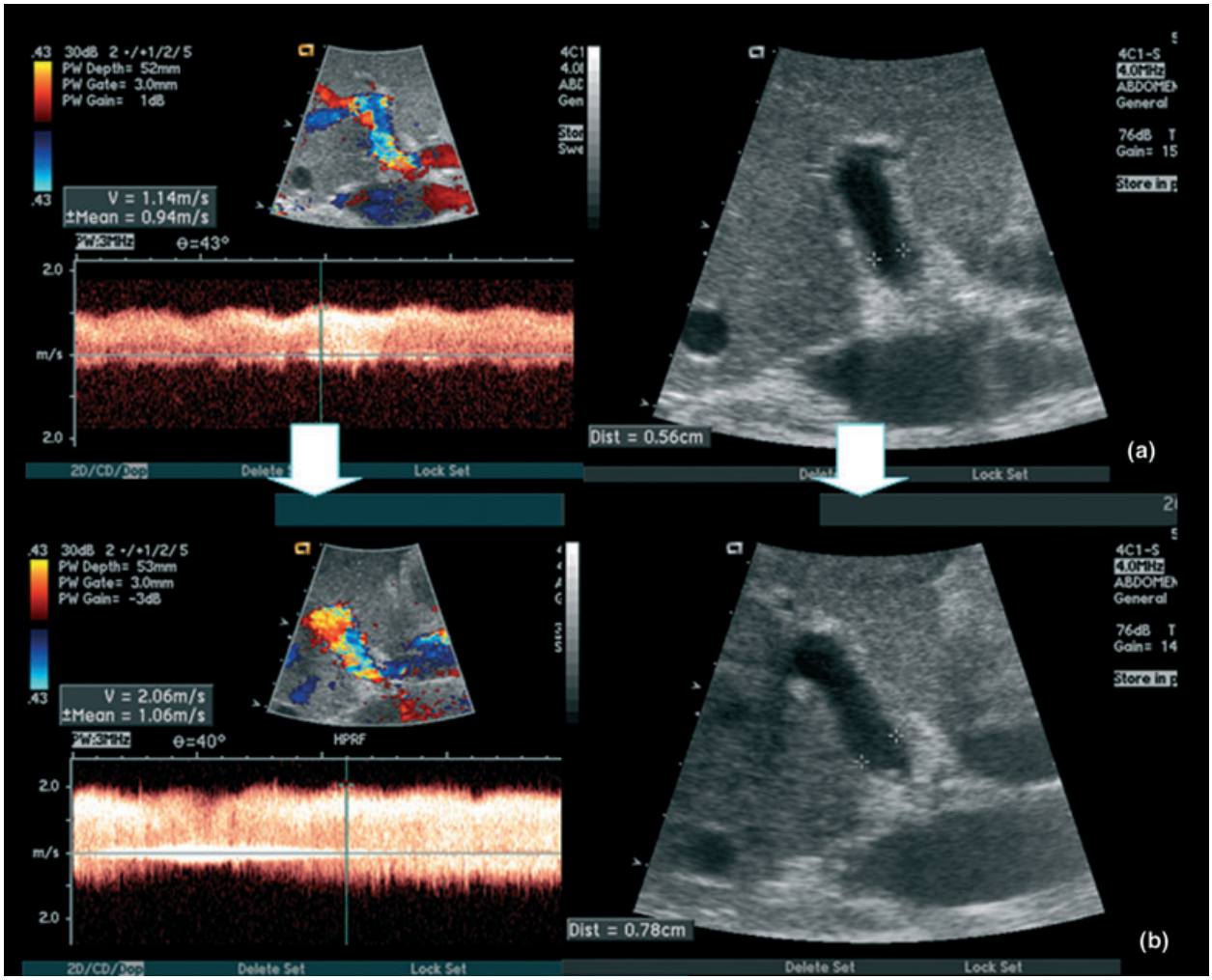

Figure 1 Intra-operative Doppler ultrasonography examination for the effect of left renal vein (LRV) ligation. (a) Doppler ultrasonography displayed portal flow velocity (114 cm/s), portal flow (1560 ml/min), and stenotic main portal vein (PV) (5.6-mm diameter) just after engraftment. (b) The increment of portal flow velocity (206 cm/s), portal flow (2850 ml/min), and stenotic main PV (7.8-mm diameter) was noted after LRV ligation.

Table 1. Changes of renal function before and after living donor liver transplantation with ligation of left renal vein.

	Number of patients (%)		
	Before surgery	1 day after surgery	3 months after surgery
Poor urine output	0	4 (9.1)	0
Proteinuria	7 (15.9)	22 (50.0)	1 (2.3)
Hematuria*	11 (25.0)	43 (97.7)	3 (6.8)
Serum creatinine (≥1.5 mg/dl)	4 (9.1)	22 (50.0)	4 (9.1)
Blood urea nitrogen (BUN) (≥26 mg/dl)	2 (4.5)	44 (100)	13 (29.5)

Values in parentheses are percentages.
*Significant difference between before and 3 months after surgery: $P < 0.05$.

noted in one patient (2.3%) and three patients (6.8%) 3 months after surgery respectively.

The mean duration of proteinuria and hematuria were 10.5 ± 8.5 days and 20.9 ± 58.4 days, respectively. Immediately after surgery, poor urine output (<1000 ml/day) was observed in four patients (9.1%), who received continuous venovenous hemofiltration. Dialysis was discontinued in all four patients after the urine output had normalized (average duration 6 days, range: 3–14 days).

Pre-operative serum creatinine level was 0.9 ± 0.4 mg/dl (range: 0.3–2.1 mg/dl). An increase in serum creatinine was seen in all but one patient (43/ 44, 97.7%) after LRV ligation. However, its value did not increase above 1.5 mg/dl in half of the patients (22/44, 50%), which was acceptable range as a post-LT renal function. It

reached a peak, 1.9 ± 1.0 mg/dl (range: 0.8–5.8 mg/dl), during the first 3 postoperative days and then decreased <1.5 mg/dl in 40 (40/44, 90.5%) patients by 3rd postoperative month. Remaining four (4/44, 9.5%) patients showed above 2.0 mg/dl in serum creatinine and three of them had diabetes mellitus (two patients) and chronic glomerulonephritis (one patient) pre-operatively.

Classifying the changes of left kidney after ligation of LRV on the basis of postoperative 7th day CT scan, that is, hypo-attenuation and normal attenuation of left kidney, 34 (77.3%) patients revealed hypo-attenuation when compared to normally looking right kidney. Interval change of size of left kidneys was 7.0 ± 5.9 mm (range: 0–20 mm) increase on the 7th day of ligation of LRV ($P < 0.001$). However, the size of left kidney decreased 4.7 ± 8.8 mm (range: 26 to −22 mm) on 3rd month after operation when compared to pre-operative size ($P < 0.001$) in 33 (75%) patients. Nine of the first 10 examined patients revealed decreased perfusion and uptake of left kidney on postoperative 3rd week DTPA-renal scan regardless of normalization of urinary output and serum creatinine.

All 44 patients recovered well without retransplantation, and 43 patients are alive now with median follow-up 17 months except one patient died of recurrence of hepatocellular carcinoma at 13 months after LDLT.

Discussion

Small-for-size liver graft transplanted to the large recipient should undergo early accelerated regeneration to meet the metabolic demands of the recipient in the immediate post-transplant period [9]. Adequate portal inflow is essential to the regeneration of partial liver graft after LDLT [10]. Pre-existing hyperdynamic splanchnic flow of cirrhotic recipient due to portal hypertension, which is going to concentrate on the partial liver graft with smaller volume after LDLT, enhances an increase in intrahepatic vascular resistance [2]. In adult LDLT for the cirrhotic patients with large collateral shunts, life threatening portal flow steal through the collaterals can occur because of high intrahepatic vascular resistance [11]. Although controversies exit, some authors have presented the evidences of the negative effects of the persistence of the spontaneous portosystemic shunts after LDLT with a small-for-size graft and their closure was recommended [2,4]. Excessive or impaired portal venous inflow may significantly reduce hepatic function in small-for-size liver graft. To deal with small-for-size graft successfully, both the avoidance of graft overperfusion by excessive portal hypertension and the prevention of portal flow steal through large spontaneous collaterals are equally important. Since 2002, our institute have performed ligation of large collateral vessels routinely even in very small-for-size graft (<0.6% GRWR) during adult LDLT after experiencing a mortality case related with devastating ''portal flow steal''.

Ligation of LRV was first performed to expedite resection of a retroperitoneal tumor [12], and secondly to facilitate exposure of the renal arteries after penetrating trauma [13] or proximal aorta in aortic reconstructive surgery [14] However, this is the first report that ligation of LRV is used for interruption of SRS as a prophylactic procedure of possible portal flow steal during LDLT.

Intra-operative DUS is a useful tool to assess portal hemodynamics by measuring flow velocity during LT. It can also be used to select patients who would benefit from ligation of their collaterals [15]. Fujimoto *et al.* [4] have suggested that collaterals should be ligated during LDLT in patients with a portal blood flow <10 ml/min/kg. However, two patients with normal portal flow during LT died of graft failure due in part to portal hypoperfusion. Therefore, we should be cautious to use DUS as a guidance of collateral ligation, because all reported portal steal cases had sufficient portal venous flow just after reperfusion, and DUS could not give us correct information about the completeness of interruption of collaterals due to confounding factors related to various tortuous collateral vessels around splenic hilum, and radiologist-dependent results.

Instead, after routine pre-operative check on collateral vessels by 3-D CT and DUS and deciding whether to ligate it or not intra-operatively by visual inspection of portal flow augmentation from the cut-end of PV after clamping LRV, we have not experience any ''portal flow steal''- related graft failure regardless of not-infrequent occurrence of acute rejection among a total of 665 adult LDLTs performed from October 2001 to January 2005 at the Asan Medical Center. As a result, ligation of LRV for the interruption of SRS is an effective method. When we consider there was no procedure-related complication during ligation of LRV, it is also a safe method.

However, there might be some debate about the safety of the left kidney. From clinical experiences, ligation of LRV is reported to be safe procedure by many investigators [12,13,16]. Especially in surgery of advanced hepatobiliary malignancy invading PV and inferior vena cava, LRV were resected from the confluence of inferior vena cava and LRV to the portion just distal to the renal-azygous and the gonadal vein, without any permanent and/or serious renal dysfunction [16]. However, some investigators cautioned its application due to occurrence of postoperative renal complications [17,18].

Among 44 patients ligated LRV, four patients had elevated serum creatinine level above 1.5 mg/dl without

poor urine output pre-operatively, and none needed artificial renal support. Some patients had pre-operative proteinuria and hematuria, and which increased during immediate postoperative period after ligation of LRV. However, most of the patients have been living without those findings after post-transplant 3rd month. Four patients who needed postoperative renal support from poor urine output recovered <2 weeks, and three of them except for remaining one patient who had diabetes pre-operatively have normal serum creatinine level below 1.5 mg/dl. Our experiences indicate ligation of LRV for the patients with large SRS was not a harmful procedure, and it can be performed more often as a life-saving procedure to cope with possible portal flow steal. However, considering three of four patients with continuous azotemia after ligation of LRV were pre-operative diabetics or glomerulonephritis who had relatively high creatinine value above 1.4 mg/dl, we have to pay special attention to those patients in view of pre-operative selection of patient ligating the LRV, intra-operative approaches for SRS, and postoperative management.

Morphologically, the left kidneys after ligation of LRV showed size-increase and also hypo-attenuation (34/44, 77.3%) on CT scan during immediate postoperative period, and then its size decrease smaller than that of pre-operation (33/44, 75%). These are corresponding to the previous reports [19,20]. However, the morphology of kidneys in a quarter of the patients was not affected from ligation of LRV, that might be explained by abundant collateral vessels such as SRS resulted from previous portal hypertension.

Meanwhile, it is known that high portal pressure in small-for-size LDLT induces liver sinusoidal injury through the excessive shear stress, and even can cause primary nonfunction [21]. Splenic arterial ligation to reduce the excessive portal hypertension and overperfusion into the liver graft can be applied for the prevention of such injury [22,23]. Among the patients with LRV ligation, six patients received small-for-size grafts <0.8% of GRWR (range: 0.49–0.79). Splenic arterial ligation was added and the adequate hepatic venous outflow reconstruction was thoroughly provided to avoid graft congestion in all patients [24].

From the above results, ligation of LRV for the patients with large spontaneous SRS in LDLT is a good graft salvaging procedure because of eradication of the possibility of portal flow steal and maintenance of the adequate portal inflow. However, the safety of the procedure cannot be guaranteed completely yet, because the elevated serum creatinine level persisted postoperatively in a few patients. Therefore, we need to perform prospective study to clarify the safety of ligation of LRV by comparing the postoperative renal function between the LDLT patients undergone ligation of LRV for SRS and the other LDLT patients without SRS, that is not performed ligation of LRV, in the future.

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