Canadian Society of Transplantation consensus guidelines on eligibility for kidney transplantation

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Since 1980, the incidence and prevalence of end-stage renal disease (ESRD) have increased each year in Canada and throughout the world.[1,2] From 1981 to 1999, the number of new patients with ESRD grew at a compound annual rate of 7.3%[1] and similar trends were documented worldwide.[2] By 31 Dec. 2000, 24 921 Canadians were receiving life-sustaining treatment for ESRD; dialysis was the treatment modality for 14 567 patients and the remaining 10 354 patients (41.5%) had a functioning kidney transplant.[3] The development of ESRD is associated with a substantial reduction in health-related quality of life[4,5] and premature death.[6] Kidney transplantation is the treatment of choice for ESRD as it prolongs survival,[7] improves quality of life[4,5] and is less costly than dialysis.[4]

Despite the benefits of kidney transplantation, not all patients with ESRD take this route and there is considerable variation in transplantation rates across Canada; for example, the renal transplantation rate (per million population) is only 27.4 in Saskatchewan compared with 51.8 in the Atlantic provinces.[3] It is not known to what extent this variation is due to differences in rates of referral and acceptance for transplantation (i.e., perceived eligibility) or to differences in availability of donors. The purpose of this consensus document was to outline which patients, in the growing Canadian ESRD population, are currently eligible for transplantation. We hope that these guidelines will lead to consistency in determining which patients are eligible and accepted for kidney transplantation.

Canadian patients with ESRD comprise a unique mixture including minority groups[8,9] who receive treatment in a universally funded health care system. Health care coverage or insurance should not be an issue in determining transplantation eligibility in Canada as it may be in other regions of the world.[10] The methods used to develop these guidelines were designed to ensure that the recommendations reflect a Canadian consensus so that they would be adopted across the country.

These guidelines are based on the best available evidence. However, clinical judgment plays a role in decision-making and, thus, there will still be variability in clinical practice across the country. This consensus document specifically addresses eligibility criteria for kidney transplantation and is not meant to outline the individual tests required for assessment or reassessment of patients awaiting kidney transplantation. Published clinical practice guidelines from the United States and Europe already exist in this area.[10–12]

These guidelines were developed with a wide audience in mind. General recommendations are provided in summary form for review by health care workers and physicians working in primary care, who may want to know whether their patient with ESRD is eligible for transplantation. We also expand on the recommendations for those interested in more detail. The guidelines refer to both children and adults and, as such, will be of interest to health care workers and physicians treating either age group.

Methods

The Kidney Transplant Working Group, a subcommittee of the Canadian Society of Transplantation (CST), was asked to prepare eligibility criteria for renal transplantation by the CST president and the Executive Council. Dr. E. Cole, the chair of the Kidney Transplant Working Group, appointed a guidelines steering committee made up of 7 other physicians from the working group (the authors of this article) based on geographic representation (British Columbia, Alberta, Manitoba, Ontario, Quebec, Atlantic Provinces) as well as specialty (adult and pediatric nephrology).

The chair and the members of the guidelines committee developed a list of 19 items that would be reviewed in these guidelines. Each of the 19 topics was assigned to a committee member. The author for each topic was given the responsibility of performing a comprehensive literature review and creating the first draft of each guideline. The guidelines committee met in person to review the draft guidelines. The recommendations were critiqued by the committee and revised accordingly until consensus was reached. No formal voting took place, but rather the documents were repeatedly revised until all members of the committee were satisfied with the content of the recommendations.

The strength of evidence supporting each recommendation was graded using the system developed by the Canadian Task Force on Preventive Health Care[13] as follows:

Grade A — There is **good** evidence to support
Grade B — There is **fair** evidence to support
Grade C — The existing evidence is **conflicting**, but other factors may influence decision-making
Grade D — There is **fair** evidence to recommend against
Grade E — There is **good** evidence to recommend against

Once the guidelines committee had reached consensus, the resulting document was circulated to all members of the

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Kidney Transplant Working Group. This larger group included both transplant physicians and transplant surgeons representing all of the Canadian renal transplant programs (adult and pediatric). Members of the Kidney Transplant Working Group were asked to share the draft guidelines with other transplant professionals at their institutions for further comment. The draft guidelines were then presented at the annual Kidney Transplant Working Group meeting, which is held in conjunction with the CST's Annual Meeting. At this meeting, comments and criticism were reviewed and the guidelines document was finalized. Again, no formal voting took place but rather the guidelines were reworked until the recommendations were acceptable to the members of the working group.

The Kidney Transplant Working Group received unrestricted grants from the following organizations to hold the in-person meetings needed to create these guidelines: Fujisawa Canada (now known as Astellas Pharma Canada), Novartis Pharmaceuticals Canada, Hoffmann-La Roche, Wyeth Canada and SangStat Canada (now known as Genzyme Canada). In addition, the Kidney Transplant Working Group received financial support from the Canadian Council for Donation and Transplantation to publish these guidelines. Representatives of these sponsors were allowed to attend the committee and working group meetings; however, none of the sponsors reviewed the draft documents or provided input into the content. Also, no sponsor had to review the final set of guidelines before publication.

General considerations

Recommendations

1. All patients with end-stage renal disease should be considered for kidney transplantation provided no absolute contraindications exist (Grade A).
2. Eligibility for kidney transplantation should be determined on medical and surgical grounds. Criteria for eligibility should be transparent and made available to patients and the public. Eligibility should not be based on social status, gender, race or personal or public appeal (Grade C).
3. A patient declined for transplantation should routinely be offered a second opinion from an alternative physician or surgeon or a committee able to assess the relative risks and benefits of kidney transplantation (Grade C).

Renal transplantation is the treatment of choice for many patients with ESRD. Despite an increased risk of death in the early post-transplant period, transplantation improves long-term survival and quality of life compared with dialysis.[7,14,15] A report from the United States Renal Data System (USRDS), in which a time-dependent non-proportional hazards model was adjusted for such covariates as age, race, gender and cause of ESRD in more than 250 000 patients initiating renal replacement therapy (RRT) between 1991 and 1996, revealed that the long-term mortality rate of patients who received a first deceased-donor renal transplant was 48–82% lower than that of patients who remained on the waiting list.[7] Although greater benefits were seen among younger patients with or without diabetes, the survival benefit extended to those between 60 and 74 years of age. Thus, the decision regarding eligibility for transplantation must be made in the best interests of the patient and be based on medical and surgical grounds.

There are relatively few absolute contraindications to kidney transplantation. It is contraindicated in the context of *active* infection, malignancy, substance abuse or non-adherence to therapy; or in cases where comorbidities are expected to limit life expectancy and the ability to benefit from kidney transplantation significantly. Many of these barriers to transplantation may be overcome with appropriate intervention followed by a period of observation to evaluate the success of the intervention. Selected patients with ESRD and other types of organ failure may be considered for combined organ transplantation, performed either simultaneously or sequentially (e.g., liver–kidney transplantation in a patient with cirrhosis who has developed kidney failure). Each of the following sections addresses the absolute and relative contraindications in greater detail. However, it is important to identify early in the assessment process candidates who are unlikely to ever receive a kidney transplant. When patients with obvious contraindications are referred for assessment, not only are scarce resources used inappropriately, but the patients also suffer unnecessary psychological stress.

Timing of referral

Recommendations

1. Potential transplant recipients should be referred for evaluation by a transplant program once renal replacement therapy is expected to be required within the next 12 months (Grade C).
2. Patients already requiring dialysis support should be referred for transplant evaluation as soon as their medical condition stabilizes (Grade C).

Referral to a transplant program should occur sufficiently early so that preemptive transplantation from a living donor remains a realistic goal for those not yet requiring RRT. For those already requiring dialysis, referral should occur as early as possible to minimize the wait time for kidney transplantation, as time on dialysis is an important determinant of long-term outcome.[16–18] This is particularly important for dialysis-dependent patients who may have a living donor. For patients without a living donor, the timing of referral and completion of assessment may not be as critical, provided these steps do not unnecessarily prolong the waiting time for a deceased-donor transplant. Currently, most Canadian transplant programs use the date of initiation of dialysis as the point at which waiting time starts to accumulate, even if there are significant delays in the referral for or completion of the transplant assessment. Similarly, most prograd not deduct the waiting time during which a patient may be on temporary "hold" or "inactive" status for acute issues. In the absence of a uniform national policy, each program should evaluate its

practices regarding the timing of referral and listing to minimize waiting time on dialysis.

The process of evaluation for transplantation may be complex and involve health professionals from multiple disciplines, many of whom may be external to the transplant program. In a patient with significant comorbid conditions, completion of the evaluation may take as long as 6–12 months. Sufficient time must also be allowed for patients to receive adequate information concerning the risks and benefits of transplantation and the options with respect to type of transplantation (living donor vs. deceased donor, usual vs. extended-criteria deceased-donor kidneys, kidney transplantation alone vs. a combined procedure, such as simultaneous kidney–pancreas transplantation, etc.). For patients planning a preemptive transplant from a living donor, the time of referral for evaluation must also take into account the time required to assess the potential living donor(s).

Although timely referral for transplant assessment is desired, premature referral should be discouraged in most cases. Valuable resources may be inappropriately used in these assessments and attempts to slow progression of native renal disease may not be pursued to the maximum extent possible.

Renal function

Recommendations

1. Preemptive kidney transplantation is the preferred form of renal replacement therapy and should be encouraged where feasible (Grade A).
2. Preemptive kidney transplantation should not proceed unless the measured or calculated glomerular filtration rate is < 20 mL/minute *and* there is evidence of progressive and irreversible deterioration in renal function over the previous 6–12 months. Exceptions may be made for patients receiving combined organ transplants where a kidney transplant is combined with a non-renal organ. However, the appropriate policy on this issue is not clear at this time (Grade C).

Preemptive kidney transplantation is the preferred treatment option for patients with ESRD. It requires a careful estimate of when the patient will need RRT, such that the benefits of maximizing the use of native renal function are realized and the risk that dialysis must be initiated is reduced. Preemptive transplantation is associated with multiple benefits for both the patient and health care system. It avoids the morbidity and cost of dialysis and dialysis access procedures and is associated with improved long-term survival of both the patient and graft.[16–23] Preliminary data suggest that these benefits occur across all age groups.[24] The procedure may also minimize disruption in work and education and promote the return to usual activities. Although concerns have been expressed that permitting preemptive transplants from either living or deceased donors may result in premature transplantation, this has not been supported by clinical experience.[25]

The ability of a transplant program to deliver preemptive transplantation is heavily dependent on donor sources and current waiting times for deceased-donor kidneys. In many jurisdictions, prolonged waiting times for deceased-donor kidneys mean that preemptive transplantation is only feasible in the context of living kidney donors.

Age and functional capacity

Recommendations

1. Advanced age per se is not a contraindication to kidney transplantation (Grade B).
2. Transplant candidates should have a reasonable probability of surviving beyond current waiting times for transplantation, given the resources required to assess and maintain patients on the renal transplant waiting list (Grade C).
3. Very young age and small size should not prevent early referral for transplant evaluation (Grade B).
4. Cognitive or neurodevelopmental delay is not an absolute contraindication to renal transplantation in children (Grade B).

Older patients with ESRD who have no medical or surgical contraindications should be considered for kidney transplantation. Over the last decade, there has been marked increase in the proportion of patients receiving dialysis support who are over 65 year of age. This population has an age-specific rate of ESRD several-fold that of younger people; by 2003, almost 54% of patients initiating RRT were in this age category.[26] Improved patient and graft survival with current immunosuppressive protocols has broadened the application of kidney transplantation to selected elderly patients and increasing numbers of patients over the age of 65 are receiving transplants. Although life expectancy is less, such recipients experience death-censored graft survival rates that are at least as good as those of younger patients.[27,28] Moreover, survival of the older patient is superior with transplantation compared with remaining on the waiting list.[7,29,30] The older recipient is at greater risk of perioperative complications, including death, largely due to infection[31] and cardiovascular disease.[32]

Older patients, as well as younger patients with significant comorbidities, should be encouraged to consider their current quality of life on RRT in the context of what they could reasonably expect following kidney transplantation. Because physiologic age and the burden of comorbid conditions is more likely to influence outcome, a detailed evaluation with emphasis on screening for cardiovascular disease, occult gastrointestinal disease, infection and malignancy is warranted. The decision regarding eligibility for transplantation must be made in the best interests of the patient and be based on medical and surgical grounds. These patients should also be reviewed regularly while they are on the waiting list for transplantation.

Although there are few data on the influence of functional capacity or pretransplant nutritional status on outcomes, extrapolation from other disease states suggests that poor functional capacity or protein malnutrition is associated with greater probability of adverse events including death while

waiting for transplantation and perioperative morbidity and mortality. Poorer functional capacity may limit the success of rehabilitation and return to premorbid activities. Careful evaluation of potential for improvement in current functional status and participation in a rehabilitation program may be helpful adjuncts in the assessment process for some patients. Investigation of the etiology of poor nutrition is indicated; patients may benefit from additional medication to control gastrointestinal symptoms, the use of dietary supplements to meet daily requirements and modifications in the dialysis prescription to control uremic symptoms better. In some cases, a period of supplemental feeding with enteral feeds may be warranted.

In the decision to proceed with wait listing and transplantation, consideration must be given to the length of current waiting times and the probability of surviving beyond that period given the current scarcity of donor organs. Full evaluation and maintenance on the waiting list consumes considerable resources; there should be a reasonable expectation that the patient will survive long enough following kidney transplantation to realize the benefits.

Elderly patients or those with poor functional capacity may be more likely to be offered an extended-criteria donor kidney; discussions should occur at the time of listing regarding the risk–benefit ratio of accepting such an offer, particularly in regions where waiting times may otherwise be prolonged. Recent data suggest that this strategy may produce acceptable results.[33,34]

The timing of transplantation in small children is influenced in part by the technical challenges inherent in performing the transplant operation with an adult-sized donor kidney, especially in infants less than 1 year of age. Small size, however, is not an absolute contraindication to transplantation, and centres with expertise in the transplantation of infant recipients have been successful in achieving graft outcomes that are similar to those in older children.[35–37] To avoid the deleterious effects on growth and development associated with uremia, children should be considered for preemptive transplantation whenever possible. Initiation of the evaluation for transplantation should, therefore, not be delayed until children are large enough to undergo transplantation; rather it should allow a transplant to be performed at the earliest date that it is technically feasible.

Children with developmental delay and their caregivers may benefit from an improved quality of life associated with freedom from dialysis. The transplant procedure can be performed safely in children with developmental delay, and graft outcomes are similar to those in other children.[38,39] Renal transplantation has also been associated with improvements in cognitive and psychomotor function.[40] This may allow children with developmental delay to reach their maximum potential. Thus, children, who would otherwise be considered for RRT, should not be excluded from consideration for transplantation solely on the basis of diminished cognitive or physical capacity. The decision to embark on RRT in children with severe developmental delay is made in consultation with the treating physician and family and considering the best interests of the child with regard to the benefits and morbidity of RRTs.

Obesity

Recommendations

1. Few data exist to suggest which, if any, obese (body mass index [BMI] ≥ 30 kg/m²) patients should be denied transplantation based on obesity per se (Grade C).
2. Supervised weight-loss therapy is recommended for obese candidates, with target BMI < 30 kg/m² (95th percentile in children) (Grade B).

An estimated 10–18% of patients evaluated for kidney transplantation are obese as defined by body mass index (BMI) ≥ 30 kg/m².[10] Obesity has been associated with hypertension, the development of type 2 diabetes mellitus and increased risk of death in the general population. Obese patients undergoing kidney transplantation are similarly at risk of adverse outcomes. They are at higher risk of delayed graft function10,[41,42] and suffer from more wound complications,[10,43,44] resulting in increased length of hospital stay and greater cost of transplantation. In a recent analysis of USRDS data, obesity was an independent risk factor for the development of new onset diabetes after kidney transplantation, with a relative risk of 1.73 ($p < 0.0001$).[45] Obesity has also been associated with a higher risk of graft loss and death-censored graft loss in some[10,42,45] but not all studies.[44,46,47] In some analyses, patient survival was also adversely affected by obesity.[10,42] In patients with a BMI above 33 kg/m², the risks of transplantation may be even greater. Based on an analysis of USRDS data, the increased risk of death first becomes significant when BMI is 34–36 kg/m².[42] The relative risk of death is even greater when BMI at transplant is above 36 kg/m².[42] These data suggest that transplantation at this level of BMI may be associated with unacceptably higher risk and will need careful consideration.

It is prudent to strongly recommend weight reduction to a BMI < 30 kg/m² before kidney transplantation. Obese patients should be referred to a multidisciplinary program targeting obesity to optimize chances of success. The role of surgical intervention for weight loss in this patient population is uncertain but may be considered in extreme cases. Obese patients should be carefully evaluated for pretransplant abnormalities in glucose metabolism, dyslipidemias and cardiovascular disease. Whether a patient should be denied kidney transplantation solely on the basis of obesity is a matter of debate. The risk of perioperative complications and inferior outcomes (graft and patient survival, rehabilitation potential and quality of life) must be balanced against the considerable risk of remaining on dialysis.

Cause of end-stage renal disease

Recommendations

1. There are few contraindications to kidney transplantation solely on the basis of the cause of ESRD, although the appropriate timing of transplantation, the type of transplant recommended, the risk of recurrent disease and the out-

come of kidney transplantation may be influenced by the cause of ESRD (Grade A).
2. Despite the risk of recurrent glomerulonephritis, there is no contraindication to a first kidney transplant in patients with ESRD due to primary glomerulonephritis, independent of the specific histologic type (Grade A).
3. Retransplantation should be considered in otherwise eligible patients who experienced recurrence of primary glomerulonephritis in a prior renal allograft. Further recurrence may occur in up to 80% of such patients in some settings, but the rate of progression of recurrent disease is unpredictable (Grade A).
4. Patients developing ESRD in the context of a prior non-renal transplant should be considered for kidney transplantation based on the same eligibility criteria used for kidney transplantation in general (Grade C).

The cause of ESRD may influence several aspects of kidney transplantation, including the appropriate timing, the risk of early or late recurrent disease and both short-term and long-term graft survival. It is well recognized that many forms of both primary and secondary renal disease may recur in the renal allograft. Notable exceptions include polycystic kidney disease, chronic pyelonephritis and Alport's syndrome. Assessment of the risk of recurrence is confounded by the significant proportion of patients experiencing ESRD of unknown etiology, the lack of biopsy information in a significant proportion of renal allograft recipients with deteriorating allograft function and the variable duration of follow-up. Issues related to transplantation in patients with ESRD due to inherited or acquired systemic disorders are addressed in the following section.

Recurrent glomerulonephritis has been reported in 5–20% of patients transplanted for ESRD due to glomerulonephritis and the prevalence of recurrence increases with duration of follow-up.[10,11,48] Allograft loss due to recurrent disease occurred in 8.4% of Australian patients transplanted for ESRD due to glomerulonephritis over 10 years of follow-up; it was the third leading cause of graft loss after chronic rejection and death with a functioning graft.[48] The type of glomerulonephritis was an independent predictor of graft loss, with the greatest risk of graft loss occurring in those with focal segmental glomerulosclerosis (FSGS; hazard ratio 2.03) and membranoproliferative glomerulonephritis (MPGN) type I (hazard ratio 2.91). Graft loss tended to occur earlier in patients with these forms of recurrent disease. The risk of recurrence is particularly high with FSGS (15–50%), MPGN type I (20–50%), MPGN type II (most recur) and IgA nephropathy (20–40% and may approach 100% by 10–20 years follow-up).[10,11] Factors such as rate of progression of the primary disease, duration of pretransplant dialysis, the degree of matching of donor and recipient human leukocyte antigen (HLA) and younger age of onset have variably been reported to predict the risk of recurrent glomerulonephritis. However, it is difficult to predict either the risk of recurrence or the aggressiveness with which recurrent disease may progress in an individual transplant recipient. Thus, otherwise eligible patients should be offered transplantation, and patients should be made aware of the risk of recurrent disease during their pretransplant education.

It is reasonable to proceed with living-donor kidney transplantation despite the risk of recurrent glomerulonephritis. Although some analyses have suggested a higher risk of recurrent FSGS resulting in premature graft loss in recipients of HLA-identical live-donor grafts, a recent analysis of the USRDS database suggests that annually adjusted death-censored graft loss was lowest in recipients of such grafts; recipients of mismatched living-donor kidney transplants also experienced better death-censored graft survival than recipients of either HLA-matched or mismatched deceased-donor kidneys.[49] Living kidney donors should be made aware of the possibility of recurrent disease and the potential impact this may have on long-term graft survival in the recipient.

Every effort should be made to define the cause of previous allograft failure, as the risk of recurrence in a second transplant approaches 80% in some settings. Of particular concern is the risk of recurrent FSGS leading to premature graft failure in a patient who has already experienced graft loss from recurrent FSGS; some have suggested that this is a relative contraindication to retransplantation with a living-donor kidney.[10]

Issues related to the transplantation of patients with ESRD due to urologic abnormalities or systemic disease processes are addressed in sections below. Patients with ESRD due to drug nephrotoxicity (i.e., lithium, analgesics) should be considered for kidney transplantation although consideration should also be given to conversion to alternative non-nephrotoxic agents before transplantation. Patients with ESRD due to calcineurin nephrotoxicity or other causes in the setting of a prior non-renal solid organ transplant should be considered for kidney transplantation based on the same eligibility criteria used for kidney transplantation in general.

Systemic diseases

Recommendations

1. Systemic diseases leading to end-stage renal failure are usually not a contraindication to renal transplantation (Grade C). The presence and severity of extra-renal disease will usually be more important in deciding suitability for transplantation.
2. The eligibility of patients with ESRD secondary to **diabetes mellitus** should be based on the presence of diabetic complications, particularly cardiovascular disease, and other comorbid conditions using the same eligibility criteria applied to the non-diabetic population (Grade B). Simultaneous kidney–pancreas transplantation should be considered in selected patients with type 1 diabetes mellitus.
3. Renal transplant candidates with **primary hyperoxaluria** should be considered for isolated renal transplantation if they are pyridoxine-sensitive and have minimal oxalate deposition (Grade B). Combined liver–kidney transplantation should be considered in patients with severe systemic oxalosis (Grade B).
4. Renal transplant candidates with **Fabry disease** should be

considered for renal transplantation if the systemic disease is not severe (Grade B).

5. Renal transplant candidates with **sickle-cell disease** should be considered for renal transplantation if the systemic disease is not severe (Grade B).
6. Renal transplant candidates with **anti-glomerular basement membrane** (anti-GBM) disease should be considered for renal transplantation if the circulating anti-GBM antibody is undetectable and they have quiescent disease (off cytotoxic agents) for at least 6 months post-treatment (Grade C).
7. Renal transplant candidates with **amyloidosis** (primary or secondary) should be considered for renal transplantation if there is no evidence of cardiac involvement (Grade B). Patients with primary amyloidosis should not undergo renal transplantation if there is associated multiple myeloma (Grade B). Patients with secondary amyloidosis should not undergo renal transplantation until the underlying inflammatory condition is in remission (Grade C). Patients with familial Mediterranean fever should receive colchicine to prevent recurrent disease in the allograft (Grade B).
8. Renal transplant candidates with **systemic lupus erythematosus** should be considered for renal transplantation if they have clinically quiescent disease for at least 6 months off cytotoxic agents (Grade C).
9. Renal transplant candidates with **scleroderma** should be considered for renal transplantation if they have quiescent disease for at least 6 months off cytotoxic agents and have limited extra-renal disease (Grade C).
10. Renal transplant candidates with **vasculitis** (Wegener's granulomatosis, microscopic polyangiitis, pauci-immune necrotizing glomerulonephritis, Henoch-Schonlein purpura) should be considered for renal transplantation if they have quiescent disease for at least 12 months off cytotoxic agents (Grade C).
11. Pretransplant anti-neutrophil cytoplasmic antibodies are not predictive of outcome and may still be positive at the time of transplantation (Grade B).
12. Patients with **thrombotic microangiopathy** or **hemolytic uremic syndrome** (HUS) should be considered for renal transplantation if they have quiescent disease (Grade C).
13. Renal transplant candidates with **congenital nephrotic syndrome** should be considered for renal transplantation after undergoing bilateral nephrectomy (Grade B).
14. Renal transplant candidates with **cystinosis** should be considered for renal transplantation (Grade B).
15. Renal transplant candidates with **autosomal recessive polycystic kidney disease** should be considered for renal transplantation (Grade A). Screening for evidence of portal hypertension and evaluation for unilateral or bilateral nephrectomy should occur before transplantation (Grade B).

Systemic diseases can recur in the transplanted kidney, but the risk for a specific patient is difficult to predict.[10] The studies examining recurrence have been problematic because in most patients cause of ESRD is not confirmed before transplant, the length of follow-up is highly variable and the reasons for biopsy (routine versus clinical indication) are different from study to study.[10] In the guidelines that follow, the influence of the systemic disease on outcome is evaluated by comparing allograft survival rate to the overall allograft survival rate published by the United Network for Organ Sharing (UNOS). In the most recent UNOS cohort, the 1- and 3-year deceased-donor renal allograft survival rates were 90.9% and 81.5%, respectively.[50]

Diabetes mellitus is the single leading cause of ESRD in Canada; over 40% of patients requiring RRT are diabetic. Patients with diabetes derive the same benefits from kidney transplantation as non-diabetic people, including greater survival compared with their dialysis-dependent wait-listed counterparts.[7] The assessment of eligibility of a diabetic patient with ESRD should be guided by the same principles applied to non-diabetic patients.[10] Due to their high risk for cardiovascular disease, particular attention should be paid to the assessment of vascular health. Periodic reassessment during the wait time is recommended, although controversy exists about the optimal screening method (see sections on cardiac and peripheral vascular disease). Diabetic nephropathy may recur in a renal allograft, although it rarely leads to graft failure. Although there are no outcome data, it is likely that the risk of recurrent diabetic nephropathy would be ameliorated by the same strategies used in the general population, namely tight control of glucose and blood pressure. Patients with diabetes should be warned that glucose metabolism is influenced by some of the immunosuppressive agents employed and by resolution of uremia. This may necessitate significant changes to therapy, particularly for patients previously controlled with lifestyle or oral hypoglycemic agents.

Patients with primary hyperoxaluria (type I) have an enzyme deficiency that leads to increased excretion of calcium oxalate. Recurrent stones and nephrocalcinosis lead to ESRD. The recurrence rate is high following renal transplantation without forced diuresis and pyridoxine.[10] It is controversial whether patients should undergo kidney transplantation alone or combined liver–kidney transplantation. An analysis of the USRDS database[51] showed that recipients of a combined liver–kidney transplant had improved death-censored renal allograft survival compared with isolated renal transplant recipients with oxalosis. However, there was no difference in patient survival. Another analysis from the United States[52] showed similar patient and renal allograft survival rates for patients receiving combined liver–kidney transplant or isolated renal transplants. The authors suggest that isolated renal transplantation is an option for patients with oxalosis, as liver–kidney transplantation can still be performed if the initial renal allograft fails. Good renal outcomes have been reported in pyridoxine-sensitive patients who received isolated renal transplants.[53] Recent UNOS data also suggest good outcomes for patients with oxalosis. From 1998 to 2001, in the 20 patients who received an isolated deceased-donor renal transplant for oxalosis, the 1- and 3-year renal allograft survival rates were 89.4% and 89.4%, respectively.[54]

It is recommended that isolated kidney transplantation be offered to patients with primary hyperoxaluria who are pyridoxine-sensitive with minimal oxalate deposition. Preemptive, living donation should also be encouraged to minimize

tissue oxalosis as native renal function declines. Combined liver–kidney transplantation should be offered to patients with severe systemic oxalosis.

Patients with Fabry's disease have an enzyme deficiency that results in the systemic accumulation of glycosphingolipid. Histologic recurrence of disease is very common but rarely leads to allograft failure.[10] In an analysis of the USRDS database, 5-year patient and allograft survival rates were found to be no different for the 93 patients with Fabry's disease compared with a matched control group.[55] From 1998 to 2001, 20 patients received a deceased-donor renal transplant for Fabry's disease; their 1- and 3-year renal allograft survival rates were 94.7% and 94.7%, respectively.[54] It is not clear whether the use of recombinant enzyme replacement will improve outcomes. We recommend that patients with Fabry's disease be considered for renal transplantation if the systemic disease is not severe.

Patients with sickle-cell disease can develop recurrent renal disease following transplantation; however, long-term allograft outcome is really dependent on patient survival.[10] Patients with sickle-cell disease have a risk of death following transplantation that is 7.9 times that of patients with IgA nephropathy.[56] The 3-year renal graft survival rate was 48% for patients with sickle-cell disease compared with 60% for a control group of African-Americans; however, patient survival for those transplanted was much better than for similar patients with sickle-cell disease who remained on the wait list.[57] From 1998 to 2001, among the 33 patients who received a deceased-donor renal transplant for sickle-cell disease, the 1- and 3-year renal allograft survival rates were 80.1% and 74.4%, respectively, which was far below the national average.[50,54] Patients with sickle-cell disease should be considered for renal transplantation if the systemic disease is not severe.[10] Transplantation should probably be delayed if there are frequent sickle-cell crises, but there are no data to support this recommendation.[10]

Patients with anti-glomerular basement membrane (anti-GBM) disease can have histologic recurrence in up to 50% of cases, but clinical recurrence in less than 10%.[10] Recurrent cases reported in the literature usually had circulating anti-GBM antibody present at the time of transplantation.[11] In a recent study, none of the 44 patients with anti-GBM disease had graft failure due to recurrent disease.[48] From 1998 to 2001, for the 56 patients who received a deceased-donor renal transplant for anti-GBM disease, the 1- and 3-year renal allograft survival rates were 88.1% and 83.5%, respectively.[54] Patients with anti-GBM disease should be considered for renal transplantation if the circulating anti-GBM antibody is undetectable and they have quiescent disease (off cytotoxic agents) for at least 6 months post-treatment.

Patients with systemic amyloidosis (primary or secondary) can develop recurrent disease in 10–40% of cases following renal transplantation.[10,11] Several studies have shown decreased patient survival following renal transplantation for those with amyloidosis.[56,58,59] In 1 study, the risk of death post-transplantation was increased 3.7 times compared with recipients with IgA nephropathy.[56] The outcome after kidney transplantation is mainly influenced by the severity of systemic (cardiac) disease.[10] From 1998 to 2001, 31 patients received a deceased-donor renal transplant for amyloidosis.[54] The 1- and 3-year renal allograft survival rates were 90.1% and 76.1%, respectively.

We recommend that patients with amyloidosis be considered for renal transplantation if there is no evidence of cardiac involvement. Patients with primary amyloidosis should not undergo renal transplantation if there is associated multiple myeloma. Patients with secondary amyloidosis should not undergo renal transplantation until the underlying inflammatory condition is in remission. Patients with familial Mediterranean fever should receive colchicine to prevent recurrent disease in the allograft.[10,11] Auto stem cell transplant may be curative and could be considered before renal transplantation in primary amyloidosis.[60]

Patients with systemic lupus erythematosus (SLE) were thought to have recurrent disease in fewer than 10% of renal transplants.[10] However, a recent report found histologic recurrence in 30% of patients with SLE.[61] Recurrent SLE rarely leads to allograft failure.[11,61,62] From 1998 to 2001, 824 patients received a deceased-donor renal transplant for SLE.[54] The 1- and 3-year renal allograft survival rates were 90.4% and 78.1%, respectively. Patients with SLE should be considered for renal transplantation if they have quiescent disease for at least 6 months off cytotoxic agents. Patients may still be on low-dose prednisone (≤ 10 mg/day) at the time of transplantation. Patients with SLE have a higher incidence of coagulation abnormalities and may benefit from screening (see section on hematologic disorders).

Patients with scleroderma develop recurrent disease in approximately 20% of cases post-transplantation.[10] An analysis of the UNOS database from 1987 to 1997 showed that the 5-year renal graft survival was 47% for the 86 patients with scleroderma.[63] This allograft survival rate was similar to that of a group of patients with SLE transplanted during the same period.[63] However, patients with scleroderma have a risk of death following transplantation that is 2.6 times greater than patients with IgA nephropathy.[56] From 1998 to 2001, 32 patients received a deceased-donor renal transplant for scleroderma.[54] The 1- and 3-year renal allograft survival rates were 68.6% and 54.3%, respectively. Patients with scleroderma should be considered for renal transplantation if they have quiescent disease for at least 6 months off cytotoxic agents. The presence of extra-renal disease (gastrointestinal, cardiac and pulmonary) must be evaluated closely before proceeding with transplantation.

Patients with vasculitis (Wegener's granulomatosis, microscopic polyangiitis, pauci-immune necrotizing glomerulonephritis and Henoch-Schonlein purpura) have a 17% incidence of recurrent disease post-transplantation.[64] Graft loss due to recurrent disease occurred in only 2% of 102 patients with vasculitis.[48] The type of underlying vasculitis appears to have no influence on disease recurrence.[48,64] The presence of circulating anti-neutrophil cytoplasmic antibodies at the time of transplantation was also not predictive of disease recurrence.[48,64] From 1998 to 2001, 130 patients received a deceased-donor renal transplant for vasculitis.[54] The 1- and 3-year renal allograft survival rates were 93.0% and 78.7%,

respectively. Patients with vasculitis should be considered for renal transplantation if they have quiescent disease for at least 12 months off cytotoxic agents.

In a recent meta-analysis,[65] 28% of patients with hemolytic uremic syndrome (HUS) or thrombotic thrombocytopenic purpura (TTP) experienced recurrent disease; recurrence was associated with significantly poorer graft survival. Factors associated with an increased risk of recurrence included older age of onset, shorter interval between HUS onset and transplantation, a living-donor kidney and the use of calcineurin inhibitors. Of interest, there was no difference in the rate of recurrence between first and second transplants and the duration of dialysis before transplantation had no impact on recurrence. The risk of recurrent disease is greatest with familial HUS; epidemic HUS (associated with toxigenic *Escherichia coli*) rarely recurs.[10,11] It seems reasonable to recommend that kidney transplantation in patients with HUS or TTP be deferred until the disease process is quiescent.

Non-epidemic HUS in children is associated with a 21% recurrence rate post-transplantation, but the rate may be as high as 45% in children with HUS associated with factor H deficiency.[66] Currently, there are no specific features that reliably predict recurrence of non-epidemic HUS in children after the first transplantation.[66] In autosomal dominant forms of HUS, there is the risk that related donors may later develop HUS themselves, if they carry the same mutation.[66] Potential living donors and recipient must be made aware of these risks, so that they may provide fully informed consent.

Congenital nephrotic syndrome due either to Finnish-type nephrotic syndrome or diffuse mesangial sclerosis is associated with growth delay, a high risk of thrombotic complications and death due to sepsis. Experience with early bilateral nephrectomy, especially in patients with Finnish-type nephrotic syndrome, demonstrates that good growth, freedom from infectious and thrombotic complications and, ultimately, renal transplantation can be achieved.[66–70] Children with diffuse mesangial sclerosis present the additional challenge of increased risk of Wilms' tumour considering the association of diffuse mesangial sclerosis with the Denys–Drash syndrome. Serial screening by ultrasound every 3 months has been advocated for these patients until bilateral nephrectomy can be performed.[70]

Patients with cystinosis have a defective lysosomal cysteine carrier that causes intracellular accumulation of cysteine. Compared with other causes of ESRD, patients with cystinosis have among the best renal allograft survival rates, and although cysteine crystals have been demonstrated in graft-infiltrating cells, there is no significant recurrence of renal disease after transplantation.[71,72] Although patients approaching ESRD often have significant polyuria and proteinuria, these have not been associated with an increased risk of thrombotic complications with transplantation, and preemptive transplantation should be considered when feasible.[73] Extra-renal disease continues to progress after transplantation, and continued treatment with cysteamine is strongly recommended to attenuate this process.[74]

Although renal transplantation is successful in treating the renal failure associated with autosomal recessive polycystic kidney disease, the extra-renal manifestations can result in significant morbidity, including hepatic fibrosis with the development of portal hypertension and the risk of variceal bleeding, feeding disturbances and pulmonary compromise related to mass effects from the markedly enlarged kidneys.[75,76] Portal hypertension typically develops in the second decade of life and is progressive with the appearance of splenomegaly, cytopenia and gastrointestinal bleeding. In 1 large series, it was responsible for 4 deaths post-transplantation (29% mortality risk) and had a long-term prevalence of 63%.[77] In children born without pulmonary hypoplasia, growth of the abnormal kidneys postnatally may compress the stomach, resulting in feeding difficulties, or may compress the diaphragm causing respiratory compromise. Optimum management in this case is either unilateral or bilateral nephrectomy.[75,78,79] Evaluation for transplantation may also require consideration of nephrectomy to allow sufficient space for a young child recipient to accommodate an adult donor allograft.

Infections

Recommendations

1. Patients should be free of active infection, whether of viral, bacterial or fungal origin (Grade B).
2. Where possible, transplant candidates should receive immunizations for infections that are prevalent or potentially life-threatening. This includes the usual immunizations recommended for the pediatric population and those for hepatitis B, influenza and pneumococcal pneumonia. *Varicella* vaccine should be given to those without antibodies. Vaccinations should be administered early in the course of renal disease, as response rates are generally superior with better kidney function (Grade A).
3. Peritonitis, tunnel infections and vascular access-related infections in patients on peritoneal or hemodialysis should be fully treated before transplantation. There are no data to recommend an optimum infection-free interval before transplantation, but documentation of the eradication of infection after completion of antibiotic therapy is appropriate (Grade C).
4. Transplant candidates should be screened for exposure to mycobacteria with a careful clinical history, chest radiography and purified protein derivative (PPD) skin testing. Patients with active tuberculosis (positive cultures, clinical signs and symptoms or positive imaging studies) should receive adequate therapy with documented microbiologic and radiologic resolution before transplantation. Patients with latent tuberculosis (positive skin test not induced by vaccination or chest radiograph suggesting quiescent tuberculosis) without a history of adequate treatment or prophylaxis should be considered for prophylaxis pre- or post-transplant, provided no contraindications exist. Referral to a specialist in infectious diseases may be appropriate to assess fully the risk of reactivation of mycobacterial disease (Grade C).
5. Serostatus for cytomegalovirus (CMV) and Epstein-Barr

virus should be assessed before transplant but should not determine eligibility for transplantation as there are appropriate techniques for monitoring and managing such infections (Grade A).

6. All patients being assessed for kidney transplantation should be screened for HIV infection (Grade A).
7. HIV-infected patients with end-stage kidney failure may be considered for kidney transplantation if they meet the following criteria (Grade B):
   - Demonstrated adherence to a highly active anti-retroviral therapy (HAART) regimen
   - Undetectable (< 50 copies/mL) HIV viral load for > 3 months
   - CD4 lymphocyte count > 200/mL for > 6 months
   - No opportunistic infections
   - Willingness to use prophylaxis against congenital CMV, *Herpes simplex* virus, *Pneumocystis carinii* pneumonia and fungal infection
   - Freedom from neoplasia, except for treated basal or squamous cell carcinoma of the skin, in situ anogenital carcinoma (human papilloma virus-associated anal intraepithelial neoplasia), solid tumours treated with curative therapy and disease-free at 5 years
   - Usual kidney transplantation eligibility criteria are met.
8. Kidney transplantation in HIV-infected patients should only be performed in centres where staff have extensive experience in the management of both HIV infection and kidney transplantation (Grade C).
9. Retransplantation should be considered in otherwise eligible patients who have experienced prior renal allograft loss due to polyomavirus-associated nephropathy. The role of transplant nephrectomy and monitoring of urine or plasma BK viral load before transplant remain unclear (Grade B).

Patients with sepsis, including active tuberculosis, parasitic or viral disease should be excluded from transplantation until the infection is fully resolved and antimicrobial therapy has been discontinued without evidence of recurrence. The number of different infections to be considered is large and beyond the scope of this document. The reader is referred to the recently published and comprehensive guidelines addressing the infectious diseases occurring in the context of solid organ transplantation for a more complete discussion.[80] Our recommendations concerning eligibility for kidney transplantation are consistent with these published practice guidelines. Recommendations concerning hepatitis B and C are discussed in the section on liver disease.

A careful clinical history should be obtained to identify factors that may increase the risk of developing serious infections post-transplant, including prior splenectomy, prior chemotherapy or prior exposure to anti-proliferative immunosuppressive therapy, prior bone marrow transplantation or the presence of inherited or acquired immunodeficiencies, such as hypogammaglobulinemia. Although the presence of these conditions should not necessarily preclude transplantation, consultation with experts in hematology or infectious disease or both may be warranted to determine fully the risks of post-transplant immunosuppression and to devise optimum prophylaxis strategies to reduce the risk. In addition to routine vaccination against the usual childhood infections, ESRD patients should receive immunizations against influenza, pneumococcal infection and hepatitis B. Patients at risk of infection with encapsulated organisms, such as asplenic individuals, should also be considered for vaccination against *Haemophilus influenzae* and *Meningococcus*. Ideally, vaccinations should be administered as early as possible in the course of renal disease as response rates are superior with better kidney function. Patients who are seronegative for *Varicella zoster* virus should be immunized before transplantation. Vaccination against *Varicella* reduces the risk, morbidity and cost of post-transplant infection and should be administered to all children without protective antibody titers.[81,82] If transplantation is imminent, vaccination may be withheld pretransplantation as the *Varicella* vaccine is live attenuated.

Dialysis-related infections (peritonitis, tunnel infections, catheter- or arteriovenous graft-related bacteremia, etc.) should be fully treated and their eradication documented before transplantation. This may be particularly important in the context of recurrent peritonitis or bacteremia with organisms predisposed to seeding of joints or leading to endocarditis. An appropriate interval between an adequately treated infection and transplantation has not been defined. Early removal of a peritoneal dialysis catheter post-transplantation may reduce the risk of subsequent peritonitis.[83,84]

Occult dental infections have also been reported post-transplant, and an international survey suggests that most transplant centres include a dental examination and treatment as part of their pretransplant assessment.[85] It seems reasonable to delay kidney transplantation until dental infections have been eradicated.

There appears to be an increased incidence of mycobacterial disease in both dialysis and transplant patients.[86] In uremic patients, these infections may be asymptomatic; the diagnosis is made more difficult by the frequency of anergy in this patient population. Post-transplant exposure to immunosuppressive therapy may result in disseminated aggressive disease, the therapy of which is complicated by interactions between certain anti-tuberculous therapy and the immunosuppressive medications. Therefore, it is critical to determine the risk of reactivation of mycobacterial disease as part of the pretransplant assessment. Obtaining a clinical history regarding risk factors, duration and type of prior tuberculous therapy, PPD skin testing and review of recent chest radiography are appropriate initial steps. It is less clear whether prophylaxis reduces the incidence of reactivation of tuberculosis.[87] However most centres currently require pre- or post-transplant prophylaxis in patients with a positive PPD skin test in the absence of prior treatment, provided there are no contraindications to therapy.[88,89] Referral to an infectious disease specialist may be warranted in such cases.

The incidence and severity of post-transplant infections with CMV or Epstein-Barr virus depend on multiple factors including the presence of latent infection in the donor, the serostatus of the recipient and the immunosuppressive proto-

col employed.[90,91] Over the last decade, tremendous strides have been made in developing highly sensitive assays that permit prospective monitoring of viral load post-transplant, prophylaxis strategies and preemptive therapy to reduce the severity of infection, and improved treatment protocols for those with active infection. Thus, although serologic status for these infections should be determined as part of the routine transplant assessment, the results should not otherwise influence eligibility for transplantation. Patients at higher risk of such infections, particularly those at risk for primary infection with CMV or Epstein-Barr virus, should be informed of their increased risk and appropriate monitoring and management protocols should be implemented post-transplant based on current practice guidelines.

Those infected with HIV have historically been excluded from consideration for organ transplantation because of the potential impact of immunosuppressive therapy on the risk of opportunistic infections and post-transplant neoplasia.[92] Additional concerns include the presence of co-infection with hepatitis B or C, the risk of transmission of HIV to health care workers and drug interactions between certain anti-retroviral agents and the immunosuppressive medications. With the advent of highly active anti-retroviral therapy (HAART) and improved infection prophylaxis, the morbidity and mortality of patients infected with HIV has decreased dramatically. End-stage organ failure from HIV, co-existing infection with the viral hepatitides or unrelated disease processes now influence life expectancy more than HIV disease itself. Recent clinical experience with liver or kidney transplantation in highly selected HIV-infected patients has been favourable, yielding short-term results similar to those in uninfected people.[93–97] and leading to reconsideration of HIV infection as an absolute contraindication to solid organ transplantation.[98–100] Current prospective clinical trials are underway to better define the risks and outcomes of kidney transplantation in HIV-infected people. Until those results are available, it seems prudent to restrict kidney transplantation to HIV-positive ESRD patients who have no AIDS-defining complications, have undetectable viral loads and CD4 counts exceeding 200–300/mL and who are able to tolerate a HAART protocol. Special considerations may apply to HIV-positive patients, who are co-infected with hepatitis C virus, as they require an assessment for the presence of cirrhosis, frequent monitoring of their liver disease and consideration of pretransplant therapy for hepatitis C (see liver disease, below). Eligible patients should be treated in centres whose personnel are experienced in the management of both HIV infection and kidney transplantation. If possible, HIV-positive patients should be enrolled in clinical trials being conducted in this patient population to help define the risks and outcomes of kidney transplantation.

BK virus infection has emerged as a significant clinical problem, with current immunosuppressive protocols leading to premature renal allograft failure in many people with this complication.[101,102] Infection is ubiquitous, affecting up to 90% of the population. Thus, the great majority of renal transplant recipients are already infected at the time of transplantation. Polyomavirus persists in the renal epithelium in a latent state, and reactivation and viral shedding in the urine occur frequently in the context of immunosuppression. The relative roles of donor-derived vs. recipient-derived virus are unclear. Emerging data suggest that retransplantation in patients who have experienced prior allograft failure due to polyomavirus-associated nephropathy may be successful,[103–107] although recurrences of viral nephropathy have been reported. At present, there is no consensus regarding the need for transplant nephrectomy before retransplantation; recurrences have been described despite removal of the previous allograft. Although some have suggested delaying retransplantation until urine and plasma viral loads have become negative, there are few prospective data to support this recommendation. Nor is there sufficient evidence to recommend a particular immunosuppressive protocol in patients undergoing retransplantation.

Malignancy

Recommendations

1. Renal transplant candidates with a previous history of malignancy should be tumour free before proceeding with transplantation (Grade A).
2. Most renal transplant candidates with a history of malignancy should wait a period of time between successful treatment and transplantation. The length of time will depend on the type of malignancy (Grade B).
3. Patients being evaluated for kidney transplantation, particularly those over 50 years of age, should be screened for pretransplant malignancy according to clinical practice guidelines developed for the general population as part of the periodic health examination (Grade C).
4. Most renal transplant candidates with a history of **bladder cancer** should wait 2 years from successful treatment to renal transplantation, although superficial low-grade lesions may not require any waiting time (Grade B).
5. Pretransplant screening cystoscopy should be considered for high-risk patients with past exposure to cyclophosphamide or those with analgesic nephropathy (Grade C).
6. Most renal transplant candidates with a history of **breast cancer** should wait at least 5 years from successful treatment to transplantation (Grade B), although patients with early in situ (e.g., ductal carcinoma in situ) lesions may only require a 2-year wait (Grade C).
7. Patients with advanced breast cancer (stage III or IV) should not undergo renal transplantation (Grade B).
8. Most renal transplant candidates with a history of successfully treated, localized **cervical cancer** should wait at least 2 years from treatment to transplantation (Grade B). No firm recommendation can be made for patients with more invasive cervical cancer (Grade C). Patients with in situ cervical lesions may proceed with transplantation after waiting less than 2 years (Grade B).
9. Most renal transplant candidates with a history of **colorectal cancer** should wait at least 5 years from successful treatment to transplantation, although a shorter waiting time of 2–5 years may be sufficient in patients with localized disease (Duke's stage A or B1) (Grade B).

10. Renal transplant candidates with a history of **Hodgkin's disease**, **non-Hodgkin's lymphoma**, **post-transplant lymphoproliferative disorder** or **leukemia** should wait at least 2 years from successful treatment to transplantation (Grade C).
11. Renal transplant candidates with a history of **lung cancer** should wait at least 2 years from successful treatment to transplantation (Grade C).
12. Most renal transplant candidates with a history of **melanoma** should wait at least 5 years from successful treatment to transplantation, although patients with in situ melanoma may be considered for transplantation after a waiting period of 2 years (Grade B).
13. Most patients with **multiple myeloma** should not undergo renal transplantation (Grade C).
14. Renal transplant candidates with a history of **basal cell carcinoma of the skin** do not require any waiting time after successful removal before proceeding with transplantation (Grade C). No firm recommendation about a waiting period can be made for patients with a history of **squamous cell carcinoma** of the skin (Grade C).
15. Most renal transplant candidates with a history of **prostate cancer** should wait at least 2 years from successful treatment to transplantation (Grade B), although patients with focal, microscopic low-grade (Gleason's grade ≤3), low-risk (T1a, T1c) disease may not require any waiting period (Grade C). Patients with advanced disease (grade 4 or 5, T3c, T4, N+, M+) should not undergo renal transplantation (Grade B).
16. Most renal transplant candidates with a history of **renal cell carcinoma** should wait at least 2 years from successful treatment to transplantation, although patients with small, incidental tumours may not require any waiting period (Grade B). Patients with large or invasive or symptomatic tumours may require a waiting period of 5 years (Grade B).
17. Renal transplant candidates with a history of **Wilms' tumour** should wait at least 1 year from successful treatment to transplantation (Grade B).
18. Renal transplant candidates with a history of **testicular cancer** should wait at least 2 years from successful treatment to transplantation (Grade B).
19. Renal transplant candidates with a history of **thyroid cancer** should wait at least 2 years from successful treatment to transplantation (Grade B).

Malignancy accounts for 9–12% of deaths following transplantation; elimination of cancer in transplant candidates is expected to decrease post-transplant mortality.[10] Patients with successfully treated cancer are generally considered candidates for renal transplantation.[10] The decision regarding suitability for transplantation should be made in consultation with the appropriate cancer specialist (medical oncologist, radiation oncologist, surgical oncologist, urologist, general surgeon, etc.). A past or current history of malignancy does not preclude referral for evaluation for kidney transplantation; earlier referral may define the recommended waiting times in specific types of malignancy or influence the choice of therapy recommended in some forms of low-grade malignancy.

For most cancers, post-transplant recurrence rate increases as the waiting time from treatment to transplantation is reduced.[10] For example, the cancer recurrence rate was 54% in those who waited less than 2 years from cancer treatment to renal transplantation, 33% for those who waited 2–5 years and 13% in those who waited more than 5 years before transplantation. Waiting times for specific cancers are addressed below.

Screening for pretransplant malignancy is particularly important in the older patient. Except in specific circumstances, identified below, screening should be performed according to clinical practice guidelines developed for the general population for breast cancer, cervical cancer, colorectal cancer and prostate cancer. As these guidelines are frequently revised, transplant programs should periodically review them and adapt their assessment process accordingly. At present, it seems reasonable to require a screening mammogram in all women 50 years and older and those with a family history of breast cancer as recommended by the Canadian Task Force on Preventive Health Care.[108] Female transplant candidates should undergo pretransplant cervical cytology testing and pelvic examination.[10] Chest radiography should be part of the routine pretransplant evaluation.[10] Screening tests for colorectal cancer should be undertaken according to risk level; patients at higher risk include those with longstanding inflammatory bowel disease, a personal or family history of familial adenomatous polyposis or hereditary nonpolyposis colorectal cancer. Screening for prostate cancer in the general population is controversial, and there are no universally accepted guidelines. However, pretransplant digital rectal examination should be considered for male renal transplant candidates 50 years of age and older.

Patients with preexisting bladder carcinoma have a recurrence rate of 18–26% following transplantation.[109,110] Most recurrences have been in patients who waited less than 2 years from treatment to transplantation.[110] Patients with a prior history of invasive bladder cancer should wait a minimum of 2 years from cancer treatment to renal transplantation. Patients with superficial lesions (pTa, unifocal, grade 1 disease) have a high risk of local recurrence (up to 60%) but a low risk of invasive or metastatic disease. These patients may not require any waiting period between treatment and transplantation,[10] but should undergo periodic surveillance with imaging of the upper urinary tract, urine cytology and cystoscopy as recommended by the urologist both pre- and post-transplant. Carcinoma in situ is considered a high-grade lesion; such patients should undergo treatment and be disease-free for 2 years before renal transplantation.

There are few data to support cystoscopy as a routine screening procedure before transplantation. However, patients at high-risk for cancer (analgesic nephropathy, cyclophosphamide use) should be considered for pretransplant cystoscopy.[10]

Patients with preexisting breast carcinoma have a recurrence rate of 5.4–63.6% following transplantation.[10,110,111] The stage at presentation seems to be the most important factor influencing recurrence; patients with stage I and stage II disease had a recurrence rate of 5.4% and 8%, respectively,

whereas those with stage III disease had a recurrence rate of 63.6% following transplantation.[111] The mortality rate from breast cancer after transplantation varies from 4% to 76% and again depends on stage of the cancer at presentation.[10,111] Most patients studied have waited at least 5 years from treatment to transplantation.[110,111] Thus, patients with a past history of breast cancer should wait at least 5 years from treatment to transplantation. Patients with advanced disease at presentation (stages III and IV) should not be offered transplantation because of the high risk of recurrence. Patients with in situ lesions (e.g., ductal carcinoma in situ) at presentation may require only a 2-year wait.

Patients with preexisting cervical carcinoma have a recurrence rate of 5–6% following transplantation.[110,112] Most patients studied have waited longer than 5 years from treatment to transplantation.[110,112] The mortality rate from recurrent cervical cancer after transplantation was 66% in 1 study.[110] The prognosis for those with in situ lesions is more favourable and these patients may require shorter waiting times.[110] Patients with successfully treated, localized cervical cancer should wait at least 2 years from treatment to transplantation.[10] No firm recommendation can be made for patients with more invasive disease, but they should probably wait at least 5 years before transplantation.[10] Patients with in situ cervical lesions may proceed with transplantation after waiting less than 2 years as long as gynecologic surveillance is ongoing.

Patients with preexisting colorectal carcinoma have an overall recurrence rate of 12–21% following renal transplantation.[10,110,113] Patients with Duke's stage A or B1 disease (no extension into pericolic fat or nodes) have recurrence rates of 14% and 19%, respectively; patients with more advanced disease have a recurrence rate of 42%.[113] Most recurrences have occurred in patients who waited 2–5 years from treatment to transplantation.[10] Mortality from recurrent colorectal cancer following transplantation was as high as 63% in 1 report.[110] Patients with successfully treated colorectal cancer should wait at least 5 years from treatment to transplantation.[10] Patients with Duke's stage A or B1 disease have lower recurrence rates and could be considered for transplantation after waiting 2–5 years.[10]

Patients with preexisting lymphoma (Hodgkin's disease and non-Hodgkin's lymphoma) have a recurrence rate of 11% following renal transplantation.[10,110] Records show that most patients (72%) with lymphoma had waited at least 5 years from treatment to transplantation.[110] Patients with successfully treated lymphoma should wait at least 2 years from treatment to transplantation.[10] Although there are limited data on recurrence of leukemia following renal transplantation, it seems prudent for patients with successfully treated leukemia to wait at least 2 years from treatment to transplantation.[10]

Post-transplant lymphoproliferative disorder (PTLD) may result in allograft failure leading to repeat transplantation. The overall recurrence rate of PTLD in repeat transplantation is 3%, with the median interval from diagnosis to repeat transplantation of 37 months.[114] The survival rate of renal transplant recipients is greater than that of recipients of other solid organs.[114] For patients with successfully treated PTLD, it seems prudent to wait at least 2 years from treatment to repeat transplantation.[114]

There are limited data on the recurrence of lung cancer following renal transplantation; however, for patients with successfully treated lung cancer it seems prudent to wait at least 2 years from treatment to transplantation.[10]

Patients with preexisting melanoma have a recurrence rate of 21% following renal transplantation.[10] In 1 report, the mortality rate with recurrence was 100%.[110] Most patients (83%) with recurrent melanoma waited less than 5 years before transplantation.[110] The rate of recurrence of in situ lesions is lower than that of invasive disease.[10] Patients with successfully treated melanoma should wait at least 5 years from treatment to transplantation, although patients with in situ melanoma may be considered for transplantation after a waiting period of 2 years.[10]

Patients with preexisting multiple myeloma have a recurrence rate of 67% following renal transplantation.[10] The mortality rate with recurrence following transplantation was 100% in 1 report.[110] We recommend that patients with multiple myeloma not undergo renal transplantation.[10] Newer regimens (e.g., bone marrow transplantation) may lead to long-term remission. However, there are insufficient data to make a recommendation on waiting time from successful bone marrow transplantation to renal transplantation.

Patients with preexisting non-melanoma skin cancer have a recurrence rate of 48–62% following renal transplantation.[10,110] Squamous cell carcinoma of the skin can lead to local invasion, metastases and death in this setting.[110] Of the patients with recurrent disease, 61% had been treated less than 2 years before transplantation, 35% between 2 and 5 years and 4% had been treated more than 5 years before transplantation.[110] A waiting period of 2 years may eliminate some recurrent skin cancers but the impact of this intervention is unknown given the potent immunosuppressive regimens in use today.[10] There are few data on which to base a recommendation for a specific waiting time for verrucous or human papillomavirus-related cancers, although concerns exist regarding the recurrence rate in the setting of immunosuppression. It seems prudent to recommend a minimum 2-year waiting time before transplantation. Patients with basal cell carcinomas do not require any waiting time after successful removal.[10]

Prostate cancer is common and affects 30% of men over the age of 50. One in 8–10 men will develop clinically significant prostate cancer. Most will be Gleason's grade 3 disease with a doubling time of 2 to 3 years. The medium-risk population has a life expectancy of about 10 years if the cancer is untreated. Patients with preexisting prostate cancer have a recurrence rate of 18% following renal transplantation.[10,115] Those with localized disease (T1 and T2) had recurrence rates of 14–16% and those whose disease extended beyond the prostate capsule (T3+) had a recurrence rate of 36% and a mortality rate of 27%.[115] Of those with recurrent disease, 40% had been treated less than 2 years before transplantation.[110] Most patients with a past history of prostate cancer should wait at least 2 years between treatment and transplantation. Patients with advanced disease (outside the prostate capsule; T3+, T4, N+, M+) at presentation should not be offered transplantation because of the high risk of recurrence. Patients with

low-risk prostate cancer may not require any waiting period.

Patients with a history of symptomatic renal cell cancer have a recurrence rate of 30% following renal transplantation.[110] Of the patients with recurrent disease, 61% had been treated less than 2 years before transplantation, 33% between 2 and 5 years before transplantation and 6% had been treated more than 5 years before transplantation.[110] Death due to recurrent disease may be as high as 80%.[10] The recurrence rate of incidentally discovered renal cell carcinoma is less than 1%.[10] Most patients with a past history of symptomatic renal cell carcinoma should wait at least 2 years from treatment to transplantation.[10] Large (≥ 5 cm) or invasive renal cell cancers may require a 5-year waiting period because of their higher risk of recurrence.[10] Small (< 5 cm), incidentally discovered renal cell cancers may not require any waiting period before transplantation.[10]

Wilms' tumour is a common childhood malignancy that presents as unilateral or bilateral disease or in association with extra-renal findings, such as aniridia, or as part of the syndrome of male pseudohermaphrodism, gonadal dysgenesis and diffuse mesangial sclerosis known as the Denys–Drash syndrome. These syndromes are commonly associated with mutations in the Wilms' tumour suppressor gene WT1.[116,117] Bilateral nephrectomy before transplantation is advocated for children with bilateral Wilms' tumour or with the Denys–Drash syndrome to be certain of removing tissue with potential malignancy.[118] In the future, identification of mutations in WT1 may be helpful in determining which patients may benefit from pretransplant nephrectomy. Survival, in general, is poorer for patients with bilateral Wilms' tumour compared with unilateral disease.[119,120] The recurrence risk is greatest when transplantation is performed less than 1 year after completion of chemotherapy; thus, renal transplantation should be delayed until at least 1 year after completion of treatment,[118,120] although some advocate a delay of 2 years or more.[121]

Patients with a history of testicular cancer have a recurrence rate of 3–12% following renal transplantation[110,122] with most (> 75%) recurrences appearing within 2 years. Mortality due to recurrent disease ranges from 0% to 8%.[110,122] Most patients have waited more than 5 years before transplantation.[110,122] Patients with a history of testicular cancer should wait at least 2 years from treatment to transplantation.[10]

Patients with a history of thyroid cancer have a recurrence rate of 7–8% following renal transplantation.[110,123] Low-grade papillary tumours and those incidentally discovered at the time of parathyroidectomy portend a favourable prognosis.[10] Patients with a history of thyroid cancer should wait at least 2 years from treatment to transplantation.[10]

Pulmonary disease

Recommendations

1. Patients with the following respiratory conditions and severity are not candidates for kidney transplantation:
   - Requirement for home oxygen therapy (Grade C)
   - Uncontrolled asthma (Grade C)
   - Severe cor pulmonale
   - Severe chronic obstructive pulmonary disease (COPD)–pulmonary fibrosis or restrictive disease with any of the following parameters (Grade C):
     - best forced expiratory volume in 1 s (FEV_1) < 25% predicted value
     - Po_2 room air < 60 mmHg with exercise desaturation, Sao_2 < 90%
     - > 4 lower respiratory infections in the last 12 months
     - moderate disease with evidence of progression
2. Patients with moderate COPD–pulmonary fibrosis or restrictive disease with any of the following parameters have a relative contraindication for kidney transplantation (Grade C):
   - Best FEV_1 25–50% of predicted value
   - Po_2 room air < 60–70 mmHg
   - Restrictive disease with exercise desaturation, Sao_2 90%
3. Patients should be strongly encouraged to stop smoking before kidney transplantation. Patients who continue to smoke may be eligible for kidney transplantation with full informed consent regarding their increased risk (Grade C).
4. Children with bronchopulmonary dysplasia, pulmonary hypoplasia or other significant chronic lung disease should be evaluated for transplantation in consultation with a pediatric respirologist (Grade C).

For patients with irreversible lung disease, the issues in determining eligibility for kidney transplantation include both long-term survival and short-term operative risks.[10,11] Patients in the critical contraindication category have mortality rates that are quite high; a best FEV_1 of < 40% of the predicted value is associated with a 50% survival rate at 6 years follow-up.[124] Patients with an FEV_1 < 25% of predicted value would be expected to have an even lower survival rate. The prognosis in patients requiring home oxygen therapy is also significantly worse, with 5-year survival rates as low as 30%.[125] Patients in the relative contraindication category are also at significant risk, especially if they are older, still smoking or have evidence of progression of the underlying lung disease. The lower survival rates significantly limit the benefits of transplantation. In addition, both groups of patients are likely to have higher postoperative complications. The usefulness of routine spirometry in clinical evaluation to predict postoperative complications is uncertain despite evidence suggesting that arterial blood gas and spirometry are significant predictors of short-term postoperative complications.[126]

Preoperative assessment for kidney transplantation should be the same as for those patients undergoing abdominal surgery. In addition to routine evaluation with medical history and physical examination, posteroanterior and lateral chest radiographs should be obtained. Additional tests should be ordered as indicated, including arterial blood gases, pulmonary function tests or chest CT scan (helical, high resolution). Patients with abnormal chest radiographic findings (nodules or atelectasis) should be further evaluated, particularly older patients or those with a significant smoking history. Lung cancer is still the most fatal cancer in the general population; a full evaluation pretransplant is recommended to reduce the likelihood of performing kidney transplant in patients with lung cancer.

Patients who are current smokers are at increased risk of perioperative complications, post-transplant ischemic heart disease and inferior survival rates post-transplantation, even in the absence of significant clinical lung disease.[10,11] All patients being considered for kidney transplantation should be strongly encouraged to stop smoking. Consideration should be given to making smoking cessation mandatory in patients with underlying lung disease or cardiovascular disease likely to be exacerbated by ongoing smoking. Patients who continue to smoke may still be offered kidney transplantation in most situations with full informed consent regarding their increased risks.

Cardiac disease

Recommendations

1. All patients should be assessed for the presence of ischemic heart disease (IHD) before kidney transplantation. The minimum required investigations include history, physical examination, electrocardiogram (ECG) and a chest radiograph (Grade A).
2. Further testing for IHD depends on the pretest probability of coronary artery disease (CAD). The following patients should have further non-invasive testing:
   I. Symptomatic patients or patients with a prior history of CAD including
      - Previous history of myocardial infarction (Grade A)
      - Symptoms of angina (Grade A)
      - Signs or symptoms of congestive heart failure (Grade A)

   II. Asymptomatic patients with
      - Diabetes (type 1 or type 2) (Grade B)
      - Multiple risk factors for CAD (3 or more) (Grade B)
        - age > 50 years
        - prolonged duration of chronic kidney disease
        - family history of CAD (first-degree relative)
        - significant smoking history
        - dyslipidemia (high-density lipoprotein level < 0.9 mmol/L or total cholesterol > 5.2 mmol/L), BMI ≥ 30 kg/m^2
        - history of hypertension
3. All patients with a positive non-invasive test should be assessed by a cardiologist with a view to undergoing angiography (Grade B).
4. Very high-risk patients should be considered for angiography even with a negative non-invasive test (Grade C).
5. Patients with IHD should be eligible for kidney transplantation if they fall into 1 of the following categories:
   - Low-risk asymptomatic patients (Grade A)
   - Asymptomatic patients with negative non-invasive testing (Grade B)
   - Patients who have undergone successful intervention (Grade B)
   - Patients who on angiography have non-critical disease and are on appropriate medical therapy (Grade C)
6. Kidney transplantation is contraindicated in patients with IHD in the following situations:
   - Patients with progressive symptoms of angina (Grade A)
   - Patients with a myocardial infarction within 6 months (Grade A)
   - Patients without an appropriate cardiac workup (Grade C)
   - Patients with severe diffuse disease, especially with positive non-invasive tests in whom intervention is not possible and in whom expected survival is sufficiently compromised so that transplantation is not reasonable (Grade C)
7. Patients with IHD should be re-evaluated on a regular basis.
   - Re-evaluation should include history, physical examination, ECG and non-invasive testing (Grade C)
   - Re-evaluation should occur any time a patient becomes symptomatic (Grade A)
   - Re-evaluation should occur annually in all patients who are at high risk (see previous recommendation for high-risk groups) (Grade C)
   - A repeat angiogram may be considered in patients with known IHD before transplantation if waiting time has been prolonged and it is known that a transplant is likely within the next year (Grade C)
   - All high-risk patients on the waiting list should be treated aggressively with risk-factor reduction strategies (Grade A)
8. Left ventricular (LV) dysfunction is not necessarily a contraindication to kidney transplantation. LV function should be evaluated in all patients being assessed for transplantation with history, physical examination, ECG and chest radiography (Grade A). An echocardiogram should be performed in patients with evidence of LV dysfunction (Grade B) or in patients at high risk for LV dysfunction (patients with diabetes, CAD, longstanding hypertension, longstanding kidney disease or known valvular heart disease) (Grade C).
9. Uremic LV dysfunction may improve after transplantation; thus it is not necessarily a contraindication to wait listing (Grade B).
10. Patients with severe irreversible (non-uremic) cardiac dysfunction should not be listed for kidney transplantation alone. Selected patients may be candidates for combined heart–kidney transplants (Grade C).
11. Children with evidence of cardiomyopathy on echocardiography or with congenital heart disease should be evaluated for transplantation in consultation with a pediatric cardiologist (Grade C).
12. All patients should be monitored for aortic stenosis by history, physical examination and echocardiogram where clinical suspicion is high (Grade C).
13. Patients with aortic stenosis should have regular follow-up echocardiograms, and consideration should be given to early surgical intervention as the disease is accelerated in renal failure (Grade C).

Ischemic heart disease (IHD) is the leading cause of death after renal transplantation. Nearly half of the deaths that occur in the first 30 days post-transplantation are due to myocardial infarction. Hence, identification of IHD in transplant recipients and determination of its severity is an important

part of the pretransplant workup. It will provide a tool for the assessment of risk both during and after surgery. It will identify patients who are candidates for interventions before transplant, which will improve cardiac outcomes. Finally, it will identify patients who are candidates for risk-factor modification both before and after transplantation.

Patients with progressive kidney disease have multiple risk factors for CAD and the prevalence of IHD in these patients at the time of their evaluation for transplant is high. Thus all patients should be screened for IHD, but the degree of screening should depend on the prior likelihood of their having significant disease. Routine screening in all patients should consist of a history, physical examination, ECG and chest radiography.[10] Patients with a positive finding should be investigated further. This approach will miss a significant number of asymptomatic patients with disease; hence, asymptomatic high-risk patients should undergo further testing. High-risk patients include all those with diabetes and patients with multiple risk factors for IHD.

The most appropriate non-invasive test for IHD in these patients is subject to debate. No non-invasive test is ideal and all perform more poorly when the pretest probability of disease is low. The ideal screening test would have a high positive and negative predictive value for angiographically demonstrable coronary disease and would also have predictive value for perioperative surgical risk. In most transplant centres, available non-invasive tests include thallium or sestamibi nuclear imaging with exercise or dipyridamole and exercise or dobutamine echocardiography. Exercise or dipyridamole single-photon emission computed tomography use is becoming more widespread but is not available at all centres.

Both nuclear imaging and stress echocardiography testing have been evaluated in potential renal transplant recipients and these tests have been correlated with angiographically proven lesions as well with clinical cardiac events post-transplantation. However, the literature is conflicting with respect to the performance of these non-invasive tests. In 1 study[127] of 80 diabetic patients with a 53% incidence of angiographically proven disease, dipyridamole persantine scans had a positive predictive value of 82% and a negative predictive value of 83% for at least a single 70% occlusion on angiography. In other studies,[128] nuclear scans have not performed as well. Nuclear studies generally perform well in identifying patients who will not have cardiac events post-transplant (high negative predictive value), but their positive predictive value is not as good.[129–131]

Evaluation of high-risk patients using stress echocardiography has shown similar results with varying negative and positive predictive values for angiographically proven lesions as well as post-transplant coronary events.[132–134] Thus, either nuclear imaging or echocardiographic studies are reasonable non-invasive tests to screen high-risk patients and the choice depends on the expertise of the personnel performing the study.[10]

Patients who have positive non-invasive tests should undergo further cardiologic assessment, which will usually include coronary angiography. Very high-risk asymptomatic patients with negative non-invasive tests may also be appropriate candidates for further assessment. Symptomatic patients should have a cardiologic review.

A single study[135] shows that asymptomatic diabetic patients have better transplantation when they have undergone revascularization procedures (bypass surgery or angioplasty with or without stenting) as opposed to medical management. Thus, patients with critical disease should be considered for revascularization. The appropriate intervention for asymptomatic patients with less than critical disease is unknown, but they require reassessment on an ongoing basis once they are on the waiting list for transplant. As the risk of progression is high, this population should be targeted for aggressive risk-factor modification. Re-evaluation should occur on a yearly basis and testing should be repeated if patients become symptomatic.[12] As non-invasive tests are relatively good predictors of perioperative risk, repeat testing should be considered before transplantation if it is possible to determine when the transplant will occur based on position on the waiting list and allocation criteria.

Although few patients are truly at low risk for underlying cardiac disease, these patients may be listed without further investigation, as their risk of perioperative events is low. It is also reasonable to list asymptomatic patients with negative non-invasive screening tests, as both nuclear imaging and echocardiographic stress testing are reasonably good at predicting which patients are at low risk for perioperative events and, to a lesser degree, later cardiac events.[10,127–134] Patients who have undergone a successful revascularization procedure (bypass or angioplasty with or without stenting) are at lower risk of postoperative events and hence can be wait listed.[135] The most uncertainty surrounds patients who have disease but not to the point where revascularization is indicated. It seems reasonable to maximize their medical therapy and reevaluate them on a regular basis.[136]

Many studies in the non-transplant literature suggest that anginal symptoms and a myocardial infarction within the past 6 months are strong predictors of perioperative events and hence should preclude transplantation.[137,138] As previously discussed, the frequency of asymptomatic severe disease is high; therefore, patients should not be listed until they have undergone screening. Patients with severe and non-correctable disease should be reviewed by a cardiologist. It is difficult to predict life expectancy in such patients; however, in our opinion, if the natural history of the cardiac disease is such that the patient will likely die within 3 years of a transplant then transplantation should be precluded. Clinical judgment plays a major role but positive non-invasive tests are strong predictors of poor outcomes.[129,130,133]

As progression of IHD is rapid in the renal failure population, rescreening of patients with prolonged waiting times is important.[136] Patients who develop new symptoms of coronary disease should be placed on hold from the waiting list and reevaluated. It is unclear how frequently asymptomatic patients should be re-evaluated. Matas and colleagues[136] recently proposed that high-risk patients be re-evaluated annually and diabetic patients have non-invasive testing annually. As no non-invasive test has perfect negative predictive value and patients who remain on dialysis for prolonged periods with

known disease are at high risk of progression of the disease, it is reasonable to consider them for coronary angiography as they near the top of the wait list. This will identify patients who may benefit from intervention or who have progressed to the point where a transplant is contraindicated. Numerous studies have shown that risk reduction improves outcome in patients with coronary disease in the general population and some have been validated in the renal failure population, thus making these interventions (treatment of hypertension, use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers and cholesterol-lowering agents) strongly indicated to reduce further events.[139]

The prevalence of LV dysfunction is high in patients with progressive kidney disease. In studies looking at the clinical diagnosis of congestive heart failure manifest by volume overload, the prevalence is up to 50%.[140] LV dysfunction, based on echocardiographic findings, is present in close to 20% of patients starting dialysis.[141] Screening for LV dysfunction should include a history and physical examination, ECG and chest radiography. Patients with abnormal findings or high-risk patients (those with diabetes, valvular heart disease, hypertension, CAD) should undergo echocardiography. The cause of the LV dysfunction should be determined and corrected if possible. Because LV dysfunction may improve significantly after renal transplantation, it should not be an absolute exclusion criterion; however, severe and irreversible LV dysfunction likely precludes renal transplant alone.[142] Patients with ESRD and severe LV dysfunction may be candidates for combined heart–kidney transplants.

Aortic-valve calcification is the most common valvular abnormality found in patients with renal disease. Progressive calcification of the aortic-valve leaflets may lead to aortic stenosis. Aortic-valve calcification occurs more frequently and progresses more rapidly in patients with chronic kidney disease than in the general population, and the incidence of clinically significant aortic stenosis is 3.3% in dialysis patients.[143] Even patients with severe aortic stenosis may be asymptomatic for some time, but there are typical clinical findings. Severe aortic stenosis has a very poor prognosis without aortic-valve replacement.[143] We recommend that patients with moderate to severe aortic stenosis be considered for valve replacement before renal transplantation and that patients be followed yearly with echocardiograms to document progression of stenosis.

Cerebral vascular disease

Recommendations

1. Kidney transplantation should be deferred in patients with a history of stroke or transient ischemic attack for at least 6 months following the event. The patient should be stable, fully evaluated and treated with risk-reduction strategies before kidney transplantation (Grade A).

The risk of stroke in the dialysis population is quite high (6 times that of the general population) and confers high morbidity and mortality.[144] Understandably, the risk of recurrent stroke is also likely to be quite high (7% per year in the general population). A stroke after transplantation is associated with a high mortality rate (50% at 3 months post-stroke).[145]

Patients at high risk of stroke should be fully evaluated for cerebrovascular disease, including laboratory parameters, ECG (to rule out atrial fibrillation), computed tomography or magnetic resonance imaging and carotid doppler or magnetic resonance angiography. This includes patients with a history of stroke or transient ischemic attack (TIA) and patients with autosomal dominant polycystic kidney disease (ADPKD) and family history of stroke. The Canadian Task Force on Preventive Health Care does not currently recommend investigation of an asymptomatic carotid bruit.[146]

Patients with a history of stroke, atrial fibrillation, TIA and carotid stenosis should be treated by best medical practice,[147] a high-level evidence is available for control of blood pressure, anti-thrombotic therapy for atrial fibrillation and antiplatelet therapy for high-risk patients. Studies are underway on secondary prevention of stroke with statins. Studies in populations at high risk for IHD have demonstrated a lower risk of stroke with statin therapy.[148] Therefore, patients should be stable, evaluated and treated with risk-reduction strategies before transplantation.

Patients with symptomatic or asymptomatic carotid vascular disease who meet certain criteria should be considered for pretransplant endarterectomy as recommended by the American Heart Association.[149] However, Canadian guidelines are more conservative.[150] The Canadian Task Force on Preventive Health Care has not updated its guidelines on the role of screening for carotid disease in the general population since 1994.[146]

The risk of recurrent stroke in patients undergoing surgery is about 3% compared with < 0.3% in the general population. The optimum waiting time is unknown, but a wait of 2–3 months is recommended.[151] Prior stroke is listed in some postoperative cardiac risk indexes for non-vascular surgery.[152] However, the impact is minor compared with other variables, which suggests that the relative or absolute contraindication relating to stroke should be taken in context with other clinical variables.

Patients with a TIA should be considered at high risk given the high rate of stroke after a TIA. In the general population, the 90-day stroke risk following at TIA is 11%. For patients with carotid stenosis > 70%, the 90-day stroke rate is 25% (this rate exceeds the rate of recurrent stroke).[153] Therefore, patients with a TIA should be considered to be at as great a risk as a patient with a completed stroke.

Screening for cerebral aneurysms in patients with ADPKD has been recommended.[154] However detected aneurysms are often small, and rates of progression are variable and difficult to predict.[155] Screening of high-risk patients with ADPKD (i.e., family history of subarachnoid hemorrhage, symptoms of possible aneurysm or prior stroke) has been recommended, although there is no good evidence to support routine screening of all patients with ADPKD. Nor is it reasonable to deny access to kidney transplantation based on the absence of screening.[156] Recommendations from the Stroke Council of the American Heart Association are less aggressive, but agree that large aneurysms in relatively young pa-

tients be considered for surgery.[157,158] Any patient with a symptomatic cerebral aneurysm > 10 mm should have intervention and patients with asymptomatic cerebral aneurysms > 10 mm should also be considered for intervention.[157] The final decision would be based on the opinion of the neurosurgeon and his or her estimate of prognosis.

Peripheral vascular disease

Recommendations

1. The presence of pretransplant peripheral vascular disease (PVD) is not an absolute contraindication to kidney transplantation. However, the risk of death is increased and the presence of PVD should be considered in the context of other comorbidities in determining eligibility for kidney transplantation (Grade B).
2. Patients with large uncorrectable abdominal aneurysms, severe occlusive common iliac disease, active gangrene or recent atheroembolic events are not candidates for kidney transplantation (Grade C).

In the general population, mortality in patients with symptomatic peripheral arterial disease (PVD) is high (50% survival at 6 years).[159] These patients have a 15-fold greater risk of dying from cardiovascular disease than the general population.

Most studies quantifying the risk factors for death after kidney transplantation have either not included PVD or have not reported whether it was examined as a risk factor.[160] Tarek and co-workers[161] recently described a cohort of 775 patients who received a transplant in Winnipeg or Newfoundland between 1969 and 1998. Of these, 45 patients (6%) had PVD (defined as an amputation or revascularization procedure) before the transplant. PVD was strongly associated with the development of congestive heart failure (odds ratio [OR] 3.2, 95% confidence interval [CI] 1.3–7.4) which in turn predicted death (OR 1.8, 95% CI 1.2–2.6) but not IHD. PVD is present in about 15% of patients starting dialysis and has been shown to be associated with increased mortality (adjusted hazard ratio 1.9, 95% CI 1.6–2.3).[162]

Sung and associates[163] reported cumulative 5- and 10-year incidences of PVD after transplant of 4.2% and 5.9%, respectively. In this study, 8 of 14 patients (57%) with pretransplant PVD had additional PVD events; and 21 of 650 patients experienced de novo PVD (3.2%, $p < 0.0001$). Patients with recurrent PVD had a 10-year survival rate of 26% vs. 80% in those without recurrent PVD. Although stable PVD is not an absolute contraindication for transplantation, it is likely to be associated with increased mortality and should be considered in the context of other comorbidities.

In addition to a general medical history and physical examination, peripheral pulses of these patients should be assessed. Patients with a history of PVD, who are absent pulses or bruits on physical examination, should undergo further testing. Additional testing may include abdominal ultrasound, doppler flow studies or magnetic resonance angiography.

Patients with large aneurysms at high risk of rupture, who are not considered candidates for repair, are not candidates for kidney transplantation. Patients with abdominal aneurysms 5–5.9 cm and ≥ 6 cm in diameter have rupture rates of 4–14% and > 20% per year, respectively.[164] These rupture rates may be higher in women. Patients who rupture have a high mortality rate. In addition, they could experience allograft failure as these aneurysms would be located above the renal transplant anastomosis. Thus, the transplanted kidney would be subject not only to reduced flow during rupture, but also atheroemboli. Patients with severe bilateral occlusive disease that cannot be corrected are also not candidates for transplant because the reduced flow to the graft may compromise function. Primary arterial anastomosis may not be possible or may result in early graft failure in patients with severe iliac disease. Atheroemboli can also cause graft loss, although transplantation after atheroemboli has been reported.[165,166] Nonetheless, kidney transplantation in patients with unstable PVD (gangrene or atheroemboli) should be deferred until existing lesions are healed. There should be no evidence of ongoing atheroembolic events.

Gastrointestinal disease

Recommendations

1. Patients with active peptic ulcer disease should not be transplanted until the disease is successfully treated (Grade C).
2. The use of upper gastrointestinal endoscopy before transplant should be considered in selected patients (i.e., those with symptoms or prior peptic ulcer disease) (Grade C).
3. The presence of asymptomatic cholelithiasis is not a contraindication to kidney transplantation (Grade A).
4. Patients with previous cholecystitis or suggestive symptoms should be investigated for the presence of gallstones. If gallstones are found, these patients should be considered for cholecystectomy before kidney transplantation (Grade C).
5. Patients with a history of diverticulitis should be evaluated and considered for partial colectomy before transplant (Grade C).
6. Acute pancreatitis within 6 months is a contraindication to kidney transplantation (Grade C).
7. Chronic pancreatitis in remission for less than 1 year is a relative contraindication to transplantation (Grade C).
8. Active inflammatory bowel disease is a contraindication to transplantation (Grade C).

Although direct evidence is lacking, it is recommended that kidney transplantation be deferred in patients with active peptic ulcer disease until they have been fully treated and are asymptomatic.[10] Repeat endoscopy may be valuable in selected individuals. There is no role for routine screening for peptic ulcer disease in asymptomatic patients. Nor is routine serologic testing for Helicobacter pylori recommended. Pretransplant prevalence of positive serology for H. pylori was 31% in 1 study ($n = 500$); there was no correlation between H. pylori serological status and postoperative course.[167]

Patients with previous cholecystitis or suggestive symp-

toms should be investigated for the presence of gallstones before transplantation. If gallstones are present, these patients should be considered for cholecystectomy before kidney transplantation. Asymptomatic gallstones are commonly identified in the course of transplant assessment. Controversy exists regarding the need for routine pretransplant screening and cholecystectomy.[10]

Asymptomatic gallstones were found on ultrasound in 10% of 406 wait-listed patients; these were treated by cholecystectomy with no morbidity.[168] Historical controls (n = 88) had 14% morbidity and 7% mortality. In another study,[169] 7% of 211 transplanted patients had asymptomatic gallstones on ultrasound; only 1 patient developed cholecystitis during a 3-year follow up. Finally, 52 out of 662 patients (7.8%) required post-transplant cholecystectomy for symptomatic gallstones; there was negligible morbidity, no mortality and no effect on graft outcome.[170]

Current practice guidelines do not recommend routine screening for diverticular disease before kidney transplantation.[10] The prevalence of diverticular disease in wait-listed patients over 50 years of age has been reported to be about 2% (n = 1000); none of these patients developed diverticulitis or colonic perforation post-transplant.[171] Although the prevalence of diverticular disease in ADPKD is reported to be as high as 20–80%, there is no evidence to suggest that patients with ADPKD should be treated differently. Moreover, in 1 study,[172] diverticular disease was found to be equally prevalent in patients with ADPKD, non-ADPKD patients with ESRD and a control group. Although immunosuppressive therapy increases the risk of complications from diverticular disease, the incidence of both diverticulitis and colonic perforation post-transplant is low at about 0.5%.[171,173] Patients with a prior history of diverticulitis are at higher risk. They should undergo screening studies and be considered for elective partial colectomy before kidney transplantation.[10]

There are no data regarding the incidence or effects of either acute or chronic pancreatitis in renal transplant patients, but it seems prudent to defer kidney transplantation for at least 6 months after an episode of acute pancreatitis; chronic pancreatitis should be in remission for at least 1 year before proceeding with transplantation.

Liver disease

Recommendations

1. All transplant candidates should be screened for evidence of liver disease (medical history, physical examination, serum bilirubin and liver enzyme levels and serological tests for hepatitis B and hepatitis C). While awaiting kidney transplantation, all dialysis patients should be regularly monitored for hepatitis B surface antigen (HBsAg), antibody to surface antigen (HBsAb) and anti-body to core antigen (HBcAb) with appropriate follow-up testing should the virologic parameters change (Grade C).
2. Patients with liver disease should be followed by a gastroenterologist, who should re-evaluate their condition (with laboratory testing and diagnostic imaging) as clinically indicated for evidence of progression to cirrhosis and development of hepatocellular carcinoma (Grade C).
3. Transplant candidates with cirrhosis should not be considered for kidney transplantation alone, but may be considered for combined liver–kidney transplantation (Grade C).
4. Patients who are HBsAg negative should be vaccinated against hepatitis B virus (HBV) if they are not already immunized. At least 1 dose of vaccine should be given before transplantation. HBV antibody status should be monitored and booster doses given when antibody concentrations fall below protective levels (Grade C).
5. Long-term mortality after renal transplantation is higher in HBV-infected patients (i.e., HBsAg+) and they should, therefore, be fully informed (Grade B).
6. All transplant candidates infected with HBV should be assessed for evidence of viral replication by testing for serum transaminases, hepatitis B e-antigen (HBeAg) and HBV deoxyribonucleic acid (DNA). They should also undergo liver biopsy (Grade C).
7. Patients with active liver disease (including chronic active hepatitis) should be treated with lamivudine or interferon-alpha in the pre- and post-transplant period. Patients treated in the pretransplant period who do not respond to therapy are at high risk for progressive liver disease after transplantation. They may still be listed for kidney transplantation after careful consideration and with full informed consent (Grade C).
8. Patients with hepatitis C virus (HCV) should be considered for kidney transplantation as the procedure is not associated with increased short-term mortality compared with dialysis (Grade B).
9. All transplant candidates with anti-HCV antibodies should be tested for the presence of HCV ribonucleic acid (RNA) and cryoglobulinemia. Testing for HCV RNA should also be considered in patients with evidence of liver disease even in cases where anti-HCV antibodies are not detectable (Grade C).
10. HCV RNA positive patients with no clinical evidence of cirrhosis should undergo pretransplant liver biopsy (Grade C).
11. HCV-infected patients with documented HCV-viremia may be offered a kidney from an HCV-infected donor with informed consent. This possibility should be discussed with the patient at the time of wait listing to determine their willingness to receive such a kidney. Any potential risks of an HCV-positive donor kidney in this setting may be ameliorated by the benefit of a shortened waiting time frequently associated with accepting such a donor kidney (Grade B).
12. Patients at high risk for liver cancer (i.e., patients with chronic HBV or HCV infection or both) should be screened using abdominal CT or ultrasound and alpha-fetoprotein testing as part of their pretransplant assessment (Grade C).
13. Renal transplantation is generally not recommended for patients with liver cancer unless it is part of a treatment strategy that includes liver transplantation (Grade C).

Liver disease is a significant cause of late morbidity and mortality in patients with kidney transplants. Death from liver

failure has been reported in 8–28% of long-term kidney recipients.[174,175] Hepatitis B and C are the most common viral infections causing liver disease among end-stage renal failure patients, and each can have a significant impact on kidney transplant recipients.[176,177] Every effort should be made to identify infection with HBV or HCV and to treat these conditions appropriately before and after kidney transplantation.[10,11,176,177] Liver biopsy is a useful tool for assessment of disease severity because serum transaminase concentrations do not necessarily reflect the extent of underlying disease.[176,177] Vaccination against HBV is recommended for patients who are HBsAg negative and not already immunized.[178–182]

Existing data suggest that HBsAg positive patients are at greater risk of death after kidney transplantation than patients without evidence of HBV infection.[183–188] However, poor prognosis established in early studies may not reflect the current situation as the earlier studies did not necessarily take into account factors such as viral replication and liver histology, and treatment for HBV infection was unavailable.

Patients with signs of viral replication are at high risk for progressive liver disease and should be treated with the best available therapy for HBV infection in ESRD.[176] Persistent viral replication is associated with poor prognosis and such patients may be best advised not to undergo kidney transplantation.[176] It is not known whether the survival advantage conferred by transplantation is outweighed by the risk of progressive liver disease.[7] Patients with persistent viral replication should be fully informed of the risks and benefits of kidney transplantation and may be considered for listing after careful consideration.

Pre- and post-transplant treatment with lamivudine of patients with signs of viral replication is currently recommended.[176] Pretransplant therapy with interferon-alpha is generally not well tolerated in patients with ESRD, but may be useful in patients with low levels of viral replication. The appropriate duration of therapy post-transplant is unclear, and the benefit of long-term therapy must be weighed against the possible emergence of viral resistance.

Patients with existing HBV cirrhosis are at risk for progressive liver disease and hepatocellular carcinoma and should either remain on dialysis or be considered for combined liver–kidney transplantation when appropriate.[176]

HCV RNA positive patients are at risk for post-transplant liver dysfunction,[189] and other complications including proteinuria, glomerular disease and possibly post-transplant diabetes mellitus.[177,190] The long-term impact on patient and graft survival is unknown. Liver enzymes correlate poorly with histology in HCV-infected patients with ESRD.[176] HCV RNA positive patients without clinical evidence of cirrhosis should undergo pretransplant liver biopsy.[80,176]

Dialysis patients have an increased risk of liver cancer,[191,192] particularly if they are chronically infected with hepatitis viruses.[174,191,193] There are few data to suggest that routine screening of dialysis patients is indicated, but it is reasonable to screen high-risk patient using abdominal CT or ultrasound and alpha-fetoprotein testing.[80]

Genitourinary disease

Recommendations

1. A urologic cause of ESRD is not necessarily a contraindication to kidney transplantation provided appropriate urinary tract drainage can be achieved (Grade A).
2. Kidney transplantation is not contraindicated in patients with a dysfunctional bladder. Most patients can be managed without surgery using self-catheterization, if necessary. A surgical approach, if needed, should be individualized (Grade C).
3. Persistent infection of the native kidneys may be a relative contraindication to immunosuppressive therapy. To reduce the risk of post-transplant complications, consideration should be given to the need for native nephrectomy in selected patients (Grade C).
4. Massive kidneys in the setting of autosomal dominant polycystic kidney disease may preclude placement of a renal allograft. Such patients may require unilateral or bilateral native nephrectomy before renal transplantation (Grade C).
5. Bladder dysfunction in children should be identified and treated before proceeding with renal transplantation (Grade B). A voiding cystourethrogram and urodynamic studies should be included as part of the transplant evaluation in all patients with congenital obstructive uropathy or known bladder dysfunction, history of urinary tract infection, vesicoureteric reflux (VUR) or renal hypoplasia–dysplasia and in young children where the cause of ESRD is unknown (Grade B).
6. High-grade VUR predisposes patients to infection post-transplantation, and corrective surgery should be considered before transplantation (Grade C).

Incidence of genitourinary abnormalities needing specific therapy in patients with no urologic history is extremely low;[194,195] thus, routine urologic assessment beyond a history and physical examination is not warranted. In contrast, patients with genitourinary abnormalities require evaluation by a urologist. The need for a voiding cystourethrogram (VCUG), cystoscopy or a retrograde pyelogram should be determined on an individual basis during the pretransplant surgical assessment. Appropriate urinary drainage is required for successful transplantation; the need for urologic surgery before transplantation should be carefully assessed in patients with a dysfunctional bladder. Many patients can be managed with intermittent self-catheterization, but some patients may require bladder augmentation or urinary diversion before transplant. Morbidity and quality of life are superior with intermittent self-catheterization compared with surgical approaches.[196] Patients with an ileal conduit require a loopogram to document the course and length of the conduit before transplantation. Consideration should be given to urinary undiversion before transplantation in selected patients.

The need for a native nephrectomy depends on the individual patient. Polycystic kidneys should be removed before transplantation only in patients who have massive kidneys that would preclude surgical placement of the allograft or in the presence

of symptomatic cyst-related complications.[197,198] Pretransplant nephrectomy may be indicated in some patients with chronic parenchymal infection, infectious stones or obstructive uropathy complicated by chronic infections. Bilateral nephrectomy may be indicated in patients with persistent nephrotic syndrome despite optimal medical management.[199] Nephrectomy may also be considered in candidates with poorly controlled hypertension despite optimal medical management.[200,201]

The evaluation of patients with ESRD for urologic malignancy should be specific to each patient and based on risk as outlined in published practice guidelines.[10,11] Eligibility of patients with urologic malignancy has been addressed in the section on malignancy.

Congenital urologic disease and renal malformations are among the most common causes of ESRD requiring renal transplantation in children. As noted, bladder dysfunction in transplant recipients is associated with an increased risk of urinary tract infection and may affect graft outcome.[202] This is particularly true for patients with small, non-compliant bladders.[203] Augmentation cystoplasty and urinary conduit surgery have been performed safely in children pretransplantation and, with subsequent clean intermittent catheterization, afford outcomes similar to those in children with normal bladder function.[204–208] Thus, most authors recommend identification of bladder dysfunction and normalization of bladder pressure with treatment before transplantation.[206,208–210] Children at risk for bladder dysfunction include those with known congenital urologic anomalies, such as posterior urethral valves, ESRD from obstructive uropathy, previous urinary tract infections and renal hypoplasia–dysplasia.[211,212] There may also be an increased risk in young children with ESRD due to unknown cause and children who are found, on ultrasound, to have thickened bladder walls.[211,212] In collaboration with a pediatric urologist, these children should be evaluated pretransplant with VCUG and urodynamic studies so that medical or surgical treatment for the pretransplant and peritransplant periods can be planned.[203,209,211]

High-grade vesicoureteric reflux (VUR) that is left untreated post-transplantation is associated with an increased risk of urinary tract infection, even if urinary tract infection was not a problem before transplantation.[213] Surgical options for treatment — ureteric reimplantation or nephrectomy — have been associated with a reduced risk of infection post-transplantation.[213,214] Endoscopic collagen injection has been used successfully to treat children with VUR (including during preparation for transplantation) and is associated with less morbidity than surgery.[215–217] Although no approach is specifically favoured, the combination of megaureter and an associated non-functioning kidney may present a heightened risk for infectious complications post-transplantation and nephrectomy may be preferred.

Hematologic disorders

Recommendations

1. The presence of thrombophilia, hypercoagulable state or cytopenias is not an absolute contraindication to kidney transplantation, but these conditions should be fully investigated (Grade C).
2. Patients requiring long-term anticoagulation for recurrent deep venous thrombosis, atrial fibrillation, prosthetic heart valves or hypercoagulable states are candidates for kidney transplantation. A perioperative anticoagulation plan should be developed as part of the transplant assessment. Patients should be informed of the risk of bleeding, including life-threatening hemorrhage, with perioperative anticoagulation (Grade C).

The routine hematologic assessment of a renal transplant candidate should include a complete blood count, a differential white cell count and assessment of partial thromboplastin time and international normalized ratio. Additional investigations, such as a hypercoagulability screen, bone marrow evaluation or review by a hematologist, are recommended in cases of thrombophilia or hypercoagulability, monoclonal gammopathy and persistently abnormal blood counts.

Increased graft thrombosis and rejection may be seen in patients with thrombophilia or hypercoagulability.[218] Routine screening of all kidney transplant candidates is likely to result in a low yield.[219] However, those with a prior history of graft thrombosis, arterial or venous thrombosis, recurrent thrombosis of hemodialysis access (other than central venous catheters) or SLE could benefit from screening. Several recent studies have outlined strategies for evaluation and prevention of complications; however, none of these state that thrombophilia is an absolute contraindication to kidney transplantation.[218–222] The impact of screening or preventive therapy has not been tested in a randomized controlled trial and post-transplant anticoagulation is associated with significant bleeding. In a prospective screening strategy, 1.4% of hypercoagulable patients (no prior history) were detected with a cost of $2200 per screened patient. Prophylactic anticoagulation with heparin was associated with significant bleeding. In those with a prior history of hypercoagulability, treatment may have reduced the thrombosis rate by 50–60%.[223] Surprisingly a number of patients with 1 of the above causes of thrombophilia and clinical clotting events on dialysis experienced biochemical correction of deficiencies after transplantation.[224]

Monoclonal gammopathy of unclear significance can develop in renal transplant patients (up to 14% within 2 years); it may be related to the intensity of therapy and is associated with increased interleukin-6 levels.[225,226] It is not clear whether conversion to myeloma is any higher after transplant than in the general population, where it tends to be low (5% per year).[227] However, the rates of myeloma are higher in the dialysis population.[191] Monoclonal gammopathy alone is not a contraindication to kidney transplantation, but does require pretransplantation evaluation by a hematologist. Multiple myeloma is usually considered a contraindication to kidney transplantation (see section on malignancy).

Patients with disorders resulting in abnormal platelet, white blood cell or red blood cell counts are encountered frequently. Anemia can be the result of uremia (hyperparathyroidism, low erythropoietin, blood loss on dialysis,

etc.), iron deficiency and many other causes, and often improves dramatically with transplantation. However, a pretransplant evaluation to identify and treat reversible causes and rule out malignancy is recommended. Patients with chronically abnormal platelet or white blood cell counts should be referred to a hematologist for an opinion. Immunosuppressive therapy post-transplant may need to be tailored in the presence of cytopenias. Patients discovered on evaluation to have cancer or severe myelodysplasia should not proceed with kidney transplantation (see malignancy section).

Hyperparathyroidism

Recommendations

1. Calcium, phosphorus and parathyroid hormone levels should be measured as part of the pretransplant evaluation (Grade A).
2. Parathyroidectomy should be considered for those who have failed medical management or have severe, persistent complications of hyperparathyroidism (Grade B).

Bone disease is common in patients with ESRD, and successful renal transplantation is often the best therapy.[228,230] However, persistence of hyperparathyroidism is common following renal transplantation.[228–231] In patients with hypercalcemia and hyperparathyroidism before transplant, severe post-transplant hyperparathyroidism can occur. Thus, pretransplant parathyroidectomy has been recommended for those with symptomatic secondary hyperparathyroidism and those with hypercalcemia and severe elevations of parathyroid hormone.[10]

Psychosocial considerations

Recommendations

1. Given the importance of adherence to therapy in transplant outcomes, all patients should have a pretransplant psychosocial evaluation by an experienced competent individual to assess for:
   - Cognitive impairment (Grade C)
   - Mental illness (Grade C)
   - Non-adherence to therapy, laboratory monitoring or follow-up (Grade C)
   - Drug or alcohol abuse (Grade C)
2. Cognitive impairment is not an absolute contraindication to kidney transplantation (Grade B). However, particular care must be taken to ensure that informed consent can be obtained and that a support system is in place to ensure adherence to therapy and patient safety.
3. A history of psychiatric illness is not an absolute contraindication to kidney transplantation. Such patients should be assessed to ensure that they are capable of giving informed consent and adhering to therapy (Grade B).
4. Patient non-adherence to therapy is a contraindication to kidney transplantation, given the use of immunosuppressive agents with a narrow therapeutic window, the impact of non-adherence to therapy on risk of acute rejection and premature graft loss, and the scarcity of donor organs (Grade A). Patients should be informed of the importance of adherence to therapy as well as the number of medications, clinic visits and blood work required before transplant (Grade B).
5. Kidney transplantation should be delayed until patients have demonstrated adherence to therapy (attendance for dialysis and compliance with medications) for at least 6 months (Grade C).
6. Kidney transplantation should be delayed until the patient has demonstrated freedom from substance abuse for at least 6 months (Grade C).

All transplant recipients should have a psychosocial evaluation to look for issues that might adversely affect transplant outcome. Although centres differ in their approach to the evaluation, it should be conducted by a professional who is knowledgeable and experienced in pretransplant evaluation. In many programs, the social worker performs an initial evaluation and those with significant problems are referred to a psychiatrist or psychologist.

In those with cognitive impairment, reversible causes should be excluded. Cognitive impairment is not an absolute contraindication to transplantation. However patients need to understand risks and benefits to give informed consent and must be compliant or have an adequate support system to ensure compliance with medications, laboratory monitoring and clinic visits.[232] If the patient is not competent to make his or her own health care decisions, then a legally acceptable surrogate decision-maker must be identified and provided with the appropriate information regarding the risks and benefits of kidney transplantation. In addition to making the best decision on behalf of the patient, the decision-maker should ensure that an appropriate support system is in place to facilitate patient adherence to therapy, laboratory monitoring and long-term follow-up.

Successful transplantation has been achieved in patients with major psychoses, depression or bipolar disorders following satisfactory treatment.[233–235] Thus, these are not an absolute contraindication to kidney transplantation if the symptoms are controlled. However, perioperative events and some medications (e.g., steroids) may exacerbate psychiatric illness and uncontrolled disease may interfere with adherence to therapy and follow-up. If a patient is controlled by agents that are potentially nephrotoxic or where dosing is strongly influenced by renal function (i.e., lithium), efforts should be made to convert the patient to a non-nephrotoxic agent before transplant.

Non-adherence to therapy is an important cause of graft failure.[236–238] Ethanol or drug abuse can interfere with patient compliance[233] and kidney transplantation should be deferred in otherwise eligible patients until the patient has demonstrated freedom from substance abuse for at least 6 months.

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