

Evaluation of Prospective Donors and Recipients

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All patients should be considered for transplantation when it is determined that renal replacement therapy will someday be required. In some cases, the evaluation can be completed and the patient can receive transplantation before initiating chronic maintenance dialysis. Prospective candidates for transplantation must be carefully screened for potentially fatal cancers and infections that are made worse by immunosuppression. Hepatic, pulmonary, cardiovascular, and gastrointestinal disorders all may increase the risks of surgery and chronic immunosuppression. Patients must be carefully screened for these disorders. In many cases, intervention before transplantation may help reduce the recipient's risks of transplantation. Detailed guidelines have been established to evaluate prospective candidates for transplantation [1].

Living donors offer the recipient optimal graft survival, reduced waiting time, and an opportunity for preemptive transplantation (*ie*, before initiating dialysis). The evaluation of prospective living donors must ensure that the donation is safe for both donor and recipient. However, the primary focus of this evaluation must always be on protecting the well-being of the prospective donor. Both the short-term surgical risks and the long-term risks of having a single kidney must be carefully defined. The evaluation also must ensure the donor has no disease that could be transmitted with the kidney. Guidelines have been developed for the evaluation of living prospective donors [2].

When no suitable living donors are available, the prospective recipient can be placed on the waiting list for a cadaveric kidney. Unfortunately, because the number of patients needing cadaveric kidneys has grown much faster than has the number of available kidneys, the median waiting time is now over 2 years. This shortage has led many transplantation centers to use cadaveric kidneys, which are associated with reduced graft survival. In particular, graft survival is affected by the age of the kidney donor. Many centers are expanding the age limits of acceptability to reduce waiting times. A detailed discussion of the selection, retrieval, preservation, and allocation of cadaveric kidneys is beyond the scope of this review.

CHAPTER

12

Evaluation of Prospective Transplantation Recipients

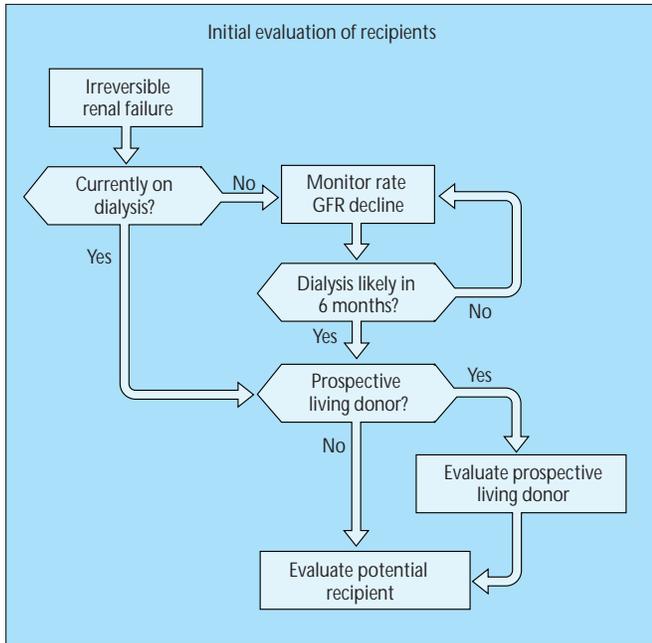


FIGURE 12-1

Initiating the evaluation. Before transplantation it must be clearly established that renal failure in the patient is irreversible. When the prospective recipient is not already on chronic maintenance dialysis, however, preemptive transplantation (*ie*, transplantation before initiating dialysis) should be considered. Because the waiting time for a cadaveric kidney is generally long, preemptive transplantation usually is possible only when a prospective living donor is available. In any case, the rate of decline in the glomerular filtration rate (GFR) must be monitored closely in patients with progressive renal disease. The evaluation process should begin when it is anticipated that transplantation may be required within 6 months. (From Kasiske and coworkers. [1]; with permission.)

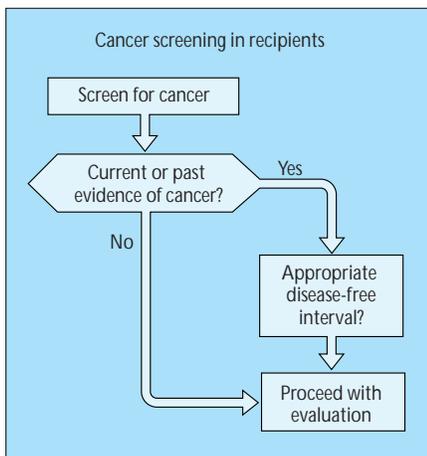


FIGURE 12-2

Screening for cancer. An active malignancy is an absolute contraindication to transplantation. Effective screening measures for patients at risk include chest radiograph, mammogram, PAP test, stool Hemocult, digital rectal examination, and flexible sigmoidoscopy examination. Patients who have had a life-threatening malignancy but are potentially cured may be candidates for transplantation when there has been an appropriate disease-free interval. This interval generally is at least 2 years, and longer in the case of some malignancies. (From Kasiske and coworkers [1].)

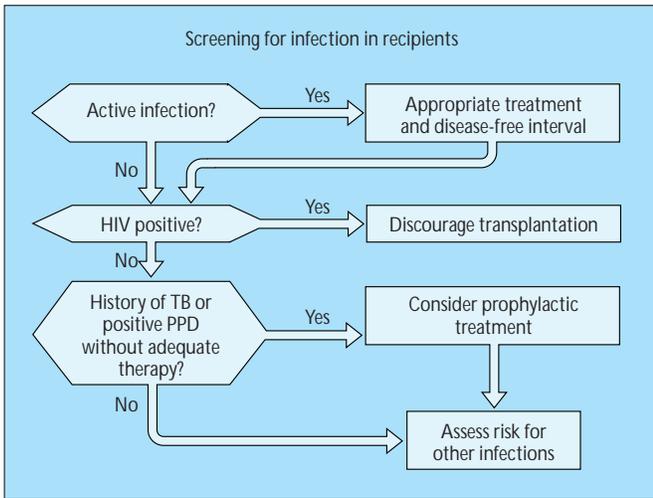


FIGURE 12-3

Screening for infection. An active potentially life-threatening infection is a contraindication to transplantation. Patients with human immunodeficiency virus (HIV) are usually not candidates for transplantation. Patients with a history of tuberculosis (TB) or a positive purified protein derivative (PPD) skin test who have not been adequately treated should generally receive prophylactic therapy. (From Kasiske and coworkers [1].)

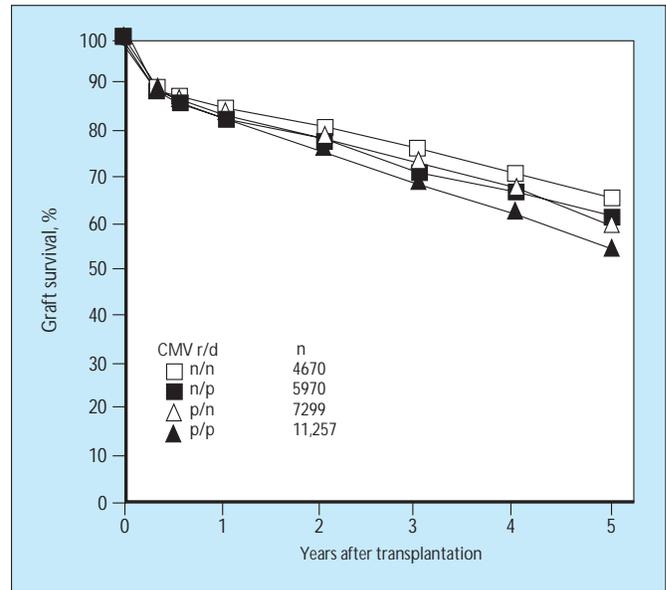


FIGURE 12-4

Assessing the risks of cytomegalovirus (CMV) infection after transplantation. CMV is a major cause of morbidity and mortality after transplantation. The incidence and severity of CMV are associated with the serologic status of the donor (d) and recipient (r), the risks generally being the following: recipient negative–donor negative less than recipient positive–donor negative less than recipient positive–donor positive. As shown in these data from the United Network for Organ Sharing Scientific Registry, the rate of graft survival tends to be less in recipients of kidneys from donors who test positive for CMV infection. The serologic status of both the donor and recipient is often used to determine which patients are candidates for prophylactic or pre-emptive anti-CMV therapy after transplantation. (From Cecka [3]; with permission.)

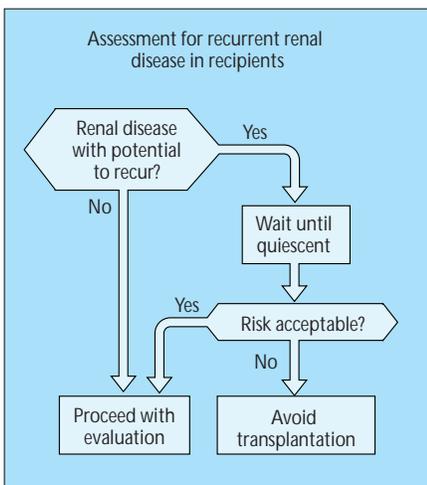


FIGURE 12-5

Assessing the risk of renal disease recurrence. Although the risk for recurrence of the underlying renal disease is rarely great enough to preclude transplantation, patients and physicians must be aware of this risk. In some cases it may be prudent to delay transplantation until the underlying disease is quiescent. (From Kasiske and coworkers [1].)

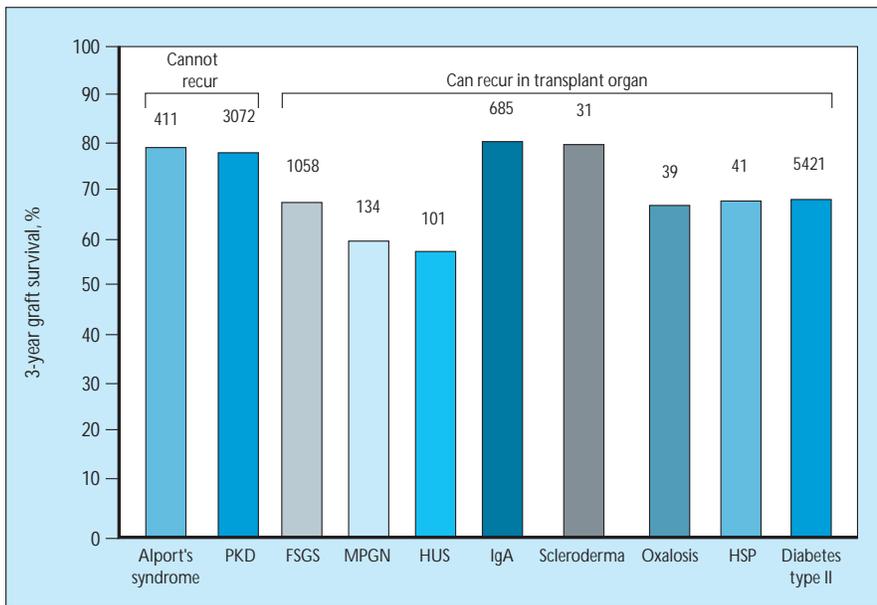


FIGURE 12-6

The influence of underlying renal disease on graft survival. As shown in these data from the United Network for Organ Sharing Scientific Registry, 3-year graft survival rates in groups of patients with different underlying causes of renal failure vary substantially. The 3-year graft survival rates for recipients with renal diseases that do not recur (eg, Alport's syndrome and polycystic kidney disease [PKD]) were about 80%. Graft survival rates for patients with diseases that may recur in the transplanted kidney varied from 60% to 83%. Of course, most of these differences in graft survival may be due to factors associated with the underlying cause of renal failure (eg, cardiovascular disease) and not disease recurrence itself. Focal segmental glomerulosclerosis (FSGS), hemolytic uremic syndrome (HUS), Henoch-Schönlein purpura (HSP), and hereditary oxalosis can cause graft failure relatively soon after transplantation. Membranoproliferative glomerulonephritis (MPGN), scleroderma, IgA nephropathy, and diabetes generally cause graft failure only after several years. *Numbers above bars indicate number of patients who had that disease.* (From Cecka [3]; with permission.)

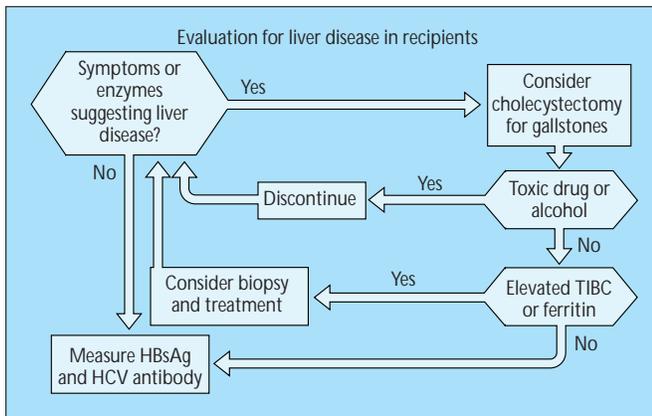


FIGURE 12-7

Evaluation of patients with signs and symptoms of liver disease. Patients with cholecystitis should be considered for cholecystectomy. For other patients with signs and symptoms of liver disease, potential hepatic toxins should be considered. The incidence of liver disease from iron deposition has declined with the diminishing use of blood transfusions in dialysis patients, but may be seen occasionally in patients with a high total iron binding capacity (TIBC) or ferritin. All prospective candidates for transplantation must be screened for hepatitis B and C by testing for the presence of hepatitis B surface antigen (HBsAg) and hepatitis C virus (HCV) antibodies. Both viruses can cause potentially fatal liver disease after transplantation. Fortunately, the incidence of hepatitis B is declining among patients with renal disease, largely as a result of the use of effective vaccination programs. (From Kasiske and coworkers [1]; with permission.)

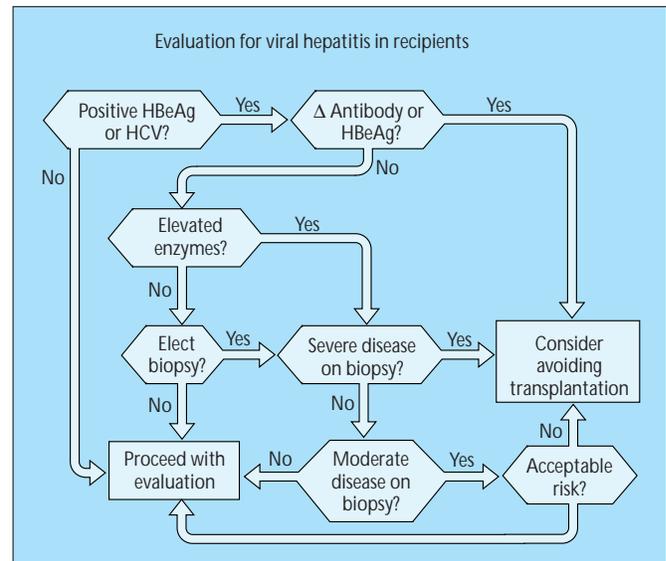


FIGURE 12-8

Viral hepatitis. Patients whose test results are positive for Δ antibodies or hepatitis e-antigen (HBeAg) are at high risk for succumbing to liver disease and most likely are not candidates for transplantation. A liver biopsy should be considered for all patients with hepatitis C virus (HCV) antibodies or hepatitis B surface antigen. Patients with severe chronic active hepatitis or cirrhosis on biopsy generally are not candidates for renal transplantation unless simultaneous liver transplantation is being considered. Whether antiviral therapy before transplantation can increase the number of patients who are candidates for transplantation is unclear. (From Kasiske and coworkers [1]; with permission.)

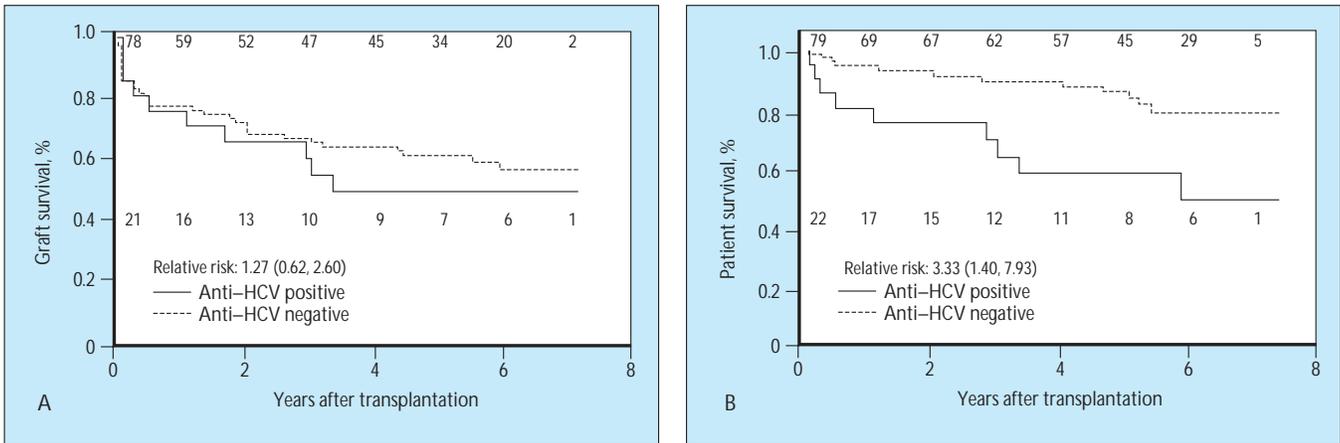


FIGURE 12-9 Effects of pretransplantation hepatitis C virus (HCV) serology results on survival of the graft (A) and patient (B). Numbers above (anti-HCV negative) and below (anti-HCV positive) survival curves indicate the number of patients at risk during that time interval. The relative risk after transplantation associated with the patient testing positive for HCV antibodies before

transplantation also is shown, along with 95% confidence intervals. Although no statistically significant effect of HCV on graft survival was seen, patient survival was significantly diminished among those who tested positive for HCV after transplantation. Not all investigators have confirmed these findings. (From Periera and coworkers [4]; with permission.)

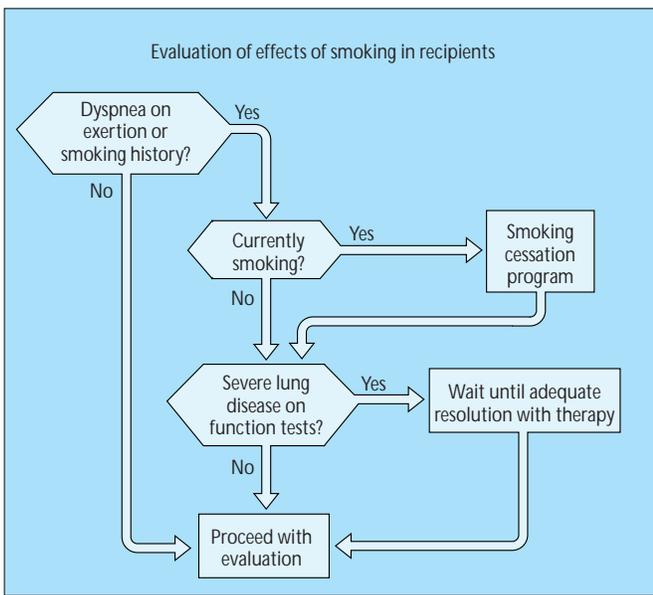


FIGURE 12-10 Lung disease. Few studies exist that address the effects of cigarette smoking on outcome after renal transplantation. Because the risks of transplantation surgery no doubt are increased by cigarette smoking, candidates for transplantation should be referred to smoking cessation programs. (From Kasiske and coworkers [1]; with permission.)

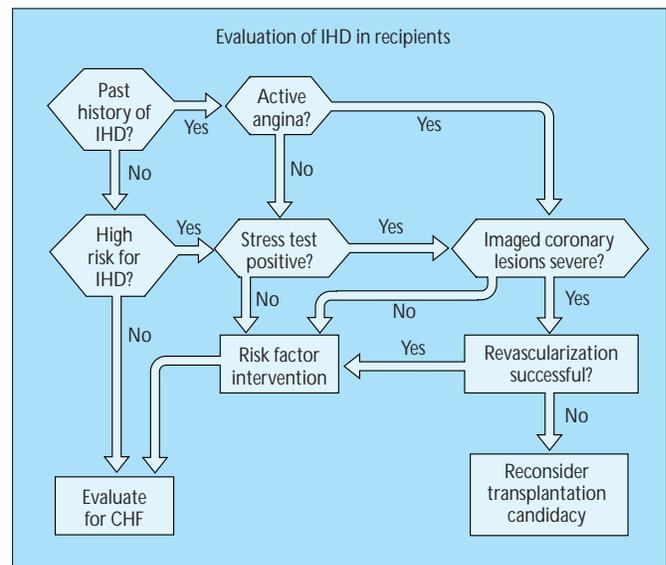


FIGURE 12-11 Ischemic heart disease (IHD). The incidence of IHD is several fold higher in renal transplantation recipients compared with the general population. Patients with IHD before transplantation are at high risk to develop IHD events after transplantation. Therefore, angiography should be considered in candidates for transplantation who have angina pectoris. Candidates with currently asymptomatic IHD and those at high risk for IHD should undergo a stress test. Patients with severe coronary artery disease on angiography must be considered for a revascularization procedure before transplantation. Aggressive management of risk factors is appropriate for all patients, with or without IHD. (From Kasiske and coworkers [1]; with permission.)

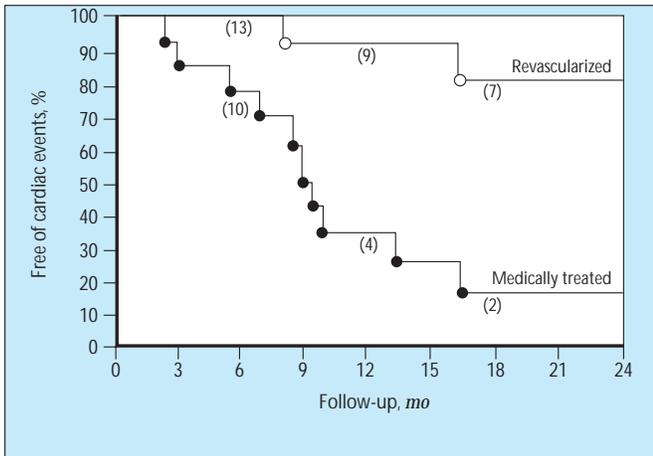


FIGURE 12-12

Effects of surgical versus medical management of coronary disease before renal transplantation in candidates who have insulin-dependent diabetes. In this study, 26 patients with insulin-dependent diabetes who were found to have over 75% stenoses in one or more coronary arteries were randomly allocated to either medical management or a revascularization procedure before transplantation. Ten of the 13 patients who were managed medically and 2 of the 13 who had revascularization performed had a cardiovascular disease end point within a median of 8.4 months after transplantation ($P < 0.01$). These findings suggest that transplantation candidates who have diabetes should be screened for silent coronary artery disease because revascularization decreases morbidity and mortality after transplantation. The numbers in parentheses indicate the number of patients being followed at that time. (From Manske and coworkers [5]; with permission.)

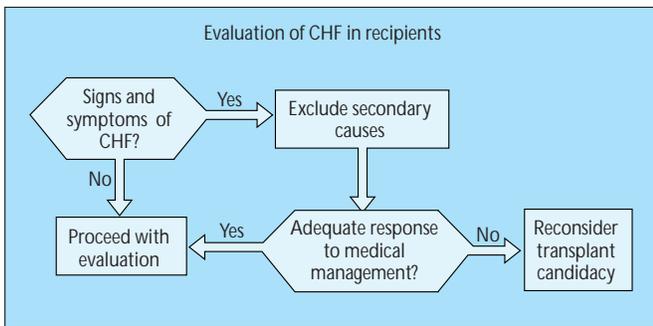


FIGURE 12-13

Congestive heart failure (CHF). Myocardial performance has been shown to improve in some patients after renal transplantation. Thus, a low ejection fraction alone does not automatically exclude patients from transplantation. In contrast, patients with severe irreversible myocardial disease may not be good candidates for transplantation. Occasionally, patients may be candidates for simultaneous heart and kidney transplantation. (From Kasiske and coworkers [1]; with permission.)

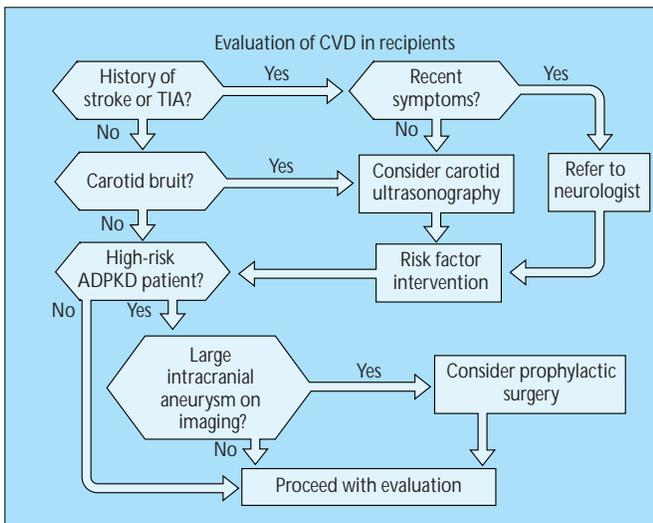


FIGURE 12-14

Cerebral vascular disease (CVD). Patients must not undergo surgery within 6 months of a stroke or transient ischemic attack (TIA). Asymptomatic patients with a carotid bruit should be considered for carotid ultrasonography because patients with severe carotid disease may be candidates for prophylactic surgery. Patients with autosomal dominant polycystic kidney disease (ADPKD) and either a previous episode or a positive family history of a ruptured intracranial aneurysm must be screened with computed tomography or magnetic resonance imaging. Patients found to have an aneurysm over 7 mm in diameter may benefit from prophylactic surgery. (From Kasiske and coworkers [1]; with permission.)

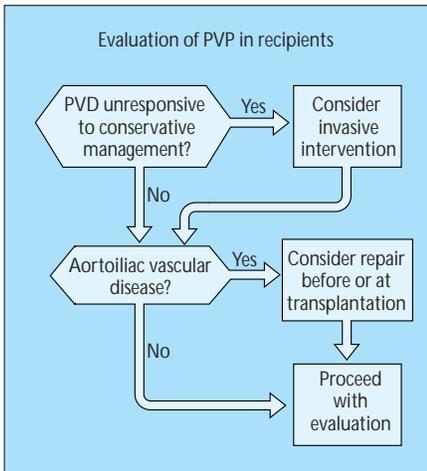


FIGURE 12-15

Peripheral vascular disease (PVD). Peripheral vascular disease is commonly associated with coronary artery disease, cerebral vascular disease, or both. However, PVD itself may require intervention before transplantation to prevent infection and sepsis after transplantation. In addition, some patients may have aortoiliac disease severe enough to require intervention before transplantation. Rarely, vascular disease is severe enough to make it difficult to find an artery suitable for the anastomosis of the allograft renal artery. (From Kasiske and coworkers [1]; with permission.)

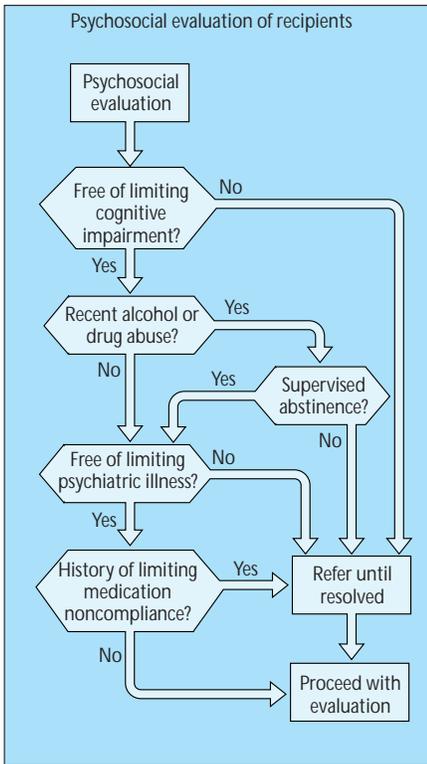


FIGURE 12-16

Psychosocial evaluation. Patients must be free of cognitive impairments and able to give informed consent. Most transplantation centers require patients with a history of alcohol or drug abuse to demonstrate a period of supervised abstinence, generally 6 months or more [6]. Similarly, patients with a past history of medication adherence poor enough to suspect that the immunosuppressive regimen will be compromised may need to delay transplantation until reasonable adherence can be demonstrated [6]. (From Kasiske and coworkers [1]; with permission.)

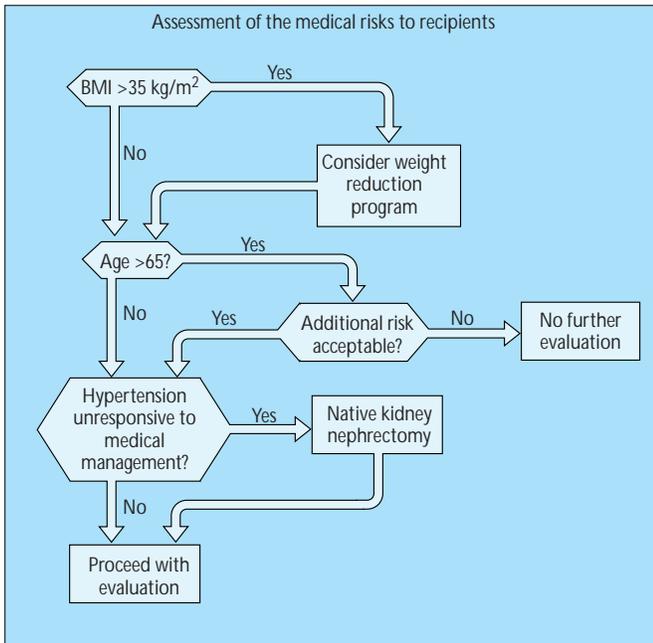


FIGURE 12-17

Assessing the medical risks of transplantation surgery. Obesity increases the risks of surgery, and a weight reduction program before transplantation must be considered for very obese patients. Older age is a relative contraindication to transplantation; however, it is difficult to precisely define an upper age limit for all patients. Rather, age and overall medical condition must be considered together. Hypertension should be controlled before transplantation. When control of hypertension is difficult, bilateral nephrectomy should be considered before transplantation. BMI—body mass index. (From Kasiske and coworkers [1]; with permission.)

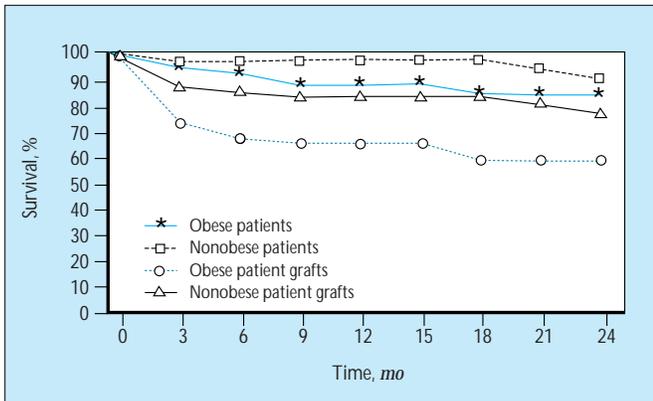


FIGURE 12-18

Effects of obesity on patient and graft survival. In this case-control study, 46 obese (body mass index > 30 kg/m²) recipients of cadaveric renal transplantation were compared with nonobese controls matched for the following after transplantation: age, gender, diabetes, panel reactive antibody status, graft number, cardiovascular disease, date of transplantation, and immunosuppression. Survival of patients and grafts was significantly less among obese patients compared with controls ($P < 0.01$ and $P < 0.05$, respectively). The following occurred more often in obese versus nonobese patients: delayed graft function, postoperative complications, wound complications, and new-onset diabetes. (From Holley and coworkers [7]; with permission.)

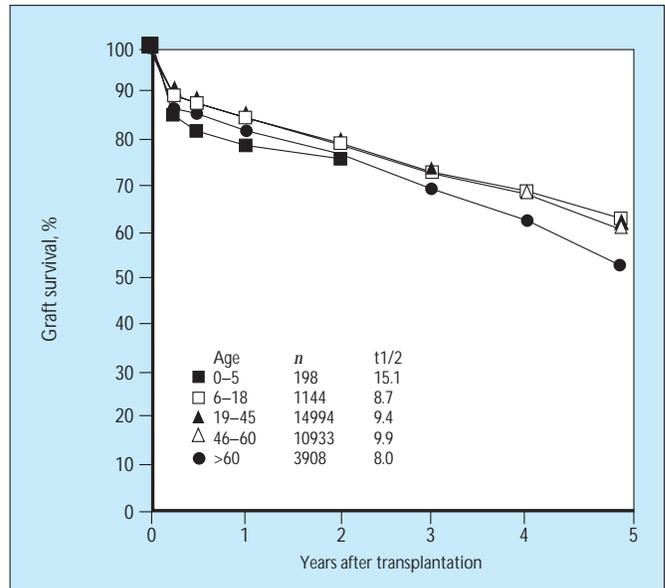


FIGURE 12-19

Effects of the recipient's age on renal allograft survival. Data from the United Network for Organ Sharing Scientific Registry indicate that recipients over the age of 60 have slightly less allograft survival compared with younger recipients. t1/2—graft survival half-life (in years) the first year after transplantation. (From Cecka [3]; with permission.)

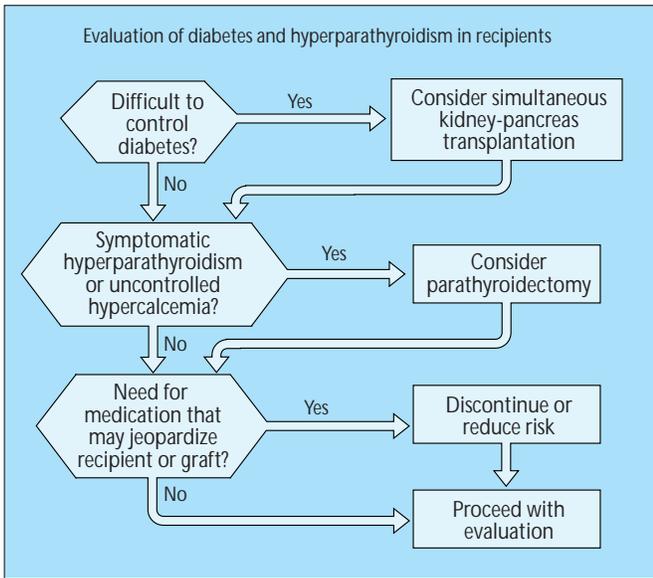


FIGURE 12-20

Diabetes and hyperparathyroidism. Patients with difficult to control diabetes may be candidates for simultaneous kidney-pancreas transplantation. However, patients with diabetes who have a living donor are generally better off undergoing transplantation with the living donor kidney alone. Patients with symptomatic hyperparathyroidism or uncontrolled hypercalcemia should be considered for parathyroidectomy before transplantation. Medications that interfere with the metabolism of immunosuppressive agents such as cyclosporine should be substituted with appropriate alternatives, if possible, before transplantation. (From Kasiske and coworkers [1]; with permission.)

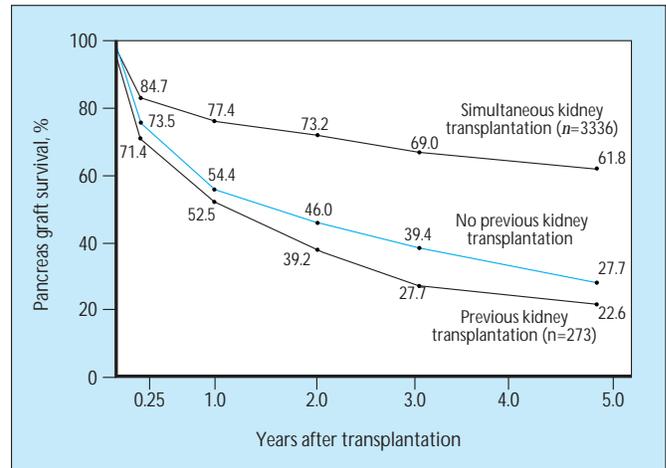


FIGURE 12-21

Pancreas graft survival in recipients of pancreatic transplantation with simultaneous, no previous, and previous kidney transplantation. Survival rates of pancreatic grafts are best when pancreatic and kidney transplantations are performed at the same time. (Data from the United Network for Organ Sharing Scientific Registry [8].)

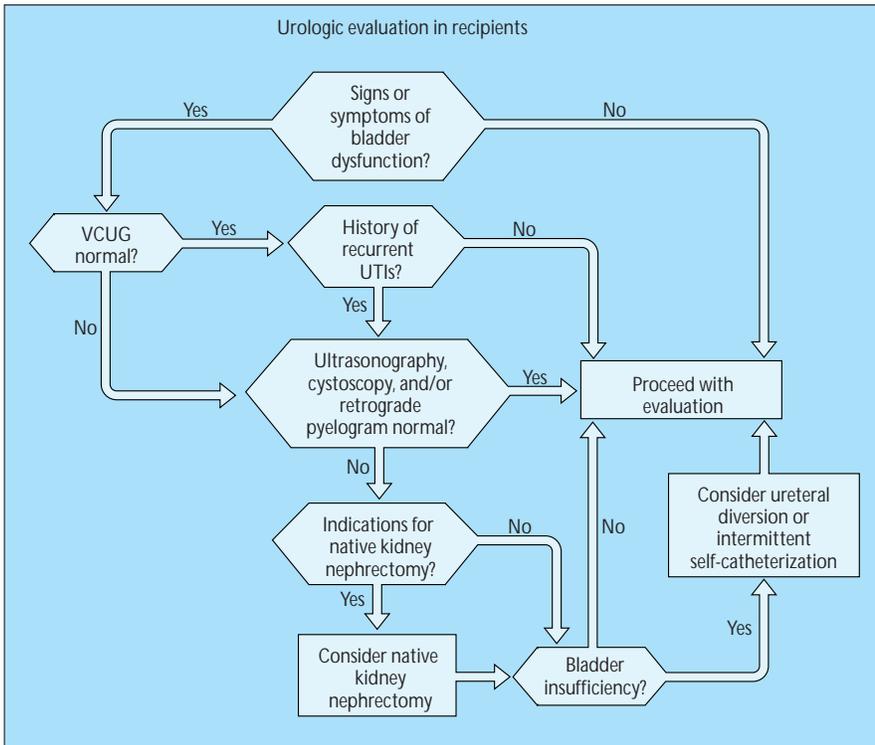


FIGURE 12-22

Urologic evaluation of transplantation recipients. Patients without signs and symptoms of bladder dysfunction generally do not need additional urologic testing. However, patients with bladder dysfunction must be evaluated to ensure that the bladder is functional after transplantation and that potential sources of urinary tract infection (UTI) are eliminated. Such patients can be screened initially with voiding cystourethrography (VCUG). (From Kasiske and coworkers [1]; with permission.)

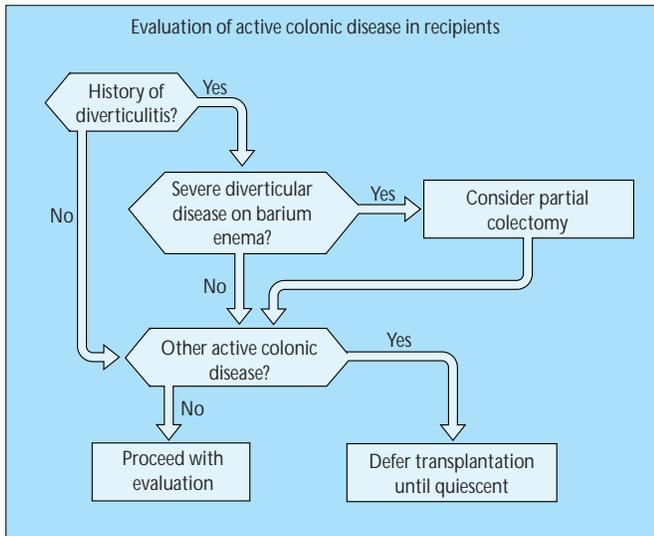


FIGURE 12-23 Diverticulitis and inflammatory bowel disease. Patients with a history of symptomatic diverticulitis must be evaluated for partial colectomy before transplantation. Inflammatory bowel disease generally should be quiescent at the time of transplantation. (From Kasiske and coworkers [1]; with permission.)

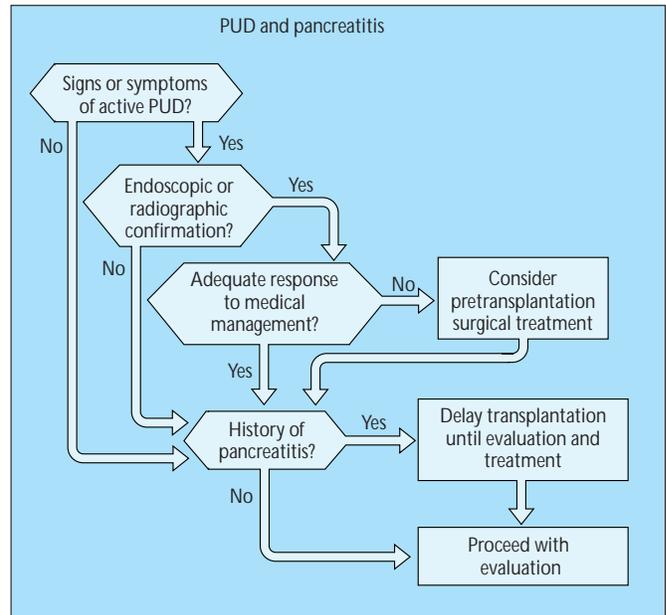


FIGURE 12-24 Peptic ulcer disease (PUD) and pancreatitis. Patients with PUD or pancreatitis must undergo evaluation and treatment before transplantation. Both conditions may be exacerbated by corticosteroids used after transplantation. (From Kasiske and coworkers [1]; with permission.)

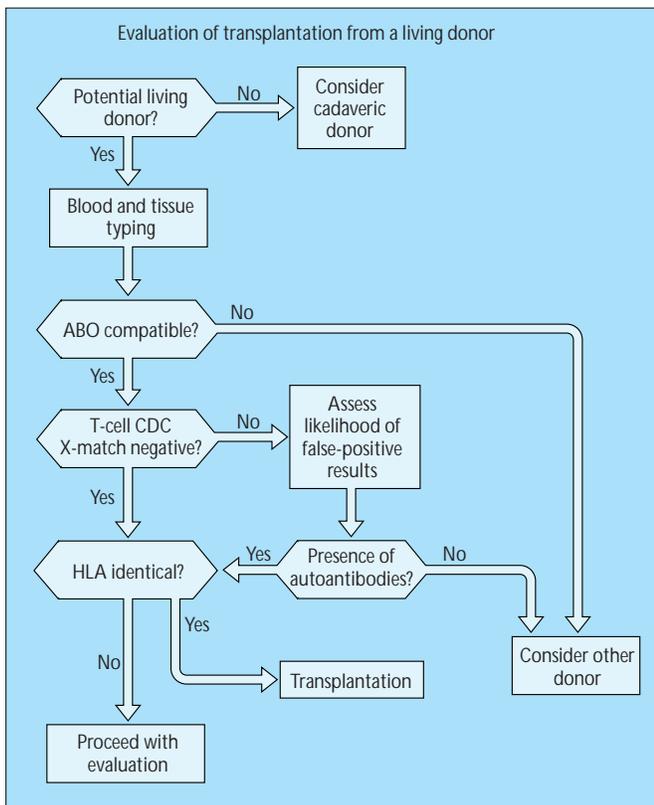


FIGURE 12-25 Immunologic evaluation for living donor transplantation. Generally, transplantation donors and recipients must have compatible blood groups. Tissue typing is also carried out, and the degree of human leukocyte antigen (HLA) matching may be taken into account in selecting the best living donor when more than one donor is available. Just before transplantation, the recipient's serum is tested against donor cells to be certain no preformed antibodies are present in the recipient that may cause a hyperacute rejection. A positive cross-match (X-match) generally precludes transplantation from that donor. CDC—cell-dependent cytotoxicity. (From Kasiske and coworkers [1]; with permission.)

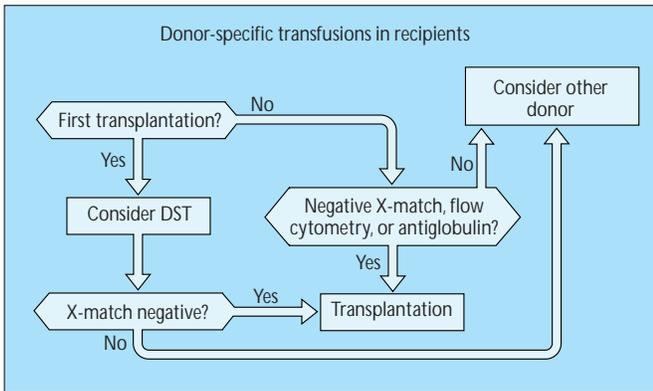


FIGURE 12-26

Donor-specific transfusion (DST). When the living donor is non-human leukocyte antigen identical and it is the recipient's first transplantation, some centers use donor-specific blood transfusions before transplantation to enhance graft survival. Unfortunately, donor-specific transfusions may induce the formation of antibodies against the donor that will preclude the transplantation. Most centers have abandoned the use of random blood transfusions as part of the preparation of recipients for cadaveric transplantation. X-match—cross-match. (From Kasiske and coworkers [1]; with permission.)

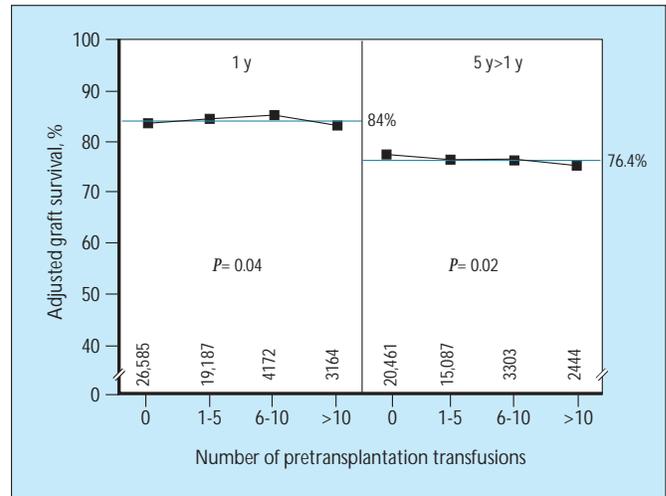


FIGURE 12-27

Effects of random blood transfusions on first cadaveric renal allograft survival. Blood transfusions before transplantation had a small but statistically significant beneficial effect on 1-year graft survival. However, a small reduction occurred in 5-year graft survival (among patients who survived at least 1 year with a functioning kidney) that was attributable to random donor blood transfusions before transplantation (From Gjertson [9]; with permission.)

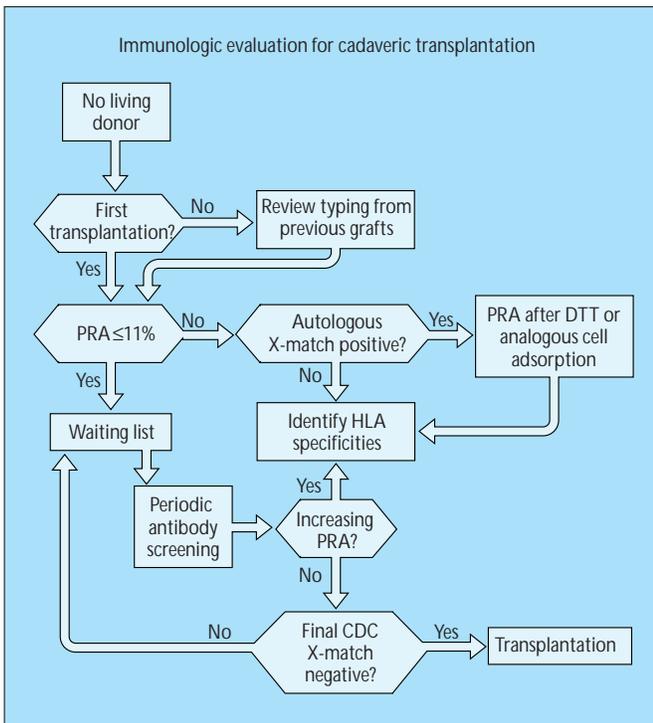


FIGURE 12-28

Immunologic evaluation for cadaveric transplantation. Donors and recipients must have compatible blood groups. Tissue typing is carried out, and the degree of matching is used in the allocation of cadaveric organs. Some data suggest that the presence of human leukocyte antigen (HLA) mismatches that were also mismatched in a previous graft (especially at the DR locus) may lead to early graft loss. Thus, it may be wise to avoid these mismatches. When the percentage of panel reactive antibodies (PRA) is over 10%, tests may be carried out to determine whether some of the antibodies are autoreactive rather than alloreactive. Autoreactive antibodies may not increase the risk for graft loss as do alloreactive antibodies. The presence of high titers of alloreactive antibodies usually is due to previous pregnancies, transplantations, and blood transfusions. Determining antibody specificities may be useful in avoiding certain HLA antigens. In the highly sensitized patient (PRA > 50%) it may be difficult to find a complement-dependent cytotoxicity (CDC) cross-matched (X-match) negative donor. Avoiding blood transfusions may help the titer decrease over time. DTT—1, 4-dithiothreitol (DTT). (From Kasiske and coworkers [1]; with permission.)

Evaluation of Prospective Living Donors

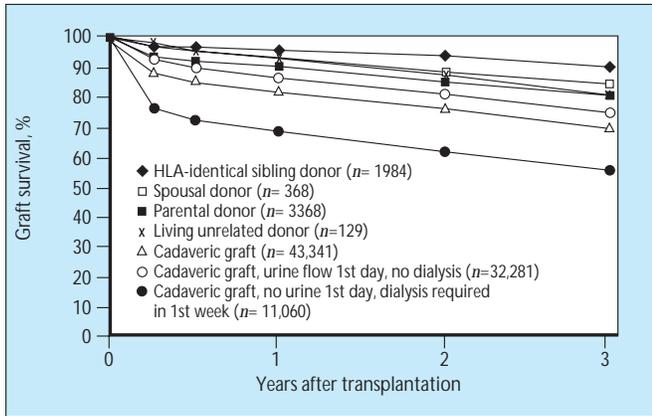


FIGURE 12-29

Effects of donor source on renal allograft survival. Data from the United Network for Organ Sharing Scientific Registry were used to compare 3-year graft survival rates between recipients of kidneys from different donor sources. The best graft survival was seen in recipients of human leukocyte antigen (HLA)-identical sibling donors. Grafts from spouses and other living unrelated donors, however, survived just as well as did grafts from parental donors and better than grafts from cadaveric donors. These data have encouraged centers to use emotionally related donors to avoid the long waiting times for cadaveric kidneys. (From Terasaki and coworkers [10]; with permission.)

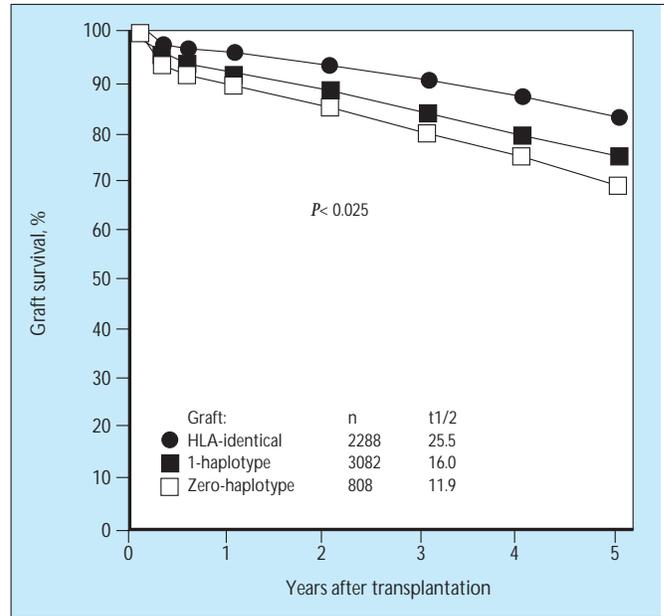


FIGURE 12-30

Effects of human leukocyte antigen (HLA) matching on living related graft survival. Graft survival is best for HLA-identical grafts from siblings and next best for one-haplotype mismatched grafts. Importantly, the half-life (t1/2) of grafts that survived at least 1 year is proportional to the degree of matching. This information can be used along with other factors to select the most suitable among two or more living prospective donors. (From Cecka [3]; with permission.)

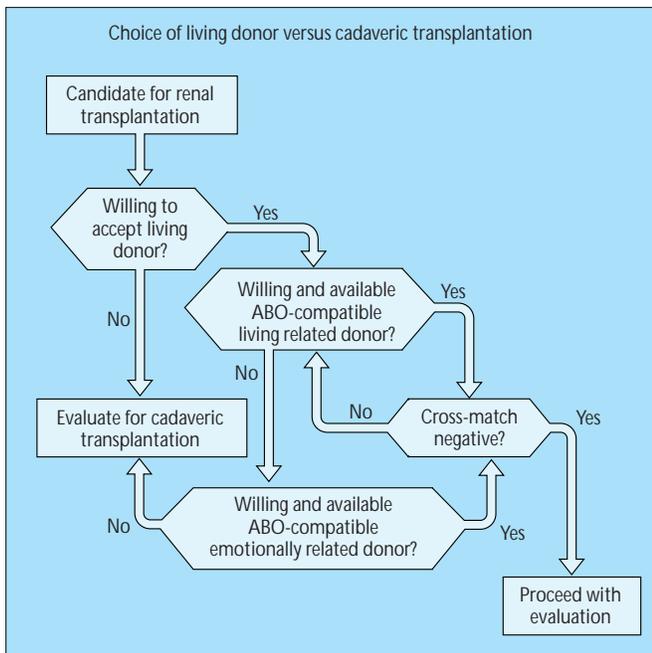


FIGURE 12-31

Use of living donors. A suitable living donor is better than a cadaveric donor because graft survival is better and preemptive transplantation is possible. The best donor usually is a family member. Psychosocial and biological factors must be taken into account when choosing among two or more living prospective donors. Every effort must be made to ensure that the donation is truly voluntary. Caregivers should tell prospective donors that if they do not wish to donate, then friends and relatives will be told "the donor was not medically suitable." (From Kasiske and coworkers [2]; with permission.)

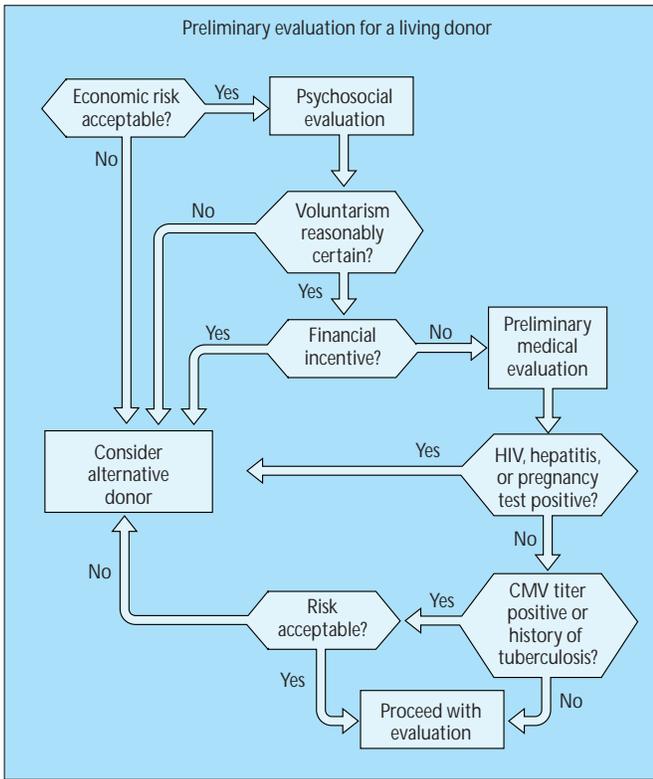


FIGURE 12-32 Preliminary evaluation of a living prospective donor. The prospective donor must be made aware of the possible costs associated with donation, including travel to and from the transplantation center and time away from work. The prospective donor must undergo a psychological evaluation to ensure the donation is voluntary. A preliminary medical evaluation should assess the risks of transmitting infectious diseases with the kidney, eg, infection with human immunodeficiency virus (HIV) and cytomegalovirus (CMV). (From Kasiske and coworkers [2]; with permission.)

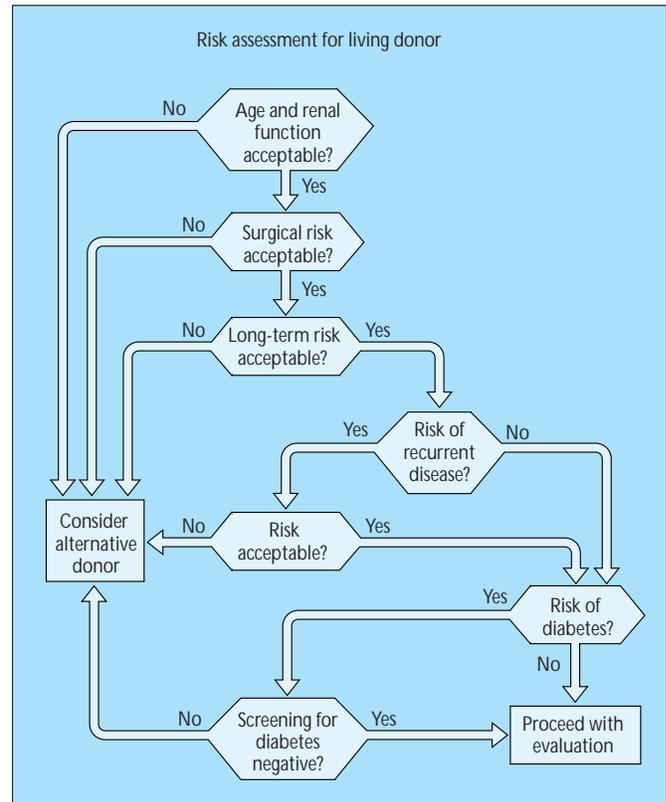


FIGURE 12-33 Assessing risks. Older age may place the living prospective donor at greater surgical risk and may be associated with reduced graft survival for the recipient. The prospective donor must be informed of both the short-term surgical risks (very low in the absence of cardiovascular disease and other risk factors) and the long-term consequences of having only one kidney. With regard to long-term risks, it should be considered whether there is a familial disease that the living donor may be at risk to acquire and whether having only one kidney would alter the natural history of renal disease progression. These questions are often most pertinent for relatives of patients with diabetes. (From Kasiske and coworkers [2]; with permission.)

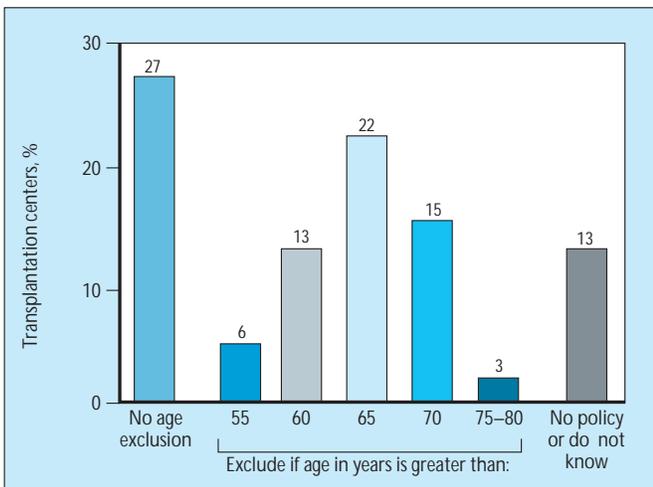


FIGURE 12-34 Donor age restrictions used by transplantation centers. Results of an American Society of Transplantation survey of the United Network for Organ Sharing centers showed that many centers either use no specific age exclusion criteria or have no policy. Among those that use an upper age limit, there appears to be a bell-shaped curve, with 65 years of age at the median. (From Bia and coworkers [11]; with permission.)

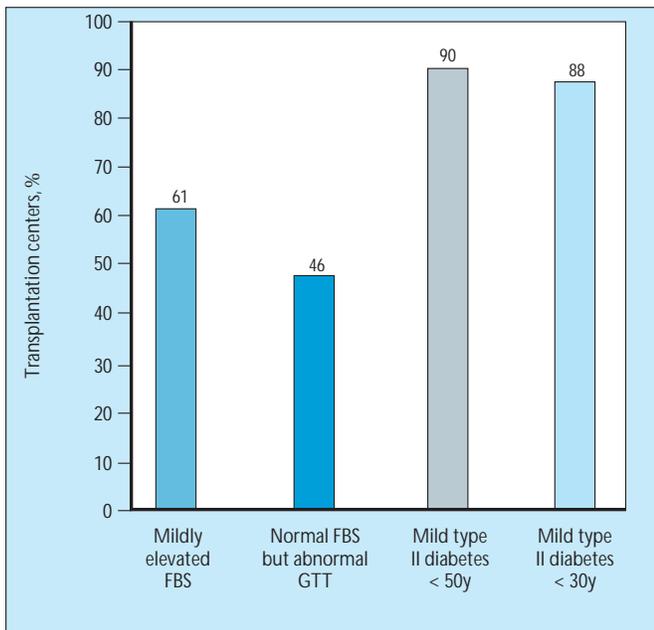


FIGURE 12-35 Screening living prospective donors for diabetes. Results of the survey of the United Network for Organ Sharing centers showed that most centers exclude patients with a mildly elevated fasting blood sugar (FBS) and patients with normal FBS but an abnormal glucose tolerance test (GTT). Most centers exclude donors with mild type II diabetes. (From Bia and coworkers [11]; with permission.)

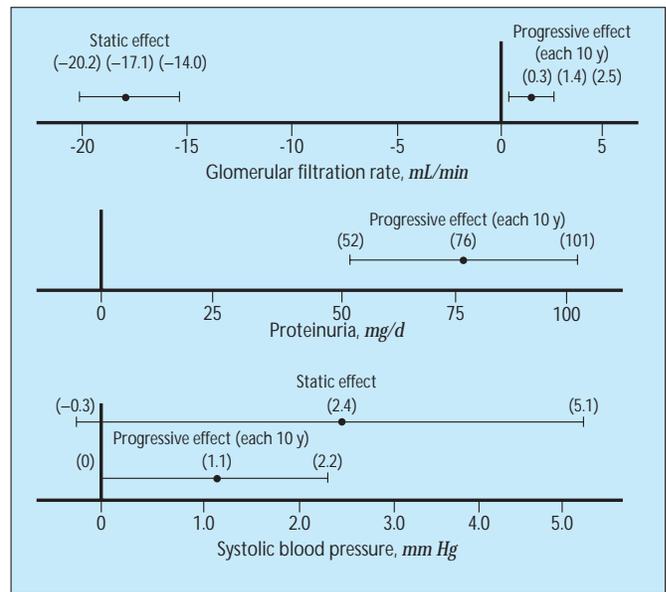


FIGURE 12-36 Long-term risks of kidney donation. In a meta-analysis combining 48 studies of the long-term effects of reduced renal mass in humans, no evidence was found of a progressive decline in renal function after a 50% reduction in renal mass. Indeed, a small but statistically significant increase occurred over time in the glomerular filtration rate. A small increase in urine protein excretion occurred; however, the rate of increase per decade was less than that generally considered an abnormal amount of protein excretion, eg, 150 mg/d. A small increase in systolic blood pressure was noted; however, it was not enough to lead to an increase in the incidence of hypertension. Thus, it appears that the long-term risks of kidney donation are very small. Shown are multiple linear regression coefficients and 95% confidence intervals. Failure of the confidence interval to include zero indicates $P < 0.05$. (From Kasiske and coworkers [12]; with permission.)

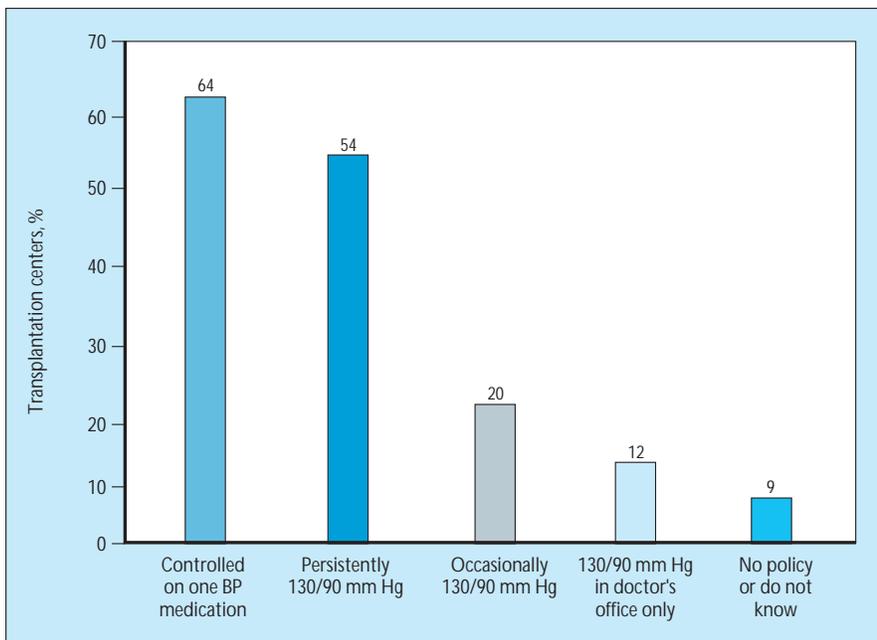


FIGURE 12-37 Blood pressure (BP) criteria for excluding living prospective donors. Results of the survey of the United Network for Organ Sharing centers showed that most exclude prospective donors who require antihypertensive medication or whose BP is persistently elevated over 130/80 mm Hg. However, most centers do not exclude living prospective donors who occasionally have BP readings over 130/80 mm Hg or patients with so-called white coat hypertension. (From Bia and coworkers [11]; with permission.)

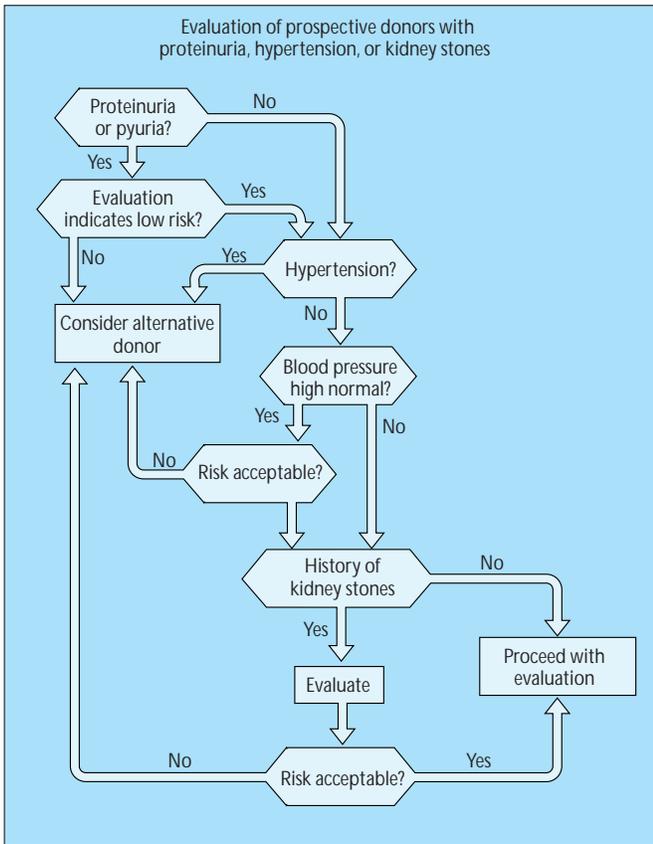


FIGURE 12-38 Proteinuria, hypertension, or kidney stones in living prospective donors. Prospective donors with pyuria must be evaluated for possible infection and other reversible abnormalities. Proteinuria is generally a contraindication to donation. Hypertension also must be considered at least a relative contraindication to donation. Patients with a history of nephrolithiasis but no current or recent stones may be considered for donation after first undergoing urologic and metabolic evaluations for stones. (From Kasiske and coworkers [2]; with permission.)

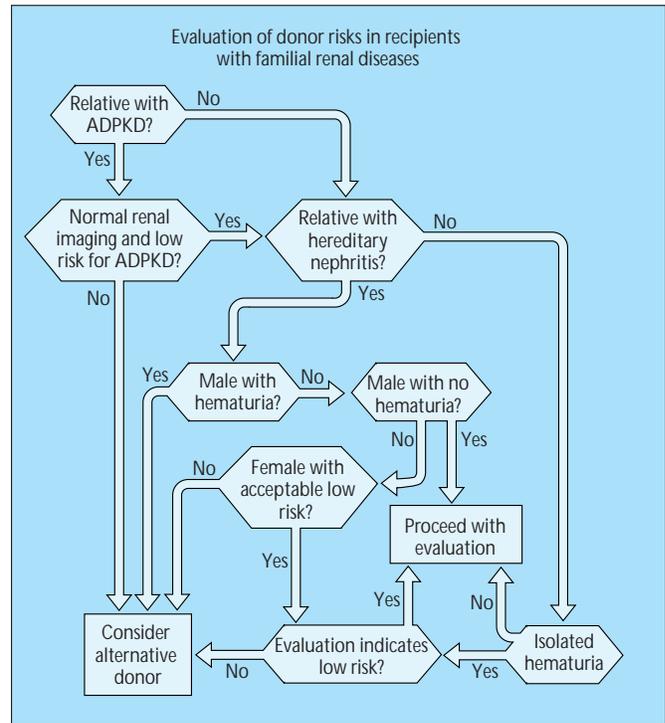


FIGURE 12-39 Risks to the related donor when the recipient has familial renal disease. Donors for relatives with autosomal dominant polycystic kidney disease (ADPKD) may be permitted to donate if over 25 years old and results on renal imaging are negative for cysts. Some younger persons may be permitted to donate if genetic studies indicate that the risk for subsequent ADPKD is very low. Male relatives of individuals with hereditary nephritis can be donors if they do not have hematuria. Male relatives with hematuria cannot be donors. Female relatives without hematuria may donate; however, women of child-bearing age who might be carriers must consider the possibility of someday donating a kidney to a child of their own with the disease. Female relatives with hematuria should not donate when other evidence of renal disease exists; however, in the absence of such evidence the exact risk of donation is unknown. Occasionally, donors with isolated microhematuria (not hereditary) and a negative evaluation may be suitable donors. (From Kasiske and coworkers [2]; with permission.)

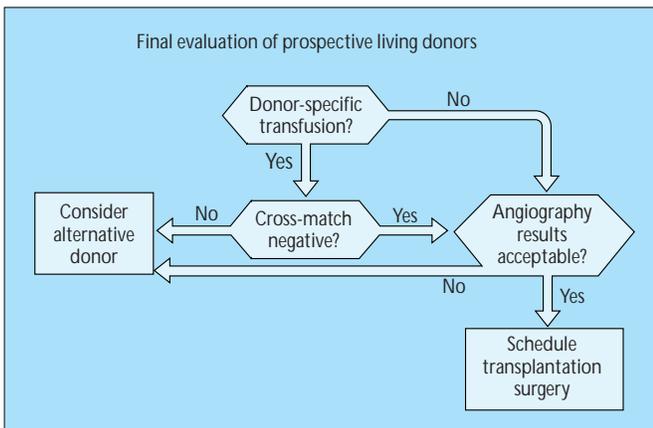


FIGURE 12-40 Final steps in evaluating a living prospective donor. Renal artery angiography is performed to define the anatomy of the renal artery system and exclude other previously undetected abnormalities. Recent studies have shown that spiral computerized tomography can replace angiography without loss of sensitivity or specificity and with less risk and inconvenience to the prospective donor. (From Kasiske and coworkers [2]; with permission.)

Use of Marginal Cadaveric Donor Kidneys

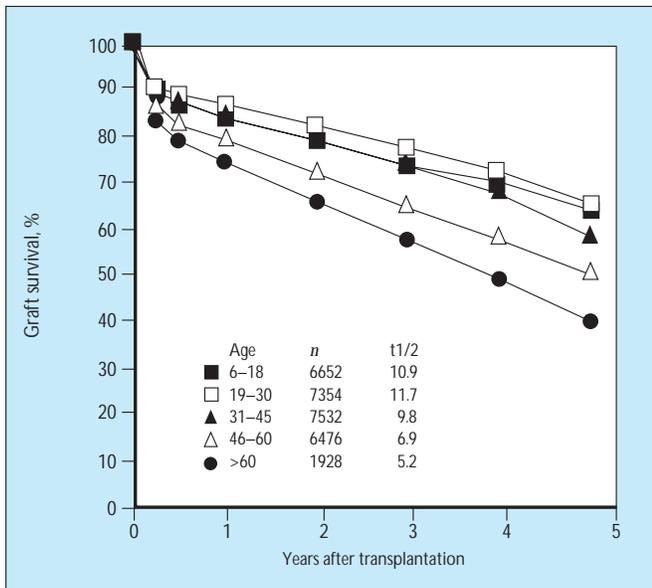


FIGURE 12-41

Donor age. When there are no suitable living donors, recipients are placed on the cadaveric waiting list. The transplantation center must always decide whether a particular cadaveric kidney being offered for transplantation is suitable for the individual recipient. The shortage of organs and long waiting times have caused many centers to accept kidneys from older donors and kidneys that may be damaged. Data from the United Network for Organ Sharing clearly demonstrate the decreased graft survival rates of kidneys from older donors. As a compromise, some advocate using kidneys from older donors for older recipients. In any case, so-called marginal kidneys should be offered to recipients with appropriate informed consent. (From Cecka [3]; with permission.)

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