

CONTROLLED DOCUMENT

Renal guidelines for liver transplant candidates and recipients

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IMPORTANT NOTE:

THIS DOCUMENT SHOULD BE USED TO GUIDE PATIENT CARE AND SHOULD ONLY BE USED IN THE CORRECT CLINICAL CONTEXT. ALWAYS CONFIRM MEDICATION DOSES WITH THE BNF AND WHEN UNCERTAIN DISCUSS WITH THE LIVER UNIT CONSULTANTS.

Assessment of renal function in patients on the waiting list and criteria for combined liver/kidney transplantation

Defining renal failure pre transplantation is important but difficult. Renal dysfunction in patients with cirrhosis is often multi factorial. Common causes include;

- Hepatorenal syndrome (Criteria for hepato-renal syndrome; Cirrhosis; serum Creatinine > 133 $\mu\text{mol/l}$; absence of shock and hypovolaemia (no sustained improvement in renal function (sCr < 133 $\mu\text{mol/l}$) after 2 days of diuretic withdrawal or albumen 1g/kg/d); no current nephrotoxic drugs; absence of parenchymal renal disease (proteinuria < 0.5 g/d, no micro-haematuria (<50 rbc/hpf), normal renal ultrasound)
- Medications (NSAID's, ACE inhibitors, diuretics, CNI's)
- Hypovolaemia (Variceal bleeding, large volume paracentesis)
- Sepsis (in particular spontaneous bacterial peritonitis)
- Parenchymal (membranoproliferative glomerulonephritis in hepatitis C, diabetic nephropathy and autoimmune hepatitis/PBC and IgA nephropathy)

It is important to distinguish between acute and chronic causes, to identify any intrinsic renal pathology and predict reversibility. Renal impairment on the list should be managed as per the liver medical protocols.

- All patients should have a serum Cre, eGFR, urine test for ACR/haematuria and a renal ultrasound. Any patients being considered for a combined liver/kidney transplant should have a formal isotopic GFR.
- An albumin creatinine ratio of > 30mg/mmol (or total urinary protein loss > 0.5 g/24hrs) reflects significant parenchymal renal disease and is associated with both cardiovascular morbidity and mortality. It should initiate a search for the underlying cause. In patients with diabetes, microalbuminuria (ACR > 2.5 mg/mmol in men or > 3.5 mg/mmol in women) is also clinically significant.
- Serum Cre and eGFR should be monitored regularly on the waiting list
- Current UK criteria for listing for Simultaneous Liver and Kidney Transplantation.
 - Genetic liver kidney syndromes; Oxalosis, Glycogen storage disease type 1
 - Chronic liver disease meeting at least one of the three current criteria for transplant selection + end-stage renal disease on long-term dialysis program.
 - Chronic liver disease meeting at least one of the three current criteria for transplant selection + HRS with serum creatinine > 200 and dialysis > 8 weeks
 - Chronic liver disease meeting at least one of the three current criteria for transplant selection + MDRD stage 3b or *GFR < 30 ml/min or renal biopsy showing > 30% fibrosis and/or glomerulosclerosis.
 - All other cases referred to the Appeals Panel.

Peri operative renal sparing strategies

Peri operative techniques

A number of factors are associated with a peri operative decline in renal function

- Hypovolaemia/haemorrhage
- Damage to vascular endothelium during reperfusion
- Nephrotoxic drugs

The use of vena cava preservation surgery is advocated but large randomised controlled trials have not been performed. The use of anti oxidant agents such as N acetyl cysteine to prevent ischaemia/reperfusion damage requires further study.

CNI withdrawal/minimisation

There is evidence that minimising CNI exposure leads to improved renal function at one year. This can be achieved by aiming for low dose of CNI in combination with a stronger antiproliferative agent (mycophenolate) or by avoiding a CNI for the first 5 days in combination with an antiproliferative agent, steroids and monoclonal antibody induction therapy. At present the evidence does not exist to support CNI delay without antibody induction therapy. Of note concerns do exist about IL2 RA induction therapy in patients with hepatitis C and its potential for causing more aggressive recurrence.

Therefore in patients with risk factors suggesting impaired renal function at one year

- Pre operative eGFR <60mls/min/1.73m
- extensive operative blood loss
- diuretic resistant ascites

we suggest either;

- low dose tacrolimus (trough 5 ng/ml) until day 5 then trough 5-10ng/ml
- oral MMF 1g BD
- Steroids as per protocol

Or

- No tacrolimus until day 5 and then low dose (trough 5-10 ng/ml)
- Intravenous IL2RA (Basiliximab) 20mg at day 0 and day 4
- Oral MMF 1g BD
- Steroids as per protocol

Of note although patients with both acute liver failure and recipients of non heart beating donors experience high levels of peri operative renal failure this does not seem to effect renal function at one year, therefore they should follow standard protocols.

Late renal sparing immunosuppressive strategies

A decline in eGFR of > 5 ml/min/1.73m² over one year or 10 ml/min/1.73m² over 5 years has been defined as progressive renal disease. All patients should have a yearly ACR and urine dip stick.

The following cases should be referred to a nephrologist for joint management;

- Stage 4 or 5 CKD with/without diabetes
- ACR > 70 mg/mmol without haematuria
- ACR > 30 with haematuria
- Decline in eGFR of > 5 ml/min/1.73m² over one year or 10 ml/min/1.73m² over 5 years

The following late renal sparing strategies are effective

- CNI withdrawal and substitution either with MMF or MMF and corticosteroids
- CNI minimization (trough 3-5ng/ml) with/without additional immunosuppression

Early treatment is beneficial and should begin once the eGFR falls below 60ml/min.

Management of Hypertension and Hyperuricaemia

Hypertension

In the presence or absence of renal dysfunction a calcium channel blocker (CCB) should be the first line antihypertensive treatment after liver transplantation. In patients with significant proteinuria > 0.5 g/day or those with diabetes consider an ACEi. A combination of CCB and ACEi (or angiotensin receptor blocker) \pm Doxazosin is recommended in hypertension which is difficult to control or to maintain at target blood pressure.

Hyperuricaemia

Hyperuricaemia is common in liver transplant population. Screen patients with renal dysfunction. Improvement in serum creatinine may be seen in treating asymptomatic hyperuricaemia with allopurinol.