

Efforts to expand the donor pool for liver transplantation

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Abstract

Liver transplantation has become a victim of its own success in that there are no longer enough suitable livers for transplantation while at the same time the indications for transplantation increase. Efforts to expand the number of recipients who benefit from this life-saving procedure are being made, in particular through the use of split grafts and live donors. However, such grafts are associated with increased morbidity and mortality related to their reduced size.

Introduction and context

Liver transplantation is currently the treatment of choice for end-stage liver disease, including acute liver failure and some metabolic disorders [1]. However, there is a mismatch between potential recipients requiring transplantation and the availability of suitable livers, resulting in the deaths of patients on the waiting list. This has been compounded by a broadening in the accepted indications for transplantation despite reductions in those transplanted for chronic viral hepatitis [2]. For example, it has been shown that older recipients and those with other medical problems such as obesity can also do well and benefit from transplantation [3]. A further compounding factor has been a reduction in cadaveric donors from road traffic accidents as road safety has improved over the last 20 years. Accommodating this increase in potential recipients requires an increase in the donor pool and methods to achieve this include the use of split livers, in which one liver is used for two recipients, and live donation.

Recent advances

Surgical splitting of a graft allows one liver to be used for two recipients. The increased surgical expertise such techniques demand has contributed to the increasing use of live donation of a partial liver graft. Split liver transplants (SLTs) conventionally generate an extended

right graft consisting of segments I and IV-VIII suitable for transplantation in adults and a left lateral graft of segments II and III for use in a child. The use of SLT and live donation has greatly reduced mortality of children waiting for liver transplantation. One limiting factor in SLT and live donation is the size of the graft for adult recipients. In SLT, a full right (segments V-VIII) and full left (segments I-IV) can be created but often are not adequate in size for two adult recipients. If the graft is too small for the recipient, the metabolic demands for the individual are not met and small for size syndrome (SFSS) develops. This can be seen after both cadaveric and live donations. SFSS is characterised as the triad of postoperative ascites, cholestasis, and coagulopathy [4], which is associated with increased mortality. Small for size can be determined as either a graft weight/recipient weight ratio of less than 0.8% [5] or a graft volume/standard liver volume ratio of less than 40% [6].

Increased understanding of SFSS has led to the recognition that factors other than size, in particular the graft haemodynamics and quality, contribute to SFSS [7]. Portal hyperperfusion and impaired drainage in small grafts contribute significantly to SFSS and can be modulated to reduce portal venous inflow and ensure adequate outflow (Table 1), thereby allowing the safe transplantation of smaller grafts [8]. Even in cases in

Table 1. Methods to modulate graft haemodynamics

Inflow	Outflow
Splenectomy Splenic artery ligation	Wide anastomosis Drainage of all segments using interpositional grafts if required
Portosystemic shunting	

which SFSS is established postoperatively, delayed splenic artery occlusion can be performed either at reoperation or radiologically with improvement in graft function [9].

Another approach to overcome the size issue is the use of left lateral segments from two different donors. This has been pioneered in Seoul to ensure adequate hepatic volume to the recipient [10,11]. It may be useful in situations in which the donor left lateral segments are insufficient to meet the demands of the recipient and the donation of the right hemi-liver would leave the donor with an insufficient residual liver volume. This does increase the risk of performing a procedure to two otherwise healthy donors. Alternatively, left lateral segments from a living donor can be transplanted together with the left segments from a cadaveric donor (with the right-side graft used on its own in another adult recipient); however, there are significant logistical barriers [12].

Auxiliary liver transplantation is another method in which small grafts may be used. The recipient's native liver is left *in situ* either completely or partially, and usually a reduced graft is transplanted orthotopically (due to inferior outcomes from heterotopic transplantation [13]). This has been used primarily in acute liver failure as a means to provide time for the recipient's own liver to recover [14]. Following recovery, the graft may be removed or alternatively immunosuppression may be stopped.

The main technical consideration with auxiliary grafts is haemodynamic, with circulatory competition between the graft and native liver. To improve the circulation in auxiliary liver transplantation, reno-portal anastomosis that avoids disturbing the vasculature to the native liver has been described [15]. Remarkably, in some cases, the auxiliary graft has been successfully retransplanted to another recipient following recovery of the native liver [16].

Implications for clinical practice

With increased understanding of the factors associated with SFSS, it is possible to use smaller grafts in recipients with acceptable outcomes, especially where there is a

shortage of suitably donated organs. This has special pertinence in live liver donation, in which there is a real risk of causing severe morbidity and mortality in a healthy individual. Due to the size factor, the larger right hemi-liver may be donated to larger recipients. However, this has an increased risk compared with left-sided donations and has resulted in at least three reported cases in which donors have subsequently required liver transplants themselves after being left with inadequate liver volumes [17].

Recipient selection is another critical factor to be considered when deciding on whether to transplant a partial graft with the associated higher risk of failure or dysfunction. A balance must be struck between the risk of transplanting the graft and the risk that the patient will deteriorate on the waiting list. This dilemma can be framed in the context of whether one considers the best outcome for an individual recipient or the best use of the graft. Generally, patients with lower MELD (Model for End-Stage Liver Disease) scores have better outcomes, especially with the use of marginal, live donor, or split grafts as they can tolerate initial graft dysfunction better. However, by definition, those with higher scores are those more urgently in need of grafting, and despite the higher risk of graft dysfunction and failure, the benefit to the recipient may be greater [18,19]. The donor shortage in liver transplantation has led not only to surgical innovations to expand the donor pool but also to complex ethical issues surrounding patient selection, marginal organ donation, and liver donation, and future work needs to focus on optimising outcomes for patients while making the best use of the scarce donor resource.

Abbreviations

SFSS, small for size syndrome; SLT, split liver transplant.

Competing interests

The authors declare that they have no competing interests.

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