

**American College of Radiology  
ACR Appropriateness Criteria®**

**Clinical Condition:**      **Renal Transplant Dysfunction**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><u>RRL</u>*</b>
US kidney transplant	9		O
Tc-99m MAG3 scan kidney	7		☢ ☢ ☢
Tc-99m DTPA scan kidney	5		☢ ☢ ☢
CT abdomen and pelvis with contrast	5		☢ ☢ ☢ ☢
Arteriography kidney	5	After noninvasive vascular assessment has been performed. To confirm RAS or other vascular abnormality and guide treatment.	☢ ☢ ☢
CT abdomen and pelvis without and with contrast	4	Noncontrast phase may be beneficial in assessing hemorrhage, vascular calcifications, and stones.	☢ ☢ ☢ ☢
CT abdomen and pelvis without contrast	4		☢ ☢ ☢ ☢
MRI abdomen and pelvis without and with contrast	4	See statement regarding contrast in text under "Anticipated Exceptions."	O
MRI abdomen and pelvis without contrast	4		O
X-ray intravenous urography	1		☢ ☢ ☢
X-ray antegrade pyelography	1		☢ ☢ ☢
<b><u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate</b>			<b>*Relative Radiation Level</b>

# RENAL TRANSPLANT DYSFUNCTION

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## **Summary of Literature Review**

### **Introduction/Background**

According to the Organ Procurement and Transplantation Network of the U.S. Health Resources and Services Administration, almost 330,000 renal transplants have been performed in the United States since 1988 [1]. In 2011 alone, 16,813 renal transplants were performed, of which 11,043 were from deceased donors and 5,770 were from living donors. Renal transplant dysfunction can lead to renal failure, a devastating event, and every effort is made to address dysfunction by management of immunosuppression and transplant complications. Five-year survival rates for the graft in renal transplant patients range from 72%-99%, with the best rates seen in patients receiving kidneys from living donors.

Causes for renal transplant dysfunction include acute tubular necrosis (ATN), rejection, toxicity from medications, renal artery stenosis, renal vein thrombosis, and postbiopsy renal arteriovenous malformations. ATN is seen in the immediate post-transplant period in a high percentage of cadaver grafts but only infrequently in living related donors. Acute rejection typically occurs at least 4-5 days after transplantation [2]. The incidence of renal artery stenosis varies from 1.8%-12% in the literature and presents as refractory hypertension or increasing serum urea and creatinine levels [3].

Ultrasound (US) is the modality of choice to evaluate renal transplants early in the postoperative period but also in long-term follow-up as well. US is also used to guide diagnostic and therapeutic interventions such as biopsy or fluid aspiration. Radionuclide imaging is an excellent modality for assessing graft function both qualitatively and quantitatively [4]. Computed tomography (CT) and magnetic resonance imaging (MRI) can provide information about structural abnormalities like stenosis and thrombosis. Angiography is used for treatment of complications like stenosis or arteriovenous malformations.

### **Ultrasound**

As renal transplants typically are located anteriorly in the pelvis, they usually are readily visible with US. US is a valuable tool in the immediate post-transplant period as well as for long-term follow-up. Typically, gray scale images are obtained to evaluate for transplant hydronephrosis, peritransplant fluid collections, and renal cortical thickness. Color Doppler images are obtained to evaluate the patency and direction of flow in transplant arteries and veins. Spectral analysis of vascular waveforms and velocities can provide information about a range of pathologies such as renal artery stenosis. The lack of potentially nephrotoxic iodinated contrast agents is an advantage of US over CT. Furthermore, an advantage of US over MRI is avoidance of the risk of developing nephrogenic systemic fibrosis (NSF) as a result of gadolinium-based contrast agents. The operator dependence of US is, however, a relative limitation.

US is used as a routine study to evaluate the transplant within the first 24 hours after transplantation to detect or rule out vascular pathology. In the perioperative period, US can detect renal artery thrombosis or renal vein thrombosis. It is also commonly used for first-line evaluation in the setting of transplant dysfunction. B-mode appearance seen on US include a reduction in corticomedullary differentiation, reduction in renal sinus echoes, increased and reduced renal parenchymal echoes, increased cortical reflectivity. However, these features occur

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well after the onset of the dysfunction and are arbitrary and inconsistent and hence of limited value. Studies have suggested that resistive index (RI) measured by duplex Doppler US is not sensitive or specific in identifying the cause of functional transplant dysfunction [5,6]. In 145 examinations of 81 patients, Rifkin et al [7] found a sensitivity of 13%, a specificity of 100%, a positive predictive value (PPV) of 100%, and a negative predictive value (NPV) of 66% in making the diagnosis of acute rejection with duplex Doppler US. Genkins et al [8] found a sensitivity of 9%, specificity of 91%, PPV of 29% and a NPV of 70% using an RI cut off of 0.90 for the diagnosis of allograft rejection. However, recent studies have shown that renal arterial RI is useful in predicting graft survival [9], especially when using a lower RI cut-off of 0.8. Using a cut-off of 0.80, Radermacher et al [9] found that 47% of patients with RI >0.80 developed chronic allograft nephropathy (CAN) compared to 9% of patients with RI <0.80 in the first 3 months after transplantation. McArthur et al [10] found both RI and pulsatility index (PI) measured between week 1 and 3 months significantly correlated with the 1-year estimated glomerular filtration rate (eGFR). Abnormal resistive indices indicate allograft dysfunction but do not reliably demonstrate the cause.

Doppler US is also a very reliable and noninvasive tool to monitor the effectiveness of revascularization in patients with renal artery stenosis [11]. Tardus parvus waveform can be seen within the kidney downstream to the stenosis; however, due to the superficial location of the transplant kidney, evaluation of the main renal artery is better. Peak systolic velocity (PSV) in the renal artery is commonly used as the parameter to assess for the presence of renal artery stenosis on US. Cut-off values of 200-300 cm/second have been proposed in various studies [12,13]. De Morais et al [14] reported a sensitivity of 90%-96.8% and a specificity of 87.5%-70% using PSV in the main renal artery and a sensitivity of 100% and specificity of 96.7% using an acceleration time (AT) of 0.09 or less as normal. Another parameter that can be used is the renal to iliac artery ratio (RIR), which has been shown to have a sensitivity of 90% and specificity of 96.7% using a cut off value of 1.8. A recent study by Aburahma et al found that a PSV of 285 cm/s or renal-aortic ratio (RAR) of 3.7 alone was better than any combination of PSVs, EDVs, or RARs in detecting  $\geq 60\%$  stenosis [15].

As for other modalities, the evaluation of accessory arteries may contribute to reduced sensitivity and specificity for arterial stenosis. As evaluation for renal artery stenosis with US is operator dependent, magnetic resonance angiography (MRA) or CT angiography (CTA) may be more reliable in centers with little experience evaluating for renal artery stenosis with US. US appearance of renal artery thrombosis is striking, with complete absence of flow in the renal vessels on color flow and spectral analysis. It is important to remember, however, that absent flow within the kidney can also be seen in patients with hyperacute rejection and renal vein thrombosis [16]. Reversal of flow in the renal artery in diastole has been seen in renal vein thrombosis [17]; however, this reversal has been shown in ATN, rejection, low cardiac output, and nephrosclerosis as well [18]. US is a useful tool for detection of post-biopsy arteriovenous fistulas, which can affect allograft function if they are large.

US can identify postoperative fluid collections like abscess, hematoma, lymphocele, and urinoma, but it cannot differentiate between them. In order to differentiate these entities, aspiration is required, and this is commonly performed with US guidance. Hydronephrosis can also be easily identified with US; however, it should be interpreted in correlation with biochemical data since reflux can give a similar appearance as well. Urine leak may appear as a fluid collection on US, but isotope scan would be more helpful [16].

US is also useful in guiding renal transplant biopsies since serum creatinine is insensitive for detecting early graft pathology and cannot be relied on for assessment of adequacy of immunosuppression. The complication rate from renal transplant biopsies is low, with a reported rate of 0.4%-1% graft loss in approximately 2,500 biopsies [19].

Contrast-enhanced ultrasound (CES) has been used by some investigators to evaluate graft perfusion not only in large arteries but within the cortex as well. Fischer et al [20] were able to identify patients with vascular rejection using CES. Schwenger et al [21] found that patients with CAN had significantly lower blood flow values quantified by CES compared to patients without CAN.

### **Computed Tomography**

CT has not been typically used to evaluate renal transplant dysfunction due to concerns of nephrotoxicity from iodinated contrast; however, in patients with suspected renal artery stenosis, CT can provide additional information before a percutaneous angiography is performed. CT angiography (CTA) allows for anatomic depiction in great detail and has a high diagnostic accuracy for detecting vascular complications. Data about the usefulness of CT in evaluating transplant renal artery stenosis are limited. Helck et al [22] in their study found abnormalities on CT in 42% of cases, like renal infarction, renal vein stenosis, and arteriovenous fistula, when US was unremarkable. Rountas et al [23] in their study found that CTA and MR angiography (MRA) appear to have comparable negative predictive accuracy in evaluating suspected renal artery stenosis. They found that CTA had

sensitivity, specificity, PPV, and NPV of 94%, 93%, 71%, and 99%, respectively. CTA, however, has the drawback of contrast-induced nephrotoxicity and radiation exposure in addition to insensitivity to mild renal artery stenosis [24]. Hence iodinated contrast agents should be used with caution in patients with renal dysfunction due to potential nephrotoxicity. In addition to vascular complications, a noncontrast CT could also be used to assess for hydronephrosis and change in the size of fluid collections.

### **Magnetic Resonance Imaging**

MRI is being increasingly used for renal arterial visualization in renal transplants to assess for renal artery stenosis [25]. In addition there are concerns about toxicity from gadolinium in this patient population causing NSF [26]. However, due to the noninvasive nature of the examination, MRA has been used for evaluating renal artery stenosis in post-transplantation patients.

MRA increased the diagnostic confidence in referring patients for conventional angiography with a change in management in approximately 65% of patients [27]. Sharafuddin et al [28] in their study involving both native and transplant renal arteries found that preprocedural planning with use of gadolinium-enhanced MRA significantly reduced the iodinated contrast material requirement during percutaneous renal artery interventions, in addition to shortening the procedure duration. Rountas et al [23] in their study on native renal arteries found that MRA had sensitivity, specificity, PPV, and NPV of 90%, 94.1%, 75%, and 98%, respectively, while Law et al [29] found sensitivity, specificity, PPV, and NPV of 97%, 67%, 90%, and 86% respectively for diagnosing renal artery stenosis. MRA, however, suffers from a few pitfalls that may lead to false diagnosis of stenosis or overestimation of a stenosis. These include artifacts caused by metallic surgical clips near the transplant artery that result in signal drop overlying the vessel, giving the false impression of stenosis, and bright signal at the margin of the signal drop in the soft tissue next to the renal allograft due to metallic clips, and venous overlaps due to inaccurate timing of the arterial bolus. Careful evaluation of the source images and multiplanar reformats will help solve these problems [30]. In addition to depicting areas of stenosis in the main renal artery, MRA is also able to depict areas of infarction within the kidney which may be seen as areas of heterogeneous T1 and T2 signal intensity and as focal areas of nonenhancement on the postcontrast images. Ismaeel et al in their study on transplant renal arteries showed a sensitivity of 93.7%, specificity of 80%, and accuracy of 88.5% [31]. In addition, outer cortical necrosis, cortical necrosis with large patches, diffuse cortical necrosis, and both cortical and medullary necrosis are also visualized on postcontrast images [32]. Changes in the corticomedullary differentiation have been described in postrenal transplant patients with cyclosporine toxicity, rejection, and ATN [6,33,34]. Hricak et al [35] described high MRI accuracy in diagnosing rejection when the corticomedullary differentiation is lost on postcontrast MRI compared to scintigraphy and US, with sensitivity, specificity, and PPV of 98%, 75%, and 72%, respectively; however this finding is nonspecific since it is seen in other etiologies as mentioned previously.

Newer techniques like nonenhanced MRA with steady-state free precession imaging can help avoid contrast in these patients and avoid the risk of NSF [36]. Blood oxygen level dependent (BOLD) imaging depends on contrast generated by changing levels of paramagnetic deoxyhemoglobin with a decrease in intrarenal T2 during hypoxia taken as a reflection of increasing concentrations of deoxyhemoglobin. BOLD imaging can noninvasively detect change in intrarenal oxygenation and renal hypoxia induced by RAS [37]. Parallel imaging has the major virtue of reducing acquisition times while preserving spatial resolution. Schoenberg et al [38] demonstrated that parallel imaging could be used in renal MRA to improve spatial resolution while maintaining a reasonable acquisition time: the authors achieved resolution on the order of 1 mm<sup>3</sup>.

### **X-ray Intravenous Urography and Pyelography**

X-ray intravenous urography and pyelography are no longer used for evaluation of the renal transplant.

### **Nuclear Medicine**

Radionuclide tests are valuable in renal transplantation since they provide a noninvasive means to evaluate transplant function qualitatively and also screen for surgical complications. Only scintigraphic studies are able to separate function of the graft from residual function of the native kidneys or any remaining prior failed graft [2]. There are a wide variety of techniques advocated in renal transplants [2]. The most commonly used procedure is renal scintigraphy with combined imaging. In many centers, baseline scintigraphic studies are obtained shortly after transplant; in others they are only done when complications occur. An advantage of renography is that it provides functional information at the time of the study, while creatinine lags behind function and radiographic studies are primarily anatomic. Because of this it can be helpful in evaluating the return of function after ATN or rejection.

Use in differential diagnosis of ATN and rejection is controversial. Heaf et al [39] in their study found that renogram performed early after transplantation could predict primary graft nonfunction, long time to graft function, low discharge Cr EDTA clearance, and low 1- and 5-year graft survival, while renogram performed at discharge could predict late (>6 months) graft loss. However, the renogram changes did not contribute to the differential diagnosis between acute rejection, acute tubulointerstitial nephropathy, and cyclosporine toxicity. In obstruction it can be used with Lasix as it is in native kidneys. Urinary leaks may be identified by the presence of radioactivity in an abnormal location. If hypertension develops in the patient, captopril renography can definitively identify the transplant and renal artery stenosis as the cause. In some centers and especially in Europe renal clearances are performed serially to evaluate renal function. These are done less frequently in the United States.

Numerous quantitative indices are used to evaluate transplants, but no single one has achieved acceptance, although it appears they may be useful. Tc-99m DTPA or Tc-99m MAG3 may be used to follow the transplant. MAG3 is preferred because of the better images it provides. Usually both renograms and images are obtained simultaneously [40]. DTPA offers similar information when assessing renal function.

### Angiography

Percutaneous therapeutic angioplasty (PTA) and stenting (PTAS) is the treatment of choice for renal artery stenosis, with a reported success rate of 65%-100% [41-52]. The complication rate of PTA and PTAS is low at approximately 0%-10% compared to surgery, which has a graft loss rate of 15% and mortality rate of 5%. However, in one long-term study over a 24-year period, Pegerin et al [48] found a complication rate of 25.5% (usually without clinical sequela); however, similar data is not available for surgical cases. The restenosis rate after PTA alone is higher than with PTAS, with a rate of 10%-33% over 6-8 months [53]. Pappas et al [47] in their study found a technical success rate of 100% with no acute complications and amelioration of arterial hypertension and improvement of graft function within 7 postoperative days. In the follow-up period, 81.8% of their patients had normal blood pressure and creatinine levels. In a large study by Ghanzanfar et al [44] involving 44 patients, the technical success rate was 100% and the clinical success rate was 86%, suggesting that PTA and PTAS are safe procedures to perform in renal transplant patients. Superselective embolization is also effective in treating postbiopsy arteriovenous fistulae in renal transplants with minimal loss of renal parenchyma [54].

### Summary

- Renal transplant dysfunction is a devastating event and appropriate management of the immunosuppression and complications that arise in these patients is necessary to avoid graft failure.
- US is the primary modality for evaluating renal transplant dysfunction.
- Radionuclide tests using Tc-99m MAG3 or Tc-99m DTPA can evaluate renal transplant function qualitatively and screen for surgical complications.
- MRI and CT can also be used for evaluating renal transplants; however, MRI suffers from lack of resolution and concerns about gadolinium toxicity in a population at risk of renal dysfunction.

### Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (ie, <30 mL/min/1.73m<sup>2</sup>), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73m<sup>2</sup>. For more information, please see the [ACR Manual on Contrast Media](#) [55].

### Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the

long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations		
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
○	0 mSv	0 mSv
⊕	<0.1 mSv	<0.03 mSv
⊕ ⊕	0.1-1 mSv	0.03-0.3 mSv
⊕ ⊕ ⊕	1-10 mSv	0.3-3 mSv
⊕ ⊕ ⊕ ⊕	10-30 mSv	3-10 mSv
⊕ ⊕ ⊕ ⊕ ⊕	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as “Varies”.		

## Supporting Documents

- [ACR Appropriateness Criteria® Overview](#)
- [Procedure Information](#)
- [Evidence Table](#)

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.