Preparation of the dialysis patient for transplantation

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Introduction

Successful kidney transplantation improves the quality of life and prolongs the survival of uraemic patients compared to long-term dialysis treatment [1–3]. Nevertheless renal transplantation is plagued by several problems. To minimize the complications during the peri- and postoperative period careful evaluation of the recipient prior to transplantation is essential. In addition regular check ups are necessary while the patient is on the waiting list.

It is useful to proceed according to a ‘shopping-list’ (Table 1) which specifies which examinations are required at what point in time.

Cardiovascular investigation—vessels and heart

Stenosis of iliac and lower extremity vessels prior to transplantation

The iliac vessels must be evaluated to establish whether vascular anastomosis between graft and iliac vessels is possible. It is necessary to exclude by appropriate examination stenosis of the pre-anastomotic iliac vessels [4] (which after transplantation will cause a clinical tableau resembling graft artery stenosis), as well as stenosis of post-anastomotic arteries (which will cause ischaemia of the ipsilateral leg because, as a result of a steal phenomenon, the graft will siphon off the blood destined for the lower extremity). Appropriate procedures to detect such a stenosis are Doppler/duplex sonography or angiography. These examinations are particularly indicated in patients with signs of peripheral vascular occlusive disease [5]. When angiography is considered, the diagnostic benefit must be balanced against the risk that radiocontrast medium impairs residual renal function. It is particularly the CAPD patient for whom residual renal function is very important [6]. An alternative option, devoid of side-effects on residual renal function, is magnetic resonance angiography.

Vascular pathology resulting from increased vascular remodelling or calcification is another important issue to consider prior to renal transplantation [7]. The finding of Mönckeberg type calcification of the media of large arteries on plain X-ray indicates that vascular stiffness is increased and that the patient is at high risk because of: (i) a higher rate of technical problems in the immediate postoperative course (e.g. intimal dissection), (ii) higher cardiovascular mortality predicted by a high blood pressure amplitude [7], (iii) impaired coronary perfusion during diastole because of an accelerated decline in diastolic pressure and (iv) a higher risk of left ventricular hypertrophy [8]. Apart from diabetes or a history of long-standing hypertension, poor control of serum phosphate concentration contributes further to a high cardiovascular risk.

Cardiac performance of the patient on the waiting list

The cardiac performance of a uraemic patient is the most important determinant influencing the decision whether a dialysis patient should be posted on the waiting list. Mainly two diseases must be excluded which are common in dialysis patients, (i) coronary artery stenosis (present in 40% of the patients at the start of dialysis; [9]) and (ii) aortic valve calcification and stenosis [10]. Non-invasive procedures such as stress-echocardiography are investigator dependent and not sufficiently sensitive to firmly exclude cardiac ischaemia, but echocardiography is definitely useful to establish the diagnosis of valvular diseases. If the electrocardiogram reveals signs indicating a history of myocardial infarction (Q-waves) or if echocardiography points to the presence of dyskinetic wall motion, coronary angiography is strongly recommended as the diagnostic gold standard to document or exclude coronary stenosis. Because of the high cardiac risk, coronary angiography is obligatory prior to transplantation in diabetic patients even when they are asymptomatic, if the criteria proposed by Manske [11] are met. Restoration of coronary perfusion by angioplasty with stent implantation or bypass surgery is necessary before the patient is put on the waiting
Bypass surgery in dialysis patients is nowadays a routine procedure with a mortality comparable to that of non-renal patients [12].

**Evaluation of carotid arteries**

Evaluation of supraaortic vessels by Doppler duplex technique is helpful, since carotid artery disease is a strong predictor of coronary artery stenosis [13]. There is no consensus, however, concerning the indications for carotid artery surgery or dilatation in patients with carotid artery disease. In polycystic kidney disease aneurysms should be excluded by magnetic resonance angiography, particularly when there is a family history of cerebral haemorrhage [14].

**Cardiovascular prevention**

**Blood pressure control**

High blood pressure is common in dialysis patients. The most important cause is volume overload. Achieving ‘dry weight’ and normalizing of blood pressure continues to be a challenge to the nephrologist on the dialysis unit. It is interesting that hypertension on dialysis predicts the later occurrence of high blood pressure after successful renal transplantation [15]. This point is important, since post-transplant hypertension has an adverse effect on graft outcome [16].

**Control of serum phosphate concentration and hyperparathyroidism**

Hyperphosphataemia is not only deleterious for the skeleton, but is also a predictor for cardiovascular death. High serum phosphate concentrations cause increased vascular stiffness and calcification of atherosclerotic plaques, e.g. coronary plaques [17]. Compliance of patients with phosphate binder therapy is notoriously poor. Regular tests of serum-phosphate concentrations are necessary and dialysis patients should frequently receive advice concerning diet and, more importantly, phosphate binders. Treatment of hyperparathyroidism is important, because it further increases the risk of vascular and valvular calcification and predisposes to skeletal complications after renal transplantation. If possible, treatment should first be medical. If this is not successful parathyroidectomy should be performed before transplantation, because after transplantation involution of grossly hyperplastic parathyroids cannot be expected. Furthermore if parathyroidectomy is performed after transplantation, serum creatinine concentration usually increases for reasons which are not completely understood [18].

**Control of dyslipidaemia**

Dyslipidaemia potentiates the risk of cardiovascular disease in end-stage renal disease patients. In patients with end-stage renal failure coronary artery disease progresses rapidly as documented by angiography [19]. In uraemic patients it was shown that increased LDL and decreased HDL concentrations were more strongly related to the length of hospital stay than body mass index [20]. Administration of cholesterol lowering drugs, particularly statins is definitely rational despite the absence of controlled data. In an ongoing study the effect of atorvastatin on dyslipidaemia is evaluated in dialysed type 2 diabetic patients [21].

**Treatment of anaemia**

Haemoglobin levels in end-stage renal disease patients are correlated to survival on chronic dialysis. If the haemoglobin concentration is lower by 1 g/dl, the risk of left ventricular hypertrophy is higher by 6% [22]. Unfortunately administration of erythropoetin to reverse anaemia fails to reliably abrogate prevalent left ventricular hypertrophy and LV-dilatation (although the frequency of de novo cardiac dilatation is reduced). This is a strong argument for prevention of anaemia by administration of erythropoetin, although admittedly prospective data to prove the effectiveness of this policy are not available.
An additional benefit of erythropoietin therapy is the avoidance of iron overload and secondary iron storage disease as well as the elimination of the risk of viral infections, particularly hepatitis B and C.

Exclusion of chronic bacterial or viral infections

Chronic bacterial infections

It is important to carefully investigate the patient to exclude the presence of chronic infectious foci. Chronic asymptomatic sinus infections and dental root abscesses are notoriously overlooked, but may later cause problems when the patient receives immunosuppression. Cholecystolithiasis and sigma diverticulosis are also potential sites of bacterial infection. Resection is mandatory when there have been episodes of symptomatic cholecystitis or diverticulitis. The vascular access (particularly PTFE grafts) or the CAPD catheter may also be the site of chronic infection and should be examined by clinical assessment and screened by ultrasound. Urinary tract infection, vesico-ureteral reflux, urinary flow obstruction and renal stone disease must be excluded. Nephrectomy is absolutely necessary if the kidney is infected. In polycystic kidney disease nephrectomy may be necessary if the bulk of the polycystic kidney is excessive or if there is a history of infection and/or recurrent bleeding. Overall only a small proportion of PKD patients requires nephrectomy. Bilateral nephrectomy because of uncontrolled hypertension was once popular, but has become uncommon today.

Figure 1a–c shows examples of uraemic patients on the waiting list presenting with various types of chronic infections requiring pre-transplant eradication.

Chronic viral infections

Hepatitis B and C have a major impact on patient outcome after renal transplantation. Hepatitis B and C infections reduce patient survival (10% excess mortality in patients with hepatitis B). In patients with hepatitis C there is an increased risk of severe postoperative bacterial infections [23]. In the long-term transplanted patients with hepatitis C have also an increased risk of hepatic cirrhosis and hepatocellular carcinoma. The renal graft may also be lost in patients with hepatitis C as a result of cryoglobulinaemia causing glomerulonephritis [24].

Fig. 1. (a) Vesico-ureteral reflux in a chronic haemodialysis patient on the waiting list (X-ray). Nephrectomy was necessary because of recurrent urinary tract infection. (b) Massive enlargement of liver and kidneys in a patient with polycystic kidney disease. Unilateral nephrectomy was necessary to accommodate the renal allograft (CT-scan). (c) Tunnel infection in a CAPD patient on the transplant waiting list (ultrasonography). Temporary 'non-transplant' status is necessary until the tunnel infection is cured or the catheter removed.
Serum transaminases do not reflect the severity of hepatic inflammation and the risk of cirrhosis. Pretransplant liver biopsies are therefore necessary to accurately assess the hepatic prognosis. In addition, if treatment with pegylated interferon and lamivudine in hepatitis B or interferon in hepatitis C patients is indicated, the patient must be treated prior to transplantation. The response rate is approximately 30 to 40% [24]. Interferon therapy after transplantation is contraindicated, because of the high risk that it may trigger episodes of acute rejection [24].

Patients with human immunodeficiency virus infections are currently excluded from renal transplantation programmes.

Information on cytomegalovirus carrier state [25] is important. The information will be crucial for postoperative prophylaxis with antiviral drugs, e.g. ganciclovir or valaciclovir [26].

Malignancy in uraemic patients on the waiting list

The prevalence of malignant tumours in the dialysis population is not increased, but the risk of malignancy is definitely excessive after transplantation [27]. The risk of recurrence of a known malignancy after transplantation depends on the type and size of the tumour. Tumours with a high recurrence rate are carcinoma of the bladder, sarcoma, malignant melanoma, symptomatic renal cell carcinoma, non-melanoma skin cancer and myeloma [28]. The recurrence rate is high during the first 2 years after treatment of the malignancy (53%) and decreases to 13% after 5 years [28]. There is consensus that—with the exception of spinocellular carcinoma of the skin—a waiting period of 5 years should be respected before the patient is put on the waiting list. Some known risk factors predispose to malignancy after transplantation; for instance analgesic abuse (uroepithelial carcinoma of the renal pelvis or bladder) or von Hippel-Lindau disease (renal cell carcinoma) [29]. Non-melanoma skin cancers are frequent after transplantation. Exposure to UV light plays a major role. As a prophylactic measure patients should avoid excessive exposure to UV-light, use sun blockers, and be screened by a dermatologist on a regular basis (while on the transplant programme).

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Recurrence of native kidney disease [30]

Several glomerular and non-glomerular diseases may recur in the renal allograft. This risk does not automatically exclude these patients from the waiting list. The diagnosis of the primary renal disease and consideration of the risk of recurrence are important for the management of the patient after transplantation, however. High recurrence rates are seen in patients with focal segmental sclerosis (early) and IgA glomerulonephritis (late). Although the frequency with which recurring IgA-nephropathy diagnosed by immunohistological examination is high, but the clinical spectrum of recurrent IgA-nephropathy varies widely. Recognition of recurrence is important, since an increase of immunosuppression is beneficial and exposes the patient unnecessarily to risks if renal failure is due to recurrence. Other renal diseases with a suspected risk of recurrence are haemolytic uraemic syndrome, particularly cases with a familial history and genetic abnormalities of the complement system.

Immunological investigation of patients on the waiting list

Information on blood group, HLA-types and presence of cytotoxic HLA antibody titers is indispensable. Such information is of great importance to select an appropriate immunsuppressive protocol, e.g. induction with or without T-cell antibodies [31].

Feasibility of living donor transplantation

Despite a growing number of uraemic patients on the waiting list for renal transplantation the number of cadaver organ donors has not substantially increased. This is regrettable, since the time on the waiting list has an independent effect on graft and patient survival [32]. New approaches to increase the pool of organ donors include the use of living unrelated kidney donors and even cross-over living related transplantation [33]. The results are encouraging and living related/unrelated kidney transplantation should be evaluated in all uraemic patients who qualify for the transplant waiting list.

References


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