

Renal replacement therapy and transplantation

What is renal replacement therapy?

Renal replacement therapy (life-supporting treatments for severe [acute kidney injury](#) or stage 5 [chronic kidney disease](#)) includes haemodialysis, haemofiltration, haemodiafiltration, peritoneal dialysis and kidney transplantation^[1].

Most patients with chronic kidney disease (CKD) stage 4-5 (estimated glomerular filtration rate (eGFR) <30 ml/minute/1.73 m²) or with CKD stage 3 and rapidly deteriorating renal function should be referred for assessment by a nephrologist. Patients should ideally be referred at least a year before they might be anticipated to require renal replacement therapy^[2]. Three choices for renal replacement therapy are available for patients with end-stage kidney disease:

- Conservative care and symptom control.
- Dialysis (either peritoneal dialysis or haemodialysis).
- Kidney transplant (from a living or cadaveric donor).

Conservative care in end-stage chronic kidney disease

- Dialysis may not improve quality of life in patients with extensive comorbidities. Very elderly patients may not have the length of their lives prolonged by dialysis.
- In these circumstances, many patients opt for symptom control without dialysis, using erythropoietin, vitamin D analogues, dietary control, antipruritics and antiemetics as necessary.

- Such patients often have significantly better quality of life, fewer hospital admissions (eg, from dialysis-related complications) and are more likely to die finally at home, rather than in hospital, than patients receiving dialysis.
- Conservative care still involves active management of the complications of CKD. Patient and carer participation in care provision and a multidisciplinary team approach including nurses, doctors and counsellors are crucial to effective patient management and support.

Dialysis^[2]

The National Institute for Health and Care Excellence (NICE) recommends:

- Consider starting dialysis when indicated by the impact of symptoms of uraemia on daily living, or biochemical measures or uncontrollable fluid overload, or at an estimated glomerular filtration rate (eGFR) of around 5 to 7 ml/min/1.73 m² if there are no symptoms.
- Ensure the decision to start dialysis is made jointly by the person (or, where appropriate, their family members or carers) and their healthcare team.
- Before starting dialysis in response to symptoms, be aware that some symptoms may be caused by non-renal conditions.

CKD^[2]

- There is no good evidence that starting dialysis earlier is of any benefit to patients but, if dialysis is delayed for too long, patients can become very malnourished.
- Early referral for specialist renal care before renal replacement therapy is required can significantly delay the need for dialysis and reduce early morbidity and mortality - ie when GFR falls below 30 mL/minute (stage 4 CKD).
- All people with stage 5 CKD should be offered a choice of peritoneal dialysis or haemodialysis, if appropriate. However, peritoneal dialysis should be considered as the first choice of treatment for children aged 2 years or younger.

- All people who choose peritoneal dialysis should be offered a choice of continuous ambulatory peritoneal dialysis, or automated peritoneal dialysis, if this is medically appropriate.

Indications for dialysis in AKI^[2] ^[3]

- Presence of clinical features of uraemia (eg, pericarditis, gastritis, hypothermia, fits or encephalopathy).
- Fluid retention leading to pulmonary oedema: inability to reduce excess volume with diuretics with urine volume under 200 mL in twelve hours.
- Severe hyperkalaemia (potassium above 6.5 mmol/L) unresponsive to medical management.
- Serum sodium above 155 mmol/L or below 120 mmol/L.
- Severe acid-base disturbance (pH under 7.0) that cannot be controlled by sodium bicarbonate.
- Severe renal failure (urea greater than 30 mmol/L, creatinine greater than 500 µmol/L).
- Toxicity with drugs that can be dialysed.

Continuous renal replacement therapy is commonly used to provide renal support for critically ill patients with acute kidney injury, particularly patients who are haemodynamically unstable. A variety of techniques that differ in their mode of solute clearance may be used, including^[4] :

- Continuous venovenous haemofiltration with predominantly convective solute clearance.
- Continuous venovenous haemodialysis with predominantly diffusive solute clearance.
- Continuous venovenous haemodiafiltration, which combines both dialysis and haemofiltration.

Haemodialysis^[5]

- Haemodialysis involves pumping blood from the body through an artificial kidney in which the blood is surrounded by a solution of electrolytes (the dialysate), whose concentration can be varied precisely. Solutes present in the blood at high concentration (eg, urea, potassium, creatinine) diffuse into the dialysate and are removed. Blood is drawn from an arteriovenous fistula and then circulated through the dialyser and returned into the fistula. Heparin is constantly infused.
- Changing the concentration of solutes in the dialysate can alter the electrolyte composition of the blood – eg, raising the dialysate calcium above the serum concentration can increase serum calcium in patients with hypocalcaemia.
- Ultrafiltration is used to regulate the distribution of water between the blood and dialysate. The volume of water to be removed from the patient's blood can be controlled by altering the pressures on either side of the membrane separating the blood from the dialysate.
- Patients are exposed to vast volumes of water so the danger from impurities is high. High-flux dialysis requires the use of ultra-pure water.
- Patients need very good vascular access, which is obtained by creating a fistula between a peripheral artery and vein (usually radial or brachial), or a permanent plastic catheter inserted into an internal jugular or subclavian vein. The fistula takes several weeks to mature and should ideally be fashioned 3–6 months before starting haemodialysis.
- Haemodialysis can be carried out in a hospital centre or in the patient's home. Dialysis for CKD is usually performed three times each week for about four hours. Some patients opt for daily haemodialysis (usually six days/week), which provides the best control of fluid balance and biochemistry but is very intensive.

Complications of haemodialysis^[6]

- Access-related: local infection, endocarditis, osteomyelitis, creation of stenosis, thrombosis or aneurysm.
- Hypotension (common), cardiac arrhythmias, air embolism.

- Nausea and vomiting, headache, cramps.
- Fever: infected central lines.
- Dialyser reactions: anaphylactic reaction to sterilising agents.
- Heparin-induced thrombocytopenia, haemolysis.
- Disequilibrium syndrome: restlessness, headache, tremors, fits and coma.
- Depression.

Percutaneous endovascular forearm arteriovenous fistula creation for haemodialysis access

NICE has produced new interventional procedures guidance on the percutaneous endovascular forearm arteriovenous fistula creation for haemodialysis access^[7]. It notes that evidence for this procedure raises no major safety concerns. However, since evidence on its efficacy is limited in quantity and quality, NICE recommends that this procedure should only be used with special arrangements for clinical governance, consent, and audit or research.

Peritoneal dialysis^[8]

Peritoneal dialysis is now used widely for the long-term treatment of end-stage renal disease. Technical innovations in peritoneal dialysis have significantly reduced therapy-related complications, allowing patients to be maintained on peritoneal dialysis for longer periods. The survival rate for patients treated with peritoneal dialysis is now equivalent to that with in-centre haemodialysis.

- A dialysate is infused into the peritoneal cavity and the blood flowing through peritoneal capillaries acts as the blood source.
- Ultrafiltration is controlled by altering the osmolality of the dialysate solution and thus drawing water out of the patient's blood. This can be achieved with glucose or other large molecular weight solutes in the dialysate. The glucose load may cause poor diabetes control and weight gain.

- A catheter is inserted into the patient's peritoneum under local or general anaesthetic, which remains in place permanently and through which dialysate is infused. The waste solutes are removed by exchanging the peritoneal fluid for a fresh solution.
- Patients can be trained to perform continuous ambulatory peritoneal dialysis (CAPD), which usually involves four exchanges of about 20 minutes spaced throughout the day. Alternatively, an automated peritoneal dialysis can be used to do a number of exchanges overnight while the patient is asleep, then with only one or two daytime exchanges required.
- Peritoneal dialysis can be performed at home, at work or while on holiday. It therefore allows a high degree of independence and control; however, a great deal of support is still required.

Contra-indications to peritoneal dialysis

- Intra-abdominal adhesions and abdominal wall stoma.
- Obesity, intestinal disease, respiratory disease and hernias are relative contra-indications.

Complications of peritoneal dialysis

- Peritonitis, sclerosing peritonitis.
- Catheter problems: infection, blockage, kinking, leaks or slow drainage.
- Constipation, fluid retention, hyperglycaemia, weight gain.
- Hernias (incisional, inguinal, umbilical).
- Back pain.
- Malnutrition.
- Depression.

Renal transplantation ^[9]

- A kidney transplant provides the best long-term outcome for patients with end-stage kidney disease. The kidney may come from a cadaveric donor (85–90%) or from a living donor.

- All patients with end-stage kidney disease should be considered for a renal transplant. Age is not a major determinant of outcome but the presence of comorbid disease adversely affects survival.
- Ischaemia times for the donor kidney:
 - Warm ischaemia: time between death and chilling plus time out of ice at transplantation. The maximum allowable time before irreversible damage is one hour.
 - Cold ischaemia: time in ice - usually the maximum is 30 hours.
- Patients do not generally have their native kidneys removed and the transplanted kidney is placed extraperitoneally in the iliac fossa.
- Patients require frequent follow-up after discharge (two or three times each week initially).
- To prevent renal transplant rejection, the recipients receive induction at the time of transplant with either depleting or non-depleting monoclonal or polyclonal antibodies directed against T cells - eg, antithymocyte globulin, basiliximab or alemtuzumab. Maintenance immunosuppression is then required in the long term to prevent rejection^[10].
- Patients need to be followed up for life and this includes annual screening for cancers, drug toxicity and cardiovascular disease.

Contra-indications for transplantation

- Cancer.
- Active infection.
- Uncontrolled ischaemic heart disease.
- Acquired immunodeficiency disease with opportunistic infections.
- Active viral hepatitis.
- Extensive peripheral vascular disease.
- Mental incapacity.

Benefits of renal transplantation

- Can stop dialysis.
- Improved quality of life with normal diet and activity, relaxation of fluid restriction.
- Reversal of anaemia and renal bone disease.

Risks of renal transplantation

- Immediate operative complications (local infection, pain, pneumonia, deep vein thrombosis).
- Immediate graft failure.
- Arterial or venous thrombosis in the transplant.
- Infections (viral, bacterial, fungal).
- Cancer (skin, lymphoma).
- Side-effects of immunosuppressive drugs.

Complications of renal transplantation and subsequent immunosuppression treatment

- Postoperative problems - eg, deep vein thrombosis, pulmonary embolism and pneumonia.
- Opportunistic infections: viral (particularly herpes simplex in the first four weeks and then cytomegalovirus (CMV) later), fungal and bacterial.
- Malignancies (especially lymphomas and skin cancers) ^[11] .
- Drug toxicity, bone marrow suppression.
- Recurrence of the original disease in the transplant.
- Urinary tract obstruction.
- Cardiovascular disease, hypertension, dyslipidaemia.

- Graft rejection:
 - Hyperacute: occurs within minutes of insertion. Is now rare due to more accurate cross-matching. Requires removal of graft.
 - Accelerated: aggressive mainly T-cell-mediated crisis can occur within a few days in patients previously sensitised. Presents with fever, swollen transplanted kidney and rapidly increasing serum creatinine. Can be salvaged with high-dose steroids plus antilymphocyte antibodies but long-term survival is affected.
 - Acute cellular: occurs in around 25% of patients usually in 1-3 weeks but can occur up to 12 weeks. Clinical signs are fluid retention, rising blood pressure and rapid increase in creatinine. Treatment is with intravenous steroids after diagnosis by biopsy. Latest induction regimens can reduce incidence of acute rejection to 10%.
 - Chronic: presents with a gradual rise in serum creatinine and proteinuria, resistant hypertension. Graft biopsy shows vascular changes, fibrosis, and tubular atrophy. It is not responsive to increasing immunosuppression therapy.

Prognosis

- The outcome of renal transplantation has steadily improved. One-year and ten-year graft survival rates are 89% and 67% for adult kidneys from 'brain death donors' and 96% and 78% for kidneys from live donors. Survival of the transplant recipient at ten years for cadaveric and live donor transplants is 71% and 89% respectively ^[10] .
- Acute rejection and early graft loss are becoming increasingly less common.
- Cadaveric donor renal transplantation, more human leukocyte antigen (HLA) mismatches, increased donor age, cold ischaemia time greater than 24 hours and a history of diabetic nephropathy all increase the risk of graft failure, return to dialysis and death.

Further reading

- [Renal Replacement Therapy Services](#); NICE Quality Standard, Nov 2014 - last updated Oct 2018
- [Guidelines for Living Donor Kidney Transplantation, United Kingdom Guidelines](#); The Renal Association (March 2018)
- [UK Kidney Association](#)
- [Zimmerman AM](#); Peritoneal dialysis: increasing global utilization as an option for renal replacement therapy. *J Glob Health*. 2019 Dec;9(2):020316. doi: 10.7189/jogh.09.020316.
- [Ashby D, Borman N, Burton J, et al](#); Renal Association Clinical Practice Guideline on Haemodialysis. *BMC Nephrol*. 2019 Oct 17;20(1):379. doi: 10.1186/s12882-019-1527-3.

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