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# Experience of Living Donor Liver Transplantation at Fukuoka University Hospital
## —Review of Referred Cases in Last Two Years—

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**Abstract：** Introduction：In the last 2 years, living donor liver transplantation (LDLT) has been performed at Fukuoka University Hospital, however, only one quarter of the referred patients actually undergo LDLT. We herein review our experience and find out the problems in the patients that were not indicated to undergo LDLT. Subjects and Methods：The medical records of all patients that were referred to the Department of Gastroenterological Surgery (formerly the 2nd Department of Surgery), Fukuoka University Hospital to be considered for liver transplantation from December 2004 to November 2006 were analyzed. Results：Fourteen patients were referred for consideration to undergo liver transplantation. They included nine with hepatitis C related liver cirrhosis, three with fulminant hepatitis, one with non-B non-C liver cirrhosis, and one with hepatitis B virus (HBV) related acute hepatitis. Of the 9 hepatitis C related liver cirrhosis patients, 7 had hepatocellular carcinoma (HCC). Of these, 3 patients (21.4%) had undergone LDLT. The model for end-stage liver disease (MELD) score of LDLT group tended to be lower than that of no-LDLT group, although those parameters did not show any statistical difference. The contraindication for these patients was advanced HCC beyond the Milan criteria, refusal of LDLT by the patient and multi-system organ failure (MOF). The contraindication for the donor was a graft size mismatch and ABO incompatibility. Discussion：The general condition of the patient, status of liver tumor and necessary and sufficient condition of live donor should thus be take account when determining the indications for LDLT. Conclusion：Efforts to educate general practitioners who take care of the patients suffering from end-stage liver disease are thus called for to increase the referral of appropriate patients for LDLT.

**Key words：Living Donor Liver Transplantation (LDLT)**

## Introduction

Since the first living donor liver transplantation (LDLT) in Japan was performed in 1989, LDLT has been commonly applied to treat end-stage liver disease. To the end of 2004, 3218 LDLT has been performed all over the country.[1)] It has been almost two years since our first LDLT was successfully performed at Fukuoka University Hospital on May 14, 2005.[2)] During that period, we have had 14 patients who were referred to undergo liver transplantation (LTx). However, among these 14 patients, only 3 actually underwent LDLT. The remaining 11 patients were initially considered to be indicated for LTx, but finally found not to be indicated for LDLT after preoperative evaluations. In this article, we review our experience over the last

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2 years including all the referred patients for LDLT, and find out the problems in the patients who were determined to not be indicated for LDLT.

## Subjects and Methods

All patients who were referred to the Department of Gastroenterological Surgery (formerly the 2nd Department of Surgery), Fukuoka University Hospital for consideration to undergo liver transplantation from December 2004 to November 2006 were enrolled. The medical records of those patients were all reviewed retrospectively, and the patient's characteristics, liver function parameters, Child–Pugh score, the model for end–stage liver disease (MELD) score, indications and clinical course of each patient were analyzed.[3] The expected graft volume was calculated by three dimensional image of multi–detector computed tomography (MD－CT). Graft–size matching was judged based on the standard liver volume (SLV) given by the body surface area of the patient.[4] The difference between the patients who underwent LDLT (LDLT group) and those who did not undergo LDLT (no－LDLT group) was compared. The difference in the liver function parameters of each group was tested by Mann–Whitney's U–test.

## Results

Fourteen patients were referred to our department for consideration to undergo liver transplantation. Five patients were referred by hepatologists in Fukuoka University Hospital, and 9 patients were referred from outside. Of those 14 patients, 9 were males and 4 were females. The age of patients ranged from 30 to 66 years old, and the median age was 55.5 years old. The diagnosis of the patients were, nine with hepatitis C related liver cirrhosis, three with fulminant hepatitis, one with non–B non–C liver cirrhosis, and one with HBV related acute hepatitis. Of the 9 with hepatitis C related liver cirrhosis, 7 had hepatocellular carcinoma (HCC). Overall, the Child–Pugh score was 8.8±2.1, and MELD score was 13.9±7.2. The characteristic of each patient is shown in Table 1.

Among the 14 patients, only 3 patients (21.4%) had undergone LDLT, and all of those 3 patients are still surviving. The remaining 11 patients did not undergo LDLT.

A comparison of the parameters of the patients between LDLT group and non–LDLT group excluding the patients who refused LDLT or had any problems with their donor is summarized in Table 2. The MELD score of the LDLT group tended to be lower than that of the non–LDLT group, although those parameters did not show any statistical difference.

The indications and contraindications of each patient were summarized in Table 3. The reason for being referred to undergo LDLT was 3 chronic hepatic failures, 7 chronic hepatic failures with repeat recurrence of HCC, and 4 cases of fulminant hepatitis. In 11 patients that did not undergo LDLT (non－LDLT group), 5 had problems regarding the patient and the other 6 patients had problems regarding the donor. The contraindications for the patients included advanced HCC beyond the Milan criteria,[5] refusal of LDLT by the patient and multi–system organ failure(MOF). The graft size mismatch was considered in 4 donors. In 2 of 4 donors, the graft volume was less than 40% of recipient's SLV even though their right liver had been scheduled to be harvested. In the remaining 2 donors, their expected remnant liver volume were less than 30% of their original liver volume which may cause postoperative liver failure in the donor. ABO incompatibility in 4 donors led to the patients not being indicated for LDLT.

## Discussion

Three LDLT have been performed at Fukuoka University Hospital during the last 2 years. Two of these 3 patients have been followed up by our hepatologists and the other one patient has been followed up by a physician of another hospital. Most of the patients that did not undergo LDLT were referred from outside of our hospital.

All referred patients thought to be indicated for LDLT based on their liver function findings when they first came to our hospital. However, over three quarters of the patients were finally determined to not be indicated for LDLT. This discrepancy was thought to arise from problems regarding both the patient and the donor.

**Table 1.** Characteristics of the patients

| Case # | Age | Sex | Diagnosis | T.B. (mg/dl) | Alb. (g/dl) | INR | Cr. (mg/dl) | Ascites | Encephalopathy | Child-Pugh score | Child Class | MELD score |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **1** | **60** | **M** | **Hepatitis C, Liver cirrhosis, Hepatocellular carcinoma (HCC)** | **0.5** | **2.9** | **1.15** | **1** | **No** | **Controlled medically** | **7** | **B** | **5** |
| 2 | 57 | M | Hepatitis C, Liver cirrhosis, Hepatocellular carcinoma (HCC) | 3.4 | 3.7 | 1.46 | 0.5 | No | No Encephalopathy | 7 | B | 9 |
| 3 | 66 | F | Liver cirrhosis (non B non C) | 5.9 | 2.7 | 1.86 | 1.2 | Controlled medically | No | 11 | C | 22 |
| 4 | 58 | F | Hepatitis C, Liver cirrhosis, Hepatocellular carcinoma (HCC) | 1.9 | 2.7 | 1.12 | 0.9 | No | No | 7 | B | 9 |
| 5 | 52 | M | Hepatitis C, Liver cirrhosis, Hepatocellular carcinoma (HCC) | 2 | 2.8 | 1.48 | 0.73 | No | No | 7 | B | 10 |
| 6 | 50 | M | Acute hepatic failure due to rapid proreferation of HBV during lamibudine therapy | 19.67 | 3.1 | 2.83 | 1.13 | Controlled medically | No | 11 | C | 31 |
| **7** | **30** | **F** | **Fluminant hepatitis** | **9.6** | **3.2** | **1.42** | **0.3** | **Controlled medically** | **Poorly controlled** | **10** | **C** | **7** |
| 8 | 43 | M | Fluminant hepatitis | 10.7 | 2.6 | 1.54 | 0.8 | Controlled medically | Controlled medically | 11 | C | 18 |
| 9 | 62 | F | Hepatitis C, Liver cirrhosis, Hepatocellular carcinoma (HCC) | 5.9 | 3 | 1.4 | 0.63 | Controlled medically | No | 9 | B | 12 |
| 10 | 54 | M | Hepatitis C, Liver cirrhosis, Hepatocellular carcinoma (HCC) | 3 | 3.1 | 0 | 0.69 | No | No | 7 | B | 11 |
| **11** | **59** | **M** | **Hepatitis C, Liver cirrhosis, Hepatocellular carcinoma (HCC)** | **1.5** | **2.5** | **1.36** | **0.9** | **No** | **No** | **7** | **B** | **10** |
| 12 | 30 | M | Fuluminant hepatic failure due to heatstroke | 0.76 | 5.4 | 0.98 | 1.75 | No | Controlled medically | 6 | A | 11 |
| 13 | 44 | M | Hepatitis C, Liver cirrhosis | 4.3 | 2.4 | 1.5 | 1.2 | Poorly controlled | No | 11 | C | 18 |
| 14 | 62 | F | Hepatitis C, Liver cirrhosis | 12.5 | 2.7 | 1.91 | 0.9 | Controlled medically | Controlled medically | 12 | C | 22 |

**Table 2.** Comparison of the parameters between the LDLT group and the non-LDLT group excluding the patients who refused LDLT or had any problems regarding the donor

| | LDLT group (n=3) | no LDLT group (n=3) | |
|---|---|---|---|
| Age | 49.7±17.0 | 49.7±17.2 | p>0.99 |
| Total Bilirubin (mg/dl) | 3.9±5.0 | 3.4±2.6 | p=0.83 |
| Albumin (g/dl) | 2.9±0.35 | 4.0±1.23 | p=0.13 |
| INR | 1.31±0.14 | 1.28±0.26 | p=0.83 |
| Creatinine (mg/dl) | 0.73±0.38 | 0.96±0.69 | p=0.83 |
| Child-Pugh score | 8.0±1.7 | 7.3±1.5 | p=0.51 |
| MELD score | 7.3±2.5 | 10.7±1.5 | p=0.13 |

In adult to adult liver transplantation, hepatitis C related liver cirrhosis is a major etiology. Therefore, the status of HCC must be concerned. Mazzaferro et al. addressed that liver transplant patients who had early HCC, defined as a single tumor measuring less than 5 cm in diameter or two to three tumors all less than 3 cm in diameter, showed a similar survival to those without HCC (so-called Milan criteria).[5] Based on these data, Japanese public health insurance system partly supports the cost of LDLT to the patients who have liver cirrhosis with HCC within the Milan criteria. In our series, 2 patients were determined to be contraindicated for LDLT because of advanced HCC be-

**Table 3.** Indications and Contraindications for each case

| Case # | Reason of reference (Indication of LTx) | LDLT done or not | Contraindicatin of LTx. in patient | Contraindication of LDLT in donor |
|---|---|---|---|---|
| **1** | **Chronic hepatic failure, Repeat recurrence of HCC** | **LDLT** | **none** | **none** |
| 2 | Chronic hepatic failure, Repeat recurrence of HCC | No LDLT | Mutiple HCC beyond Milan Criteria | none |
| 3 | Chronic hepatic failure | No LDLT | none | Graft size mismatch |
| 4 | Chronic hepatic failure, Repeat recurrence of HCC | No LDLT | Refusal of LDLT | none |
| 5 | Chronic hepatic failure, Repeat recurrence of HCC | No LDLT | none | 1st candidate for donor : ABO incompatible<br>2nd candidate for donor : Graft size mismatch |
| 6 | Fluminant hepatic failure | No LDLT | Refusal of LDLT | none |
| **7** | **Fluminant hepatic failure** | **LDLT** | **none** | **none** |
| 8 | Fluminant hepatic failure | No LDLT | none | Grasft size mismatch |
| 9 | Chronic hepatic failure, Repeat recurrence of HCC | No LDLT | Portal vein involvement of HCC | none |
| 10 | Chronic hepatic failure, Repeat recurrence of HCC | No LDLT | none | ABO incompatible |
| **11** | **Chronic hepatic failure, Repeat recurrence of HCC** | **LDLT** | **none** | **none** |
| 12 | Fluminant hepatic failure | No LDLT | Multisystem organ failure (MOF) | none |
| 13 | Chronic hepatic failure | No LDLT | none | ABO incompatible |
| 14 | Chronic hepatic failure | No LDLT | none | 1st candidate for donor : Alcoholic hepatitis<br>2nd candidate for donor : Graft size mismatch |

yond Milan criteria, although they were initially thought to be indicated for LTx.

Graft size mismatch is a major problem for live liver donation in adult to adult LDLT. When the graft volume is too small for satisfy the recipient's metabolic demand, the recipient may thus experience small-for-size liver syndrome such as variceal bleeding, persistent ascites and jaundice. To avoid small-for-size liver syndrome, the volume of partial liver graft should be over 40% of recipient's standard liver volume.[6] The greater volume of live liver graft procurement imposes a greater risk on donor because the remnant liver in the donor would thus become smaller. From the point of donor safety, the remnant liver volume should be at least 30% of the original liver volume in the donor.[7]

ABO incompatibility is another issue in LTx. Currently we do not indicate LDLT from ABO incompatible donors. The Vancouver Forum on the Care of the Live Organ Donor held on September 15 and 16, 2005 recommends a compatible ABO blood type live donor transplant.[7] Although new immunosuppressive protocols have been established,[8][9] the outcome of ABO incompatible LTx is still not good in adult to adult LDLT. The 1, 3 and 5 year survival after ABO incompatible LDLT has been reported to be 69.1%, 66.4% and 64.1%, respectively in Japan.[1]

The MELD score of our LDLT group tended to be lower than that of the non-LDLT group. That means the patients who undergo LDLT had better risk than that of the non-LDLT group. In other words, these patients were referred to our hospital for LDLT before the patient's general condition had fallen into a severe state. The 3-month mortality rate of hospitalized cirrhotic patients whose MELD score greater than 20 was higher than that of the patients whose MELD score less than 19.[3] Moreover, the postoperative survival of LDLT recipients whose preoperative MELD score was greater than 25 was worse than that of those below 25.[10] The ideal timing of decision-making of LTx for chronic hepatic failure or HCC thus still remains controversial.

In conclusion, all patients suffering from end-stage liver disease of any etiology may potentially be candidates for LTx. However, the general condition of the patient, status of liver tumor and necessary and a sufficient condition of the live donor all have to be considered before determining a

positive indication for LDLT. Hepatologists and transplant surgeons therefore have to improve the education of general practitioners who take care of the patient suffering from end-stage liver disease in regard to the appropriate indications for LDLT.

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