

Postoperative Liver Regeneration and Complication In Live Liver Donor after Partial Hepatectomy for Living Donor Liver Transplantation

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The safety of donor is the first priority during whole procedure in living donor liver transplantation. We evaluated the short-term results of partial living donor liver transplantation in the view of donor safety. We prospectively evaluated the extent of liver regeneration, the recovery of liver function, and the perioperative complications in 41 live liver donors for partial liver transplantation at our institution. We developed novel personal computer volumetry program for the evaluation of liver regeneration. Serial CAT scan was performed preoperatively, at postoperative day (POD) #7 and POD #30 and liver volume was measure by using volumetry program. The serum level of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and total bilirubin (T.bil.) was serially monitored. There were 34 males and 7 females. The mean preoperative liver volume was 1320.6 cm³. The remained mean liver volume was 687.8 cm³ after harvest, and increased to 954.4 cm³ (144.6%) at POD #7, and 1169.5 cm³ (81.4%) at POD #30, which was 88.5% of preoperative total liver volume. The serum level of ALT/AST and T.bil. peaked at POD #1 and declined thereafter, and finally returned to preoperative level at POD #30. The regeneration rate was significantly different by age, type and size of graft according to the donors. Six donors experienced postoperative complications and they were four pleural effusions, one wound infection and one case of bile duct stenosis that was treated by endoscopic nasal biliary drainage. All of them were right lobe donors. In conclusion, the donor liver regenerated up to 88.5% of preoperative volume with full recovery of liver function at POD #30. Right lobe donors suffered more complications and need more meticulous

operative and postoperative care than left lobe or left lateral segment donors.

Key Words: Living, partial liver transplantation, donor, safety

INTRODUCTION

Liver transplantation has been considered as a main therapy for patients with end-stage liver disease. Before the development of idea and technique of partial liver transplantation, cadaveric liver transplantation has been performed over the whole world. But the number of people on the liver waiting list has increased and living donor liver transplantation, using left lateral segment, left lobe and finally right lobe, has been developed to solve this problem. However, in the living donor liver transplantation, there has been a possibility of small sized graft, which caused graft insufficiency or finally transplantation failure. Many authors have reviewed the results of recipients received left lateral segment, left lobe or right lobe. But evaluation of donor safety was reported little.

Hereby, we reported our results of the liver regeneration and surgical complications from the standpoint of donor safety after living liver transplantation.

MATERIALS AND METHODS

Between June 1 1999 and June 30 2003, 41 donors were underwent donor hepatectomy for 40 living liver transplantations in the Department of

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Surgery, Yonsei University College of Medicine including a case of dual transplantation. We prospectively evaluated the extent of liver regeneration, the recovery of liver function, and the perioperative complications in these 41 donors.

The indication for living donor was basically defined as estimated graft volume/recipient body weight ratio > 1.0% or estimated graft volume > 50% of standard liver volume of recipient. Because of donor safety, authors should not included middle hepatic vein in the graft.

Liver volume was measured by novel volumetry program using personal computer, which was made by one of our colleague (KS Kim). Serial CAT scan was performed preoperatively, at POD #7 and POD #30 and liver volume was measured by a donor surgeon (JS Choi) by using volumetry program.

The liver biopsy was carried out through small celiotomy prior to major resection. If the steatosis exceeded 20% by frozen section pathology, no further operation would be proceeded.

The serum level of AST, ALT and total bilirubin level of these 41 donors were serially monitored preoperatively, at POD #1, 2, 3, 5, 7, and twice a week thereafter until POD #30. All values are indicated its mean \pm standard deviation.

Statistical analysis was done using the Statistical Package for the Social Science (SPSS) version 11.0 (SPSS, Inc. Chicago, IL, USA). The student's t-test and ANOVA test were used. A *p* value < 0.05 was considered statistically significant.

RESULTS

Of the 41 donors, 34 were male and 7 were female. The age distribution of donor was 11 cases in 10's, 15 cases in 20's, 12 cases in 30's and 3 cases in 40's. The mean age was 27.8years (range 16-49). The mean body weight and height were 67.3kg (range 42-96) and 170.3 cm (range 153-180). The ABO blood type was A in 16 cases, B in 13 cases, O in 10 cases, and AB in 2 cases. There were 31 related donors, most of them were sons, and 10 unrelated donors. The types of graft harvest were right lobectomy (RL) in 34 cases, left lobectomy (LL) in 4 cases, and left lateral segmentectomy (LLS) in 3 cases, respectively.

The preoperative liver volume measured by volumetry program was $1320.6 \pm 213.1 \text{ cm}^3$ in total (TLV), $831.1 \pm 152.1 \text{ cm}^3$ in right lobe, and $489.5 \pm 127.0 \text{ cm}^3$ in left lobe, respectively. The actual graft volume was $715.5 \pm 107.7 \text{ cm}^3$ in RL, and $414.2 \pm 194.5 \text{ cm}^3$ in LL or LLS, respectively. The ratio of graft to total liver volume (TLV) was 0.55 ± 0.06 in RL donors, and 0.30 ± 0.10 in LL or LLS donors, respectively. The remained liver volume was $642.0 \pm 161.8 \text{ cm}^3$ after RL, and $969.0 \pm 261.8 \text{ cm}^3$ after LL or LLS, respectively.

The donor remnant liver volume increased to $954.4 \pm 182.9 \text{ cm}^3$ from $687.8 \pm 208.3 \text{ cm}^3$ which was $144.6 \pm 33.3\%$ increase in the volume at POD #7, and increased to $1169.5 \pm 194.5 \text{ cm}^3$ ($181.4 \pm 42.6\%$) at POD #30 that was 88.5% of preoperative TLV.

The ALT, AST and T.bil. showed their peak level at POD #1 and declined gradually. The AST and ALT returned to normal level at POD #30.

Serum level of ALT was $240.1 \pm 159.3 \text{ IU/dl}$ at POD #0, and showed its peak level of $275.9 \pm 162.3 \text{ IU/dl}$ at POD #1. After then it declined gradually and reached $118 \pm 75.9 \text{ IU/dl}$ at POD #7, and $37.3 \pm 8.8 \text{ IU/dl}$ at POD #30.

The serum level of AST also showed serial change as ALT. That was $221.1 \pm 102.8 \text{ IU/dl}$ at POD #0, $240.2 \pm 109.6 \text{ IU/dl}$ at POD #1, $78 \pm 49.6 \text{ IU/dl}$ at POD #7, and $30.9 \pm 13.2 \text{ IU/dl}$ at POD #30, respectively.

The T.bil. returned to normal level at POD #7 except one donor. The serum level of T-bill showed serial change of $2.46 \pm 1.21 \text{ mg/dl}$ at POD #0, $2.83 \pm 1.2 \text{ mg/dl}$ at POD #1, $1.12 \pm 0.61 \text{ mg/dl}$ at POD #7, and $0.63 \pm 0.24 \text{ mg/dl}$ at POD #30, respectively (Fig. 1).

No complication occurred in LLS and LL donors. But complications occurred in RL donors, they were pleural effusion in 4 donors, wound infection in 1 donor, and bile duct stenosis in 1 donor. The T.bil. level of bile duct stenosis donor was 7.4 mg/dL at POD #10. The endoscopic retrograde cholangio pancreaticography (ERCP) revealed mild segmental stenosis of common hepatic duct. By applying the endoscopic nasal bile drainage (ENBD), the serum level of T.bil. return to base line level at POD#17. The ENBD was removed at POD#24 and he discharged without any problem.

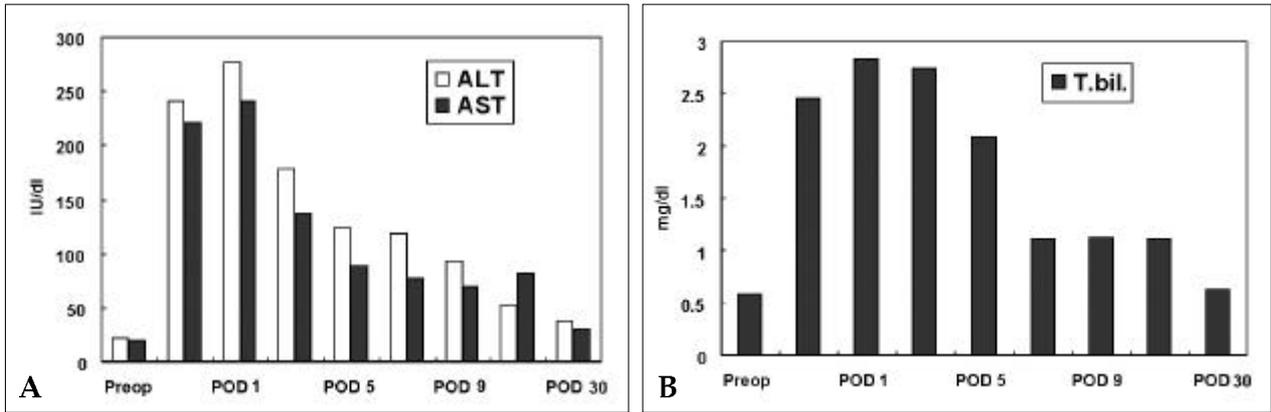


Fig. 1. Change in the ALT/AST (A) and T.bil. (B) before and after a hepatectomy for the living donor liver transplantation.

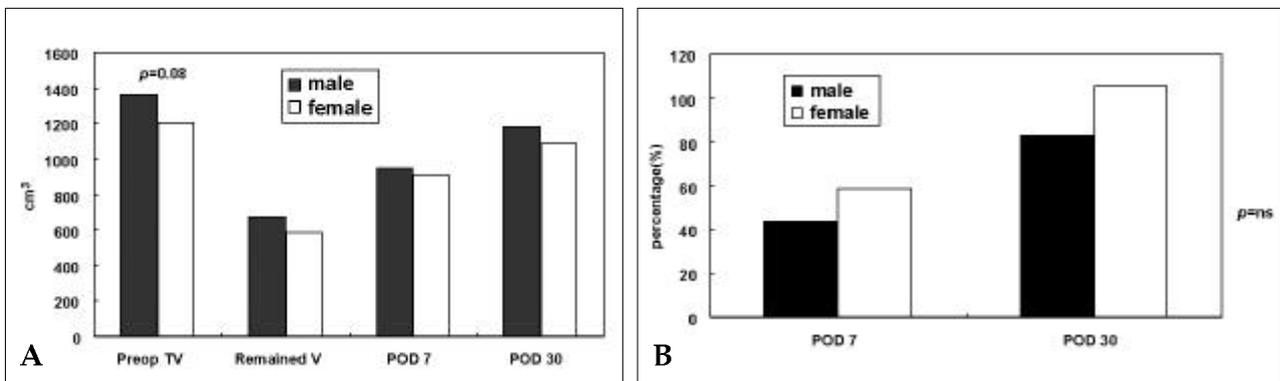


Fig. 2. Postoperative volume (A) and increased ratio (B) of remnant liver according to gender.

Liver regeneration and function recovery; according to donor sex

Right lobectomy was carried out in all 7 female donors and 30 male donors. The preoperative TLV was $1360.1 \pm 192.5 \text{ cm}^3$ in male, and $1199.2 \pm 268.6 \text{ cm}^3$ in female ($p=ns$). The volume of right lobe was $869.1 \pm 148.9 \text{ cm}^3$ in male and $712.6 \pm 106.9 \text{ cm}^3$ in female ($p=0.0009$). The graft volume was $729.6 \pm 165.6 \text{ cm}^3$ (53.6% of TLV) in male and $650.4 \pm 105.1 \text{ cm}^3$ (54.2% of TLV) in female ($p=ns$). The remnant liver volume increased to $965 \pm 188.5 \text{ cm}^3$ at POD #7 and $1184.0 \pm 184.7 \text{ cm}^3$ at POD #30 in male, and it also increased in female to $909.9 \pm 165.1 \text{ cm}^3$ at POD #7 and $1087.9 \pm 250.6 \text{ cm}^3$ at POD #30, respectively. The difference of regeneration between male and female was not significant (Fig. 2).

The serial serum levels of AST (IU/dl) at POD

#0, #1, #7, and #30 were 216.5, 230.1, 73.7 and 31.6 in male, and 243.1, 289.4, 98.9 and 27.3 in female ($p=ns$, respectively)

The serial serum levels of ALT (IU/dl) at POD #0, #1, #7, and #30 were 250.7, 276.0, 125 and 39.3 in male, and 188.6, 275.6, 88.6 and 27.2 in female ($p=ns$, respectively).

The serial serum levels of T.bil. (mg/dL) at POD #0, #1, #7, and #30 were 2.43, 2.72, 1.10 and 0.62 in male, and 2.56, 3.43, 1.2 and 0.67 in female ($p=ns$, respectively)(Fig. 3).

Liver regeneration and function recovery; according to donor age

All RL donors were analyzed. There were 10 in 10's, 12 in 20's, 10 in 30's and 2 in 40's of donor age.

The preoperative TLV, mean right liver volume, mean left liver volume showed no significant

difference between age groups.

The preoperative TLV was 1372.2 cm³ in teenagers, 1289.4 cm³ in 20's, 1290.4 cm³ in 30's, and 1443.2 cm³ in 40's, respectively (*p*=ns). The mean graft volume was 703.1 cm³ in teenagers, 706.0 cm³ in 20's, 698.8 cm³ in 30's, and 865.0 cm³ in 40's, respectively. The remnant liver volume was 742.4 cm³ in teenagers, 563.6 cm³ in 20's, 633.1 cm³ in 30's, and 578.0 cm³ in 40's.

At POD #7, the remnant liver volume increased to 903.4 cm³ (121.7%) in teenagers, to 955.0 cm³ (169.4%) in 20's, to 946.4 cm³ (149.5%) in 30's, and to 953.3 cm³ (164.9%) in 40's respectively. Regeneration of remnant liver occurred slowly in teenage donors than others (*p*=0.039). At POD #30, the remnant liver volume increased to 1174.6 cm³ (158.2%) in teenagers, to 1164.3 cm³ (206.6%) in

20's, to 1128.2 cm³ (178.2%) in 30's, and to 1240.6 cm³ (214.6%) in 40's, respectively (*p*=ns, respectively) (Fig. 4).

The serial change of AST, ALT and T.bil. showed no significant difference between ages (Fig. 5).

Liver regeneration and function recovery; according to fatty change of donor liver

All donors were divided into four groups, such as no fatty degeneration group (within normal limit: WNL), group with fatty change less than 5%, group with fatty change between 5 and 10%, and group with fatty change more than 10%.

There was no significant difference between groups on regenerated liver volume and serial AST, ALT, and T.bil. level (Fig. 6 and 7).

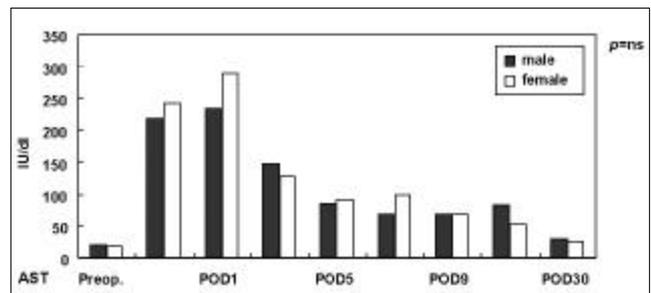
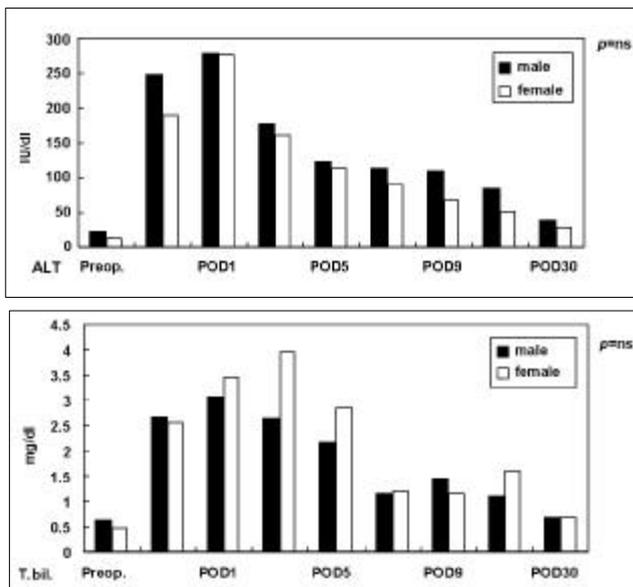


Fig. 3. Changing pattern of the laboratory findings according to gender.

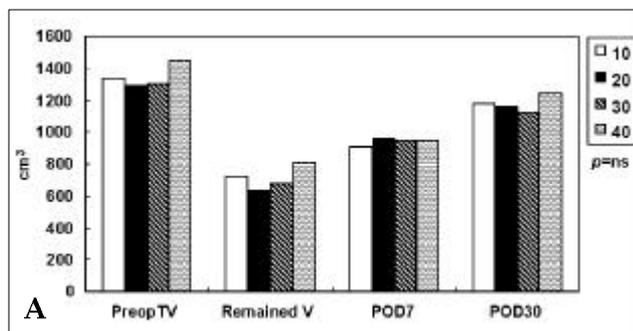


Fig. 4. Postoperative volume (A) and increased ratio (B) of remnant liver according to age.

Liver regeneration and function recovery; according to method of resection

The remnant liver volume was $642.4 \pm 161.8 \text{ cm}^3$, in RL donors, $894.0 \pm 232.2 \text{ cm}^3$ in LL donors, and $1269.0 \pm 450.2 \text{ cm}^3$ in LLS donors, respectively.

At POD #7, the remnant liver volume of RL, LL and LLS donors increased to $932.0 \pm 158.5 \text{ cm}^3$ (145.0%), $987.9 \pm 198.4 \text{ cm}^3$ (110.5%), and $1458.4 \pm 347.3 \text{ cm}^3$ (114.9%), respectively. The amount of volume increase in RL donors showed significant difference to that of LL or LLS donor ($p=0.007$).

At POD #30, the remnant liver volume of RL, LL and LLS donors increased to 1161.0 ± 172.6

cm^3 (180.7%), $1108.2 \pm 299.6 \text{ cm}^3$ (123.9%), and $1598.5 \pm 430.2 \text{ cm}^3$ (125.9%), respectively ($p=ns$).

At POD #0, the serum levels of ALT and AST were 235.9 IU/dl and 224.1 IU/dl in RL donors, 282.0 IU/dl and 188.8 IU/dl in LL donors, and 231.7 IU/dl and 229.7 IU/dl in LLS donors, respectively ($p=ns$). The serum levels of T.bil. were 2.7 mg/dl in RL donors, 1.9 mg/dl in LL donors, and 1.33 mg/dl in LLS donors, respectively ($p=ns$).

At POD #1, the serum levels of ALT in RL, LL, and LLS donors were 277.7 IU/dl, 280.3 IU/dl, and 250.7 IU/dl, respectively ($p=ns$). The serum levels of AST in RL, LL, and LLS donors were 246.0 IU/dl, 191.5 IU/dl, and 239.0 IU/dl, respectively ($p=ns$). The serum levels of T.bil. in RL, LL,

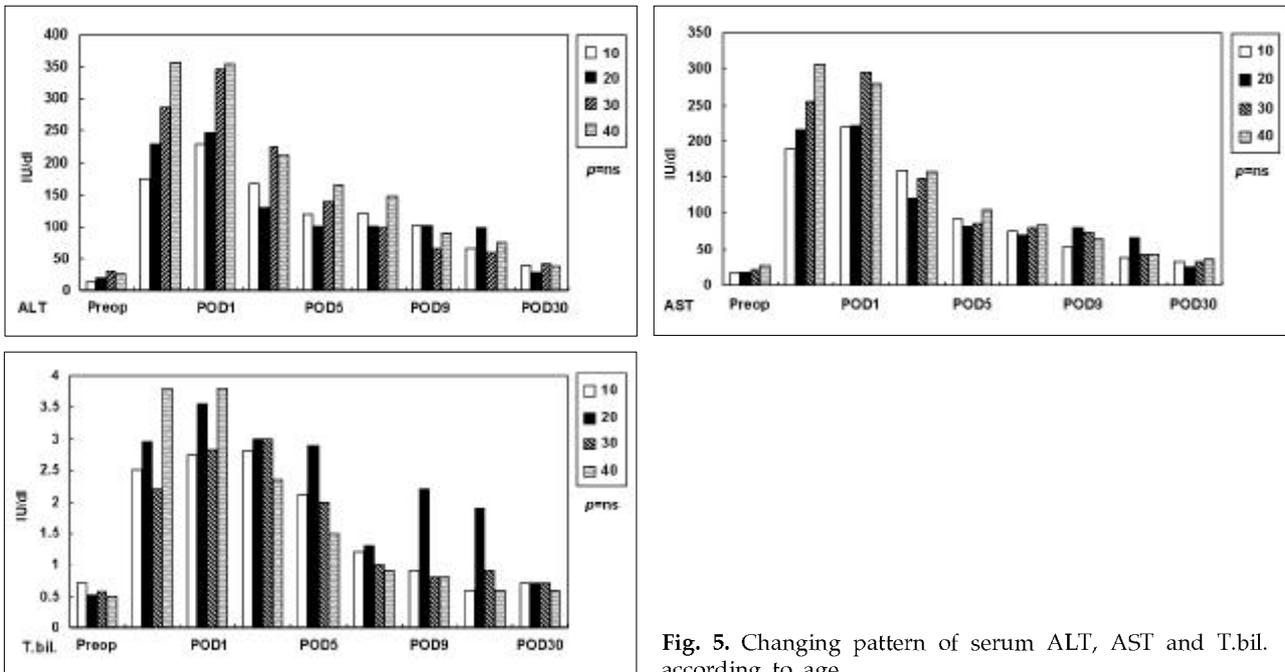


Fig. 5. Changing pattern of serum ALT, AST and T.bil. according to age.

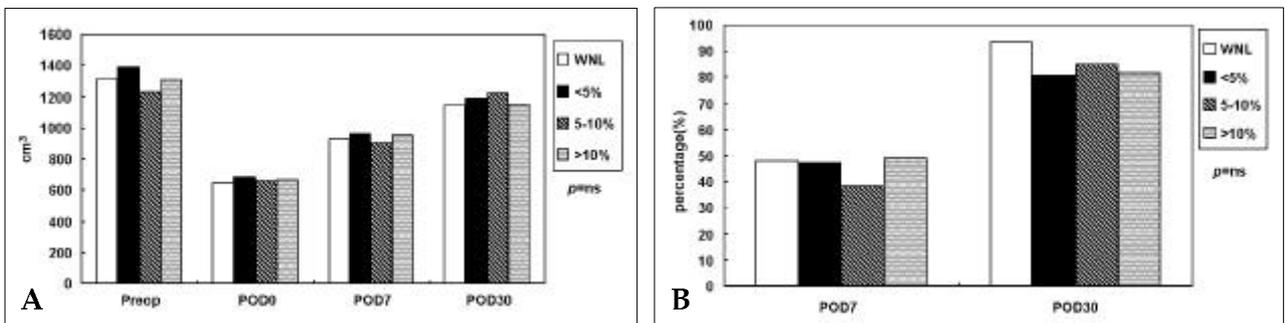


Fig. 6. Postoperative volume (A) and increased ratio (B) of remnant liver according to the degree of steatosis.

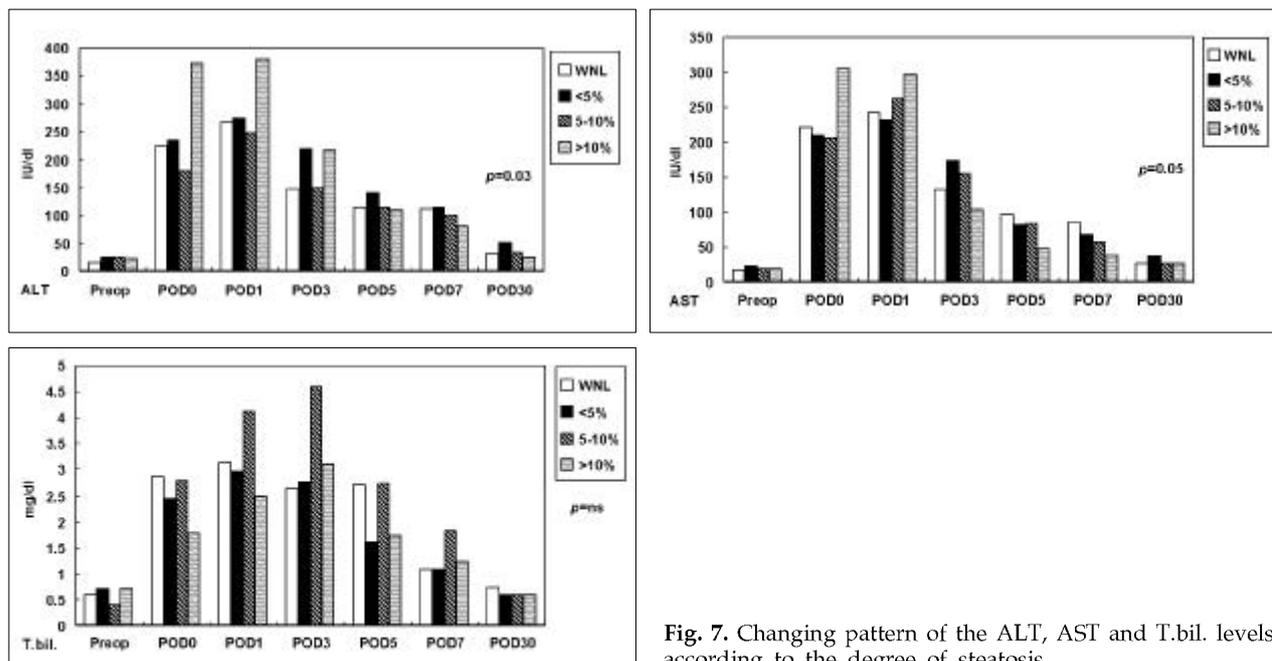


Fig. 7. Changing pattern of the ALT, AST and T.bil. levels according to the degree of steatosis.

and LLS donors were 3.1 mg/dl, 1.7 mg/dl, and 1.3 mg/dl, respectively ($p=ns$).

At POD #7, the serum levels of ALT in RL, LL, and LLS donors were 108.4 IU/dl, 212.8 IU/dl, and 105.3 IU/dl, respectively ($p=ns$). The serum levels of AST in RL, LL, and LLS donors were 74.9 IU/dl, 135.3 IU/dl, and 37.3 IU/dl, respectively ($p=ns$). The serum levels of T.bil. in RL, LL, and LLS donors were 1.16 mg/dl, 0.88 mg/dl, and 0.93 mg/dl, respectively ($p=ns$).

At POD #30, liver enzymes and T.bil. returned to the nearly normal level. The serum levels of ALT in RL, LL, and LLS donors were 35.2 IU/dl, 34.3 IU/dl, and 59.7 IU/dl, respectively ($p=ns$). The serum levels of AST in RL, LL, and LLS donors were 29.4 IU/dl, 35.7 IU/dl, and 40 IU/dl, respectively ($p=ns$). The serum levels of T.bil. in RL, LL, and LLS donors were 0.68 mg/dl, 0.4 mg/dl, and 0.37 mg/dl, respectively ($p=ns$).

Liver regeneration and function recovery; according to size of remnant liver

We divided all donors to group with remained volume less than 40% of preoperative TLV (group 1, N=3), between 40 and 49% (group 2, N=16), between 50 and 59% (group 3, N=12), and more than 60% (group 4, N=5) and then evaluated and

compared between groups.

The remained liver volume was 440.0 cm³ in group 1, 577.4 cm³ in group 2, 756.6 cm³ in group 3 and 1024.3 cm³ in group 4.

At POD #7, the remained liver volume increased to 912.5 cm³ (207.1%) in group 1, 891.9 cm³ (153.1%) in group 2, 955.1 cm³ (127.4%) in group 3 and 1162.8 cm³ (113.1%) in group 4 respectively ($p=0.0005$).

At POD #30, the remained liver increased to 1180.8 cm³ (168.3%) in group 1, 1133.7 cm³ (194.6%) in group 2, 1162.0 cm³ (159.6%) in group 3, and 1282.0 cm³ (121.2%) in group 4, respectively ($p=0.0007$) (Fig. 8).

There was no significant difference of serum level of AST and ALT between each group at any point of examination. The serum level of T-bill of group 1 significantly increased high at POD #1 and remained high level for 4 days after operation than other groups. From the POD #5, the level of T-bill didn't show significant difference between groups (Fig. 9).

DISCUSSION

In the past, recipients of living donor liver transplantation using left lateral segment or left

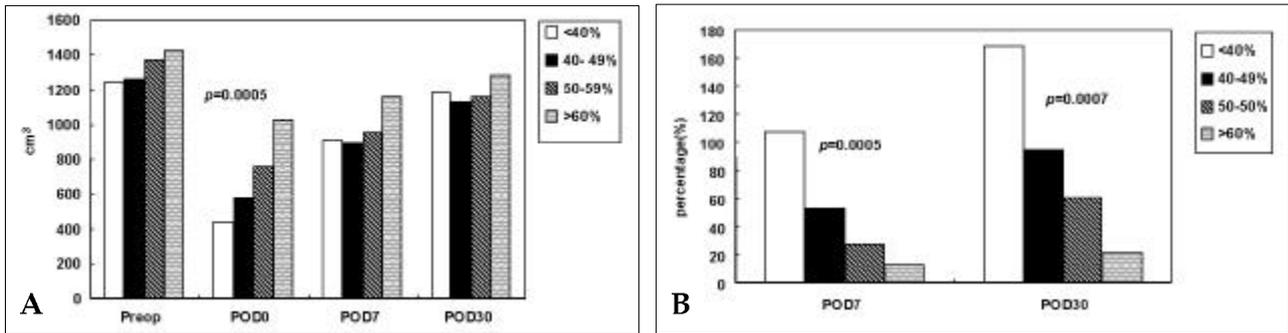


Fig. 8. Postoperative volume (A) and increased ratio (B) of the remaining liver according to the size of the remaining liver.

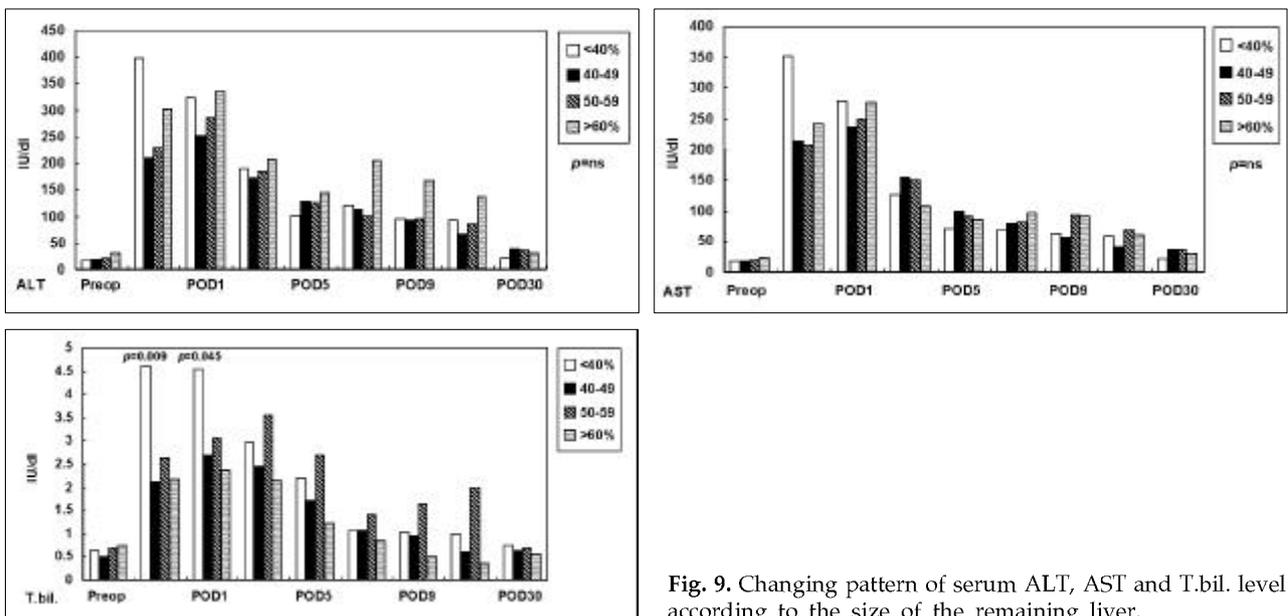


Fig. 9. Changing pattern of serum ALT, AST and T.bil. level according to the size of the remaining liver.

lobe were limited to pediatric or small body weight patients with end-stage liver disease. Currently, however, graft of the right lobe of the liver is worldwide trend for living donor liver transplantation because of enough volume and function of right lobe to meet the metabolic need of adult recipient. The development of refinements in surgical techniques, unique anatomy and physiology of the liver expands living donor partial liver transplantation.¹

Though graft harvest from living donor for liver transplantation may be a safe, the ethical debate for using live donor has increased with reports of donor deaths,²⁻⁴ and it is still a risky procedure for the donor, especially for whom with a large body mass, carrying high morbidity and mortality rates

due to complications such as portal vein thrombosis and bile leakage.⁵

There are not yet many reports on donor safety or short-term liver parenchyma regeneration or function return after right lobectomy for living donor liver transplantation, even though awareness and interests in these issues are increasing.^{6,7}

We used software program for liver volumetry that was developed by the one of author in our study (KS Kim). One of our colleagues (JS Choi) calculated the area of liver of each sagittal scanned CT image by tracing its outer borders as in a 2D CT volumetry. The volume of liver can be acquired by multiplying the area calculated from each scanned CT image and thickness of each scan and total number of images. This pro-

gram had the additional advantage of being applicable not only to CT but to MRI (Magnetic Resonance Image) that has an advantage of the evaluation of the vascular supply and biliary tree.⁸

Liver has almost unlimited regeneration power as revealed by rat model.⁹ Normal human liver also begins to regenerate within 3 days and has reached its original size by 6 months.^{10,11} There has been numerous studies addressing human hepatic regeneration but the mechanism of controlling liver regeneration is still poorly understood and few have reported hepatic regeneration in living liver donors.¹²⁻¹⁵

In this study, remnant liver restored its volume by short-term regeneration of 144.6% at POD #7 and 181.4% at POD #30, but the regeneration of remnant liver was significantly different by age of donors, type and size of graft.

The remnant liver of teen age group showed significant slow regeneration until POD #7.

We could not explain the reason of this result. The liver regeneration of this age group had no difference to others age groups at POD #30 result.

The volume of right lobe was bigger in male donors than female donors. But we harvested 53.6% of TLV in male donors and 54.2% of TLV in female donors for RL. That means both male and female donors had same amount of remnant liver and resulted in no difference in liver regeneration and AST, ALT and T.bil. level.

In our data, remnant liver regenerated more actively in order of RL, LL and LLS donors at POD #7, but not at POD #30. And remnant liver also regenerated more rapidly and persisted significantly until POD #30 in the donor who had a remnant liver volume less than 40% of TLV. The T.bil. levels increased in the donors who got a small remnant liver volume less than 40% of TLV. This elevated T.bil. decreased after POD #4 and showed no difference in recovery to the other donors. Because the portal venous flow velocity has a triggering effect on liver regeneration,¹⁶ the increased portal blood flow in the donors who got a less amount of remnant liver might influence more rapid liver regeneration. But we cannot convince this hypothesis because we did not check portal blood flow in these donors before and after harvest.

Our result showed more rapid regeneration of

liver in those who had a small remnant liver volume especially early after resection, and the remnant liver volume of more than 40% of TLV is enough to safe recovery of liver function.

Because of the risk of primary nonfunction of graft, we did not use steatotic liver as donor. It has been generally believed that more than 30% of steatosis may induce primary nonfunctioning allograft.¹⁷⁻¹⁹ And Pomfret, et al.¹⁵ demonstrated significantly slow regeneration in female donor at 12 months. The selection criteria in our program is "do not use fatty liver > 20% of steatosis by frozen liver biopsy in operation theatre".

As a result, we could not find any differences of liver regeneration and function recovery between the donor groups with different degree of steatosis.

We also observed that both morbidity and mortality did not happen after postoperative 1 month as the donor's liver functions returned to normal, and this result was different to report of Sato, et al.⁵ We experienced 4 pleural effusions, a wound infection, and a serious biliary complication of bile duct stenosis. The posterior segment bile duct of this duct stenosis donor located 3 mm apart from the bifurcation and careful division of right duct was demanded. A transient hyperbilirubinemia happened to this donor and relieved by ENBD. He has no further elevation of serum bilirubin thereafter for 9 months. Exact information of surgical anatomy and careful resection of liver may guarantee few complications.

In conclusion, the donor liver regenerated up to 88.5% of preoperative volume with full recovery of liver function at POD #30. Right lobe donors suffered more complications and need more meticulous operative and postoperative care than left lobe or left lateral segment donors. Current our series reported only early postoperative results and further study beyond 1 month should be proceeded to evaluate the late result of liver regeneration.

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