Kidney transplantation

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Abstract

Renal transplantation is well established as the treatment of choice for selected patients with end stage renal failure. A renal transplant recipient can enjoy an improved quality of life while benefiting from a reduction in the mortality associated with long-term dialysis. However, the success of transplantation is limited by the disparity between an ever growing demand for organs and an insufficient supply of organs. Expansion of the organ donor pool has been achieved through increased utilization of living donor kidneys in paired and domino transplant schemes, transplantation across HLA and ABO boundaries, as well as a greater acceptance and consideration of extended criteria allografts. While 1-year graft survival rates are significantly higher than a decade ago, the rate of chronic graft loss after the first year remains substantial. The surgical procedure can be challenging due to operating on recipients with multiple comorbidities, an increasing incidence of obesity as well as utilizing allografts with complex vascular anatomy.

Keywords Immunosuppression; kidney donation; kidney transplantation; transplant immunology

History of renal transplantation

In 1906, the first recorded transplant occurred in Lyon when Mathieu Jaboulay transplanted pig and goat kidneys on to the arm or thigh of patients with chronic renal failure. Unsurprisingly, each kidney worked only for an hour. Twenty years later, the first human kidney allograft was performed by Yu Yu Voronoy, a Soviet surgeon working in the Ukraine. The kidney was obtained from a donor dying of a head injury and was transplanted into the thigh under local anaesthetic. The donor and recipient were blood group incompatible, and the kidney never worked. The patient died after 2 days; however, at post-mortem the transplant vessels were found to be patent. In 1954 the first twin-to-twin transplant was performed in Boston. Its success led to others being performed over the following years. Many of these recipients are still alive today. Nevertheless, it was not until the 1960s when immunosuppressive agents such as prednisolone, mercaptopurine and azathioprine were introduced that kidney transplantation was facilitated as a successful treatment for chronic renal failure.

Renal transplantation in the UK

At present, more than 6000 patients are awaiting kidney transplants in the United Kingdom which represents 100 patients per million population. Adult patients wait on average 1156 days for a kidney transplant. Twenty percent of patients registered on the waiting list are transplanted within the first year, while 64% receive a kidney within 5 years of being listed. In the last year (1 April 2012 and 31 March 2013), 1750 deceased donor transplants and 1060 live donor operations were performed.

Indications for renal transplantation

Patients are considered with chronic kidney disease stage 5 (eGFR <15 ml/min/1.73 m^2) and once they fulfil medical criteria for major surgery and long-term immunosuppression. Occasionally, transplantation may also be considered in patients with an eGFR >15 ml/min/1.73 m^2 if they are suffering significant uraemic side effects. In those patients with a previous malignancy (excluding non-melanoma skin cancer), the guidelines stipulate postponing surgery for a period of 2–5 years depending on the type of malignancy and how aggressive it is. The age of the recipient is not a limitation on the decision to transplant, however, age-related comorbidity is an important consideration in the decision to proceed with transplantation.

Outcomes

Multiple studies have demonstrated that patient survival is better with renal transplantation than on dialysis. The largest study based on the United States Renal Data System (USRDS) demonstrated a lower annual death rate among transplant recipients compared with patients on the waiting list with improved survival observed amongst diabetics and in all age groups. The reasons for improved survival are unclear. It has been hypothesised that an improved clearance of uraemic toxins coupled with a lower pro-inflammatory and/or oxidative state as seen in chronic renal failure patients, may be partly responsible. In diabetic patients, transplantation restores near normal renal function which reduces the circulating levels of glycosylation products thus decelerating the progression of microvascular disease.

Patient survival post-transplantation depends on a number of factors; the type (living/deceased) of graft, the age of the patient and the spectrum and severity of a recipient's comorbidities. The leading cause of death post-transplantation remains cardiovascular disease with one third of cases arising from acute myocardial infarction. The highest number of deaths from cardiovascular causes occur immediately post-surgery. It also accounts for 30% of graft loss from death alone.

Other causes of death include infection, related to the levels of immunosuppression and malignancy.

Graft survival after first adult kidney transplant (2005–2007)

Years post-transplant	DBD	DCD	Live
1	94%	93%	96%
2	91%	92%	95%
5	85%	86%	91%

DBD, donation after brain death; DCD, donation after circulatory death

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Patient survival after first adult kidney transplant (2005–2007)

Years post-transplant	DBD	DCD	Live
1	97%	95%	99%
2	95%	93%	98%
5	89%	87%	96%

DBD, donation after brain death; DCD, donation after circulatory death

Transplant immunology

Recipient's blood group and HLA tissue type are determined as part of the assessment for transplantation. Historically, the most important antigens in transplantation are class I molecules (HLA-A and HLA-B) and class II molecule (HLA-DR). These three molecules are reported as a mismatch (MM) between recipient and donor. MM sequencing reflects the difference in HLA type between donor and recipient, and hence the potential for developing an immune response. The gene locus for each molecule is represented once on each haplotype that an individual possess, so the range of MM can range from 0–0–0 (exact match in three locus pairs) to 2–2–2 (all locus pairs are different). The degree of MM has an impact on graft survival rates; for living donor transplants with a 0–0–0 MM, the 5-year graft survival rate is 89.2%; for those with a 2–2–2 MM, the rate is 79.4%.

Recipients may also have pre-formed donor-specific antibodies (DSAs). Screening for anti-HLA antibodies is performed regularly for all patients on the transplant waiting list. Development of anti-HLA antibodies occurs in response to sensitizing events such as blood transfusion, pregnancy, or previous transplantation. The formation of these antibodies is termed pre-transplant DSA. De novo DSA can be formed post-transplantation.

For deceased donor renal transplants, optimal HLA matching between donor and recipient has a significant effect on graft outcome. The presence of an incompatible blood group or significant recipient anti-HLA antibody to donor-specific HLA is a contraindication to renal transplant without prior desensitization. Desensitization is a prolonged treatment and therefore made logistically easier when administered prior to a planned living donor renal transplant. Complete removal of antibody is impossible, so the purpose of desensitization is to minimize antibody to levels to render transplantation safe.

ABO and HLA incompatible transplantation

The principle of desensitization is similar for ABO and HLA incompatible transplants with a three pronged approach: antibody removal, reduction in antibody production and augmented immunosuppression. The recipient undergoes a period of plasma exchange or plasmaphaeresis prior to transplantation to reduce circulating antibody levels. For ABO incompatible transplants specific immunoabsorption columns are available that selectively remove anti-A or anti-B antibodies, retaining other important plasma proteins such as clotting factors. Plasma exchange may be combined with the anti-B cell monoclonal antibody rituximab or pooled immunoglobulin to minimize rebound antibody production. If antibody levels fall satisfactorily and the acute donor recipient cross match is negative, transplantation may proceed. Even though most transplant recipients develop recurrent antibodies, accommodation occurs in the majority and antibody-mediated rejection is not common.

Kidney donation

There are a number of potential sources of kidneys donors (see Figure 1).

Deceased donation

Approximately 65% of kidneys are from deceased donors the majority procured following donation after brain death (DBD). However, in the drive to expand organ numbers, there has been a steady rise in organs retrieved following circulatory death (DCD) donors.

A DBD donor is identified as a patient with an irreversible intracerebral event and confirmed as brain dead. The retrieval surgery is conducted while maintaining the donor patient on life sustaining treatment, including maintenance on a ventilator. Potential donors who do not meet brain death criteria but are identified as having no viable recovery are termed DCD donors. In this category of donor, procurement surgery is commenced once the ventilator has been disconnected, cardiac arrest has occurred and the patient is pronounced dead according to cardiopulmonary criteria (permanent absence of respiration, circulation and responsiveness).

Retrieval surgery is covered in more detail elsewhere in this issue, however the procedure involves aortic cannulation with rapid cooling of the body and dissection of the organs of interest. The kidneys are removed en-bloc and separated on the back-table. The IVC remains with the right kidney to lengthen the otherwise short right renal vein. They are flushed with a preservation fluid and transported in static cold storage.

Warm ischaemia time (WIT) is the time between cessation of perfusion of the organ by the donor's blood circulation to the point at which it is perfused with preservation fluid.

Sources of kidneys for transplantation

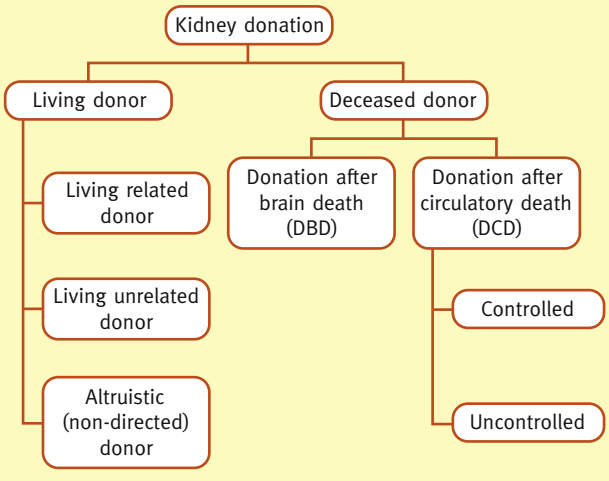

Figure 1