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Research Article

# A Single-Center Experience with Liver Transplantation from Donation after Cardiac Death

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**Abbreviations** DCD: Donation after Cardiac Death; LT: Liver Transplantation; RLT: Remedial Liver Transplantation

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## Abstract

**Background and Objective:** Liver transplantation (LT) is an effective treatment method for terminal liver disease but is limited by a lack of donors. Donation after cardiac death (DCD) would effectively alleviate this shortage. Here we summarize our experience with LT using DCD in our hospital.

**Methods:** We retrospectively analyzed the mortality and adverse reactions of 13 patients who underwent LT for terminal liver disease and their donors in our hospital between November 2011 and August 2013.

**Results:** The surgeries were successful in all 13 cases. The 1-, 2-, and 3-year survival rates were 92%, 85%, and 72%, respectively.

**Conclusions:** LT from DCD for patients with terminal liver disease will be an effective treatment method.

## Introduction

Since the first Liver Transplantation (LT) was performed by Starzl in the United States in 1963, allogeneic and orthotropic LT has been extensively performed as the only effective method to treat terminal liver disease. LT was first performed in China in 1977 and has since undergone considerable developments with technological advances and living standard improvements. Patients with terminal liver cirrhosis encounter many complications. Conservative treatment targets symptoms only, and LT is the only effective treatment method for terminal liver cirrhosis. Approximately 150 million patients are newly diagnosed with liver cancer annually, nearly 50% (600,000–700,000 cases) of which occurs in mainland China [1]. Primary liver cancer has the second highest mortality rate of all cancers in globally men [2]. Of the cases of primary liver cancer in China, >90% are associated with hepatitis B virus (HBV)-related cirrhosis or infection. LT involving total resection of the lesion is the most effective and feasible treatment method for primary liver cancer, especially in cases associated with liver cirrhosis and portal hypertension [2,3].

Due to the serious donor shortage, <10% of patients with liver failure worldwide have the opportunity to undergo LT [4]. More than 300,000 patients urgently need LT in China each year, but only a few thousand patients are able to undergo it. In the 1960s, donor livers were primarily obtained by Donation after Cardiac Death (DCD). With the great advances of DCD in research and applied technology in the late 20$^{th}$ century, the popularity of DCD increased once again [5,6]. The World Health Organization called on member states to formulate corresponding policies for DCD and promoted its application [5]. With the deepening of cognition of donors with controlled classification type (Maastricht type III or IV), LT outcomes from controlled DCD donors is gradually improving. The effect of LT from DCD had efficacy close to or even equivalent with LT from donation after brain death in some transplant centers [7-12]. Here we aim to summarize our experience with LT from DCD in our hospital.

## Patients and Methods

### Patients

In this retrospective study, 13 male patients (mean age, 48.2 years; range, 34–62 years) who underwent LT for the treatment of terminal liver disease at the Affiliated Hospital of Guilin Medical University from September 2011 to August 2013. Eight of these patients suffered from terminal cirrhosis, of which seven had HBV-related cirrhosis and one had alcoholic cirrhosis; the liver

function of each patient was Child-Pugh C. One patient with hepatitis C virus–related cirrhosis suffered from primary liver cancer with multiple tumors < 3 cm in diameter. Four patients suffered from liver cancer recurrence combined with HBV-related cirrhosis with a single recurrent tumor < 5 cm in diameter. There were 13 donors (10 males and 3 females; mean age, 37.2 years; range, 17–55 years), including 10 with traumatic brain injury and three with cerebral vascular accident hospitalized at the Affiliated Hospital of Guilin Medical University. Families of all donors had been consented their donation. All the donors were Maastricht type IV classification.

### Terminal liver disease

Terminal liver disease is defined as a variety of causes of progressive irreversible liver damage, cannot be cured using conventional means, features severe symptoms, and cannot avoid death expected in the short term (6–12 months). It includes cirrhosis of the liver, liver cancer, and fulminate hepatic failure.

### Ethics

This study received approval from the local ethics committee of the Affiliated Hospital of Guilin Medical University. The organ donation volunteer book of the local Red Cross was signed by each donor's family members. Written informed consent was provided by all recipients within the hospital. The donor donation program is shown in figure 1. The messenger, coordinator, related experts, Red Cross workers, organ harvesting doctor, and organ implanting doctor all belonged to the organ transplant organization managed by the Red Cross. None of the transplant donors were from a vulnerable population and all donors or next of kin provided written informed consent that was freely given.

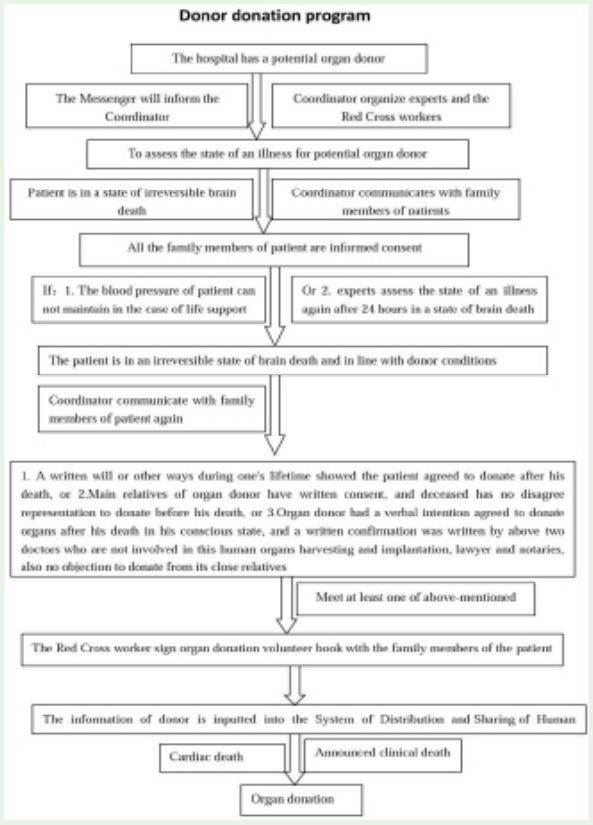


**Figure 1:** Donor donation program.

### Surgical procedure and preoperative management

All 13 patients underwent classical orthotropic LT. Above their confirmed candidacy for LT, patients were placed on a list that was sent to the China Center for Organ Transplantation to await donors. Determination of donor organ suitability was based on blood group, liver size, and medical urgency. Most of these patients were followed while waiting as outpatients. The operative time ranged from 5 hours and 30 minutes to 13 hours and 30 minutes (mean, 10 hours and 30 minutes). Cold ischemic time (the time from clamping the aorta in the donor to the time when the liver was brought out of the ice to be transplanted) ranged from 3 hours and 50 minutes to 17 hours and 20 minutes (mean, 9 hours and 20 minutes). Warm ischemic time ranged from 30 minutes to 1 hour (mean, 45 minutes). The patients were taken to an isolated special LT unit where hemodynamic and respiratory monitoring was performed in a standard postsurgical manner.

Postoperative immune suppression was instituted with a triple drug therapy regime consisting of steroids, tacrolimus, and mycophenolate 24–48 hours' post-transplantation. An intraoperative bolus of methyl prednisolone 500 mg was administered. Thereafter, prednisolone was started at a dose of 500 mg tapered to 200 mg over a 3-day period. The dose was gradually decreased from 60 mg to 5 mg at 1 month post-transplantation and then finally discontinued by the end of the third postoperative month. Tacrolimus was given at daily dose of 0.1 mg/kg twice a day for 12 h to achieve a level of 10–15 μg/L in the first month. Mycophenolate was given at 2 g twice a day to achieve a level of 6–10 ng/mL.

### Follow-up and observational values

After hospital discharge, blood work was performed twice weekly for the first 3 months, and a weekly outpatient visit. Liver function tests were closely monitored. If any abnormalities were noted, the patients were admitted for investigation. Starting at 1 year post-transplantation, blood and liver function test were performed on a monthly basis and clinic visits were performed every 2–3 months. "Death" in this study was defined as death related to liver disease or LT.

### Statistical analysis

Continuous variables are expressed as mean ± standard deviation, data between the two groups were compared by independent samples t test, rates were compared by the $\chi 2$ test, and survival rates were compared by Kaplan-Meier description. Most of the statistical analyses were completed by SPSS version 19.0 statistical software. Values of $P < 0.05$ were considered statistically significant.

## Results

### Donors

Between September 2011 and August 2013, there were 58 potential donors in the Affiliated Hospital of Guilin Medical University; of them, 15 successfully donated a liver and two other donors were diverted to other hospitals. None of them had expressed the desire while alive

**Table 1:** Donation failure causes for 43 potential donors.

| Causes | Cases (%) |
|---|---|
| Potential donors | 20 (46.51) |
| The donor had $HB^{V}$+ | 2 (4.65) |
| The donor had infection | 3 (6.97) |
| The organ conditions did not meet criteria for donation | 4 (9.3) |
| Death before family members agreed | 4 (9.3) |
| Patient's condition improved | 6 (13.95) |
| Others | 1 (2.33) |
| Family members of potential donors | 23 (53.49) |
| The relatives refuse organ donation | 19 (44.18) |
| No relatives were found | 1 (2.33) |
| Families abandoned treatment | 1 (2.33) |
| Others | 2 (4.65) |

**Table 2:** Donors' clinical features.

| Indexs | Mean /Cases |
|---|---|
| Age (year) | 37.23±11.15 |
| Gender( Male/Female) | 3-Oct |
| Body Mass Index (kg/$m^2$) | 23.11±2.74 |
| The time of demolition life support until death (minutes) | 8.15±2.44 |
| Liver weight (g) | 1876.15±496.33 |
| Causes of death | |
| Trauma | 10 |
| Cerebrovascular accident | 3 |

to donate their organs upon their death; rather, all of the organs were voluntarily donated by their family members after their death. The causes of unsuccessful donation are shown in table 1, while the preoperative diseases of the successful donors are shown in table 2.

### Recipients

The follow-up period was 2–47 months. None of the patients died intra operatively. One patient experienced intraoperative cardiac arrest, but the heartbeat was restored after open chest cardiac compression and no severe postoperative complications were noted. Patient demographics, disease indications, relevant dates, postoperative complications, mortality rates, and current status are shown in table 3.

All of the recurrent tumors were solitary and <5 cm in diameter, and none infringed upon the surrounding great vessels. All patients met the Milan criteria. All of the patients demonstrated hydrothorax and as cites, while three experienced acute rejection, one had hepatic involvement with artery embolization, one had arrhythmia, one had biliary obstruction, and one had acute cholangitis. One patient died of hepatic artery thrombosis, whereas the complications of all other patients were relieved after treatment.

The 1-, 2-, and 3-year overall survival rates were 92% (12/13), 85% (11/13), and 72% (9/13), respectively. Two patients with liver cancer died of cancer recurrence at 17 and 40 postoperative months, respectively. One patient with HBV-related cirrhosis died of hepatic artery embolization after 2 postoperative months. The blood types of this patient and his donor were A and O, respectively. Another patient with HBV-related cirrhosis died after 36 postoperative months.

## Discussion

### LT for patients with terminal liver disease

**Table 3:** Clinical features of the 13 recipients.

| Sequence number | Sex | Age (year) | Primary Diseases | Date of LT | Postoperative complications | Current status |
|---|---|---|---|---|---|---|
| 1 | Male | 45 | HBV-liver cirrhosis | 16.09.2011 | Arrhythmia; Hydrothorax and ascites | Alive |
| 2 | Male | 49 | Recurrence primary liver cancer and HBV-liver cirrhosis | 14.10.2011 | Incisional infection, Acute cholangitis; Hydrothorax and ascites | Death(23.02.2015) |
| 3 | Male | 53 | HBV- liver cirrhosis | 19.12.2011 | Hydrothorax and ascites | Death (24.12.2014) |
| 4 | Male | 62 | Recurrence primary liver cancer and HBV-liver cirrhosis | 09.02.2012 | Moderate chronic hepatitis; Hydrothorax and ascites | Alive |
| 5 | Male | 45 | HBV-liver cirrhosis | 27.04.2012 | Hepatic artery thrombosis; MODS ; GVHD; Hydrothorax and ascites | Death(17.06.2012) |
| 6 | Male | 34 | HBV-liver cirrhosis | 07.06.2012 | Acute organ rejection reaction; hydrothorax and ascites | Alive |
| 7 | Male | 57 | HBV-Liver cirrhosis | 18.07.2012 | Hoarseness of voice; Acute organ rejection reaction; hydrothorax and ascites | Alive |
| 8 | Male | 34 | Recurrence primary liver cancer and HBV-liver cirrhosis | 08.12.2012 | Canalis spinalis metastatic cance; hydrothorax and ascites | Death(07.04.2014) |
| 9 | Male | 40 | HBV-Liver cirrhosis | 07.02.2013 | Gastroparesis syndrome; Hydrothorax and ascites | Alive |
| 10 | Male | 58 | primary liver cancer and HCV-liver cirrhosis | 20.03.2013 | biliary anastomotic stenosis; Hydrothorax and ascites | Alive |
| 11 | Male | 48 | HBV-Liver cirrhosis | 21.06.2013 | Pleural effusion | Alive |
| 12 | Male | 59 | Recurrence primary liver cancer and HBV-liver cirrhosis | 25.07.2013 | Pleural effusion; Acute organ rejection reaction; Hydrothorax and ascites | Alive |
| 13 | Male | 43 | Alcholic cirrhosis | 24.08.2013 | Pulmonary infection; Hydrothorax and ascites | Alive |

LT: liver transplantation; MODS: Multiple Organ Dysfunction Syndrome; GVHD : Graft-versus-host disease.

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In the patients in our study, the 1-, 2-, and 3-year cumulative survival rates were 92%, 85%, and 72%, similar to figures reported elsewhere [13-17]. Although some complications are common after LT [18], LT is an effective treatment for patients with terminal liver disease.

Death directly attributed to technical complications occurred in one patient in this study. The recipient and his donor had type O and A blood, respectively. The patient experienced acute rejection and liver artery embolization and died 2 months postoperatively. These complications are related to hepatic artery thrombosis and multiple organ dysfunction syndromes for which interventional and thrombolytic therapies were implemented. In this case, no organ was available for re-transplant; had it been, it would be too late and sepsis would have produced inferior transplant results.

Four patients underwent LT for liver cancer recurrence, namely remedial LT (RLT). The 1-year survival rate was 100% (4/4), 1-year recurrence rate was 25% (1/4), 2-year survival rate was 75% (3/4), and 2-year recurrence rate was 75% (3/4), similar to rates reported in related studies [19]. RLT was reported by Majno et al. [20] in 2000. Patients with good liver function underwent hepatectomy first; followed by LT until cancer recurrence or functional failure, and its criteria were consistent with direct LT. Majno et al. [19] reported that the RLT strategy could save approximately 26% of donor liver resources. Studies have suggested no significant differences between RLT and direct LT in postoperative recurrence rates or survival rates [12,19] but increased preoperative complications of the RLT [20]. RLT is effective and feasible for patients with liver cancer [21,22].

### Study limitations

This was a single-center study with a small sample. Therefore, future multi-center studies with larger populations are required to validate our findings.

## Conclusions

LT from DCD may be an effective treatment method for patients with terminal liver disease.

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## Disclosure

The authors of this manuscript have no conflicts of interest to disclose.

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