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ORIGINAL ARTICLE

Congestion of the donor remnant right liver after extended left lobe donation

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Summary

The clinical importance of congestion of the remnant right lobe has not yet been fully elucidated in donors who donate their left lobe with the middle hepatic vein. The impact of congestion on clinical course and liver regeneration in 52 donor remnant livers were evaluated. The donors were divided into three groups according to the degree of the congestion: the mild [congestion ratio (CR) < 10%], moderate (CR ranged from 10% to 25%) and severe congestion groups (CR > 25%). The regeneration ratio of the graft at postoperative day 7 (7 POD) was 22.0 ± 14.3% and inversely correlated with the CR in the remnant right lobe ($P = 0.003$). Aspartate aminotransferase and alanine aminotransferase at 7 POD were significantly higher in the severe CR group in comparison to the mild CR group ($P = 0.003$ and 0.019, respectively), but those of the three groups were comparable at 30 POD. The hospital stays were significantly longer in the severe CR group ($P = 0.010$). In conclusion, the congestion of the donors' remnant right liver can lead the transient liver dysfunction and poor regeneration. Therefore, the conversion of the graft from the left to right lobe might be appropriate according to the degree of the congestion.

Introduction

Since the first report in 1989, living donor liver transplantation (LDLT) has been gradually accepted as a therapeutic modality for end-stage liver cirrhosis and hepatocellular carcinoma [1–3]. The decision of the choice between the right lobe and extended left lobe depends on the physical constitution of the recipient in LDLT [4,5].

Recent reports have demonstrated that the reconstruction of middle hepatic vein (MHV) tributaries for the drainage of the right anterior section improved the outcomes in the right lobe LDLT [6,7]. In the extended left lobe LDLT, congestion of the graft is almost free on the recipient side, as a result of a concomitant inclusion of the MHV; however, the remnant right lobe of the donor may have congestion of the right anterior section [8]. Theoretically, regional venous outflow disturbances could disrupt the function of the relevant hepatic parenchyma. In recipients, therefore, a pretransplant estimation of graft volume and congestion volume because of the occlusion of tributaries has been performed for the planning of reconstruction of the MHV [8]. The postoperative liver function and liver regeneration of the recipients in LDLT is affected by multiple factors including not only graft congestion but also graft volume [9], hyperdynamic circulation caused by portal hypertension [9,10], or ischemia-reperfusion injury [11]. However, this concept has not yet been considered in regard to the donors. The purpose of the present study is to analyze the clinical importance of congestion of the remnant right liver of donors in LDLT.

Materials and methods

Patients

Ninety-seven patients underwent LDLT between January 2005 and December 2007. Among them, 52 underwent LDLT using an extended left lobe graft and two-phase computed tomography (CT) was performed in the donors 1 week after LDLT. A total of 52 donors were thus the subjects of this study. All donations were performed after obtaining full informed consent including for exposure to X-rays during the performance of imaging studies from all donors and approval by the Liver Transplantation Committee of Kyushu University Hospital. There were 39 men and 13 women with an age range of 19–62 years (mean age, 33 years). The mean blood loss and operation time were 711 g (range 300–1600) and 438 min (range 326–636), respectively. Preoperative 3D-CT and postoperative two-phase CT [6–9 postoperative day (POD)] were performed for all donors.

Preoperative evaluation of the congestion area

Preoperative multi-detector helical computed tomography (MDCT) images were made using 2-mm-thick slices represented on a CT machine. Enhancement was achieved by an intravenous bolus of contrast non ionic medium (IopamionTM; Schering, Erlangen, Germany and M900QUADRA) at a speed of 5 ml/s. This method allows for clear visualization of the hepatic arteries, portal veins and hepatic veins including the MHV tributaries. Three-dimensional reconstructions of the liver and the graft were rendered by multi-detector helical CT using the 3D-CT software (Region Growing Software; Hitachi Medical Corporation, Chiba, Japan), which was able to calculate the total liver volume and the volume of each vessel's (both portal venous branches and hepatic venous branches) territories from their diameter and length. The 3D image reconstructed by this software could reflect the actual congestion area. The right lobe volume was calculated from the right portal vein territories and the congestion volume of each hepatic venous branch was calculated automatically (Fig. 1a and b). The preoperative estimated ratio of the remnant noncongested volume (noncongested remnant liver volume/total liver volume: NCRLV/TLV) was calculated using the following formula: (Total liver volume − Congested volume − Left lobe volume)/Total liver volume (%).

Postoperative measurement of the congestion volume

Three-dimensional reconstructions of the postoperative remnant right lobe and the congestion area of anterior

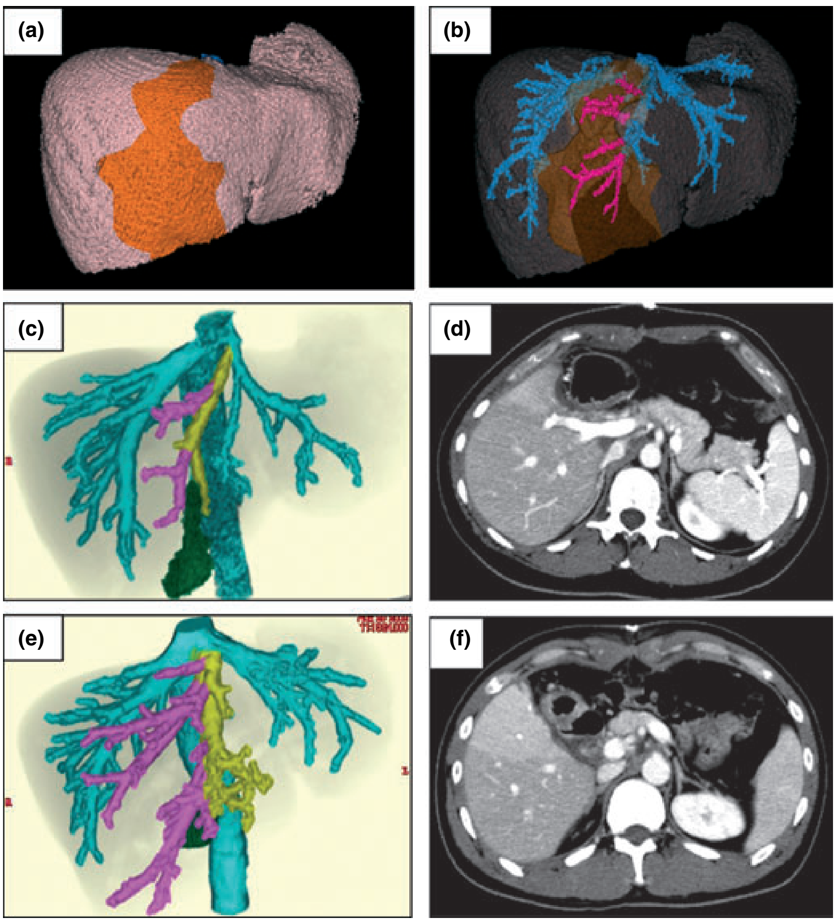

Figure 1 3D-CT image of a liver. The volume of each vessel branch can be automatically calculated using the 3D software preoperatively. (a,b) 3D image shows the perfusion area (orange color) of the tributaries of the MHV (pink color). The preoperative estimated volume of the congestion after a left lobectomy with the MHV can be calculated automatically. (c,d) Preoperative 3D reconstruction of the venous anatomy and actual postoperative congestion of the remnant right lobe in the donor, whose tributaries of MHV were small. The tributaries and main trunk of MHV are purple and yellow, respectively. Hyperattenuation area in the abdominal CT signifies the congestion. (e,f) Preoperative venous anatomy of the liver and actual postoperative congestion of the remnant right lobe in the donor whose tributaries of MHV were large.

sections were rendered by two-phase CT using a 3D-CT software program (M900QUADRA; ZIO Soft Corp, Tokyo, Japan), which was able to fix the cutoff line freely. The CT findings showed the congestion area to have become hyperattenuated because of the poor drainage of radiopaque dye [10]. The remnant right lobe and the congestion volume were calculated by using the difference of attenuation between the congestion area and the non-congestion area (Fig. 1d and f). The Donors were divided into three groups depending on the degree of congestion: mild congestion [mild CR group: proportions of the congestion area in the remnant right lobe (expressed as percentage) were <10%], moderate congestion (moderate CR group: proportions ranged from 10% to 25%) and severe congestion (severe CR group: proportions were over 25%) groups.

Analyzed clinical factors

The aspartate aminotransferase (AST) level, alanine aminotransferase (ALT) level, total bilirubin (T.Bil) level, albumin (Alb) level and international normalized ratio of prothrombin time (INR) at POD 1, 2, 3, 5, 7 and 30 were compared among the three groups. Postoperative complications were classified according to Clavien's classification [12]. Grades 1 and 2 included any deviation from the normal postoperative course without pharmacologic treatment or surgical, endoscopic and radiologic intervention. Grade 3 complications required surgical, endoscopic, or radiologic intervention. Grade 4 included life-threatening complications requiring patient management in the intensive care unit and Grade 5 included the death of a patient. Postoperative complications and hospital stays also were compared among the three groups. Univariate and multivariate analyses were performed to identify the factors associated with the occurrence of persistent liver dysfunction.

Evaluation of the regeneration rate of the right lobe

Preoperative and postoperative 3D volumetries of the right lobe were performed using 3D software (M900QUADRA; ZIO Soft Corp). The regeneration rate (expressed as percentage) was computed as Post/Pre × 100, where Pre is the preoperative estimated volume of the right lobe and Post is the estimated volume at POD 7. The regeneration rate was compared among the three groups.

Selection criteria and surgical technique

The left lobe is initially considered as the graft with respect to donor safety. A right lobe graft was selected when a left lobe graft was insufficient for the recipient and the remnant liver volume of the donor was over 35% [8]. The surgical procedure in donors has been described elsewhere [4,5]. Briefly, a parenchymal transection was performed with or without intermittent inflow occlusion of the Glissonian pedicle in the remnant side of the hepatic lobe. Pringle's maneuver was partly applied in 24 donors (average ischemic time: 21 min, range: 15–33). None of the tributaries of the MHV (V5 and V8) were reconstructed on the donor side.

Statistical analysis

The data are expressed the mean ± standard deviation. The statistical analysis was performed using Student's *t*-test, the Mann–Whitney *U*-test, Pearson's correlation coefficient. SPSS (Version 15.0) (SPSS Japan Inc., Tokyo, Japan) was used for all analyses. $P < 0.05$ was considered to be significant.

Results

Relationship between the estimated preoperative congestion volume and postoperative congestion volume using 3D-CT volumetry

The mean preoperative estimated volumes of the right lobe and congestion area were 821 ± 194 ml (range 457–1400) and 215 ± 71 ml (range 49–432), respectively. The mean postoperative volumes of remnant right lobe and actual congestion area were 986 ± 188 ml (range 619–1451) and 186 ± 99 ml (range 42–393), respectively. The preoperative and postoperative estimated congestion ratio were 26.4 ± 7.1% (range 6.9–44.6) and 19.2 ± 10.3% (range 3.8–39.7), respectively. The relationship between the preoperative and postoperative congestion ratio using 3D-CT volumetry in 49 donors was linear: $y = 19.06 + 0.379x$ ($R^2 = 0.309$, $P < 0.001$) (Fig. 2). In real cases, Fig. 1c–f shows the venous anatomies and postoperative congestions in the two cases with small and large tributaries of MHV, respectively. The donors were divided into three groups depending on the degree of the congestion evaluated by CT on 6–9 POD [mild CR group ($n = 15$), moderate CR group ($n = 21$), severe CR group ($n = 16$)].

Characteristics of the three groups

Table 1 shows the characteristics of the donors, surgical data and preoperative liver function. The clinical status, preoperative liver function and surgical data were not significantly different among the three groups. The preoperative estimated volume of the congestion area in the severe CR group was higher than those in the moderate CR or mild CR groups ($P = 0.001$ and 0.011, respectively).

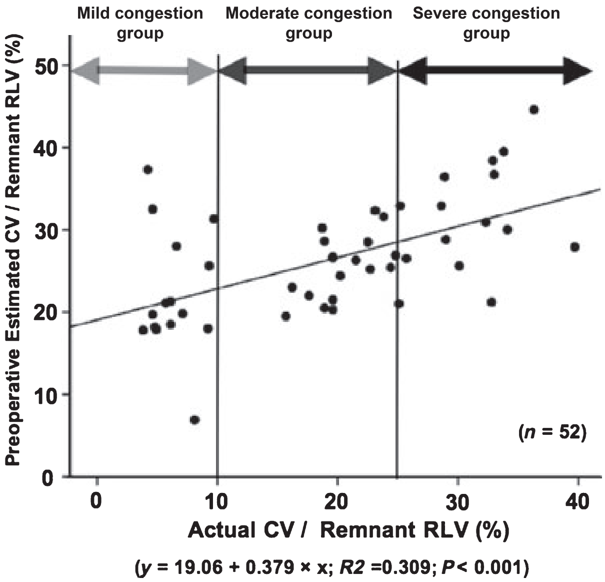

Figure 2 Correlation between the preoperative estimated and postoperative actual congestion ratio of the right liver volume using 3D-CT software: $y = 19.06 + 0.379x$ ($R^2 = 0.309$, $P < 0.001$). Donors ($n = 52$) were divided into three groups depending on the degree of congestion: severe congestion [proportions of the congested area in the remnant right lobe (%) were over 25%, $n = 15$], moderate congestion (proportions were from 10% to 25%, $n = 21$), and mild congestion (proportions were not over 10%, $n = 16$) groups.

Table 1. Comparison of the characteristics and preoperative volumetry of donors according to the degree of congestion.

Variables	Mild CR group ($n = 16$)	Moderate CR group ($n = 21$)	Severe CR group ($n = 15$)	P-value
Donor age (years)	29.8 ± 11.6	34.0 ± 9.3	35.3 ± 12.3	NS
Donor gender (female/male)	4/12	4/21	5/10	NS
Serum AST (U/l)	18.3 ± 3.7	17.1 ± 3.0	17.3 ± 3.1	NS
Serum ALT (U/l)	16.1 ± 3.7	16.8 ± 6.2	19.2 ± 6.0	NS
Serum T.Bil (mg/dl)	0.68 ± 0.20	0.83 ± 0.29	0.63 ± 0.34	NS
Operative time (min)	413 ± 46	427 ± 41	479 ± 76	NS
Intra-operative blood loss (g)	638 ± 200	830 ± 321	648 ± 178	NS
Pringle's maneuver (yes/no)	8/8	11/10	5/10	NS
Estimated RLV (%)	790 ± 105	893 ± 242	772 ± 195	NS
Estimated CV/RLV (%)	22.1 ± 7.3	25.9 ± 3.7	31.6 ± 6.7	0.001
Resected graft volume (g)	411 ± 69	407 ± 43	428 ± 89	NS
Actual CV/remnant RLV (%)	6.8 ± 2.9	20.9 ± 2.4	31.6 ± 6.7	<0.001

CR, congestion ratio; AST, aspartate aminotransferase; ALT, alanine aminotransferase; T.Bil, total bilirubin; RLV, right liver volume; CV, congestion volume; NS, not significant.

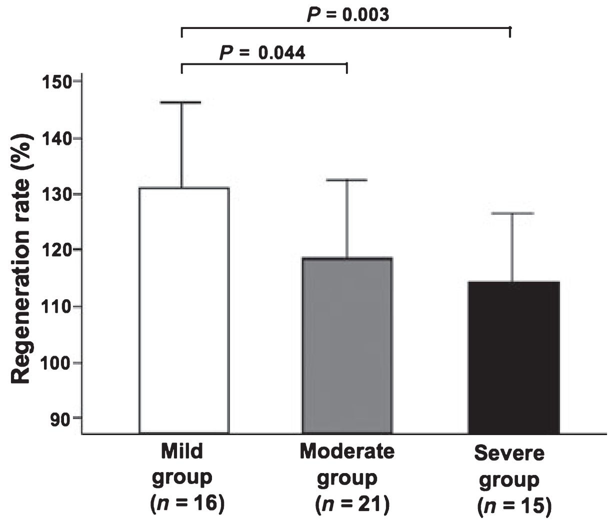

Figure 3 Comparison of the regeneration of the remnant right lobe among the three groups. The regeneration rate was significantly higher in the mild group than that in the moderate or severe groups ($P = 0.044$ and 0.003, respectively).

Regeneration rate of the remnant right lobe

The mean regeneration rate of the postoperative estimated volume of the remnant right lobe in comparison to the preoperative estimated volume of right lobe was 122.0 ± 14.3% (range −2.8–59.9). The regeneration rate was 130.9 ± 14.1% in the mild CR group, 119.5 ± 13.1% in moderate CR group and 115.3 ± 11.5% in severe CR group. The regeneration rate was significantly higher in the mild CR group than in the moderate CR and the severe CR groups ($P = 0.044$ and 0.003, respectively) (Fig. 3).

Comparisons in clinical course

To evaluate the effect of liver congestion on the clinical course, the postoperative liver function, incidence of complications and hospital stays were compared among the three groups (Fig. 4). The AST and ALT levels on 7 POD were significantly higher in the severe CR group than the same in the mild CR group ($P = 0.003$ and 0.019, respectively), however, those on 1, 2, 3, 5 and 30 POD were not significantly different among the three groups (Fig. 4a and b). The T.Bil, Alb and INR were comparable among the three groups. The liver function tests on 30 POD were improved to the normal range in almost all of the donors, even in those with severe congestion. The degree of the congestion volume transiently contributed to the delay in the recovery of the liver function. The incidence of postoperative complications was comparable at any grade of the Clavien's criteria

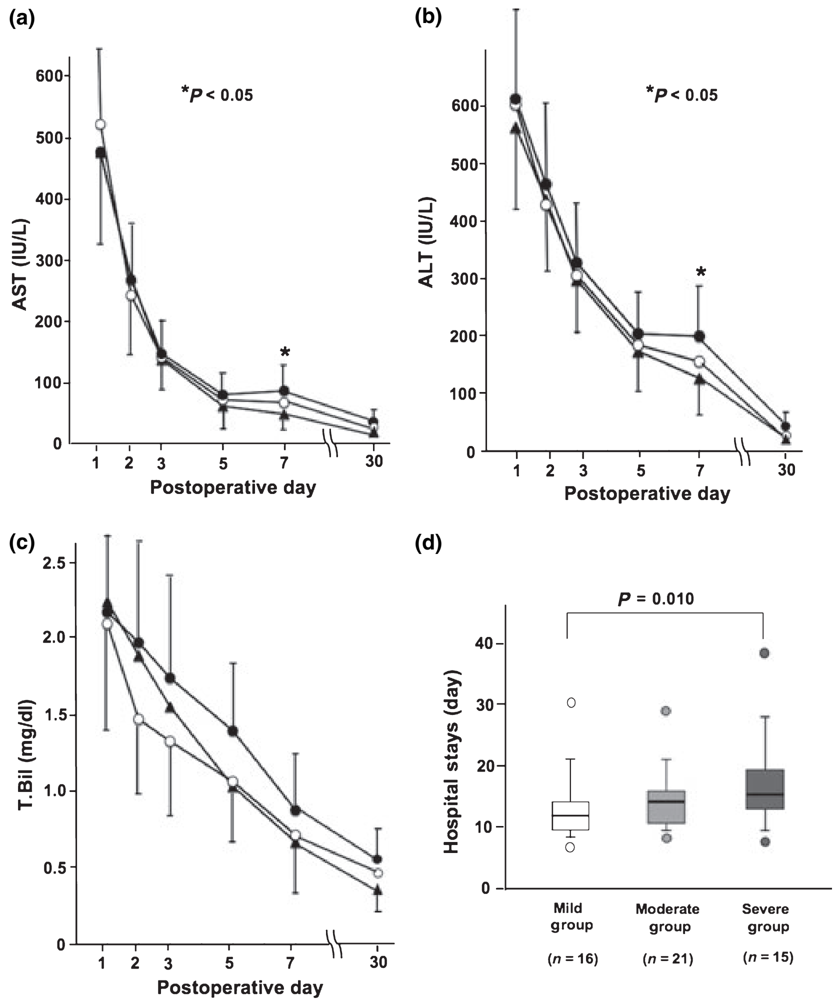

Figure 4 (a,b,c) Serial changes of postoperative aspartate aminotransferase (AST), alanine aminotransferase (ALT), and total bilirubin (T.Bil) in three groups of donors. AST and ALT after 7 postoperative days were significantly high in the severe congestion group. The triangles represent the value in Mild CR group (n = 16). The open and solid circles represent the value in Moderate CR (n = 21) and Severe CR groups (n = 15), respectively. (d) Comparison of hospital days among the three congestion groups. The hospital days were significantly longer in the severe congestion group.

Table 2. Comparison of the overall complications and classified complications by severity.

Variables	Mild CR group (n = 16)	Moderate CR group (n = 21)	Severe CR group (n = 15)	P-value
All complications	43.8	38.1	40.0	NS
Grade 1*	31.3	28.6	20.0	NS
Grade 2	0	0	6.7	NS
Grade 3	12.5	9.5	13.3	NS
Grade 4	0	0	0	NS
Grade 5	0	0	0	NS

Values are given in percentage.
NS, not significant.
*Grades are defined according to Clavien's grade [11].

among the three groups (Table 2). The mean of hospital stays was 11.6 ± 3.0 days (range 8–16) in the mild CR group, 13.1 ± 3.9 days (range 9–24) in the moderate CR group and 17.1 ± 9.4 days (range 9–47) in the severe CR group (Fig. 4d). The hospital stays in the severe CR group were significantly longer than the mild CR group (P = 0.010).

Impact of the preoperative estimated ratio of the remnant noncongested volume on postoperative clinical course

Preoperative estimated NCRLV/TLV ratios were 51.1 ± 8.8% (range 35.1–68.0). The donors were divided into two groups depending on these ratios being >40% (High NCRLV/TLV group, n = 45) and ≤40% (Low NCRLV/TLV group, n = 7). The AST levels on 5 and 7 POD and ALT on 7 POD were significantly higher in the Low NCRLV/TLV group than the High NCRLV/TLV group (P = 0.004 and 0.024, respectively) (Fig. 5a and b). The mean hospital stay in the Low NCRLV/TLV group (mean 18.6 ± 12.9, range 11–47) was longer than that in the High group (mean 12.8 ± 3.9, range 8–25) (P = 0.023).

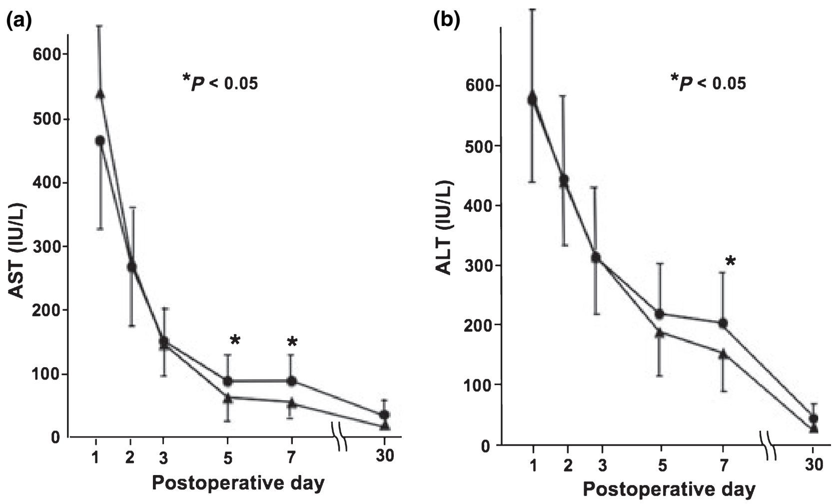

Figure 5 (a,b) Serial changes in the postoperative aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels in the two groups [the open and solid circles represent the value in High NCRLV/TLV (n = 45) and Low NCRLV/TLV groups (n = 7), respectively].

Discussion

One of the crucial prerequisites for performing LDLT is the minimization of morbidity and mortality risk to the healthy living donor [13]. Unfortunately, sporadic donor deaths associated with right liver donations have been reported in several countries [4]. It is reported that operative mortality for the right lobe donor is estimated to be as high as 0.5–1% [14]. To minimize the risk to the donor, left lobe LDLT could be an ideal option in LDLT. We previously reported that left lobe LDLT was a feasible modality to keep the chance of mortality and morbidity of donors minimal [4]. In addition, right lobe graft procurement is one of the independent risk factors for postoperative biliary complications after donor surgery [15,16]. In several cases, the congestion of the remnant right lobe caused by impaired outflow was severe, however, the impact of that congestion on the clinical course has not been elucidated in left lobe donation. The estimated congestion volume sometimes exceeded 50% of the right liver volume [8]. Therefore, the influence of this congestion on the clinical outcome in donors after LDLT cannot be ignored. In this study, the impact of the congestion of the remnant right liver on the clinical outcome was evaluated. The severe congestion of the remnant liver at 7 POD was significantly associated with poor regeneration and transient liver dysfunction. However, liver function tests at 30 POD in this analysis were almost normal, irrespective of the severity of the congestion. In addition, the preoperative estimated NCRLV/TLV ratio after extended left lobe donation was also significant risk factor for postoperative transient liver dysfunction.

In recipients using right liver grafts without the MHV, several reports demonstrated that the regeneration of the congestion area was significantly poor in comparison to that of the noncongestion area, especially during the early postoperative period [17,18]. In donors after a left lobectomy with the MHV, Maema *et al.* [19] reported that the congestion of the remnant right liver was associated with a latent disadvantage in postoperative liver volume regeneration and attenuation differences in the remnant liver were not observed after 3 postoperative months. In this study, the degree of congestion volume was inversely correlated with liver regeneration rate at POD 7. It is possible that the impaired regeneration caused by congestion is attributable to the abnormal hemodynamics of the congestion area [19]. It is possible that the outflow from the congestion area cannot be entirely compensated by the function of the pre-existing collaterals and the portal branches substitute as venous pathways by regurgitation [19]. Several reports have demonstrated that the collateral between the ligated tributaries of the MHV and the right hepatic vein is formed over several days [20,21]. The impaired liver regeneration is probably caused by these issues of hemodynamics; however, there has been no scientific basis for the explanation of this influence. In humans and experimental animal models, hepatocyte growth factor (HGF) [22,23], serotonin [24] and interleukin-6 (IL-6) [25] are cytokines, which play a critical role in liver regeneration after liver damage and ischemia. In future research, the influence of liver congestion on the cytokines associated with regeneration such as HGF, serotonin and IL-6 should be analyzed in animal models.

Several reports indicated that liver dysfunction is influenced by the imbalance between inflow and outflow of the liver [26,27]. Troisi *et al.* [28] reported the portal inflow to significantly increase because of hyperdynamic circulation in comparison to the normal liver. In the setting of the recipients, there is a possibility that not only an impaired outflow because of the congestion of right lobe graft but also an increased inflow leads to the relative small-for-size syndrome in spite of a sufficient graft volume. In recipients using a right lobe graft, the failure to effectively reestablish this communication might result in liver dysfunction and eventual graft failure [29]. Therefore, the concept of the reconstruction of tributaries (V5 and V8) of the MHV to avoid the congestion is an accepted modality [30–34]. Indeed, various interposition grafts including explanted portal vein, cryopreserved vein, saphenous vein, or jugular vein are used for reconstruction in recipients [30–34].

However, there are some problems if the reconstructions of MHV in donors are performed. In regard to donors, the reconstruction of the MHV is performed not on the back table but in situ in comparison to recipients, therefore, the surgical procedure of the reconstruction of the donor's MHV is difficult. In addition, the creation of a new wound to procure the interposition graft is necessary [34]. The use of synthetic vessel can sometimes lead the occurrence of a life-threatening infection [35]. As the imbalance between inflow and outflow can be mild in donors as compared with recipients [28], the influence of the congestion on liver function is thought to be mild in comparison to the recipients. Consequently, considering the balance between the damage caused by the harvest of the interposition graft and the transient influence, the reconstruction of the MHV is therefore considered to be unnecessary for most donors. However, the preoperative estimation of the remnant noncongested area was significantly associated with the postoperative clinical course (Fig. 5) and the clinical influence of actual postoperative congestion was also significant (Fig. 4) according to the findings of this analysis. Therefore, the conversion of the graft from the left to right lobe or the reconstruction of the MHV might lead to a better postoperative clinical course in LVLT situations involving severe congestion.

Authorship

TF: wrote the paper and performed the research. KU: designed the research. TT, KT and KM: collected and analyzed data. SN, KS and TG: performed operation. TI, AT and YM: performed operation and advised to our research. YS: designed the research mainly.

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