For over 50 years those who experience vital organ failure have had a chance to live relatively normal lives thanks to transplant surgery. However, the shortfall between recipients and donors continues to rise.

Organ transplantation
donation and surgery

By Reena Popat, MSc, MRPharmS

Since 1954, when the first successful kidney transplant was performed, transplantation surgery has dramatically changed the lives of people with end-stage organ failure. Transplantation still continues to evolve and, alongside innovations in surgery and increasing knowledge of the role of immunosuppressive medicines, the number of transplants being performed has increased. In addition, patient and graft survival rates have improved.

Sources of organs

Organs are sourced from two categories of deceased donors: heart-beating (HB) and non-heart-beating (NHB). HB donors are those who meet the criteria of brain-stem death but whose circulatory system is still working. NHB donors are becoming increasingly common and are classified into five subcategories according to Maastricht criteria (see Box 1, p42). NHB organs have prolonged warm ischaemia time (ie, the time that the organ remains at body temperature after loss of blood supply before it is cooled or reconnected to another blood supply), which often results in delayed graft function. Nevertheless, their medium- and long-term outcomes are comparable to those for organs retrieved from HB donors.

There is an increasing number of living donors who have contributed mostly to transplantations for patients with kidney or liver failure. Living donor kidney transplantation is now an established practice and represents nearly 50% of the workload in most renal transplant units. The major advantages of living donation are that it generates the possibility of pre-emptive transplantation (ie, when a transplant is performed before the patient reaches end-stage organ failure) and it has higher success rates than transplants using deceased donors’ organs. Furthermore, the risks attributable to the donor are minimal thanks to modern surgical techniques.

Despite an established organ donation scheme in the UK, there is an increasing shortfall in the number of organs available for transplantation — mainly due to the rising number of patients on transplant waiting lists (see Figure 1, p42). Recent statistics from NHS Blood and Transplant (NHSBT) suggest that, at present, around 10,000 people in the UK need a transplant. Of these, around 1,000 will die each year waiting for an organ.2 These statistics are a result of low organ donation rates in the UK compared with other European countries: around 13 donors are found per million of the UK population per year; in Spain, 35 donors are found per million of the population per year.3

To tackle the issue of organ shortages, an organ donor task force was created by NHSBT in December 2006 to...

SUMMARY

Organ transplantation is evolving and its success rates are ever increasing thanks to new technologies and innovative practices. However, a shortfall remains between the number of transplants needed and the number of suitable organs available.

Kidney transplants are the most common and have lower rates of graft rejection and patient mortality compared with other types of transplant (ie, heart, lung, liver or pancreas). However, the lessons learnt through renal transplantation have served to inform all types of transplant and increase patient outcomes across the board.

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Kidney
Several medical conditions can cause renal failure, including diabetes, hypertension, polycystic kidney disease and prolonged use of non-steroidal anti-inflammatory drugs. Renal failure is the only type of vital organ failure where life can be sustained without transplant (through dialysis). However, dialysis is not without complications; transplantation is associated with lower rates of morbidity and mortality and costs £25,000 per year less than does dialysis during the second and subsequent years after transplant. Notably, 3% of the total NHS budget is spent on end-stage renal failure services.

Before transplantation, blood group compatibility and cross matching is carried out routinely to prevent graft rejection. This involves mixing blood samples taken from the donor and the recipient. If antibodies to the donor’s human leukocyte antigen (HLA) are generated in the mixture, this is termed a “positive cross-match.” In such circumstances, the recipient is not a suitable candidate to receive the donor’s organs because hyperacute rejection of the organ is inevitable. When antibodies are not generated (a negative cross match), the patient is suitable for transplant.

Kidneys are allocated according to several factors, including the number of days a recipient has been on the waiting list and the age difference between the recipient and the donor. Paediatric recipients and those with HLA that is compatible with the donor are favoured.

Transplant surgery usually involves one kidney (although double kidney transplants have been performed). In most cases the native kidney is not removed unless there is a risk that it will affect the transplanted kidney. Renal transplantation has excellent outcomes: graft survival after one year is 95%; after 10 years it is nearly 60%. During 2008 over 2,000 renal transplants were performed in the UK.

Technological advancement Renal transplantation is at the forefront of innovations in transplantation and has surmounted many obstacles. Traditionally, transplantation could not be performed if the recipient’s blood group or HLA classification was incompatible with those of the organ donor. Now, patients who are incompatible with potential living donors can undergo planned antibody removal by undergoing:

- Plasma exchange — a process that removes plasma and antibodies from the blood (the plasma needs to be replaced)
- Immuno-absorption — a process that removes antibodies only from the blood

The availability of new immunosuppressants that target antibody-mediated rejection and the use of immunoglobulin have helped to increase the rate of transplant success, particularly among such recipients (see accompanying article, p48).

High number of transplants An organ-sharing scheme has been created whereby live incompatible donors/recipients are matched with compatible ones so that transplants can be performed. In addition, a limited amount of altruistic or non-directed donation takes place (ie, when individuals give up a kidney without dying or being asked).

The use of NHB donors is highest for renal transplantation, which has increased the numbers of transplants performed. The knowledge generated from this work has helped to increase the number of other organ transplants performed, such as for liver and pancreas.

Heart
In adults the most common causes of heart failure requiring transplantation are coronary artery disease and cardiomyopathy. A small number of paediatric patients also require transplants due to congenital heart disease.
Patients must fulfil all of the following criteria to qualify for a heart transplant:

- End-stage heart disease with a life expectancy of 12–18 months
- Stage III or IV heart failure as classified by the New York Heart Association
- Condition is refractory to medical/surgical therapy
- Patients are medically and surgically fit to receive a transplant (usually, this means they need to be under 60 years of age)

When a heart becomes available, it is allocated to the most suitable patient based on the size of the organ (ie, an organ from an adult donor is only suitable for an adult recipient) and blood group. However, a third of donated hearts go into a centrally run urgent allocation system to ensure the most critically ill patients are prioritised. Once a suitable recipient is identified and accepts the organ, he or she is anaesthetised and put onto bypass. The new heart must be sewn into the recipient's chest cavity within four hours of it being removed from the donor to prevent it suffering ischaemic damage.

Approximately 120 patients receive a heart transplant annually in the UK, although the demand is much higher. Such low numbers are attributed to the shortage of suitable organs (with the age of donors increasing, many potential organs are diseased).

Post-transplant life expectancy at one year is 85–90% and at 10 years is 50%. Failure of the donated heart to function immediately after transplantation is the primary cause of death during the first year.

**Other surgical options** Due to the shortage of donors, there is increasing use of left-ventricular assist devices (LVADs) — mechanical pumps that are surgically inserted into the chest cavity. These devices take blood from the failed ventricle and pump it into the aorta, thus supplementing the heart’s function. They have been used primarily as a bridge to transplantation for those waiting for a suitable heart to become available. However, there is increasing evidence for their use as an alternative to transplantation.

**Liver**

Several conditions lead to patients developing respiratory failure and thus the need for a lung transplant. These include cystic fibrosis, emphysema, chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis and pulmonary hypertension. In some cases combined heart and lung transplants are conducted where irreversible damage has occurred to both organs (eg, due to pulmonary hypertension).

Similarly to heart transplantation, recipient-matching is done once an organ becomes available based on the size of the organ and blood group. However, unlike for heart transplants, there is no national system for lung allocation. Instead, each transplant centre (there are five adult lung transplant centres in the UK) will assess its own patients to determine which is most in need of a transplant when an organ becomes available. Two types of lung transplants can be done:

- Single lung transplant — the preferred option in patients where the remaining lung in the recipient cannot adversely affect the function of the new lung (eg, emphysema and lung fibrosis)
- Bilateral lung transplant — the only type of lung transplant that can be used for patients with cystic fibrosis and the most common type performed in the UK and abroad (however, it is associated with higher mortality risks for the recipient than a single lung transplant)

Approximately 130 lung transplants (five of which were heart and lung transplants) were conducted during 2008 in the UK, although nearly double that number of recipients is currently waiting for a transplant. Unfortunately, due to the nature of lung failure, 20–30% of patients waiting for a transplant do not survive beyond 12 months. Post-transplant one-year survival rates are 90%, but only 50% of recipients survive for 10 years or more.

Partial lung transplantation from living donors has been performed in the UK (two were performed in 2007) and could benefit some patients who are unlikely to receive a lung from a deceased donor in time. Only a small number of transplants have been performed to date but, so far, the procedure is considered safe.

**Lung**

Lung failure can occur as a result of acute disease (following fulminant hepatitis or paracetamol overdose) or chronic disease (eg, primary biliary cirrhosis, alcoholic liver disease, cirrhosis from hepatitis B or C, and primary hepatocellular carcinoma).

Patients diagnosed with acute liver failure have a prognosis of less than three days unless they receive a liver transplant and are prioritised onto a “super urgent” waiting list. (Patients with primary liver graft non-function or early hepatic artery thrombosis are also on this list.) If there is no suitable recipient on the super urgent list when an organ becomes available, the organ is allocated according to the NHSBT nationally agreed sharing scheme. This considers recipients’ age, clinical condition and how far they are from the centre where the organ was retrieved.

UK guidelines specify that patients should only be accepted for transplantation if they have at least a 50% probability of surviving, with an acceptable quality of life, for five years after transplantation. The guidelines also

**Transplant tourism**

Because of shortages in available organs in the UK, some people seek transplant donors overseas. This “transplant tourism” occurs in developing countries, such as the Philippines, India, Pakistan and Bangladesh, where individuals are willing to sell a kidney for £1,000.

Transplant tourism has been banned in many countries but illegal activity still continues while the demand for organs in developed countries exceeds availability.

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state that should a patient's condition deteriorate while waiting for a liver to an extent that these criteria are no longer met, the patient should be removed from the list. In the case of alcoholic liver disease (ALD), there is particular controversy. ALD is the highest cause of liver failure in Europe and many believe that offering liver transplants to such individuals is a waste of a scarce resource due to the high risk of relapse post transplant.

Therefore, UK transplant centres have implemented a "six-month rule" that requires patients to abstain from alcohol for six months before being allowed onto the transplant waiting list. The reasons for this are to reduce the risk of post-transplant relapse, to improve postoperative recovery and to give patients the opportunity to recover spontaneously — thus avoiding transplantation. However, it is argued that this rule is unfair on those patients who cannot survive six months without a transplant.

Once a patient has been listed and a donor found, the donor's liver can be removed and transplanted in one of three ways:

- Whole liver
- Split liver — the whole liver is divided into two segments, the larger used for an adult and the smaller used for a child or small adult
- Cut down liver — only part of the liver is removed and transplanted

The method used depends on the needs of the recipient. Live liver transplantation, where a lobe of the liver from a living donor is removed and transplanted, is also conducted — particularly when the recipient is a child. However, there have been eight donor deaths reported worldwide following this procedure, resulting in a donor mortality rate of one in 300.

Liver transplants can be divided into three classifications:

- Orthotopic — the recipient's liver is removed and the new liver put in its place
- Heterotopic — the native liver is left in place and the new liver is put elsewhere in the abdomen
- Auxiliary orthotopic — part of the native liver is removed and a split liver segment is implanted in the space created

Over 600 liver transplants were performed in the UK during 2008. Over 90% of recipients survive beyond one year and 75–80% survive beyond five years (although the survival rate varies depending on the cause of liver failure).

Pancreas

When a pancreas is unable to secrete insulin, this results in type 1 diabetes. Patients with type 1 diabetes can suffer severe long-term complications such as retinopathy and nephropathy. Some patients with renal failure caused by diabetic nephropathy require a renal transplant. To reduce the potential for diabetic complications after transplantation, recipients can be considered for pancreas transplantation, either simultaneously with their renal transplant or afterwards. Pancreas transplants have also been performed in patients suffering life-threatening complications of insulin therapy, such as hypoglycaemic unawareness. However, such transplants are not carried out often in the UK.

Transplant surgery and lifelong immunosuppression are associated with complications that, for many patients, can be more serious than the risks associated with long-term insulin therapy. Consequently, most patients with type 1 diabetes are unsuitable for this type of surgery. Over 200 pancreas transplants were performed in the UK during 2008 and 85% of patients did not require insulin treatment for the first year after the transplant.

Research into the transplant of pancreatic islet cells is also being carried out, however success rates so far are lower than for whole pancreas transplants. Research into stem cells and genetic engineering could improve success rates of islet cell transplants.

Conclusion

In the UK there remains a chronic shortage of suitable organs available for transplantation. The work of the NHSBT organ transplant taskforce is central to increasing organ availability to match the number of patients on transplant waiting lists.

References