Current Status of Liver Transplantation — an Asian Perspective

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INTRODUCTION

Professor Tan Sri GB Ong, chair of the Department of Surgery, The University of Hong Kong between 1962 and 1983, innovated many operations for the treatment of head and neck cancer, oesophageal cancer, liver cancer and urinary bladder cancer during his tenure. He has moulded the department into one of the best surgical units in the world. Following his footsteps in pursuance of liver surgery, liver transplantation is now a routine treatment at the University of Hong Kong Medical Centre, Queen Mary Hospital for patients with terminal liver diseases. With the improvement and refinement of surgical techniques, it is believed that an even larger number of patients will benefit.

BACKGROUND

As a result of the relentless effort of Starzl in the USA and Calne in England, liver transplantation has become a standard treatment for patients with terminal liver disease since 1983. Maturity of the surgical technique, availability of the necessary equipment and prevention of graft rejection by cyclosporine and other immunosuppressive agents have contributed to the success of the operation.

In Asia, however, developments in liver transplantation could hardly keep pace with the USA and European countries. There are various reasons, including the scarcity of organ donation from brain-dead people, limitation of resources and prevalence of hepatitis B and C. Under such conditions, liver transplantation may not achieve good results. Nevertheless, in the last decade, some of these problems have been resolved. For example, hepatitis B reinfection of the graft is now successfully prevented by lamivudine monotherapy1 and live donors have been adopted to overcome graft shortage.2 The following is an account on the issues of live donor liver transplantation (LDLT), in relation to the substantial contribution of Asian liver transplant surgeons to the development of the field.

DEVELOPMENT OF LIVER TRANSPLANTATION IN ASIA

The history of LDLT started in 1989 when the first successful operation was performed by Russell Strong in Brisbane, Australia.3 Subsequently, the operation has been taken up in various parts of the world, particularly in Japan, where brain dead organ donation was not allowed. Initially, left lateral segments or left lobe grafts from an adult were transplanted to a child or adolescent. Surgeons later modified the operation by using extended left lobe grafts in adult recipients, but the initial result was unsatisfactory.4 The first successful left lobe LDLT for adults was performed by Makuuchi and his team at Shinshu University in 1993.5 The recipient suffered from primary biliary cirrhosis and the donor was her son. Later, we performed a similar operation between a husband and a wife.6

MINIMUM GRAFT VOLUME

The key question at that time was the minimum graft volume that could sustain survival. From animal data, the minimum graft weight (GW) for successful orthotopic liver transplantation was 25% of the original liver weight.7 The GW of the three patients with fulminant hepatic failure on whom we operated over the estimated standard

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liver mass (ESLM) ratio were 25%–43%. All three patients survived. However, when we performed a similar operation on two patients with pre-existing portal hypertension and cirrhosis, both patients died, even though the GW/ESLM ratio exceeded 25%.

In another study involving cadaveric grafts, patients with mostly portal hypertension and small-for-size liver graft (defined as less than 50% of ESLM), had poor outcome in terms of prolonged cholestasis and poor early graft function. Liver biopsy showed a diffuse ischaemic pattern characterized by preservation injury and cellular ballooning.8

The probable reason for failure was that a small-for-size liver graft cannot accommodate a large volume of high portal vein blood flow. That would lead to diffuse sinusoidal mechanical injury and, subsequently, aggravated portal hypertension and liver failure. To increase graft size, Kawasaki et al proposed the inclusion of the caudate lobe in a left lobe graft.9 This increased the graft volume by 5%–8%. However, the problem could not be entirely solved because other situations limited the use of the left lobe graft. For example, implanting a relatively large left lobe graft into a small recipient could be problematical because the space between the spine and the costal arch is limited. After reperfusion, the graft expands, rendering the approach to the liver hilum for hepatic artery and bilio-enteric reconstruction impossible.10

The assistant, in order to expose the liver hilum for the anxious surgeon, would invariably compress the upper portion of the liver graft onto the costal arch, thereby inducing ischaemic injury to the upper portion of the liver graft. Therefore, the effective graft volume would be much less than anticipated or calculated.

**RIGHT LOBE LDLT IN ADULTS**

To solve the problem, in 1996, we designed the right lobe LDLT between adults (Figure 1).11 In this operation, the right hepatic artery and right portal vein are isolated in the liver hilum. The right lobe is mobilized and the right hepatic vein is encircled extrahepatically. The liver is then transected on the left side of the middle hepatic vein using an ultrasonic dissector without any inflow or outflow vascular occlusion. When the recipient hepatectomy is completed, the graft is retrieved and implanted into the patient's right subphrenic cavity. With a short cold ischaemic time and adequate venous outflow reconstruction, the graft is usually soft in consistency and uniformly pink in colour. The best indicator of a successful operation is the immediate bile production. The hepatic artery is reconstructed by microvascular anastomosis. Occasionally, two independent hepatic arteries need to be reconstructed.

A larger graft volume is one of the advantages of the right lobe graft LDLT. Despite the size of the graft, it does

![Diagram](image-url)
not interfere with the hepatic artery and bili-o-enteric anastomosis, and it will not be injured by the costal arch or by the wound on closure because the graft is located in the spacious right subphrenic cavity. If the left portal vein is used for veno-venous bypass during right portal vein reconstruction, the duration of splanchnic congestion can be kept to the minimum. Finally, the right hepatic artery is usually large, thus facilitating microvascular anastomosis. In addition, the right lobe graft can provide sufficient graft volume, even though the donor is smaller in body size than the recipient. In our series of right lobe LDLTs, more than 69% of the donors were actually lighter in body weight than the recipients.

Right lobe LDLT is now accepted by many liver transplant centres round the world. However, many unsolved issues remain that include the safety of the donors, necessity of inclusion of the middle hepatic vein in the graft, the best venous outflow reconstruction, and the best technique for biliary anastomosis.

Right lobe donation is a more major operation than left lobe donation, because about 60%–65% of the liver mass is removed from the donor. We compared the outcome of the right lobe donor versus the left lobe donor. The postoperative liver function, in terms of serum bilirubin and prothrombin time, was, in fact, less satisfactory in the right lobe donors, although recovery in both groups were usually rapid. Right lobe donors also tended to stay longer in the hospital than left lobe donors.

**DONOR COMPLICATIONS**

We have experienced donor complications in our right lobe donors. There have been cholestasis (n = 3), biliary strictures (n = 2), portal vein thrombosis (n = 1), duodenal ulcer (n = 1), small bowel obstruction (n = 1) and transient peroneal nerve injury (n = 1). Cholestasis was probably related to fatty liver and small liver remnant. All three donors with cholestasis recovered with expectant treatment. Biliary stricture was due to imprecise division of the right hepatic duct. Both donors with biliary stricture recovered after adequate treatment. One donor had small bowel obstruction due to adhesion bands. She was well after enterolysis. Fortunately, there has been no donor mortality in our series.

Inclusion of middle hepatic vein in right lobe graft

Another controversy is the necessity for inclusion of the middle hepatic vein in the graft. Since the initiation of this operation in adults, we have been including the middle hepatic vein in the graft. The reason being that the middle hepatic vein is the main drainage vein of segments 5 and 8. Other transplant surgeons adopting this technique do not include the middle hepatic vein because they consider that it is the main drainage vein of segment 4 and a compromised venous drainage of segment 4 would endanger the donors. On the other hand, graft congestion has been reported repeatedly when the right lobe graft does not contain the middle hepatic vein and many surgeons now design operations that can improve venous drainage of segments 5 and 8 when the middle hepatic vein is not included. In our experience, segment 4 congestion is not a serious problem because, although the segment 4a vein needs to be sacrificed, the segment 4b vein can be preserved. On many occasions, the segment 4b vein drains into the middle hepatic vein near to the junction with the left hepatic vein and, therefore, can be preserved. In addition, an umbilical vein is frequently present and serves to drain segment 4. Even though the segment 4 hepatic vein joins the middle hepatic vein high above the junction with the inferior vena cava, venous drainage of segment 4 can be preserved if the middle hepatic vein is transected above the junction of the segment 4 hepatic vein with the middle hepatic vein. In the recipient, a longer segment of middle hepatic vein is preserved to make up the deficiency in the length of donor middle hepatic vein.

Venous Drainage

The third issue is venous drainage of the right lobe graft. Since almost all right lobe grafts, even though they meet the minimum requirement of most adults, are small-for-size, their venous drainage must be sufficient. Otherwise, the graft will suffer from severe congestion. Unlike whole liver grafts, the venous anastomosis is a little
tricky especially when the right subphrenic cavity is relatively small. This is because, after reperfusion, the graft expands and rotates to the left side. If the right hepatic vein is long, kinking will occur. Thus, the right hepatic vein must be as short and wide as possible. On the other hand, the middle hepatic vein has to be sufficiently long, especially when the graft is small, otherwise, tension will appear, leading to collapse of the vein wall and graft congestion. In addition, to avoid the purse-string effect, a growth factor is given to all hepatic vein anastomoses, in a similar manner as to vein anastomosis.

Apart from the graft consistency, the Doppler study is helpful in judging the result of hepatic vein anastomosis. The important feature is the triphasic wave form and the

![Graph showing postoperative alanine aminotransferase (ALT) level in 78 right lobe donors.](image1)

![Graph showing postoperative serum bilirubin levels in 78 right lobe donors.](image2)
postoperative International Normalized Ratio (INR) in 78 right lobe donors.

Figure 4.

reversed flow pattern in the pulse Doppler wave. The pulsatility is a reflection of cardiac contractility and also indicative of a wide and patent anastomosis, while backflow reflects that the liver is soft in consistency. Such a phenomenon is seen in the donor before harvesting. After implantation, the same finding on Doppler study is expected in the recipient. That would be an indication that a perfect anastomosis has been created.

**Biliary Reconstruction**

The incidence of complications of biliary reconstruction has been high, ranging from 22% to 64%. The reasons for this high complication rate probably include ischaemia of the right hepatic duct and a high incidence of anatomical variation leading to two or three hepatic duct orifices in the graft or even missing one or two hepatic ducts. To study the hepatic ducts thoroughly and to avoid missing one or two hepatic ducts, a high-quality cholangiogram is essential. We utilize undiluted radiographic contrast and fluoroscopy to achieve this purpose. Under fluoroscopy, the sequence of the intrahepatic duct filling is closely observed. The right posterior segment duct is filled first because it is most dependent in position. The right anterior duct is filled next, followed by the left duct and the segment 4 duct. A metal clip is placed at the site of the proposed division of the right hepatic duct. This site can be confirmed by the cholangiography allowing the precise location of the duct division to be determined.

There is additional advantage of using fluoroscopy. In a relatively small liver that rotates into the right subphrenic cavity, the right hepatic ducts are difficult to recognise and interpret. By rotating the X-ray tube to the right side of the donor to obtain an anterior oblique view, the right anterior and right posterior ducts are clearly defined.

To avoid ischaemia of the right hepatic duct, it is necessary to study the blood supply of the bile duct. The blood supply of the right hepatic duct derives from the arcades formed by the gastroduodenal artery, the left hepatic artery and right hepatic artery. After division of the right hepatic duct, the arcades are disrupted and the blood supply of the right hepatic duct is then derived from the right hepatic artery, the hilar plate and the caudate lobe. To preserve the blood supply to the right hepatic duct, it is, therefore, necessary to avoid dissection into the space between the right hepatic duct and the right hepatic artery beyond the point of the right hepatic duct division.

In addition, the line of liver transection should be deviated to the left side of the gallbladder fossa in order to provide sufficient liver tissue covering the duct. The liver tissue will also serve to provide venous drainage for the right hepatic duct. With all the modifications of the technique, we have achieved a satisfactory result with
right lobe live donor operations with an overall survival rate at 85%.

**CONCLUSION**

The use of right lobe LDLT has a major impact on the outcome of patients waiting for cadaveric grafts. When the patient's family opts for live donor operation, the waiting time can be much shortened, the transplant rate is much increased and the mortality rate while waiting can be reduced.

The same phenomenon is also observed in patients with acute liver failure. We now proactively offer right lobe LDLT to patients with acute liver failure. If the family decides on live donation, the transplant rate can be much increased. In the last 2 years, about half of the patients with acute liver failure admitted to Queen Mary Hospital with voluntary donors survived. For those without volunteers, only one of the 15 patients in the study period received a cadaver graft and survived, while all the others died.

Living donors have altered the development of liver transplantation. However, we should not rely on live donors for expansion of transplant activities because live donor operation is a major and perhaps dangerous operation. To expand the activity of liver transplantation in Asia, splitting of the liver for two recipients should be considered.

Splitting of liver and sharing of organs is not impossible in Asia and has already been carried out in Hong Kong as well as between Taiwan and Hong Kong. This task is difficult if it is carried out by one single centre. If two or more centres can collaborate in sharing of the split liver, it would be easier and many patients will benefit. Liver splitting and organ sharing should be a target in the future development of liver transplantation.

**REFERENCES**

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