

Liver retransplantation for adult recipients

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Living donor liver graft can be used for the first or second liver transplantation. The timing of retransplantation also should be stratified as 2 types according to the reoperation timing. Combination of these two classifications results in 6 types of living donor liver transplantation (LDLT)-associated retransplantation. However, late retransplantation to LDLT might have not been performed in most LDLT programs, thus other 4 types of LDLT-associated retransplantation can be taken into account. The most typical type of LDLT-associated retransplantation might be early living donor-to-deceased donor retransplantation. For early living donor-to-living donor retransplantation, its eligibility criteria might be similar to those of early living donor-to-deceased donor retransplantation. For early deceased donor-to-living donor retransplantation, its indications are exactly the same to those for aforementioned living donor-to-living donor retransplantation. Late deceased donor retransplantation after initial LDLT has the same indication for ordinary late deceased donor retransplantation. ([Korean J Hepatobiliary Pancreat Surg 2013;17:1-7](#))

Key Words: Living donor liver transplantation; Deceased donor liver transplantation; Retransplantation

INTRODUCTION

Living donor liver transplantation (LDLT) has been settled as a main type of liver transplantation. However, in spite of a large number of LDLT, living donor liver retransplantation has been uncommon and rarely reported in literature. According to a registry maintained by the Japanese Liver Transplantation Society, 2249 transplants have been performed in 49 institutions throughout Japan until the end of 2002; there were 2226 LDLTs in 2164 patients and 23 deceased donor liver transplants.¹ These data indicate that retransplantation rate following LDLT was about 2.8% and most of them were living donor-to-living donor liver retransplantation. In the series of first 1000 LDLTs and 155 deceased donor liver transplants at Asan Medical Center, there were 11 patients who underwent LDLT-associated retransplantation (retransplantation from or to LDLT): Three patients received living donor-to-living donor retransplantation and 8 patients underwent deceased donor-to-living donor or living do-

nor-to-deceased donor retransplantation.² This series shows 1.1% of LDLT-associated retransplantation rate. On the other hand, the reported rate of retransplantation from large-volume deceased donor liver transplant programs varied between 7% to 23%.³ In the University of California Los Angeles series of 3,200 liver transplants including 65 LDLTs, liver transplantation more than once was performed in 538 patients (20.2%) of overall 2,662 patients.⁴

The basic reasons why LDLT-associated retransplantation has been performed in such a low incidence comparing with deceased donor transplants might as follows: first of all, it might be very low incidence of primary non-function after LDLT, which has been the most common cause of retransplantation following deceased donor transplant. North American multi-center study group reported that 11 (2.9%) living donor liver grafts failed as primary non-function in 385 recipients and 37 patients underwent retransplantation within first year mainly due to vascular thrombosis or primary non-function.⁵ In this re-

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port, the type of reoperation might be living donor-to-deceased donor retransplantation. The detailed clinical sequences of primary non-function following LDLT have been not fully understood yet. There were only one case report of living donor-to-deceased donor retransplantation due to primary non-function of the first liver graft.⁶ The second reason for low incidence of LDLT-associated retransplantation might be progressive decrease of graft failure from technical faults of LDLT operation through advancement of surgical techniques and improvement of imaging studies for donor liver evaluation.⁷ By using various innovative techniques, the incidence of serious surgical complications after LDLT decreased significantly, by which the need for retransplantation were proportionately reduced.⁸ The third reason is definite shortage of available deceased or living donor for retransplantation.

In North America and Europe where deceased donor liver transplantation is the main type of liver transplantation, deceased donor liver graft could be available with a relatively short waiting time in high probability if an emergent retransplantation is required.⁵ This implicates that LDLT is primarily used for first liver transplantation to cope with relative shortage of deceased donor organs, and there is very low probability performing living donor-to-living donor retransplantation. Furthermore, the overall case number of LDLT in these areas is much smaller than those of Asian countries. As a result, in North America and Europe, the experience of LDLT-associated liver retransplantation would be confined to living donor-to-deceased donor retransplantation.

On the other hand, in Asian countries where deceased organ donors are in scarcity, retransplantation with either deceased donor or living donor liver graft has very low probability due to lack of donors. In this situation, serious posttransplant complication is directly related to patient death without chance of retransplantation. According to the AMC experience, the main causes of early graft failure were serious complications confined to the liver graft such as hepatic artery thrombosis, portal vein thrombosis, hepatic outflow obstruction, massive hemorrhagic necrosis or unexplained severe graft dysfunction.⁹ Retransplantation might have been attempted to most of these seriously complicated recipients if deceased liver donors were available.

LDLT-associated retransplantation can be classified as

three types according to the sequences of graft types (living donor-to-living donor, living donor-to-deceased donor and deceased donor-to-living donor) because different surgical techniques should be considered according to the different sequences. It also should be classified into two types according to reoperation timing - early and late - like in ordinary deceased donor liver retransplantation.

After applying these combinations, early retransplantation from LDLT to deceased donor transplantation might have been the most typical type in countries where deceased donor organs are available. It is also the simplest type of retransplantation because all structures belonging to the first liver grafts would be removed before formation of adhesion and new graft can be anastomosed to the recipient's native structures. On the other hand, late retransplantation to LDLT is the possible worst combination because severe adhesion, distorted structures and newly developed collateral veins would make the recipient operation very difficult or not possible. In practice, retransplantation using living donor liver graft has a limited indication only for life-saving purpose. The outcome of LDLT-associated retransplantation has not been reported yet in literature. Based on the Asan Medical Center experience with 11 cases of LDLT-associated retransplantation, 1-year survival rate after retransplantation was about 60%, which is much lower than 91% following first LDLT in 883 adult recipients.⁹ The underlying cause of such lowering of survival rate might be inevitable miss of the optimal timing for retransplantation due to donor factors.

INCIDENCE AND INDICATIONS

It is presumed that only a small number of liver recipients have undergone LDLT-associated retransplantation worldwide to date. Living donor liver graft can be used for the first or second liver transplantation. The timing of retransplantation also should be stratified as 2 types according to the reoperation timing. Combination of these two classifications results in 6 types of LDLT-associated retransplantation. However, to our knowledge, late retransplantation to LDLT might have not been performed in most LDLT programs. Considering our experience on late deceased donor retransplantation after initial LDLT or deceased donor transplant, it does not seem to be reasonable or sometimes not feasible to dissect the heavy adhe-

sion around the initial partial liver graft, especially at the conglomerated hilar structures, to make them suitable for LDLT. Thus, other 4 types of LDLT-associated retransplantation can be taken into account.

The most typical type of LDLT-associated retransplantation might be early living donor-to-deceased donor retransplantation. Any cause of early graft failure can be indicated for this type of retransplantation if a deceased donor organ is available: it includes primary non-function, early severe dysfunction or major surgical complications confined to the liver graft, which are much similar to those of deceased donor liver transplantation. Although the incidence of primary non-function following LDLT has been sporadically commented in literature, the actual incidence has been unknown so far after exclusion of the technical factors during learning curve.^{5,6,10} According to the Asan Medical Center experience, its incidence was definitely less than 1% if strict definition of primary non-function was applied. Severe initial dysfunction of the living donor liver graft was often associated with small-for-size graft, excessive venous congestion of the right lobe graft from hepatic outflow obstruction or portal flow steal syndrome. Serious hepatic artery-related complications including hepatic artery thrombosis occurred in 2-5% at large-volume LDLT programs and became a leading cause of early graft failure following LDLT.¹¹⁻¹³ Intractable biliary complication also can be an indication of retransplantation because its clinical course could be intractable and it occasionally induced life-threatening sepsis.^{14,15} If the general condition of a patient can endure the retransplantation procedure itself, there might be no absolute contraindication specific for this type of retransplantation. Thus, it shares the same retransplantation indication criteria with initial deceased donor liver transplantation.

For early living donor-to-living donor retransplantation, its eligibility criteria might be similar to those of early living donor-to-deceased donor retransplantation, but technical feasibility should be considered first. The most important point is the availability of hepatic arterial blood flow source. A reliable arterial flow source other than the hepatic artery proper is the right gastroepiploic artery because it can be easily mobilized toward the hepatic hilum after detachment from the stomach and can be promptly enlarged to facilitate size-mismatching. The clinical sig-

nificance of this artery was proven in its use for LDLT.^{11,16} If it is not possible to use this artery before reoperation, living donor retransplantation should not be attempted or fresh arterial vessel graft should be sought from deceased organ donors.

For early deceased donor-to-living donor retransplantation, its indications are exactly the same to those for aforementioned living donor-to-living donor retransplantation unless extensive hepatic artery thrombosis occurred. Hilar dissection of the failed whole liver graft is comparable to that of liver dissection during initial LDLT. If hepatic arterial thrombosis was the cause of graft failure, alternative arterial flow source such as right gastroepiploic artery should be searched first.

Late deceased donor retransplantation after initial LDLT has the same indication for ordinary late deceased donor retransplantation such as recurrence of hepatitis C cirrhosis or chronic rejection. This type of retransplantation is considered to carry an increased risk comparable to the repeated deceased donor retransplantation.¹⁷⁻²⁰ As there is no short-cut to dissect heavy adhesions, the timing of deceased donor and recipient operations should be adequately adjusted not to make the cold preservation time too much prolonged.^{21,22}

TECHNICAL CONSIDERATIONS FOR LDLT-ASSOCIATED RETRANSPLANTATION

The difficulty of the recipient operation usually depends on the timing of retransplantation. Early emergency retransplantation such as reoperation within the first week does not require difficult dissection process because there is little adhesion around the liver graft. Retransplantation after an interim period such as 1-3 months would make adhesions from mild to severe degree. Although minute collateral vasculatures are not usually developed in the adhesion of this time, meticulous sharp dissection is mandatory to secure the dissection effectively. For late retransplantation after progression of viral hepatitis or chronic rejection, heavy adhesion and new development of portal venous collaterals would be encountered. Every adhesion should be cut sharply and every bleeding point should be strictly controlled during the dissection process. Blunt dissection of such adhesion should be avoided because it can induce massive uncontrollable bleeding from

the widely dissected surface in the situation of portal hypertension. Except for early retransplantation, retransplantation operation usually takes much longer operation time for dissection than in the initial operation, so experience-based scheduling of donor and recipient operations is important not to prolong cold preservation time or living donor operation time.^{21,22}

Early living donor-to-deceased donor retransplantation

After the main operative wound for initial LDLT is opened, gentle blunt dissection with fingers would make the gelatinous or mild adhesion separate from the liver graft. Hepatic hilar structures should be manipulated gently, but the hepatic artery and common bile duct may not be suitable to reuse for deceased donor retransplantation. Retrohepatic inferior vena cava should be dissected further especially cephalad to enable deep secure clamping of the suprahepatic vena cava over the diaphragm because the hepatic vein cuffs are nearly absent. As the cephalad end of right hepatic vein orifice is located very close to the diaphragm, deep diaphragm clamping is mandatory to secure suprahepatic vena cava anastomosis.

In this type of retransplantation, the common hepatic artery may not be suitable for arterial anastomosis; adequate branch patch cannot be made because all branches other than previously anastomosed branch were ligated already. Blood outflow from the right gastroepiploic artery often appears to be too small to perfuse the whole liver graft reliably. Thus, arterial interposition graft should be taken into account. Infrarenal aortic jump graft has been preferred to supraceliac aortic graft.

After complete dissection of the old graft and inferior vena cava, the retransplantation procedure proceeds as routine like in deceased donor-to-deceased donor retransplantation. Piggyback technique with side-to-side or end-to-side cavocaval reconstruction is not recommended because the use of such methods did not seem to have no advantage when comparing with the standard technique.²³⁻²⁵ LDLT has often used duct-to-duct anastomosis, so the condition of recipient bile duct is usually not enough good to re-do duct anastomosis. Thus, Roux-en-Y choledochojejunostomy is highly recommended.^{26,27}

Early living donor-to-living donor retransplantation

For this type of retransplantation, the type of second liver graft and hepatic arterial inflow source should be considered prudently. As this retransplantation is performed in a highly morbid situation, suboptimal donor graft such as graft size smaller than 40% of the recipient's standard liver volume should not be used considering the severity of pre-retransplant condition.²⁸⁻³⁰ Donor livers with variant liver anatomy such as variant portal vein or hepatic artery cannot be used.^{11,13,31,32} If a right lobe graft is used, hepatic venous congestion should be minimized through interposition reconstruction or concurrent procurement of the middle hepatic vein.³³⁻³⁶ Arterial flow source is another important point to be considered before this type of retransplantation because it is usually not feasible to use the proper hepatic arterial branch again even in the favorable situations with no hepatic artery thrombosis. Splenic artery is usually not suitable for arterial reconstruction of LDLT due to its limited length and diameter discrepancy. It is not preferred to use the cryopreserved vessel graft for arterial reconstruction due to a high risk of arterial thrombosis or potential pseudoaneurysm formation although successful outcomes have been sporadically reported.³⁷⁻³⁹ Instead, fresh arterial graft from a deceased donor can be used like in primary LDLT for recipients with destructed hepatic artery. For such purpose, it is reasonable to procure the superior mesenteric artery graft from a deceased donor during procurement of iliac artery grafts because superior mesenteric artery has many small branches matching to right or left hepatic artery of the partial liver graft. Another reliable source of hepatic arterial flow is the right gastroepiploic artery. In practice, in such a situation requiring arterial blood flow source other than innate hepatic arteries, the right gastroepiploic artery has been the most preferable artery for LDLT because of its invariable anatomical location, size, and length. This artery often looks too small at a glance, but it can be rapidly dilated after clamping for a short time. As this artery is fed from the arterial arcades at the pancreatic head not to mention of the gastroduodenal artery, usual hepatic artery thrombosis without extension to the celiac axis usually does not have negative influence on its blood flow. These merits of the right gastroepiploic artery as a substitute source for hepatic arterial flow have led to use it

for multiple or re-do arterial reconstruction in LDLT. Preoperative selective arteriography or three-dimensional reconstruction of computed tomographic angiography can be used for its preoperative evaluation.⁴⁰

For removal of the old graft and secure anastomosis of the hepatic vein, deep secure suprahepatic vena cava clamping over the diaphragm should be prepared like in deceased donor retransplantation. As prolonged vena cava clamping is often required, active venovenous bypass would be beneficial.

After complete dissection of the old graft and inferior vena cava, the retransplantation procedure proceeds as routine like in primary LDLT. Portal vein should be cut close the old liver graft across the anastomotic line, and then suture material should be removed. Similar principle would be applied to the hepatic vein orifice. After vena caval clamping, the liver parenchyma should be cut to leave some tissue at the hepatic vein orifice. After that, suture material should be removed to preserve the edge of hepatic vein orifice intact.

Technically, the use of a partial graft of same type is of advantage for intra-abdominal space occupation and hepatic vein reconstruction. The same stump of portal vein can be usable for portal vein reconstruction. Hepatic vein stump can be used like in primary LDLT. When using the right gastroepiploic artery for alternative hepatic arterial flow source, it is necessary to straighten the anastomosis site not to make a kinking deformity. To avoid accidental excessive tension at the arterial anastomosis site, it is necessary to transfix the artery to the surrounding structure such as gastric antrum before performing other procedure. The recipient bile duct which had been used for biliary reconstruction is not acceptable for duct-to-duct anastomosis, so Roux-en-Y hepaticojejunostomy is mandatory.

Early deceased donor-to-liver donor retransplantation

This type of retransplantation has been usually applied to primary non-function of the first deceased donor liver graft. Thus, all vascular structures should remain intact. In contrast, the cause of first graft failure is vascular complication such as hepatic artery thrombosis, portal vein stenosis or vena cava stenosis, such patient may not be indicated for this type of retransplantation. Any type of

living donor liver graft can be implantable like a first LDLT, but right lobe graft is desirable due to stable settlement of the partial liver graft in the right subphrenic fossa. Hilar vascular structures and retrohepatic vena cava of the failed liver graft should be dissected like in primary LDLT. Vena cava and portal vein of the first graft should be left as interposition grafts. Hepatic artery of the first graft can be used as interposition graft, or other source of arterial blood flow such as gastroepiploic artery can be used alternatively. Since the retrohepatic inferior vena cava should be fully preserved, both supra- and infrahepatic anastomotic lines should be protected carefully. The portal vein of the first graft should be dissected, but this process is not difficult because the failed liver has nearly normal consistency and hilar structures are dissected already. It is not recommended to use the hepatic artery branch of the first graft,³ but there might be not worse than using other type of jump graft. Based on the AMC experience, this arterial interposition did not result in any arterial complication. Alternatively, the right gastroepiploic artery can be used as arterial flow source without interposition of deceased vessel graft. Duct-to-duct anastomosis is not feasible because the proximal portion of recipient bile duct had been already removed during first operation. There is no choice of biliary reconstruction other than hepaticojejunostomy.

Late living donor-to-liver donor retransplantation

It is almost not practical to perform this type of retransplantation because of heavy adhesion and distorted the hilar structures not permitting sufficient dissection.

Late living donor-to-deceased donor retransplantation

Heavy adhesion and prominent venous collateral would be encountered during recipient operation. Piggyback technique may be not feasible and not recommended due to heavy adhesion around the retrohepatic inferior vena cava. Dissection of the main portal vein which had been once dissected would require meticulous sharp dissection. Common hepatic artery patch or aortic jump graft is used. There is no choice other than Roux-en-Y choledochojejunostomy.

Late deceased donor-to-liver donor retransplantation

This type of retransplantation is also a kind of least recommended type like late living donor-to-living donor retransplantation. Surgical technique would be similar to that of early deceased donor-to-living donor retransplantation, but the difficulty of hilar dissection varies depending on the patient conditions.

OUTCOME OF LDLT-ASSOCIATED RETRANSPLANTATION

Since LDLT-associated retransplantation has been performed in a small number of patients worldwide, its outcome cannot be assessed statistically unlike in deceased donor re-transplantation. Furthermore, LDLT itself indicates shortage of deceased donor organs, so optimal retransplantation timing might have been missed in patients with failing first liver graft. Considering the real situation of deceased organ shortage and limited availability of living donor, the outcome of LDLT-associated retransplantation might be naturally worse than that of deceased donor retransplantation. Although deceased donor retransplantation revealed higher morbidity and lower survival than primary transplantation, 1-year survival in adult recipients became about 70% in recent literature.^{17,41} Considering the disadvantageous situation of LDLT-associated retransplantation, the result of about 60% 1-year survival from the Asan Medical Center series is comparable to the result from deceased donor retransplantation. Late deceased donor retransplantation has been often performed for patients with hepatitis C virus infection, but this disease was associated with lower patient and graft survival compared with retransplantation for other causes.⁴² It may be reasonable to expect the similar outcome after LDLT-associated retransplantation in patients with viral hepatitis C.

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