

**ORIGINAL****Regeneration of caudate lobe after living donor liver transplantation : Comparison with a surrogate model of left lobe graft**

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**Abstract : Background :** The aim of this study is to clarify the regeneration of the CL (caudate lobe) without any reconstructions of short hepatic veins (SHVr) after LDLT (living donor liver transplantation) and compare the regeneration of the CL after right hepatectomy (Rt. Hx), as the surrogate model of extended left lobe graft (Ex LLG) with complete SHVr. **Methods :** Eleven Ex LLGs with CL were included in this study. SHVr was not performed in all cases. The volumetry was performed before, one month and six months after LDLT. Seven patients who underwent Rt. Hx were also included in this study as the surrogate model. **Results :** In Ex LLGs with CL, the regeneration rate of the large CL (> 30 ml) was worse than that of small CL (< 30 ml). In the surrogate model, the regeneration rate of the CL was not worse than other segments. However, the regeneration rate of the large CL was also worse than that of small CL even in the presence of complete SHVr. **Conclusions :** The regeneration of the large CL was worse than that of the small CL regardless of the presence or absence of SHVr, indicating that SHVr in Ex LLG with CL might not be necessary. *J. Med. Invest.* 68:330-333, August, 2021

**Keywords :** caudate lobe, short hepatic vein, living donor liver transplantation

**INTRODUCTION**

First of all, the size of an extended left lobe graft (Ex LLG) more than doubles one month after transplantation (1), and functions as a graft for a recipient for life. However, Ex LLG has more frequent risk of small-for-size-graft (SFSG) than right lobe graft. SFSG sometimes causes graft failure after living donor liver transplantation (LDLT). However, RLG imposes a greater surgical risk on living donors. As a method of increasing the graft volume in the case of SFSG in LDLT, the Shinshu group already reported caudate lobe (CL) transplantation with an extended left lobe graft (Ex LLG) was an innovative and promising method for increasing the graft volume in LDLT (2). We have also already reported a new technique for left lobe graft harvesting proved a promising approach to gain additional volume (2). However, little is known about the fate of the CL after transplantation. As a preliminary report regarding the changes in the CL after transplantation, we already reported that regeneration rate of CL was worse than that of left lobe (LL) at one month after LDLT without any reconstructions of short hepatic veins (SHVr), which are drainage veins of CL that flow directly into inferior vena cava, however, the CL volume increased in almost all patients (1). On the other hand, it was also reported that CL could regenerate proportionally with the LL by complete SHVr (4). It means that the necessity of SHVr in Ex LLG with CL is still controversial.

As our new idea in the present study, we focused on patients after right liver resection (Rt. Hx) for liver tumors. Since CLs of those patients were remnant with SHVs as drainage veins, the patient with Rt. Hx could be used as the surrogate model of Ex LLG with complete SHVr.

Accordingly, we herein clarify the regeneration of CL in case of Ex LLG without SHVr after LDLT and compare the regeneration of CL after Rt. Hx, as the surrogate model of Ex LLG with complete SHVr.

**METHODS***Ethical permission*

This study was approved by The Tokushima University Hospital Ethics Committee and the corresponding regulatory agencies (Tokushima Clinical Trial Management, Approved No 3215) and all the experiments were carried out in accordance with the approved guidelines. Meanwhile, all the patients involved in the study signed the informed consent form and agreed to participate.

*Patients*

LDLT ; From February, 2005, to March, 2015, eleven Ex LLG with CL were included in this study. All LDLT operations were performed at Tokushima University Hospital. In all cases, SHVr did not be performed. Detailed operative techniques in LDLT were described in previous report (2).

Rt. Hx ; From December, 2005, to April, 2015, seven patients with initial Rt. Hx were included in this study (five patients with liver metastasis of colorectal cancer with no chemotherapy and two patients with liver abscess or hemangioma). These patients were used for the surrogate model of Ex LLG with complete SHVr.

**Abbreviations :**

small-for-size grafts ; SFSG, living donor liver transplantation ; LDLT, caudate lobe ; CL, extended left lobe graft ; Ex LLG, left lobe ; LL, reconstructions of short hepatic vein ; SHVr, multi-detector computed tomography ; MDCT, standard liver volume ; SLV, graft volume ; GV, liver volume ; LV

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*CT volumetry*

3D-reconstruction of the hepatic vasculature was made using data from a contrast enhanced multi-detector computed tomography (MDCT) and SYNAPSE VINCENT software (Fuji Film Medical Co. Ltd., Tokyo, Japan). The volumetry of each segment was performed by “portal segmentation function” of SYNAPSE VINCENT. The volumetry in LDLT was performed before LDLT from the donors and 1 month and 6 months after LDLT (Figure 1). In the surrogate model, the volumetry was performed as well before operation and 1 month and 6 months after operations.

*Standard liver volume (SLV), graft volume (GV), and GV/SLV estimation*

SLV was calculated according to the formula described by Urata *et al.* (5). All GV in this study was calculated by volumetry using portal segmentation function.

*Regeneration rate*

The regeneration rate was calculated as described below ; (Postoperative liver volume (LV) – Preoperative liver volume) / Preoperative liver volume × 100 (%)

*Statistical Analysis*

All results were presented as mean ± SD. Comparisons between the two groups were performed using a Chi-square test using statistical software (JMP 8.0.1., SAS Campus Drive, Cary, 27513 NC, USA). A *p*-value of less than 0.05 was considered statistically significant.

**RESULTS**

*Increasing the graft volume with CL*

The LL graft volume was 456 ± 117 ml at pre LDLT, 1,023 ± 213 ml at one month post LDLT and 1,175 ± 275 ml at six months post LDLT, corresponding to a 40%, 89% and 105% increase respectively in GV/SLV (Table 1).

The addition of the CL increased the graft volume by 30 ± 11 ml at one month post LDLT and 28 ± 13 ml at six months post LDLT, corresponding to a 2.6% and 2.5% increase respectively in GV/SLV (Table 1).

*The regeneration rate of CL in LDLT without SHVr*

The regeneration rate of CL was 18 ± 42% at one month post LDLT and 0 ± 42% at six months post LDLT (Figure 2). 3 cases showed 5% or more of volume decrease after LDLT, and their preoperative volume were all over 30 ml in volume (data were not shown). Regeneration rate of the small CL (volume ≤ 30 ml) was 39 ± 42% at one month post LDLT and 35 ± 42% at six months

Table 1. The regeneration of CL and LL

	Caudate lobe			Left lobe		
	Pre	1m	6m	Pre	1m	6m
GV (ml)	28	30	28	456	1023	1175
GV/SLV (%)	2.5	2.6	2.5	40	89	105

GV, graft volume ; SLV, standard liver volume ; m, month(s).

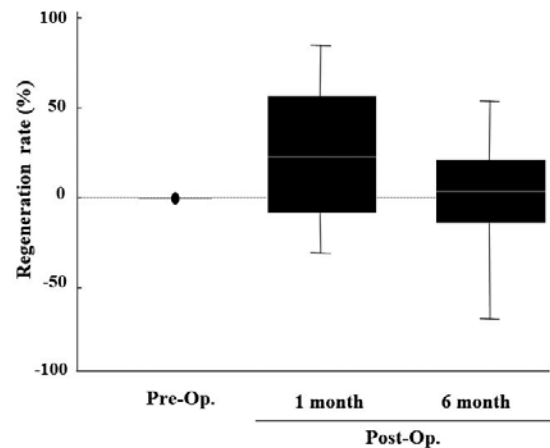


Figure 2. Regeneration rate of CL in LDLT without SHVr. The regeneration rate of CL was 18 ± 42% at one month post LDLT and 0 ± 42% at six months post LDLT.

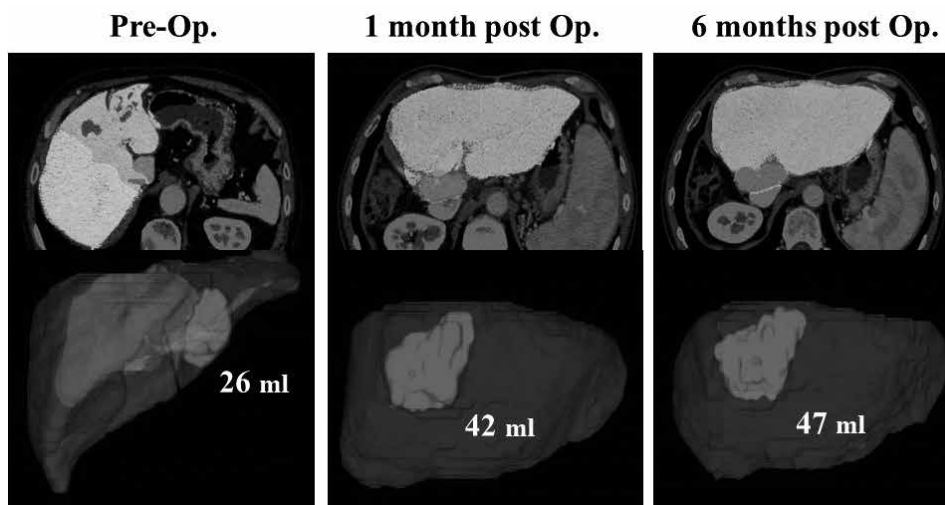


Figure 1. Volumetry of CL. The volumetry of CL was performed by “portal segmentation function” of SYNAPSE VINCENT before LDLT from the donors and 1 month and 6 months after LDLT.

post LDLT. On the other hand, regeneration rate of the large CL (volume > 30 ml) was  $-27 \pm 18\%$  at one month post LDLT and  $-54 \pm 36\%$  at six months post LDLT (Figure 3). It was suggested that the large CL had worse regeneration than the small CL in Ex LLG without SHVr.

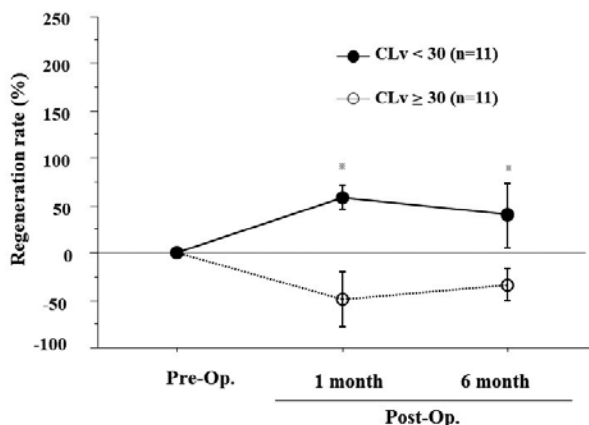


Figure 3. Comparison of the regeneration between small and large CL in LDLT without SHVr

Regeneration rate of the small CL (volume ≤ 30 ml) was  $39 \pm 42\%$  at one month post LDLT and  $35 \pm 42\%$  at six months post LDLT. On the other hand, regeneration rate of the large CL (volume > 30 ml) was  $-27 \pm 18\%$  at one month post LDLT and  $-54 \pm 36\%$  at six months post LDLT.

#### The regeneration rate of CL in in the surrogate model with complete SHVr

The regeneration rate of CL was  $49 \pm 62\%$  at one month post operation and  $113 \pm 93\%$  at six months post operation (Figure 4). Regeneration rate of the small CL (volume ≤ 30 ml) was  $56 \pm 69\%$  at one month post operation and  $164 \pm 63\%$  at six months post operation. On the other hand, regeneration rate of the large CL (volume > 30 ml) was  $17 \pm 3\%$  at one month post operation and  $12 \pm 8\%$  at six months post operation (Figure 5). It was suggested that the large CL had also worse regeneration than the small CL in the surrogate model with complete SHVr.

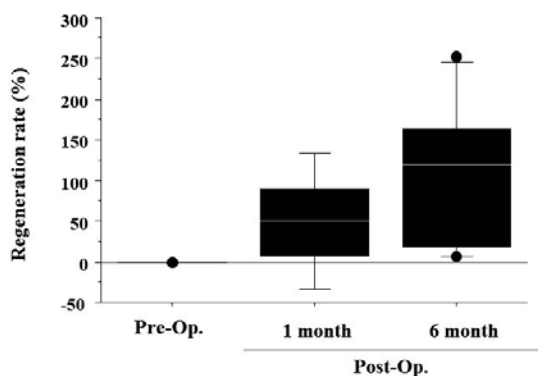


Figure 4. Regeneration rate of CL in the surrogate model with SHVr. The regeneration rate of CL was  $49 \pm 62\%$  at one month post operation and  $113 \pm 93\%$  at six months post operation.

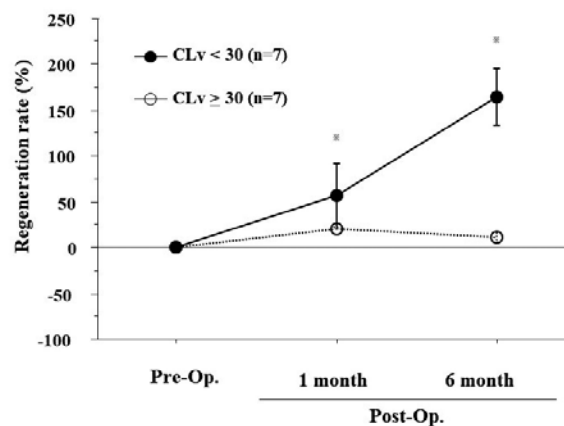


Figure 5. Comparison of the regeneration between small and large CL in the surrogate model with SHVr

Regeneration rate of the small CL (volume ≤ 30 ml) was  $56 \pm 69\%$  at one month post operation and  $164 \pm 63\%$  at six months post operation. On the other hand, regeneration rate of the large CL (volume > 30 ml) was  $17 \pm 3\%$  at one month post operation and  $12 \pm 8\%$  at six months post operation.

## DISCUSSION

The necessity of SHVr in Ex LLG with CL is still controversial. In the present study, we clarified that the regeneration of CL in case of Ex LLG without SHVr after LDLT and compare the regeneration of CL after Rt. Hx, as the surrogate model of Ex LLG with complete SHVr. It was the first report using the surrogate model of Ex LLG with complete SHVr.

Various CL venous reconstruction techniques were described as one of the feasible solutions to overcome SFSG (6-11). Although the CL volume is small, it is important when the graft volume is critical. We have already showed that the regeneration rate of the transplanted CL and other left lobe graft segments. The regeneration rate of the CL one month after transplantation was smaller ( $62 \pm 24\%$ ) than that of other left lobe graft segments ( $152 \pm 35\%$ ) (3). It was already reported that with reconstruction of the inflow (6) or outflow (7), the regeneration rate of the CL was noted to be equal to or more than that of the other left lobe graft segments. The additional functional volume afforded by CL venous reconstruction might provide an additional safety margin.

On the other hand, Mikami K *et al.* (12) reported that the GV/SLV ratio of the whole grafts after LDLT showed no difference regardless of the presence or absence of SHVr. In the present study, in the surrogate model of Ex LLG with complete SHVr, regeneration rate of the CL was not worse than other segments. However, regeneration rate of large CL (volume > 30 ml) had worse than that of the small CL (volume < 30 ml) as well as LDLT without SHVr cases. It was suggested that the size of CL seemed to be important for regeneration as a new finding.

As limitations of this study, the present study was a retrospective cohort from a single institution. Although it was necessary to add more patients in the present study, the chance of operation of open Rt. Hx with normal liver function have recently decreased. A prospective randomized trial with more patient number will be necessary in the future.

In conclusion, Ex LLG with CL was a useful method for increasing the graft volume. The regeneration of the large CL was worse than that of the small CL regardless of the presence or absence of SHVr. It was suggested that SHVr in Ex LLG with

CL might be not necessary and the graft size might be important for CL regeneration.

#### COI DISCLOSURE

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