

# Sharing Your Liver – Adult Living Donor Liver Transplantation in Singapore

By Dr Tan Kai Chah

The success of liver transplantation as a treatment for the patient with end-stage liver disease has resulted in an ever-increasing waiting list mortality, even in the West. Data in the United States shows 14,710 patients on the waiting list end of 1999 and only 4,480 liver transplants being performed that year<sup>1</sup>. This year the wait list has ballooned to 18,000 patients, with cadaveric donor procurement remaining static. Until recently, despite the prevalence of liver disease, there were only a few centers in Asia performing liver transplantation from living donors (mainly pediatric). The great majority of adult patients with end-stage liver disease were not transplanted due to the scarcity of cadaveric donor livers. The development and clinical application of adult living donor liver transplantation (ALDLT) has largely been driven by this huge discrepancy between recipient needs and the availability of donor livers.

The first living donor liver transplantation (LDLT), using the left lateral segment was attempted in 2 children in 1989 in Brazil<sup>2</sup>. The procedure has been shown to have excellent results, with graft and patient survival comparable to or even better than those of cadaveric transplants, and a low risk for donor morbidity and mortality<sup>3,4</sup>. Pediatric LDLT is today well established in most liver transplant centers. With the experience and expertise gained in pediatric LDLT, attempts were made to transplant adults initially with the left lobe<sup>5,6</sup>. However, the small graft volume limited ALDLT using the left lobe, which was often insufficient to meet the metabolic demand of an adult<sup>7</sup>. It has been estimated a graft-to-recipient weight ratio (GRWR) of more than 0.8% is necessary in LDLT and recipients of grafts with GRWR of <0.8% have

been shown to have a lower chance of survival<sup>8,9</sup>. The first ALDLT using the right lobe was attempted in 1994 in Japan<sup>10</sup>, followed shortly by a series from Hong Kong<sup>11</sup>. Given the near absence of cadaveric donor livers it is not surprising that the initial thrust to develop an alternative source of donor livers for adult patients took place in Asia<sup>12,13</sup>. The prevalence of liver disease and the existing hepatobiliary surgical expertise also provided impetus to develop this formidable but essential operation. To date almost 3,000 LDLT have been performed in Asia with no reported donor mortality.

Liver transplantation has been performed sporadically in Singapore since the early 1990's. Since 1996, due in part to the successful implementation of a pediatric LDLT programme and the occasional split liver transplantation; almost 80 liver transplants have been performed<sup>14</sup>. Like elsewhere in Asia, the main impediment to expanding the programme in Singapore has been the acute shortage of cadaveric donor livers. Despite considerable efforts to increase cadaveric organ donation in Singapore, only 10-12 such livers are retrieved each year. The number of cadaveric donor livers has actually decreased over the last 3 years and this was in the face of an ever-increasing recipient need. Given an average requirement of 12-transplants/million population/year, there should be at least 40 transplants each year in Singapore. In fact, the number of transplants needed is considerably greater with the influx of foreign patients, as currently there is no active adult liver transplant programme in any of the surrounding countries. It is not surprising that currently in Singapore, almost 70% of adult patients perish while on the wait list for a cadaveric donor liver. In an emergency situation, such as in acute

liver failure, the patients here face almost certain death.

Besides being an alternative source of donor livers, the other advantage of ALDLT over cadaveric organ donation is that it allows scheduling of the procedure. As such, the patient with decompensated liver function can be optimized prior to the operation. In addition, the quality of the graft is better as it is retrieved from a healthy donor and the cold ischaemic time is much shorter.

The most important disadvantage of ALDLT is the potential for morbidity and even mortality to a healthy donor. The reported donor mortality for LDLT worldwide is about 0.3%<sup>15-17</sup>. Donor morbidity rates vary widely, with a range of 0 - 67%<sup>18</sup>. These include wound and chest infection, abdominal discomfort and ileus, nerve palsy, phlebitis, etc. Other more serious morbidity encountered is hepatic encephalopathy and bile leakage.

As donor safety is of paramount importance, it is vital that ALDLT is performed by a surgical team experienced in hepatobiliary and transplant surgery. The procedure must be carried out in medical centers with facilities and resources over and above those required for major liver resection and cadaveric transplantation. A comprehensive assessment and consent process for both donor and recipient must be established that ensures autonomy of decision and lack of coercion. Finally, a physician, a psychiatrist and a medical social worker that are independent of the transplant programme must assess the donor.

It was with these in place that the first five successful ALDLT in Southeast Asia were performed this year in Singapore. Two patients were in acute liver failure and had liver dialysis as a bridge to liver transplantation. Two patients had cryptogenic cirrhosis and



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the fifth had alcoholic cirrhosis and hepatocellular carcinoma. All the donors were related except for one patient with acute liver failure due to a slimming drug, the donor being the fiancé. The right lobe was used in 4 cases and an extended right lobe was grafted in the fifth case. Only autologous blood was used in all the donors and they were discharged between 6 to 10 days post surgery. All but the last recipient were discharged between 18 to 32 days with normal liver function test.

In Singapore today, ALDLT remains the only effective lifesaving procedure for the patients with end-stage hepatic disease, in particular acute liver failure and hepatocellular carcinoma (HCC). The current waiting period for a cadaveric donor liver is much too long to benefit patients with these rapidly progressive diseases. Without ALDLT, it is unlikely that patients here will be transplanted before they develop fatal neurological or septic complications. In this instance, it is vital that the potential donor undergo additional counseling and psychosocial evaluation, as the urgency of the situation may not allow sufficient time to fully comprehend the risks involved<sup>19,20</sup>.

Previously, with the limited resource of cadaveric donor livers, it was important that the results for transplanting patients with HCC be comparable to those without malignant disease. As such, only patients with early stage HCC and decompensated cirrhosis were transplanted<sup>21,22</sup>. However, there have been reports that some patients with more advanced HCC may benefit from the procedure<sup>23,24</sup>. Recent studies have shown that transplantation is significantly superior to resection for the patients with HCC and cirrhosis<sup>25,26</sup>. With ALDLT, the current criteria for transplanting the patients with HCC in Asia are being greatly expanded. This is often combined with aggressive anti-tumour treatment that may include transarterial chemoembolisation or systemic chemotherapy.

Although ALDLT should still be considered a work in progress with a steep learning curve, the number of

such transplants is expected to increase substantially in Singapore in the next few years. Although we should continue to be vigilant in ensuring donor safety, our experience indicates that often family members are willing to accept far greater risks for the donor and recipient than the transplant team. A recent survey confirmed that the lay public would accept ALDLT for marginal outcome in the recipient, with donor mortality nearly 100 times the current rate<sup>27</sup>. It is clear that the risks of ALDLT deemed acceptable by the public will affect the future criteria for donor and recipient selection and must be taken into consideration by the medical community. ■

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