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Transplanted Kidney Function Evaluation

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The best option for the treatment of end-stage renal disease is kidney transplantation. Prompt diagnosis and management of early posttransplantation complications is of utmost importance for graft survival. Biochemical markers, allograft biopsies, and imaging modalities are used for the timely recognition and management of graft dysfunction. Among several other factors, improvements in imaging modalities have been regarded as one of the factors contributing to increased short-term graft survival. Each imaging procedure has its own unique contribution to the evaluation of renal transplant dysfunction. In the era of multimodality imaging and emerging clinical considerations for the improvement of graft survival, evaluating an imaging modality in its own right may not be relevant and may fall short of expectation. Recognized as being mainly a functional imaging procedure, radionuclide imaging provides valuable information on renal function that cannot be obtained with other imaging modalities. For evaluating and establishing the current place, indications, and potential applications of radionuclide renal transplant imaging, a classification of renal allograft complications based on renal allograft dysfunction is essential. The major factor affecting long-term graft loss is chronic allograft nephropathy. Its association with early posttransplantation delayed graft function and repeated acute rejection episodes is well documented. Long-term graft survival rate have not improve significantly over the years. Imaging procedures are most commonly performed during the early period after transplantation. There seems to be a need for performing more frequent late posttransplantation imaging for the evaluation of acute allograft dysfunction, subclinical pathology, and chronic allograft changes; for understanding their contribution to patient management; and for identification of pathophysiological mechanisms leading to proteinuria and hypertension. With its unique advantage of relating perfusion to function, the potential for radionuclide imaging to replace late protocol biopsies needs to be investigated.
Semin Nucl Med 44:129-145

End-stage renal disease is a cause of significant morbidity and mortality, with a worldwide increase in its incidence and prevalence. Renal replacement therapy with hemodialysis or peritoneal dialysis and transplantation of a graft from a deceased or living donor constitute the major treatment options in this patient group. Owing to persistent organ shortage and increased demand, the use of marginal kidneys from expanded criteria donor (ECD) and cardiac death donors has increased. Renal transplantation is the best choice of treatment as it is associated with better survival rates, improved quality of life, and lower costs. However, implantation of a renal graft does not mean an uneventful course. Renal transplant complications can be observed during the early posttransplantation period and on follow-up, resulting in graft dysfunction and in severe cases graft loss, necessitating hemodialysis or the use of a new transplant.

Despite the survival benefit conferred by transplantation, renal allograft recipients still have a high mortality rate compared with population controls. Posttransplantation survival rates vary depending on patient-related factors, such as age, gender, race, and presence of comorbid conditions; source of the allograft; operation-related factors; degree of immunosuppression; and postoperative complications. During the early posttransplantation period, the immune system is routinely suppressed to minimize the incidence of graft rejection. The graft failure rate has significantly decreased over the years because of improved surgical technique, better immunosuppressive therapy, and better monitoring techniques. Although short-term survival rate at 1 year after operation has improved over the past 2 decades, long-term failure rate at 5 years or more did not change significantly.[1-3] There are conflicting results in the literature about the influence of potential risk factors on long-term graft survival. The only factor shown to have a certain influence on the

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0001-2998/14/$-see front matter
http://dx.doi.org/10.1053/j.semnuclmed.2013.10.005

outcome is the source of the graft. Survival rate at 5 years was reported to be 90% for living related, 83% for non-ECD, and 69% for ECD deceased donor grafts.[1]

Owing to the importance of renal transplantation in patient management and limited availability of donor kidneys, detailed evaluation of factors that affect transplant survival is essential. Noninvasive imaging modalities have become an important part of transplantation programs for evaluating early post-transplantation vasculature and function, differential diagnosis of early allograft dysfunction, and evaluating long-term transplant complications and as a prognostic tool for short- and long-term graft survival.

Renal Transplant Complications

There are various schemes used for the classification of renal transplant complications. The most commonly used ones either classify them as surgical vs medical or, depending on the localization of the underlying etiology, as prerenal, renal, and postrenal. Surgical complications comprise fluid collections, urinary obstruction, and vascular complications. Medical complications are related to parenchymal pathologies as acute tubular necrosis (ATN), acute rejection (AR), and drug toxicity.

From the renal function point of view, renal allograft dysfunction can be in the form of primary nonfunction or most commonly delayed graft function (DGF) during the early period after transplantation. DGF is characterized with a failure of renal function tests to improve early posttransplantation. At other times, allograft dysfunction is generally diagnosed based on an acute or slow deterioration of renal function, as reflected by rising serum creatinine levels, proteinuria, hypertension, or abdominal pain. From the functional point of view, a classification scheme for the most common etiologic factors of renal transplant dysfunction is summarized in Table 1.

Table 1 Classification of Renal Transplant Complications Based on the Time and the Course of Renal Transplant Dysfunction After Transplantation

1. Delayed graft function (DGF)
   - A. Due to ischemia-reperfusion injury
     - a. Acute tubular necrosis
   - B. Nonischemic causes of DGF
     - a. Acute rejection
     - b. Drug toxicity
     - c. Vascular complications
     - d. Urinary complications
       - i. Obstruction
       - ii. Urinary leak
       - iii. Urinary bladder dysfunction
     - e. Peritransplant fluid collections
2. Acute renal allograft dysfunction
   - A. Acute rejection
   - B. Urinary tract infection
   - C. Obstruction
   - D. Tubulointerstitial nephritis
3. Slowly deteriorating graft function
   - A. Chronic allograft nephropathy
   - B. Drug toxicity
   - C. Renal artery stenosis
   - D. Transplant glomerulopathy
   - E. Infections (particulary viral infection due to cytomegalovirus)

Evaluation of Renal Transplant Complications

Nonimaging Procedures

Renal Function Tests

Renal transplant function is commonly monitored using serum creatinine level. Its production is dependent on age, gender, and muscle mass. Serum creatinine concentrations may remain within the reference range until approximately half of renal function has been lost. Plasma cystatin C level, 24-hour urinary output, and 24-hour creatinine clearance are among the measures used for the evaluation of renal function in transplant recipients. Creatinine reduction ratio and 24-hour urine creatinine excretion from posttransplant days 1-2 are shown to be effective measures of evaluating renal transplant status and for predicting graft survival.[4]

Allograft Biopsy

Percutaneous renal needle core biopsy is performed mainly in the setting of acute graft dysfunction and is the gold standard to establish the correct diagnosis. However, regardless of renal function, biopsies can also be obtained at predetermined times after renal transplantation, and these are called protocol biopsies.[5] The rationale behind the protocol biopsies is the potential benefit of early recognition of allograft pathologies, thus their earlier treatment resulting in a better long-term outcome. However, there is debate over the performance of protocol biopsies and conflicting results concerning its possible benefits.[6] Banff classification has set the widely accepted criteria for the diagnosis of renal allograft pathologies.[7]

Nonradionuclide Imaging Procedures

Renal transplant imaging is most commonly performed during the first 7-12 days after transplantation. Imaging procedures are used as necessary during follow-up based on renal function tests and clinical symptoms. Ultrasonography (US), radionuclide imaging, CT, and MRI are the main imaging procedures used in the evaluation of renal transplant status.

US with color Doppler imaging is the first-line imaging during the early posttransplantation period. This modality not only provides vascular flow information and define perirenal fluid collections but also establishes a baseline for future comparisons. It is also useful for guiding renal biopsy and drainage of large fluid collections. Limitations include relatively