ECG-gated Nonenhanced 3D Steady-State Free Precession MR Angiography in Assessment of Transplant Renal Arteries: Comparison with DSA

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Purpose:
To evaluate noncontrast material–enhanced steady-state free precession (SSFP) magnetic resonance (MR) angiography in the assessment of transplant renal arteries (RAs) by using digital subtraction angiography (DSA) as the reference standard.

Materials and Methods:
This prospective study was approved by the institutional review board; written informed consent was obtained from all participants. In 20 renal allograft recipients scheduled for DSA, the transplant RAs were assessed with electrocardiographically gated nonenhanced SSFP MR angiography performed at 1.5 T; the degree of stenosis was compared with that of DSA. Subjective image quality for SSFP MR angiography was assessed independently by two radiologists on a four-point scale (from 1, nondiagnostic to 4, excellent) in four predefined segments (I, the iliac artery; II, the main transplant artery; III, segmental branches; and IV, parenchymal branches). Sensitivity, specificity, and accuracy of SSFP MR angiography for the detection of relevant (≥50%) transplant RA stenosis (TRAS) were calculated on a per-artery basis.

Results:
One patient was excluded because SSFP MR angiography failed to adequately visualize the allograft vasculature owing to low cardiac output. The mean image quality assessed by both readers was 3.98 ± 0.16 (standard deviation), 3.5 ± 0.68, 2.71 ± 1.12 and 2.03 ± 1.09 for segments I, II, III, and IV, respectively (κ = 0.80). DSA helped identify eight relevant (≥50%) stenoses in six transplant RAs. Kinking of the transplant artery without relevant stenosis was found in seven patients. The degree of stenosis was overestimated in three patients by using SSFP MR angiography. As compared with DSA, the sensitivity, specificity, and accuracy of SSFP MR angiography to help detect relevant TRAS were 100% (six of six), 88% (14 of 16), and 91% (20 of 22), respectively.

Conclusion:
Nonenhanced SSFP MR angiography is a reliable alternative imaging technique for the assessment of transplant RAs in patients for whom contrast-enhanced MR angiography is contraindicated.

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Transplant renal artery (RA) stenosis (TRAS) is the most frequent post-transplantation vascular complication and may cause hypertension and allograft dysfunction. It may occur in up to 23% of allograft recipients (1). While the most frequent location is the site of the anastomosis (1), a stenosis may also appear at the iliac artery proximal to the anastomosis (2) or at multiple locations within the RA (3).

Doppler ultrasonography (US) is routinely used as a reliable screening tool for TRAS (4) but the results are operator dependent. This is particularly true for the evaluation of tortuous vessels seen in transplant RAs, where kinks and curves may lead to spurious elevations of US-measured peak systolic velocity, raising the chances for mistaken suspicion of TRAS (5,6). For many years, contrast material–enhanced magnetic resonance (MR) angiography has been established as the preferred imaging technique for the evaluation of transplant RAs because it does not require the use of iodinated contrast material and does not expose the patient to ionizing radiation. Gadolinium-based MR contrast media have been considered safe in transplant recipients (7) owing to the absence of nephrotoxicity at routinely applied doses. However, in 2006, two studies (8,9) reported a strong association between the development of nephrogenic systemic fibrosis and the administration of a gadolinium-based contrast medium in patients with renal insufficiency. Therefore, the use of gadolinium-based contrast medium in renal transplant recipients, especially when allograft function is impaired, is potentially problematic, and an alternative is warranted. Nonenhanced MR angiography may provide a promising alternative for the visualization of vascular structures in renal transplant recipients. Steady-state free precession (SSFP) MR angiography has been used as a nonenhanced technique for the imaging of the renal vasculature in several studies (10–14), showing a high sensitivity for the detection of RA stenosis. The purpose of this study was to evaluate nonenhanced SSFP MR angiography in the assessment of transplant RAs by using digital subtraction angiography (DSA) as the reference standard.

Materials and Methods
Two Siemens Healthcare employees (P.S., Erlangen, Germany and X.B., Chicago, Ill) assisted in the development of this MR technique. The authors that are not Siemens employees had full control of all information and data submitted for publication.

Patients
This prospective study was approved by the institutional review board. Written informed consent was obtained from all participants prior to examination. Only patients who were scheduled for conventional DSA were included in this study. The standard contraindications for MR examinations were applied.

A total of 20 renal transplant recipients (mean age, 44.4 years ± 12.9 [standard deviation]), nine women (mean age, 47.7 years ± 12.4) and 11 men (mean age, 41.7 years ± 12.2), were enrolled in this study between December 2007 and September 2008 (Fig 1). The levels of serum creatinine, urea, and hemoglobin were determined on the day of the conventional angiogram. Indications for conventional DSA included pathologic US flow profile of the iliac or transplant RA (n = 15), as well as evaluation of vessel anatomy following revision surgery (n = 4). In one patient with chronic allograft dysfunction, the transplant RA was visualized during conventional DSA of the iliac and lower-limb arteries. MR angiography was usually performed prior to DSA but in four patients, DSA was conducted first for logistical reasons. The maximum time interval between DSA and MR examinations was 4 weeks (range, 1–28 days).

Conventional Angiography
All DSA examinations were performed with an angiographic installation (Multi-Star; Siemens Medical Solutions, Forchheim, Germany). Intravenous hydration with a saline solution injected at a rate of 1 mL/kg/hr was performed for 6 hours prior to and following DSA in all patients. All conventional angiography was performed by one radiologist (A.S., with 11 years experience with DSA), who was blinded to the MR angiographic findings. The degree of stenosis was evaluated by using the same scoring system (grades 1–5) as for MR angiography (see below). For visualization of the distal portion of the aorta and the pelvic vasculature, a

Advances in Knowledge
- Noncontrast material–enhanced steady-state free precession (SSFP) MR angiography enables visualization of transplant renal arteries (RAs) up to the parenchymal branches.
- Nonenhanced SSFP MR angiography shows high sensitivity (100%, six of six), specificity (88%, 14 of 16), and accuracy (91%, 20 of 22) in assessment of transplant RAs as compared with digital subtraction angiography.
- The degree of stenosis might be overestimated by using nonenhanced SSFP MR angiography.

Implication for Patient Care
- Because the use of gadolinium-based contrast agents may be problematic in renal allograft recipients, nonenhanced SSFP MR angiography is a reliable alternative imaging technique for the assessment of transplant RAs.
power injector was used to inject 25 mL of iodinated contrast material (Imeron 300; Bracco, Milan, Italy) at a rate of 15 mL/sec. The anastomosis and the transplant RA were visualized following manual injection of 8–10 mL of contrast material per imaging series. A total of 60–110 mL of contrast material was used per examination. In three patients, intraarterial pressure measurements were obtained proximal and distal to the stenotic lesions.

MR Angiography

All examinations were performed with a 1.5-T whole-body MR system (Magnetom Avanto; Siemens Medical Solutions) with a slew rate of 200 T/m/sec. A six-channel surface coil was placed over the pelvic region. For visualization of the kidney allograft and pelvic anatomy, a T2-weighted half-Fourier acquired single-shot turbo spin-echo sequence in the transverse plane was used. The following imaging parameters were used: repetition time msec/echo time msec, 1000/92; section thickness, 6 mm; and field of view, 380 × 315. An additional two-dimensional coronal fast imaging with SSFP sequence (3.2/1.3; section thickness, 6 mm; and field of view, 420 × 420) was used to obtain a scout image for SSFP MR angiography. The nonenhanced SSFP MR angiogram was acquired by using the fast imaging with SSFP technique, essentially consisting of a segmented three-dimensional SSFP acquisition after a preceding slab-selective inversion preparation for background suppression obtained by using an imager (NATIVE TrueFISP; Siemens Medical Solutions). Electrocardiographic triggering was used to ensure proper synchronization between the arterial inflow events and data sampling. Owing to the location of the transplant vessels deep in the pelvic region, data acquisition was performed during free breathing, without any additional effort to control or correct the actual position of the diaphragm with navigator signals.

The inversion slab was carefully positioned to provide background signal suppression in the target volume. The inversion time was typically adjusted to its maximum value, which allowed the repetition time to fit in the cardiac cycle so that data acquisition took place in the end-diastolic phase. Depending on the heart rate, values between 600 and 950 msec were used. For each repetition, data acquisition was preceded by a standard fat saturation module, consisting of a Gaussian radiofrequency pulse with a flip angle of 90°, a frequency offset of 220 Hz, and subsequent spoiler gradients. Before the fast imaging with SSFP data sampling, 10 dummy radiofrequency excitations with linearly increasing flip angles were inserted to avoid artifacts arising from signal oscillations in the early transient phase of the magnetization (Figure E1 [http://radiology.rsna.jnl.org/cgi/content/full/2531082260/DC1]). The data sampling comprised 49 segments (excitations) with a flip angle of 90° and an echo spacing of 3.5 msec, followed by a single α/2 restore pulse. A transverse three-dimensional volume was imaged with the following parameters: number of sections, 80–120; field of view, 340 × 242 mm; resolution, 1.1 × 1.1 × 1.0 mm; a generalized autocalibrating partially parallel imaging factor of 2; and acquisition times between 1 minute 30 seconds and 2 minutes 30 seconds, depending on the heart rate.

Image Analysis

Axial, sagittal, and coronal sliding maximum intensity projection (MIP) reconstructions, as well as a three-dimensional MIP reconstruction, were performed with a workstation (Leonardo; Siemens Medical Solutions, Erlangen, Germany). The presence and degree of stenosis was determined independently by two radiologists (R.S.L. and D.B., with 3 and 7 years experience with MR angiography, respectively) who were blinded to the results of conventional DSA. Both readers had full information about the type of surgery, the number of accessory arteries, and the location of the anastomosis. In cases of divergent interpretations, an additional reading was undertaken by these two radiologists in consensus. The extent of TRAS was graded as follows: grade 1 indicated a stenosis of less than 20%; grade 2, 20%–49%; grade 3, 50%–74%; grade 4 75%–99%; and grade 5, total vessel occlusion. Grades 3–5 were considered as relevant stenoses. The percentage of stenosis was assessed at the optimal projection angle along the vessel axis with a digital caliper. The degree of TRAS was calculated as $(1 - (S/R)) \times 100$, where $S$ and $R$ are the diameters of the stenosis and reference vessels, respectively. A normal-appearing portion of the transplant RA distal to the stenotic lesion was defined as a reference vessel.

For analysis of image quality, four segments were defined: I, the external and internal iliac arteries, including the anastomosis; II, the main transplant RA from the site of the anastomosis to the segmental branches; III, segmental branches up to the renal parenchyma; and IV, arterial branches inside the renal parenchyma. The image quality of each segment was evaluated on the basis of a four-point scale: 1, nondiagnostic (no signal within the vessel); 2, moderate (incomplete signal within the vessel, no sharp vessel border delineation); 3, good (homogeneous signal within the vessel with slight flow artifacts, almost complete and sharp delineation of vessel border); and 4, excellent (completely homogenous signal within the vessel lumen without flow artifacts, sharp and complete delineation of vessel border) independently by the same two radiologists.

Statistics

Mean values and standard deviations were tabulated and statistical analyses were performed by using software (SPSS

Table 1: Flowchart of study patients.

<table>
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<tr>
<th>Event</th>
<th>20 patients scheduled for DSA were enrolled in the study</th>
<th>SSFP MR angiography failed to visualize allograft vasculature</th>
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<tr>
<td>1 patient was excluded</td>
<td>1 patient was excluded</td>
<td>Both SSFP MR angiography (index test) and DSA (reference standard) were performed in 19 patients</td>
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for Windows, version 15.0; SPSS, Chicago, Ill). Sensitivity, specificity, and accuracy (with 95% confidence intervals) of SSFP MR angiography in comparison with conventional DSA were calculated on a per-artery basis. Values were used to determine agreement between both readers for subjective evaluation of image quality, where a $\kappa$ value of less than 0.50 corresponds to poor agreement; $\kappa$ of 0.50–0.75, good agreement; and $\kappa$ higher than 0.75, excellent agreement.

**Results**

Of 20 patients initially included in this study, one had to be excluded because SSFP MR angiography failed to visualize the iliac and renal transplant arteries owing to low cardiac output and motion artifacts. This patient already had mitral regurgitation and hypertensive cardiomyopathy prior to transplantation. Thus, SSFP MR angiographic results in 19 patients were considered as analysis and compared with DSA.

**Digital Subtraction Angiography**

There were 22 transplant RAs evaluated in 19 patients; three patients had accessory arteries, two accessory arteries were anastomosed directly to the external iliac artery, and one accessory artery was connected to the main transplant RA by means of an end-to-side anastomosis. All main transplant RAs originated from the external iliac artery except for two arteries; in one patient, the transplant artery was anastomosed to the internal iliac artery during revision surgery and in the other, the transplant artery was anastomosed to the common iliac artery by means of a venous patch during revision surgery.

DSA did not show hemodynamically relevant stenoses during four follow-up examinations following prior revision surgery nor in one patient whose transplant RA was visualized during an examination of the pelvic vasculature. In 14 patients with pathologic flow profile in duplex US, DSA revealed kinking of the transplant artery without relevant stenosis in seven patients. Eight relevant (grades 3–5) TRAS were found in six transplant RAs in six patients. These stenoses were located at the anastomosis with the external iliac artery ($n = 3$), in the main RA ($n = 2$), in segmental branches ($n = 2$), and at the end-to-side anastomosis of the main RA with a pole artery ($n = 1$) (Table, Table E1 [http://radiology.rsna.org/cgi/content/full/2531082260/DC1]).

Intraarterial pressure measurements were obtained in three patients. In two patients with mild stenosis (grade 2) at the site of the anastomosis, pressure gradients of 4 and 5 mm Hg were found. In one patient with a high-grade kink steno-

<table>
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<tr>
<th>Imaging Method</th>
<th>Degree of Stenosis</th>
<th>Presence of Kinking with No Relevant (≥50%) Stenosis</th>
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<tr>
<td></td>
<td>Grade 1</td>
<td>Grade 2</td>
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<tr>
<td>DSA</td>
<td>7</td>
<td>9</td>
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<tr>
<td>SSFP MR angiography</td>
<td>7</td>
<td>8*</td>
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</tbody>
</table>

Note.—In two recipients, two consecutive stenoses were found in a single transplant RA.
* An aneurysm was suspected at MR angiography that could not be confirmed with DSA.

**Figure 2**

*Images in 32-year-old woman (living donor recipient) suspected of having TRAS at US. (a) DSA shows low-grade stenosis (grade 2) at anastomosis of transplant artery with external iliac artery (arrow); intraarterial pressure gradient, 4 mm Hg. (b, c) Degree of stenosis (arrow, b) determined correctly by using SSFP MR angiography with (b) coronal and (c) axial MIP reconstructions.*
sis (grade 4), a pressure gradient of 46 mm Hg was measured (Table E1).

**MR Angiography**

In 19 patients, the allograft vasculature was visualized with SSFP MR angiography (Figs 2, 3). In one patient with two transplant RAs, both arteries could not be visualized in one acquisition slab in the transverse plane because the distance between the transplanted arteries was too wide. In this particular case, each artery was independently examined in the transverse plane.

In seven other patients, SSFP MR angiography failed to help visualize both the course of the transplant RA and the entire allograft, so that parenchymal branches at the upper or lower pole of the kidney were missed, while the main artery and its segmental branches were fully included in the acquisition volume.

As compared with DSA, SSFP MR angiography helped detect all relevant stenoses. Six (75%) of eight relevant stenoses were graded correctly by using MR angiography. One grade 3 stenosis was overestimated as grade 4. A high-grade (grade 4) stenosis of an accessory artery at the site of an end-to-side anastomosis with the main RA was misdiagnosed as vessel occlusion (grade 5), owing to severe signal loss distal to the high-grade stenosis. In addition, one low-grade TRAS (grade 2) was misleadingly interpreted as a relevant stenosis (grade 3) with MR angiography. In one patient, SSFP MR angiography revealed a hyperintense round lesion next to a segmental artery, following revision surgery, that was misinterpreted as an aneurysm (Figure E2) and subsequently considered as a false-positive result. Sensitivity, specificity, and accuracy of SSFP MR angiography to help detect relevant stenosis (≥50%) on a per-artery basis were calculated as 100% (six of six, 95% confidence interval: 54%, 100%), 88% (14 of 16, 95% confidence interval: 62%, 98%), and 91% (20 of 22, 95% confidence interval: 79%, 99%), respectively.

Respective mean image quality for transplant RA segments I, II, III, and IV was 3.98 ± 0.16, 3.5 ± 0.68, 2.71 ± 1.12, and 2.03 ± 1.09 for both readers, 4.0, 3.53 ± 0.68, 2.63 ± 1.09, and 2.05 ± 1.15 for reader 1, and 3.95 ± 0.22, 3.47 ± 0.68, 2.79 ± 1.15, and 2.0 ± 1.03 for reader 2. The *k* value for overall interobserver agreement was 0.80.

Image quality was excellent or good in all patients for segment I and in 17 (89%) of 19 patients for segment II. In two patients, the main transplant RA (segment II) showed marked flow artifacts distal to stenotic lesions, which resulted in moderate image quality (Fig 4). In both of these cases, surgical clips were located next to the transplant artery, so we cannot determine whether surgical clips or flow artifacts were responsible for the impaired vessel visibility. Segmental branches (segment III, Fig 5) were rated as excellent or good in 10 patients by reader 1 and in 12 patients by reader 2. Parenchymal branches were visible in 10 (53%) of 19 patients.

**Discussion**

In our study, we evaluated an electrocardiographically gated nonenhanced three-dimensional SSFP MR angiogram of transplant RAs in comparison with DSA. Nonenhanced assessment of transplant RAs has previously been performed with phase-contrast (15) and time-of-flight (16) MR angiography. Phase-contrast MR angiography is extremely time consuming, as echo time and the velocity-encoded value need to be optimally adjusted to display the turbulent flow in stenotic lesions, whereas the SSFP technique we used has an acquisition time of approximately 1 minute 30 seconds to 2 minutes 30 seconds.

With time-of-flight MR angiography,
**Figure 4**: Images in 31-year-old man (living donor recipient) suspected of having TRAS at US. (a) DSA shows relevant TRAS (grade 3, arrow) at anastomosis with external iliac artery. (b) Extent of stenosis (arrow) is depicted correctly on coronal MIP reconstructions but signal loss is seen in main transplant artery. (c) Note excellent contrast of parenchymal branches on coronal MIP reconstructions.

**Figure 5**: Images in 30-year-old man (living donor recipient) with poor allograft function (serum creatinine, 3.3 mg/dL [3.3 μmol/L]) and suspected of having TRAS at US. (a) DSA shows relevant (grade 4, arrow) kink stenosis of segmental artery. (b) Kink stenosis was graded correctly (grade 4, arrow) at SSFP MR angiography, although stenosis is more pronounced when compared with DSA. (c) DSA shows relevant (grade 3, arrowhead) stenosis at anastomosis. (d, e) Degree of stenosis is determined correctly by using SSFP MR angiography with (d) axial and (e) coronal MIP reconstructions.
peripheral segments of RAs are not usually visualized owing to saturation effects (17). These effects are more pronounced in tortuous vessels oriented perpendicularly to the acquisition plane (18). Owing to the location of renal allografts in the pelvic fossa, transplant arteries often show these artifacts. SSFP MR angiography delivers a more consistent vessel signal, as its flow is compensated in all three spatial orientations because of its intrinsically balanced gradient structure and because it has high intrinsic blood contrast owing to a favorable T2/T1 ratio. Thus, in our study, parenchymal branches were visualized by using SSFP MR angiography in 10 of 19 recipients. The grading of RA stenosis with MR angiography is challenging (19). Overestimation of the degree of stenosis has been described for contrast-enhanced (20,21) as well as nonenhanced MR angiography (11). In our study, the degree of stenosis was consistently slightly overestimated by using SSFP MR angiography. In one case, a subtotal stenosis of an accessory artery was misdiagnosed as vessel occlusion at SSFP MR angiography.

The sensitivity of SSFP MR angiography to help detect relevant (>50%) TRAS was 100% (six of six), with a specificity of 88% (14 of 16). Our results are comparable with those obtained by using contrast-enhanced MR angiography of renal allograft vasculature, in which sensitivity and specificity ranged between 88%–100% and 67%–100%, respectively (16,22–24).

When compared with nonenhanced assessment of the native RAs, imaging of transplant RAs with SSFP MR angiography has one major advantage. As the renal allografts are located in the iliac fossa, they are not prone to respiratory artifacts. This means that SSFP MR angiography of the transplant RA can be performed without the use of a respiratory navigator pulse, which typically results in prolonged imaging times and which may not be completely able to compensate for motion effects in some patients (12).

The assessment of renal allograft venous vasculature by using SSFP MR angiography with an inversion pulse has one disadvantage when compared with contrast-enhanced MR angiography. Because of inversion pulse used for background suppression, the transplant veins cannot be evaluated with SSFP MR angiography. Venous complications are less frequent in occurrence than are arterial complications; indeed, transplant vein thrombosis may occur in only 0.3%–4.0% of cases (25). Transplant vein stenosis is rarely seen as a result of poor surgical technique. However, both can compromise arterial flow resulting in infarction and loss of the allograft (23). When visualization of venous structures is required, additional image acquisitions are mandatory, which might lead to prolonged imaging time.

Our study had several limitations. The number of patients included in this study was relatively small. In our study, only transplant recipients scheduled to undergo DSA were included. However, in view of its invasive character and the need for potentially nephrotoxic iodinated contrast material, DSA is only performed after serious consideration of the risks and benefits to the patient.

The acquisition slab and inversion prepulse should be oriented in the transverse plane to optimize vessel contrast, which primarily depends on inflowing arterial blood from outside the inverted volume. In seven patients, parenchymal branches of the upper or lower pole of the allograft were missed owing to the transverse imaging plane and the fact that the acquisition was not repeated. However, in one patient with two transplant RAs, two acquisitions were necessary to visualize the full arterial vasculature, as the distance between both arteries was too wide. Moreover, owing to the restricted transverse imaging plane, the distal portion of the aorta and parts of the iliac artery were not visualized by using SSFP MR angiography. Stenoses of the aortic bifurcation and iliac arteries are described in about 1.5% of transplant recipients (2,26) and may also be the source of allograft dysfunction. Additional images of the iliac vasculature proximal to the transplant artery may be required when stenosis is suspected at these locations. This may lead to prolonged imaging times and may become a source of misinterpretation.

DSA is considered as the diagnostic standard for TRAS (27). Depending on posttransplantation anatomy, it may require imaging with multiple oblique angles to properly visualize the anastomosis and the kinking of transplant RAs. Thus, given the limited number of views obtained, we cannot exclude that the anastomosed region and kink stenosis were not fully visualized and that the degree of stenosis was therefore not determined correctly at DSA.

In conclusion, SSFP MR angiography can reliably help assess transplant RAs without the potential risks of contrast agents and is therefore a promising MR imaging technique when stenosis of the transplant RAs is suspected and the use of gadolinium-based contrast agents is contraindicated. Because the degree of stenosis might be overestimated at SSFP MR angiography, pathologic findings should be confirmed by using contrast-enhanced imaging modalities, such as DSA.

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