Controversy

A deceased-donor liver transplant program must precede a living-donor program

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"Those who fail to read the mistakes of history are condemned to repeat them." – George Santayana

Liver transplantation is now a well-established therapeutic procedure for patients suffering from end-stage liver disease. In the last few years, partly as a response to increasing demand for organs and partly as a result of improved technical expertise, living-related liver transplantation (LRLT) has emerged as an option to the traditional deceased-donor transplant procedure. In most countries the living-related procedure has been introduced against the background of longstanding, active cadaveric programs, and the large majority of transplants are still performed from deceased donors. However, there is now a trend in some countries including India to initiate programs based mainly on the living-related procedure. Whilst this trend has already been established in some parts of the world, in the Indian context where liver transplantation is still in its early days, this is an opportunity time to examine whether it is the right way forward.

To understand the issues in this debate it may first be worthwhile to look at the historical evolution of the two procedures. In countries where liver transplants were pioneered, the operation was first performed from deceased or cadaveric donors. Over a period spanning almost three decades, the procedure was standardized, fine-tuned and gained wide acceptance. Protocols for perioperative management were laid down and validated. The results of the procedure improved dramatically from its inception in the 1970s to the 1990s. Most of these procedures were carried out in the developed world, mainly in North America and Europe.

In 1989 the living-related transplant procedure was described from Brazil and Australia. In the early 1990s centers with a strong background of cadaveric liver transplant and/or liver surgery started performing the living-related procedure in small numbers in pediatric patients. In a prospective, comprehensive, review board-supported protocol at the University of Chicago, 20 donor-recipient pairs underwent transplantation. This study incorporated elements like research ethics consultation, assignment of a donor advocate, demonstration of field strength of the institution and physician team prior to undertaking the procedure, and a cooling-off period with multiple steps in the informed consent process.

However the living-related procedure really gained numbers in the Oriental countries where either there was no law permitting removal of organs from cadaveric donors, as in Japan, or cadaveric donations were very rare for cultural reasons, as in Hong Kong. The other feature common to these countries was that they all had large experience in resectional surgery of the liver mainly due to the wide prevalence of hepatocellular carcinoma. In the mid 1990s in the USA multiple small centers, all of which did not necessarily have a background of cadaveric transplantation, started performing LRLT. On the other hand in Europe, where LT is performed as a component of national health programs (and therefore is strongly regulated) LRLT has been performed in very limited numbers and centers. In the UK, which pioneered liver transplantation in Europe, the role and relevance of LRLT is still being debated and one of the largest LT units in Europe, the Queen Elizabeth Hospital at Birmingham, has as yet not ventured into this procedure. Similarly many centers with a strong record of deceased-donor transplants have been slow and cautious in embarking on LRLT.

Most centers starting the LRLT procedures first applied it to children where the donor procedure is less formidable and therefore less risky. Also, there was a higher need for this procedure in children since age-matched cadaveric donors were not easily available. It was only after the procedure had been performed in children with success with a low incidence of donor-related problems that gradually adult-to-adult procedures were begun. The unit at Kyoto University in Japan, considered a pioneer in LRLT, performed their first adult-to-adult procedure only after performing around 200 pediatric procedures.

However, contrary to the pediatric experience, the introduction of adult-to-adult living-donor liver transplantation did not benefit from a prospective, well-defined, single-center study. In fact, the majority of institutions performing adult-to-adult living-
donor liver transplant did so without ethics committee approval. Consequently the risks and benefits associated with the procedure were difficult to quantify and were not applicable across programs. Soon, grave concerns about the haste with which the procedure was being performed were being expressed by the transplant community itself.

The single most important difference between the deceased- and living-donor procedures is the performance of a potentially life-threatening operation on a healthy person. Whilst the issue of donor safety is not the focus of this debate, it is relevant to mention that besides continuing to be a critical ethical issue, donor mortality has the potential to destroy the public image and acceptance of liver transplantation. The much publicized donor death in Mount Sinai Hospital in New York a few years back not only led to a huge public outcry but also affected organ donation rates in the US. And if there are donor mishaps early in the evolution of LT in any country this is likely to do significant damage to the development of liver transplantation as a whole. The issue of donor mortality is still plagued by hazy information and lack of transparency. The precise worldwide number of donor deaths is as yet not clear and it is accepted by many experts that the figures are often underestimated. Although there is debate over the precise figure it is significantly higher than that for kidney donors.

Equally important is the morbidity of the donor operation, especially the right lobe resection for the adult donor. Reported donor complications have ranged from liver failure needing transplantation to bile leaks and rebleeding needing re­laparotomy. It is estimated that around 20% of LRLT donors have some complication, some of which can cause significant morbidity.

When LRLT is proposed as an option to cadaveric LT, it is often not appreciated that the procedure of LRLT by its very nature increases the complexity of the operation and in turn increases the stress on the entire team. For one, since the size of the liver being transplanted is always smaller than what is needed, it is in a sense a suboptimal graft. Also, the anastomoses that need to be performed in the recipient procedure involve smaller vessels and more complex reconstructions with resultant higher rates of primary non-function and mortality. Thus for any institution or team starting a LT program to start with LRLT is like jumping into deep waters before practising the basics of swimming in the shallow part of the pool. And to start with adult-to-adult LRLT is like diving into a pool without knowing swimming at all.

The main argument of those who support the idea of starting LRLT programs before the establishment of cadaveric programs in countries like India is likely to be the lack of cadaver donors. This argument needs to be carefully examined in the light of actual experience gained over the last few years. In our institution in Mumbai where a concerted effort was initiated five years back with the appointment of a dedicated transplant coordinator and education of ICU staff, the overall consent rate (proportion of those giving consent out of those approached) is around 60%, a figure close to that in many Western countries. There have been 21 cadaver donations over the last 5 years. Amongst these, there was consent for liver donation in fifteen. However of these, only 5 livers have been used. In 4 of the donors the liver was considered unusable and in the other 6 the liver was not utilized because of lack of availability of an appropriate recipient! All through Mumbai there have been approximately 50 cadaver donations in the last 5 years. From these, only 8 livers have been used. Again, in a large number of these donors the livers were not used because of the lack of an appropriate recipient on the local waiting list or logistic problems in sharing organs with other institutions and cities.

From this limited but significant experience it seems that if there is a concerted effort by any institution to promote organ donation and identification of brain-dead donors by ICU personnel, the consent rate is likely to be fairly high. There is no reason to believe that this cannot be replicated in other parts of India. In fact in cities like Chennai and Bangalore, cadaveric kidney transplants have been performed in much larger numbers than liver transplants. It is unusual for donor families to consent for kidney donation and not for liver donation. It seems therefore that cadaveric liver transplants are not being performed not because of unavailability of cadaver organs but because of lack of infrastructure, recipients or organ-sharing mechanisms, all potentially correctable problems.

To further understand the reasons behind the jump to LRLT, it may also be worth looking at the setting in which living-related programs are presently developing in India. It is no coincidence that most of these programs are in the private sector where the market is the prime determinant of how specialty medicine develops. Thus transplant teams have to deliver quickly and are in a competitive en-
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Deceased-donor must precede living-donor liver transplant program. Also liver transplantation is becoming a part of the medical tourism phenomenon, attracting patients from other countries, especially South Asia. Whilst all this is an inevitable fallout of the way health care is evolving in liberalized India, it is prone to practices that may produce immediate results but can lead to mishaps and therefore are not sustainable in the long term.

There have already been donor deaths and major donor morbidity in India. Whilst this is a worldwide phenomenon, what distinguishes the Indian situation is the secrecy that surrounds such incidents. It is not difficult for anyone familiar with the style of practice of medicine in India to understand that the solidity of two critical components of the ethical basis of LRLT, viz., donation based on true bonding with the recipient and genuine informed consent, will be severely tested. The practice of hepatobiliary surgery is still limited in India and the importance of a broad base of hepatobiliary surgical expertise in the safe performance of LDLT has been emphasized by experts. It may also be pertinent to mention that the surgeons leading LRLT programs in India have essentially been trained in cadaveric-based programs in the UK.

Whilst the debate on jumping to LRLT before the establishment of a cadaveric program is relevant internationally, it is especially important to the Indian scenario where on one hand liver transplantation is unlikely to make a significant impact on the management of the huge numbers of patients with end-stage liver disease and where on the other, health care is largely unregulated. It is one thing to evolve a stand based on logical stepwise argument and it is another to create arguments having already been committed to a stand. In the counter-argument in this issue one cannot help feeling that it is more of the latter than the former.

References
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