Liver transplantation from non-heart beating donors

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An alternative to transplantation is lung volume reduction surgery. This reduces the size of the lungs and thereby can restore the lost circumferential pull on small airways, reduce hyperinflation, and can, on average, increase FEV_1 by about 50% in most patients.[4–8 w4] The most destroyed areas of the lung, easily identified preoperatively by high resolution computed tomography and V/Q scanning, are removed with linear staplers. This allows re-expansion and return to function of the adjacent more normal lung. But such surgery is only palliative and is associated with substantial morbidity; hence it is suitable only for selected patients needing temporary improvement in symptoms and quality of life.[4–7] Only those patients with poor exercise capacity and with emphysema localised to the upper lobe survive longer after surgery than after medical treatment.[8]

The indications for lung volume reduction surgery and transplantation overlap considerably. Younger patients with clear contraindications to lung volume reduction (such as increased pulmonary artery pressure and hypercapnia) should undergo lung transplantation, while older patients and those with contraindications to transplantation should undergo volume reduction surgery. The choice should be taken on a case by case basis, after careful discussion with the patient, keeping in mind that volume reduction surgery could also be used as a bridge to lung transplantation.

There is preliminary evidence for minimally invasive surgery such as airway bypass and bronchoscopic lung volume reduction. Both techniques aim to improve respiratory mechanics through functional exclusion of emphysematous areas of the lung without exposing patients to the risks of a conventional operation.

Airway bypass aims to improve respiratory mechanics by creating new exit pathways for the air trapped in emphysematous lungs. Under bronchoscopic guidance the surgeon punctures the wall of the segmental bronchus and inserts a stent, thereby creating an internal bronchopulmonary communication for expiration. The aim is to reduce hyperinflation, improve respiratory mechanics, and alleviate dyspnoea. The procedure has been progressively modified to improve results and prolong the period of patency of the stents. The evidence for airway bypass is at an early stage though, comprising mainly an experimental model[9] and a study of safety and efficacy in 15 patients having lobectomy for lung cancer or lung transplantation for emphysema.[10]

In bronchoscopic lung reduction surgery, one-way valves are placed in the segmental bronchi supplying the most hyperinflated parts of the emphysematous lung. Deflation and sometimes atelectasis of the target area prevent air entering from the target area of the lung while allowing air and mucus to exit. Pilot studies based on small case series show a functional improvement in selected groups of patients with heterogeneous emphysema,[11 12] and a prospective multicentre trial is comparing bronchoscopic lung volume reduction surgery with maximal medical treatment. Although the early evidence for bronchoscopic lung volume reduction is encouraging, it will take long term follow-up and randomised controlled studies to clarify the role of these interventions.

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Liver transplantation from non-heart beating donors

A promising way to increase the supply of organs

Since its inception in the 1960s liver transplantation has seen such improvements in patient selection, surgical technique, perioperative care, and immunosuppression that it is now the treatment of choice for patients with liver failure. Indeed, like most other solid organ transplants, liver transplantation has become a victim of its own success with more patients now on the waiting list as the number of organ donors declines. Among the various approaches to increasing the number of donors, one of the most promising is the use of non-heart beating donors.

In general, liver donation rates are poor in the UK (13 per million population compared with 33 per million in Spain, the best in Europe; www.uktransplant.

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org). To use this scarce resource most effectively clinicians are restricting access to transplantation to patients with a 50% chance of survival at five years. This restrictive listing excludes many patients, particularly those with hepatocellular cancer and older recipients. Even so the supply is not able to meet demand. In the UK about 60 people die on the waiting list each year and up to 80 are removed from the list as their condition deteriorates (www.uktransplant.org).

To increase the number of organs available for liver transplantation, centres have used marginal donors,[1] or split liver transplantation, or living donor transplants. Split liver transplantation has had a dramatic effect on reducing paediatric waiting list deaths but has had no impact on the situation for adults. In the UK living donor liver transplantation has not been widely adopted because of concerns about the safety of donors and morbidity in recipients. However, a recent meeting of the UK Liver Transplant Group reached consensus on encouraging more units to develop this expertise over the next few years.

Another source of organs is the non-heart beating donor. Historically, there have been concerns that organs retrieved from non-heart beating donors are "second class," but continued enthusiasm from a few specialist centres has resulted in a gradual improvement in outcome, especially in renal transplantation.[2 3]

The first international workshop on non-heart beating donors in Maastricht in 1995 devised four categories of non-heart beating donation, though this has recently been revised to five categories.[4] Essentially the donation is "uncontrolled" (Maastricht category type I and II) or "controlled" (Maastricht category III and IV), depending on the circumstances of cessation of cardiopulmonary function.

The fundamental distinction between non-heart beating donors and conventional heart beating donors is the diagnosis of death. In a non-heart beating donor diagnosis is by cardiac criteria, whereas in a heart beating donor diagnosis is by brain stem criteria. The beating heart donor is always ventilated before death and the heart remains beating at the time of retrieval, thus virtually eliminating any warm ischaemic injury to donor organs. With a non-heart beating donor (in controlled circumstances) the organs are retrieved after a "stand off" period of five minutes during which death is certified. The organs are therefore subjected to a variable period of warm ischaemia, which is detrimental to outcome and predisposes to delayed graft function[5] or at worst to complete non-functioning of the graft. After renal transplantation, non-function is not so much of a problem as there is always the back-up of dialysis, but in the case of liver transplantation the patient has to be urgently relisted for surgery.

Despite enthusiasm for non-heart beating donation in renal transplantation, its development in liver transplantation has been more difficult. The early results were far worse than those with beating heart donors. The main reason was the non-selective approach to using uncontrolled donors that were subjected to a prolonged period of warm ischaemia. Not surprisingly, early one year graft survival rates reported from Pittsburgh were less than 20%.[6] Nevertheless, with judicious donor selection, a recent analysis from the United Network of Organ Sharing showed a three year survival of 63% compared with 72% for beating heart donors.[7] At the second European meeting on transplantation from non-heart-beating donors the combined UK experience (King's, Leeds, Newcastle) showed an acceptable one year graft survival of 84% (K R Prasad, London 2004).

The major problems in non-heart beating donor liver transplantation continue to be higher rates of primary failure (12% *v* 6%) and biliary complications than those from heart beating donation.[8] However, several approaches are being explored to improve these results. One strategy is rapid in situ cooling of donor organs, particularly in the uncontrolled donor, where the duration of warm ischaemia is unpredictable. In most cases this would mean performing the cooling without consent from the next of kin as they are invariably not contactable at the time of cardiac arrest in the uncontrolled setting. The Spanish have achieved good results using a cardiopulmonary bypass model.[9] This is a grey area which has not been addressed by the UK Intensive Care Society.[10] It is not clear whether consent is needed from the next of kin or not, but the forthcoming Human Tissue Act will clarify this important issue. There have also been encouraging results from an experimental model of normothermic preservation of livers involving perfusion ex vivo at body temperature using a modified cardiopulmonary bypass circuit.[11] The British Transplantation Society has published guidelines on non-heart beating donation.[12]

A reasonable prediction would be that non-heart beating donor livers have the potential to contribute about 10-20% more organs to the donor pool, a challenge which the medical community has to take up.

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