Personal Practice

LIVER TRANSPLANTS FROM LIVING DONORS

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In the west majority liver transplantation is from deceased donors. In the Far East most liver transplant is actually done from living related donors. In the past, when experience with hepatectomy was limited, liver transplantation did not progress because of lack of cadaveric donors. With hepatectomy becoming a safe operation, liver transplant from living donors is a good alternative. Although there is a risk to donor, LRLT has certain advantages over DDLT in our country such as optimum patient preparation prior to surgery, allows use of cadaveric organs when available, for patients with primary liver turnover, for adoptive transfer of immunity in patients with hepatitis B related cirrhosis and in acute liver failure. LRLT should be promoted and safeguards built in for donor safety.

Key words: Orthotopic liver transplantation, Living related transplantation, Donor hepatectomy, Cadaveric organs.

ORTHOTOPIC LIVER TRANSPLANTATION

ORTHOTOPIC liver transplantation is a very effective form of treatment for chronic liver disease as well as for acute liver failure. In 1996, UNOS reported over 27 000 liver transplant operations in US alone [1]. With progress in liver transplantation, important advances have been made in the fields of immunology, vascular surgery and laboratory services. In spite of all this liver transplantation has so far been slow to gain momentum in our country. This has mainly been because of lack of cadaveric organs. There is no dearth of talented surgeons, doctors and anaesthetists to carry out this operation successfully in our country.

The Human Transplant Act was drafted in 1994 to deal with two main issues, one was to legalize brain stem death and the second was to curb unrelated organ transplantation. It was hoped that with the diagnosis of brain stem death, there would be enough cadaveric organ donations so that unrelated transplantation would not be necessary. This hope has not been fulfilled so far. There have been pockets where cadaveric donation has been quite successful for example the efforts of Mohan and Forte in South India [2].

So while there will be shortage of cadaveric livers at least in the foreseeable future, should liver transplantation not be done in our country? India is not the only country where there is a shortage of cadaver organs. Countries like Japan, which recognised brain stem death only a few years ago, have had a flourishing liver transplant programme for years. Why should living related transplantation not be promoted in India? In many meetings, senior doctors from all over the country have decried LRLT as being very dangerous. In this article we will discuss what are the merits and demerits of LRLT in the Indian clinical context.

OVERCOMES ORGAN SHORTAGE

Living related transplantation opens up a limitless supply of organs for transplantation. Even in the West, where there is a much higher donation rate of cadaveric organs, many patients die waiting for an organ to become available. Currently, over 60% of renal transplants in USA are from living related source [3]. In certain situations living related liver transplantation seems to be the only solution for example in patients with fulminant liver failure and those with hepatocellular carcinoma.

DONOR HEPATECTOMY IS A SAFE OPERATION

Currently, living related kidney transplantation is not frowned upon because it is perceived that donor nephrectomy is a safe operation. Donor hepatectomy is also a safe operation in the hands of trained surgeons. Makuuchi reported no mortality in over 1000 liver resections in the year 2003 [4]. A total of 7 deaths have been reported out of over 4000 live liver donations in the world [5]. Possibly, two donor deaths have occurred in our own country [6]. Donor safety is an important issue and all safeguards must be put in place before we embark on a programme of living related transplantation. Training in hepatobiliary surgery is a must. Not only training in surgical skills is important but

also the ability to read CT pictures and accurate volumetry is equally important. The transection plane should be defined on the worktable prior to operation. Only centres, which have a reported liver resection mortality of less than 5%, should venture in to living related transplantation [7].Our experience has been that in the beginning, it is helpful to have two team members from an established centre to be around while the first few transplants are happening.

LRLT ALLOWS USE OF CADAVERIC ORGANS

Many centres for liver transplantation have opened up in the country and more are likely to open seeing the success of liver transplantation in the Western world. However if these centres do not do regular liver transplant work, it is quite likely that experienced and skilled surgeons will do a shoddy job if a cadaveric liver were to suddenly become available. It has been shown in numerous studies that high volume centres when they do complicated surgery, their results are much better than those of small volume centres [8]. To keep patients active on the cadaveric list it is important to do regular transplantation, otherwise patients will either die or will not have the confidence to undergo liver transplantation. Currently, the majority of donors in North India have come through the efforts of ORBO and AIIMS. However, they have not been able to use these organs, as it does not have a waiting list of potential recipients. LRLT allows active use of cadaveric organs.

LRLT ALLOWS OPTIMUM PATIENT PREPARATION

Many patients of chronic liver disease are generally in quite poor shape and even if a cadaver organ were to become available, it is unlikely that they can be taken successfully through liver transplantation. These patients are fluid overloaded, malnourished, or in dyselectrolytemia. They may have just recovered from episodes of sepsis either from the chest or from the abdomen. Diuretic overuse would have caused hyponatremia and deranged renal function tests. Sometimes they need months of preparation before they can even be considered for transplantation. There is therefore a problem of matching supply with demand. In the western world where health care is either state run or through medical insurance, these patients have access to good health care and remain in reasonable health while waiting for transplantation. Quite often even in the West, many patients will be suspended from the waiting list if they are not doing well. Moreover, liver transplantation has been around for much longer time and therefore patients are sent for transplantation even when their general condition is well preserved. We in India are yet to reach that stage. An analogy can be drawn from renal transplantation in India where it is very difficult to maintain patients on long-term dialysis. Patients prefer to have early kidney transplantation unlike in the West where patients have been maintained on long term dialysis for years.

LRLT IS IDEAL FOR MALIGNANCIES

Many investigators have now shown dramatic results after liver transplantation for hepatocellular carcinoma [9]. Currently there is debate whether cirrhotic patients with a tumour should have primarily resection or control of tumour with local therapy such as radiofrequency ablation, percutaneous alcohol injection or chemoembolization followed by liver transplantation [10]. Previously, many patients with cirrhosis and HCC would become untransplantable during the average 6-month waiting period for a cadaveric organ [11]. The option of LRLT has done away with the debate that scarce cadaveric organs should only be used for recipients with the best long-term results. In recent months there have been many reports of successful transplant for cholangiocarcinoma using neoadjuvant chemotherapy and radiotherapy [12]. Many transplants were done in Austria for metastatic liver disease as they had one of the highest cadaveric donation rates in the world [13]. Neuroendocrine tumours have also been successfully transplanted.

LRLT MAY BE RIGHT FOR HEPATITIS B RELATED CHRONIC LIVER DISEASE

Hepatitis B related chronic liver disease is quite difficult to manage post transplantation, as traditionally they have to be given hepatitis B immunoglobulins lifelong. This is quite an expensive therapy. With living related transplantation, there seems to be data that post-living related transplantation, there seems to be fewer requirements for immunoglobulins. ST Fan has reported that with LRLT hepatitis B patients can be transplanted without HBIG prophylaxis with a breakthrough rate of only 10% [14]. Further, as there is a high rate of lamivudine resistance if given longer than for 6 months, it is usually best to give lamivudine for less than 6 months and then transplant them [15]. This kind of planned activity is only possible with LRLT.

LRLT SUITABLE FOR OVERSEAS PATIENTS

Liver transplantation is a highly skilled operation and is not an operation done in many countries. As a result they often have to travel huge distances to have a liver transplant. The wait in countries where there is only cadaveric transplantation can be very long and sometimes patients die while waiting for a transplant. Overseas patients receive a liver only when there is no suitable native recipient for a cadaveric liver. Marginal livers or sometimes split livers are often used for transplantation. When a potential liver

transplant recipient comes to a foreign country, the wait for a cadaveric liver can be agonizingly long. Living related transplantation is ideal for overseas patients as they can come on a scheduled date for operation.

LRLT IDEAL FOR PAEDIATRIC PATIENTS

Pediatrics liver transplantation has had a long history of living related transplantation all over the world. Parents are keener to donate. Since a smaller volume of graft is needed, the donor operation is relatively simpler to perform. Results of paediatrics transplants are much better with centres reporting over 100 consecutive transplants with no 6-month mortality [16]. Cadaveric organs are in short supply and whenever they do become available there is enormous pressure from adult recipients for their transplantation. Theoretically, it is possible to split a cadaveric organ in to two and then use it for one adult and one paediatric recipient. Unfortunately, this is logistically very difficult to perform unless one shares organs between different centres. Although, this would be quite appropriate but is very difficult to establish as there are factors like inter hospital rivalry, patient allegiance to different hospitals and patient confidence in different doctors.

DDLT IDEAL FOR MULTIORGAN TRANSPLANTS

Living related liver transplantation can not be performed when recipients require more than one organ transplantation. For example, patients of primary hyper-oxaluria require both kidney and liver transplantation and therefore it is not right to retrieve part of liver and one kidney as well from a donor or for that matter from two separate donors. Similarly simultaneous kidney pancreas transplants can only be done from cadaveric organs. Deceased donor liver transplant is correct for these situations.

LRLT IS MOST SUITED FOR ACUTE LIVER FAILURE

Acute liver failure is a potentially fatal condition. Causes of acute liver failure in our country are viral hepatitis, drug reactions such as with antitubercular drugs and paracetamol overdose. There are now well laid criteria to predict who will recover spontaneously and who will need liver transplantation. For example, patients where the aetiology is not clear, when the patient is either less than 10 or more than 40 years of age, or when the prothrombin time is more than 50 or when the encephalopathy to jaundice duration is more than 7 days the outcome in patients of acute liver failure is poor [17]. These patients need to be considered urgently for transplantation. However, the majority of these patients will die if a cadaveric organ does not become available quickly. These patients need to be assessed urgently for a living related liver transplantation because cerebral oedema and sepsis will soon make them untransplantable.

LRLT IS MOST SUITABLE FOR PRIMARY NON-FUNCTION

Following cadaveric transplantation the primary non-function has been reported as high as 5% in the western literature. In India, the primary non-function rates are even worse. In our own centre, we have done four cadaveric transplants and we lost one graft because of primary nonfunction. Some grafts will also be lost because of hepatic artery thrombosis and some to acute rejection as cadaveric transplant seems to have a higher rate of rejection.

DDLT IS GOOD FOR TRAINING FUTURE SURGEONS

Deceased donor liver transplantation is very good for training of future hepatobiliary surgeons as the trainee learns to mobilise liver, is able to recognise arterial variations and also becomes familiar with abdominal anatomy. It helps them to be better surgeons. Further, cadaveric transplant is a much simpler operation and the atmosphere in the theatre is quite relaxed. Trainees can be supervised to do a liver transplant operation even if they have modest skills to start with.

OUR EXPERIENCE

Our liver programme started in the year 2001 when we did the first cadaveric liver transplant in our hospital. Since then we have done a total of 43 transplants with 37 long-term survivors. Of these, 43 transplants, 41 were from live donors and none of these donors have had any problem. Currently, all donors are alive and well. In the last one-year, 17 out of 20 of our LRLT are doing well. One cadaveric transplant was done in the last year and the recipient died because of primary non-function. We have shown that LRLT is a safe operation both for donor as well as the recipient.

SUMMARY AND CONCLUSIONS

LRLT is an important advance in liver transplanation in our country and unless the facts mentioned above are recognised by our health planners, lot of time and effort will be spent to promote cadaveric liver transplantation, which may not pay dividend at least in the short term. For example, although the focus should be to promote cadaveric donation, one must also look towards the East, in countries like Japan, Korea and Hong Kong for training in liver transplantation than towards the Western world. Both the activities must continue concurrently so that recipients are waiting on the list, cadaveric organs are not wasted and transplant surgeons can continue to push for organ donation

while doing active transplant work. In the end, if there are more cadaveric organs, living related transplant work would diminish, as certainly it is a more taxing operation.

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