Renal Doppler resistance indices are associated with systemic atherosclerosis in kidney transplant recipients

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Renal Doppler resistance indices are associated with systemic atherosclerosis in kidney transplant recipients.

Background. In kidney transplant recipients, increased intrarenal resistance indices measured by duplex ultrasound are associated with poor subsequent allograft performance. It remains unclear whether high resistance indices rather reflect local renal damage or systemic vessel disease. We hypothesized that resistance indices are associated with cardiovascular risk factors and with subclinical systemic atherosclerosis in transplant recipients.

Methods. In 105 renal transplant recipients, categories of risk for coronary heart disease were determined by Framingham risk scoring. Intrarenal resistive index (RI) and pulsatility index (PI) were measured in segmental arteries at five representative locations. For assessment of subclinical atherosclerosis, common carotid intima-media thickness, and ankle-brachial blood pressure index (ABI) were determined.

Results. Transplant recipients with high coronary risk had higher intrarenal resistance indices than low-risk patients. Higher age, female gender, and lower body mass index were independently associated with increased resistance indices. Renal resistance indices were correlated with common carotid intima-media thickness [RI: \( r = 0.270 \) \( (P = 0.005) \); PI: \( r = 0.355 \) \( (P < 0.001) \)]. This association remained significant after adjusting for renal function. Renal resistance indices were increased in patients with pathologic ankle-brachial-indices compared to patients with physiologic ankle-brachial-indices [RI: \( 73.3 \pm 7.1 \) vs. \( 70.2 \pm 6.9 \) \( (P = 0.03) \); PI: \( 146.4 \pm 29.9 \) vs. \( 131.4 \pm 25.9 \) \( (P = 0.01) \)]. Renal resistance indices were neither significantly correlated with glomerular filtration rate (GFR), nor with donor age.

Conclusion. Intrarenal resistance indices are a complex integration of arterial compliance, pulsatility, and peripheral resistance. They are associated with traditional cardiovascular risk factors as well as with subclinical atherosclerotic vessel damage and should thus not be considered specific markers of renal damage.

Key words: kidney transplantation, ultrasonography, Doppler, duplex, subclinical atherosclerosis.

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Renal resistance indices (RIs) measured by duplex ultrasound have recently been shown to be associated with long-term allograft and patient survival in kidney transplant recipients. In a prospective cohort study reported by Radermacher et al [1], a resistive index of 80 or higher in a kidney transplant was a stronger predictor of allograft loss than various established risk factors such as proteinuria, donor age, or the number of human leukocyte antigen (HLA) mismatches. Increased RIs were suggested to reflect a nonspecific renal scarring process resulting in a reduction of the intrarenal vessel area and a subsequent increase in intrarenal vascular resistance (compare [2]).

However, ultrasound resistance indices do not directly reflect renovascular resistance. As discussed by Radermacher et al [1], additional intrarenal and extrarenal hemodynamic factors have a major impact on the RI in the allograft.

First, in cross-sectional studies among transplant recipients, ultrasound RIs significantly depend on the pulse pressure, which is the difference between systolic and diastolic blood pressure, and on the age of the transplant recipient, whereas neither donor age nor serum creatinine nor creatinine clearance independently predict RIs [3, 4]. Second, ex vivo data suggest that ultrasound RIs are affected by pulse pressure and by vascular compliance independently from renal vascular resistance [5–7]. Finally, a recent hemodynamic study surprisingly found a significant negative correlation between ultrasound RIs and hemodynamically assessed renal vascular resistance in renal transplant recipients before and after angioplasty and stenting of transplant artery stenosis [8].

We thus hypothesized that ultrasound renal RIs in stable transplant recipients, instead of representing selective markers of local kidney damage, are significantly associated with cardiovascular risk factors as well as with subclinical atherosclerotic disease in nonrenal organs.

METHODS

Subjects

After allogenic renal transplantation, 105 patients (60 male and 45 female) were studied between
September 2003 and July 2004. All patients had been transplanted for at least 6 months (mean 83 ± 64 months, range 6 to 237 months) and were being followed by our outpatient clinic. Patients with rapid deterioration of renal function (increase in serum creatinine >0.8 mg/dL within 28 days), with hydronephrosis of grade 2 or higher or with angiographically proven, untreated renal artery stenosis resulting in a 50% reduction in the luminal diameter were excluded.

All patients gave informed consent. Ultrasonography and data acquisition were performed by a single investigator who was blinded for the study hypothesis (M.K.G.). At study entry, blood was taken from all subjects under standardized conditions. Plasma glucose, creatinine, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), C-reactive protein (CRP), lipoprotein(a), and homocysteine were obtained using standard techniques. Adjusted estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) Study equation 3 [9]. Proteinuria was measured in morning specimens, using the protein-to-creatinine ratio [9]. According to the National Kidney Foundation-Dialysis Outcomes Quality Initiative (K-DOQI) guidelines [9], proteinuria was diagnosed in patients with a protein-to-creatinine ratio >200 mg/g.

Anthropomorphic measurements were recorded, and body mass index (BMI) was calculated as weight (kg)/height (m)^2. Systolic blood pressure (RRsys), diastolic blood pressure (RRdia), and heart rate were measured after 5 minutes of rest. Mean arterial blood pressure (RRmean) was calculated as RRdia + [(RRsys - RRdia)/3].

**Assessment of cardiovascular risk factors and comorbidity**

A standardised questionnaire was used to record a history of smoking, diabetes, a family history of premature-onset cardiovascular disease (defined as myocardial infarction or stroke by age 65 in first-degree relatives), current drug intake, and cardiovascular comorbidity. Additionally, comorbidity was assessed by chart review. Coronary artery disease was diagnosed in patients who had had a myocardial infarction or who had undergone coronary artery angioplasty, stenting, and/or bypass surgery. In patients who had had a stroke or had undergone carotid endarterectomy or stenting, cerebrovascular disease was diagnosed. Finally, in patients who had undergone nontraumatic lower extremity amputation, lower limb artery angioplasty, stenting and/or bypass surgery, peripheral artery disease was diagnosed. Patients were defined as having cardiovascular disease if they had coronary artery disease, cerebrovascular disease, and/or peripheral artery disease.

Patients with self-reported diabetes mellitus, with a nonfasting blood sugar level of >200 mg/dL, with a fasting blood sugar level of >126 mg/dL, or with current use of hypoglycemic medication were categorized as diabetic. Patients were categorized as active smokers if they were current smokers or had stopped smoking <1 month before entry into the study.

Categories of risk for coronary heart disease were determined by Framingham risk scoring. A 10-year risk for myocardial infarction and coronary death were determined using electronic calculators, which are available on the adult treatment panel (ATP) III page of the National Heart, Lung, and Blood Institute Web site (www.nhlbi.nih.gov/guidelines/cholesterol). According to the Third Report of the National Cholesterol Education Program (NCEP), patients with a Framingham risk score of >20%, with prevalent cardiovascular disease (as defined above), or with diabetes mellitus were classified to have “high coronary heart disease risk” (10-year coronary heart disease risk >20%) [10]. Accordingly, patients with a 10-year coronary heart disease risk of 10% to 20% and of <10% according to the Framingham score were defined to have “intermediate coronary heart disease risk” and “low coronary heart disease risk,” respectively.

**Renal RIs**

Color Doppler examinations were performed with a phased-array transducer (Acuson Sequoia, Mountain-view, CA, USA), B-mode frequency 5 MHz; Doppler frequency 2.5 MHz in supine position.

Intrarenal Doppler spectra were obtained from the segmental arteries at five representative locations, and the RI and pulsatility index (PI) were calculated according to the following formula:

\[
\text{RI} = \left( \frac{\text{peak systolic frequency shift}}{\text{minimum diastolic frequency shift}} \right) / \text{peak systolic frequency shift}
\]

\[
\text{PI} = \left( \frac{\text{peak systolic frequency shift}}{\text{minimum diastolic frequency shift}} \right) / \text{mean frequency shift}
\]

The average RI and PI were computed to yield an overall RI and PI for the renal transplant.

A subgroup of 32 patients had taken part in an ultrasound study performed 4 years earlier by us [11]. Present and former RI and PI measurements were compared in order to assess the stability of renal RIs over time.

Interobserver variability between the two investigators who had performed the ultrasound examinations in the present cohort (M.K.G.) and in the earlier study (G.H.H.) was assessed in a subgroup of 16 patients, in whom resistance indices were measured within 1 hour by both investigators in a blinded fashion. The mean differences in RI
and PI measurements between both observers were 2.7 ± 2.3 and 13.6 ± 10.4, respectively.

Carotid ultrasound studies

The intima-media thickness of the common carotid artery was measured from high-resolution, two-dimensional ultrasound images obtained by a linear-array 8 MHz transducer (Acuson Sequoia). With the subject in supine position and the head slightly extended and turned to the opposite direction, the distal common carotid artery and the carotid bulb were identified by longitudinal scanning. Intima-media thickness was defined as the distance between the leading edges of the lumen interface and the media-adventitia interface of the far wall.

Three representative intima-media thickness measurements were bilaterally performed in the far wall of the common carotid arteries at fixed positions (1.0, 1.5, and 2.0 cm proximal to the bifurcation), and these six intima-media thickness readings were averaged to give the mean common carotid intima-media thickness (intima-media thickness mean). Intima-media thickness was not measured at the site of a carotid plaque.

Ankle-brachial blood pressure index (ABI)

Arm blood pressure (brachial artery) and bilateral ankle blood pressure (posterior tibial artery), measured by hand-held Doppler (Handydop, Elcat, Wolfratshausen, Germany), were taken with the subject supine. ABI was measured at the site of a carotid plaque.

Participants who had an ABI >1.10 were categorized as having low ABI. Participants were categorised as having high ABI if they had an ABI measure <1.40 or if the ankle pressure of either leg could not be obtained because of arterial stiffening (pulse could not be obliterated with a pressure of >300 mm Hg). Participants were defined as having normal ABI if ABI measures were >1.10 and <1.40.

Statistics

Data management and statistical analysis were performed with the Prism 4.00 statistical software (Graphpad, San Diego, CA, USA). Unless indicated otherwise, continuous data are expressed as means ± standard deviation, and compared by Mann-Whitney U test, or by Kruskal-Wallis test followed by Dunn’s post hoc test, as appropriate.

For analyzing the association of traditional cardiovascular risk factors with renal RIs, continuous data first were categorized into tertiles. Subsequently, a multivariate linear regression analyses were used to determine independent predictors of intrarenal RIs. Model 1 included all traditional cardiovascular risk factors listed in Table 1. Model 2 additionally included the GFR.

Correlation coefficients were calculated by Spearman test. The level of significance was set at \( P < 0.05 \).

RESULTS

Patient characteristics

Among the 105 patients included, mean age was 52.5 ± 14.4 years, and mean serum creatinine was 1.7 ± 0.7 mg/dL. Twenty-seven patients suffered from diabetes mellitus and 20 patients were active smokers, as defined above.

As immunosuppressive medication, patients received cyclosporine A (\( N = 61 \)) or tacrolimus (\( N = 41 \)). Three patients had no calcineurin inhibitor. Coimmunosuppressive medication comprised azathioprine (\( N = 31 \)), mycophenolate mofetil (\( N = 7 \)), and methylprednisolone (\( N = 86 \)). Intrarenal resistance indices did not significantly differ between patients on cyclosporine A and on tacrolimus treatment (cyclosporine A RI 72.8 ± 7.2 and

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Table 1. Linear regression models of the association of cardiovascular risk factors and renal resistive indices (RI)

<table>
<thead>
<tr>
<th>Model 1</th>
<th>B</th>
<th>SD</th>
<th>( P ) value</th>
<th>Model 2</th>
<th>B</th>
<th>SD</th>
<th>( P ) value</th>
</tr>
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<tbody>
<tr>
<td>Constant</td>
<td>77.058</td>
<td>6.537</td>
<td>&lt;0.001</td>
<td>80.953</td>
<td>6.586</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Age years</td>
<td>-0.229</td>
<td>0.048</td>
<td>&lt;0.001</td>
<td>-0.237</td>
<td>0.047</td>
<td>&lt;0.001</td>
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<tr>
<td>Diabetes mellitus yes</td>
<td>2.084</td>
<td>1.482</td>
<td>0.163</td>
<td>1.739</td>
<td>1.454</td>
<td>0.235</td>
<td></td>
</tr>
<tr>
<td>Active smoking yes</td>
<td>-1.319</td>
<td>1.524</td>
<td>0.389</td>
<td>-1.217</td>
<td>1.488</td>
<td>0.416</td>
<td></td>
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<tr>
<td>Gender recipient male</td>
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<td>1.270</td>
<td>0.001</td>
<td>-4.926</td>
<td>1.258</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Mean arterial blood pressure mm Hg</td>
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<td>0.058</td>
<td>0.313</td>
<td>-0.070</td>
<td>0.057</td>
<td>0.220</td>
<td></td>
</tr>
<tr>
<td>Pulse pressure mm Hg</td>
<td>0.040</td>
<td>0.041</td>
<td>0.337</td>
<td>0.053</td>
<td>0.040</td>
<td>0.197</td>
<td></td>
</tr>
<tr>
<td>High-density lipoprotein mg/dL</td>
<td>-0.024</td>
<td>0.033</td>
<td>0.472</td>
<td>-0.013</td>
<td>0.033</td>
<td>0.685</td>
<td></td>
</tr>
<tr>
<td>Low-density lipoprotein mg/dL</td>
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<td>0.017</td>
<td>0.635</td>
<td>-0.015</td>
<td>0.017</td>
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<tr>
<td>Body mass index kg/m²</td>
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<td>0.014</td>
<td>-0.374</td>
<td>0.144</td>
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<tr>
<td>Family history yes</td>
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<td>1.273</td>
<td>0.221</td>
<td>1.494</td>
<td>1.243</td>
<td>0.233</td>
<td></td>
</tr>
</tbody>
</table>

Indicated are regression coefficients (B), their standard deviation (SD), and the level of significance (\( P \) value).
PI 144.5 ± 30.4; tacrolimus RI 71.3 ± 7.1 and PI 132.7 ± 26.0). Mean donor age was 42.5 ± 16.8 years. There was no significant correlation between intrarenal resistance indices and donor age [RI: \( r = 0.20 \) (\( P = 0.09 \)); PI: \( r = 0.17 \) (\( P = 0.16 \))].

**Association between cardiovascular risk factors and renal RIs**

According to the Framingham risk score, 46 patients had “high coronary heart disease risk” (10-year coronary heart disease risk >20%), 13 patients had “intermediate coronary heart disease risk” (10-year coronary heart disease risk 10% to 20%), and 46 patients had “low coronary heart disease risk” (10-year coronary heart disease risk <10%). Intrarenal RIs significantly differed between these three groups and high-risk patients had significantly higher RIs than low-risk patients (Fig. 1).

For analyzing the impact of traditional cardiovascular risk factors on RIs, continuous data were categorized into tertiles. High intrarenal RIs were associated with a pulse pressure >60 mm Hg, with age >60 years, with the presence of diabetes mellitus, with female gender, and with smoking abstinence. Neither LDL, nor HDL cholesterol levels, nor mean blood pressure had an impact on intrarenal RIs (Fig. 1). Among nontraditional cardiovascular risk factors, neither lipoprotein(a), nor homocysteine, nor CRP were associated with intrarenal RIs (data not shown).

A subsequent multivariate linear regression analysis, which included all traditional cardiovascular risk factors, showed that older age, female gender, and lower BMI were associated with higher intrarenal RIs (RI model 1). These associations remained significant after further adjustment for renal function (model 2).

**Stability of RIs over time**

Of the present cohort, 32 patients had taken part in an earlier ultrasound study [11]. The mean time interval between the two ultrasound examinations was 3.4 ± 0.2 years. As depicted in Figure 2, renal RIs remained remarkably stable over time, with a mean yearly increase in absolute RI and PI values of 0.2 ± 1.8 and 1.0 ± 7.1, respectively.

**Association between markers of subclinical atherosclerosis and renal RIs**

Renal RIs were significantly correlated with common carotid intima-media thickness (Fig. 3). In contrast, no significant correlation was found between renal function, described as calculated GFR, and intima-media thickness measurements \( r = -0.008 \) (\( P = 0.932 \)). The association between renal RIs and intima-media thickness remained significant after adjusting for GFR in a multivariate linear regression analysis (data not shown).

Renal RIs were significantly increased in patients with pathologic ABI compared to patients with physiologic ABI [RI: 73.3 ± 7.1 vs. 70.2 ± 6.9 (\( P = 0.03 \)); PI: 146.4 ± 29.9 vs. 131.4 ± 25.9 (\( P = 0.01 \)]. When patients with pathologically decreased and patients with pathologically increased ABI were regarded separately, a significant difference remained for intrarenal PIs, but not for intrarenal RIs (Fig. 4).

**Association between renal RIs and transplant function**

Renal RI did not significantly correlate with the GFR (Fig. 5A). In contrast, a significant correlation was found between length of the transplant, as assessed sonographically, and renal RIs (Fig. 5B). Patients with proteinuria tended to have higher RIs than patients without proteinuria [RI: 74.0 ± 7.9 vs. 71.0 ± 6.8 (\( P = 0.08 \)); PI: 149.2 ± 34.7 vs. 134.0 ± 25.8 (\( P = 0.07 \)].

**DISCUSSION**

Duplex ultrasound with measurement of intrarenal RIs has originally been introduced in kidney transplant medicine for early diagnosis of acute allograft rejection [12, 13]. However, later studies cast doubt on the sensitivity and specificity of RIs in discriminating different causes of acute allograft dysfunction, as summarized by Dupont et al [14].

Recently, intrarenal RIs have been suggested to be associated with long-term allograft and patient survival in kidney transplant recipients. Radermacher et al [1] reported a RI of 80 or higher to be the strongest predictor of allograft loss among some 44 risk factors included in a multivariate analysis, and RIs were correlated with several histologic markers of intrarenal damage [1, 2].

Again, however, the specificity of intrarenal RIs for selective assessment of intrarenal damage remains uncertain, as discussed by Radermacher et al [1]. Earlier models considered ultrasound RI and PI to directly reflect intrarenal resistance due to, for example, a reduction in the intrarenal vessel area [15], and the terms “resistive index” and “renal vascular resistance” have been used interchangeably by some authors. We however came to learn recently that the ultrasound RI is a complex composite ratio that represents a number of vascular factors and that predominantly reflects arterial compliance and pulsatility rather than renal vascular resistance [16].

Bude and Rubin [6] constructed an in vitro model in which changes in vascular compliance and vascular resistance were analyzed separately. They found ultrasound RIs to be dependent on both vascular compliance and vascular resistance, becoming less and less dependent on resistance as compliance decreased, and being
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<table>
<thead>
<tr>
<th>Low CHD risk</th>
<th>Intermediate CHD risk</th>
<th>High CHD risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>Male</td>
<td></td>
</tr>
<tr>
<td>&lt;45 years</td>
<td>45-60 years</td>
<td>&gt;60 years</td>
</tr>
<tr>
<td>RR mean &lt;105 mm Hg</td>
<td>RR mean 105-115 mm Hg</td>
<td>RR mean &gt;115 mm Hg</td>
</tr>
<tr>
<td>PP &lt;60 mm Hg</td>
<td>PP 60-70 mm Hg</td>
<td>PP &gt;70 mm Hg</td>
</tr>
<tr>
<td>HDL &lt;55 mg/dL</td>
<td>HDL 55-70 mg/dL</td>
<td>HDL &gt;70 mg/dL</td>
</tr>
<tr>
<td>LDL &lt;100 mg/dL</td>
<td>LDL 100-130 mg/dL</td>
<td>LDL &gt;130 mg/dL</td>
</tr>
<tr>
<td>No DM</td>
<td>DM</td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>Smoker</td>
<td></td>
</tr>
<tr>
<td>No Family CVD History</td>
<td>Family CVD History</td>
<td></td>
</tr>
<tr>
<td>BMI &lt;23 kg/m²</td>
<td>BMI 23-27 kg/m²</td>
<td>BMI &gt;27 kg/m²</td>
</tr>
</tbody>
</table>

### Fig. 1. Intrarenal resistive indices (RI) and pulsatility indices (PI) in renal transplant recipients categorized according to Framingham risk scores and to traditional cardiovascular risk factors. Indicated are the mean and the standard error of the mean. Abbreviations are: CHD, coronary heart disease; RR mean, mean arterial blood pressure; PP, pulse pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; DM, diabetes mellitus; CVD, cardiovascular disease; BMI, body-mass index.

### Fig. 2. Stability of intrarenal resistive indices (RI) and pulsatility indices (PI) over time in a subgroup of 32 patients. Measurements taken in the present study are compared to measurements taken in an ultrasound study 4 years earlier.

completely independent of vascular resistance when compliance was zero. In an in vivo model of acute urinary obstruction in Yorkshire pigs, Claudon et al [17] showed ultrasound RI to correlate well with ureteral pressure and with renal perfusion pressure, but poorly with vascular resistance. Finally Tublin, Tessler, and Murphy [5] reported on an ex vivo study, in which rabbit kidneys were perfused using a pulsatile perfusion system, and in which renal
vascular resistance, systolic, diastolic pressure, pulse pressure, and pulse rate were controlled. The authors found intrarenal resistance indices to rise only with marked, likely nonphysiologic increases in renal vascular resistance, whereas a linear relationship was shown between pulse pressure and intrarenal RIs. Consequently, the ultrasound “resistance index” has recently been claimed to be inappropriately named, and the term “impedance index” has been suggested instead [6].

In agreement with such in vitro and animal data, an association between ultrasound RIs and pulse pressure has been reported before in renal transplant recipients [3] and in hypertensive patients without impaired renal function [18]. In addition, the impact of vascular compliance and pulse pressure on ultrasound RIs helps to explain why recent cross-sectional studies among renal transplant recipients [3, 4, 11] found intrarenal RIs to significantly correlate with recipient age, but not with donor age, and why the intake of vasoconstrictive calcineurin inhibitors does not result in an acute rise in ultrasound RIs [11].

To our best knowledge, we are the first to show that renal transplant recipients at high cardiovascular risk, defined either by the Framingham risk score or by the presence of subclinical atherosclerosis, have increased ultrasound RIs compared to low-risk patients even after correction for transplant renal function. In contrast, we found no significant correlation between renal RIs and transplant function, which is in accordance with earlier reports [3, 4]. The association between kidney length and ultrasound RIs, which has not been reported before by other groups, might be a play of chance, as we cannot explain why kidney length rather than kidney function correlates with RIs.

Thus, with regard to our hypothesis, ultrasound renal RIs in stable transplant recipients do not represent selective markers of kidney damage, but are significantly associated with systemic vascular risk factors as well as with subclinical atherosclerotic disease in nonrenal organs.

A better understanding of the association between RIs and transplant nephropathy might have been achieved by correlating ultrasound measurements with histologic findings from renal biopsies. However, we do not perform routine renal biopsies in patients with stable transplant renal function in our transplant center, and for ethical reasons we decided not to undertake study biopsies.

The Framingham risk score has initially been established and validated among apparently healthy individuals. Even though the absolute score may underestimate cardiovascular risk in renal transplant recipients to a certain degree, the Framingham risk score has convincingly been shown to discriminate cardiovascular high-risk and low-risk transplant recipients [19]. When analyzing individual traditional risk factors separately, ultrasound RIs were significantly associated with older age, female
gender and lower BMI. The latter may be explained by the small number of obese subjects among our patients (N = 9) and by the malnutrition-inflammation-atherosclerosis syndrome (MIA syndrome), according to which in patients with chronic renal disease, a low BMI, reflecting malnutrition, is associated with systemic (micro)inflammation and accelerated atherosclerosis [20].

As markers of subclinical atherosclerosis, the ABI and common carotid intima-media thickness were measured which allow a standardized and noninvasive assessment of atherosclerotic vascular damage [21, 22].

In patients with intact renal function, renal RIs have been associated with carotid atherosclerosis assessed as carotid intima-media thickness [18, 23] or as carotid plaque score [24].

CONCLUSION

Rather than being considered specific markers of renal damage, intrarenal RIs are a complex integration of arterial compliance, arterial pulsatility, and peripheral resistance, which are associated with traditional cardiovascular risk factors and with subclinical atherosclerosis. A follow-up examination of our study cohort will have to show in how far intrarenal RIs predict long-term prognosis of kidney transplant recipients independently from markers of subclinical atherosclerosis (e.g., intima-media measurements).

In addition, future ultrasound studies will have to examine whether intrarenal RIs may be corrected for cardiovascular risk factors and for subclinical atherosclerosis, in order to allow for a more specific assessment of intrarenal damage. Finally, future studies should examine in how far the specificity of transplant renal RIs might be further increased by comparing transplant RIs to indices measured in arteries of native (nonrenal) organs, such as spleen arteries.

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REFERENCES

5. TUBLIN ME, TESSLER FN, MURPHY ME: Correlation between renal vascular resistance, pulse pressure, and the resistive index in isolated perfused rabbit kidneys. Radiology 213:258–264, 1999


