Clin J Am Soc Nephrol. 2010 Oct; 5(10): 1867–1872.
doi: 10.2215/CJN.01210210
PMCID: PMC2974388
PMID: 20616164

Original Articles

Significant Increase in 1-Year Posttransplant Renal Arterial Index Predicts Graft Loss

Mélanie Terebus Loock,[*] Jamal Bamoulid,[†‡] Cécile Courivaud,[†‡] Philippe Manzoni,[*] Dominique Simula-Faivre,[§] Jean-Marc Chalopin,[†‡§] Bruno Kastler,[*‖] and Didier Ducloux[†‡§]
Author information Article notes Copyright and License information PMC Disclaimer
*Department of Radiology, CHU Saint Jacques, Besançon, France;
Department of Nephrology, Dialysis, and Renal Transplantation, CHU Saint Jacques, Besançon, France;
INSERM, UMR645, Université de Franche-Comté, Etablissement Français du Sang, IFR133, Besançon, France;
CIC Biothérapies 506, CHU Saint Jacques, Besançon, France; and
I4S, Laboratory of Intervention, Innovation, Imagerie, Ingénierie en Santé, Université de Franche-Comté, Besançon, France
Corresponding author.
Correspondence: Dr. Didier Ducloux, Department of Nephrology and Renal Transplantation, Saint Jacques Hospital, 25000 Besançon, France., Phone: 33-381-21-87-82; Fax: 33-381-21-87; E-mail: rf.nocnaseb-uhc@xuolcudd

Go to:

Abstract

Background and objectives: Conflicting data have been reported concerning the use of kidney graft arterial resistance index (RI) measured by Doppler to predict death-censored graft loss. We hypothesized that changes in RI values could carry better information than a single measure of RI.

Design, setting, participants, & measurements: Four hundred twenty-five renal transplant recipients were included in the study. We tested whether changes in renal arterial resistance index between 4 and 12 months after transplant ($\Delta RI_{4\rightarrow12}$) were predictive of graft loss.

Results: Neither 4-month nor 1-year RI predicted graft loss. The area under the receiver operating characteristics curve of $\Delta RI_{4\rightarrow12}$ for graft loss was 0.75. A $\Delta RI_{4\rightarrow12} \geq 10\%$ had the best

sensitivity and specificity. One year after transplant, 22% of the study population had $\Delta RI_{4\rightarrow12} \geq 10\%$. Fifty-five patients (12.9%) experienced graft loss during follow-up. The annual incidence of graft loss was higher in patients with $\Delta RI_{4\rightarrow12} \geq 10\%$ (3.5 *versus* 1.3%; $P = 0.009$). In multivariate analysis, patients with $\Delta RI_{4\rightarrow12} \geq 10\%$ had an increased risk of graft loss (hazard ratio, 6.21; 95% confidence interval, 1.99 to 22.15; $P = 0.002$).

Conclusions: A variation in RI ≥10% in the first year after transplant is an independent risk factor for death-censored graft loss in renal transplant recipients.

Despite advances in the prevention of acute rejection, long-term outcomes after kidney transplantation have only modestly improved during the last years. Indeed, survival rates remain quite stable, with only 50% of kidneys from deceased donors still functioning 10-year after transplant (1). The leading cause of allograft failures is chronic allograft nephropathy, a complex phenomenon characterized by progressive renal dysfunction, chronic interstitial fibrosis, tubular atrophy, vascular occlusive changes, and glomerulosclerosis (2,3). Many risk factors are known to influence long-term graft survival, such as recipient age, race, delayed graft function (DGF), HLA mismatching, and acute rejection episodes (4,5).

Sequential biopsies may help to predict the subsequent development of chronic allograft nephropathy and the worse outcome of the graft (6,7). Nevertheless, kidney biopsies are invasive and expensive procedures. Recently, conflicting data have been reported concerning the use of kidney graft arterial resistance index (RI) measured by Doppler to evaluate kidney function and predict graft loss (8–11). We hypothesized that longitudinal changes in RI values could carry better information than a single measure of RI to predict death-censored graft loss. We tested this hypothesis in a cohort of 425 consecutive renal transplant recipients.

Go to:

Patients and Methods

Patients Characteristics

Four hundred eighty-three patients received a deceased kidney transplant in Saint-Jacques university hospital between January 1993 and December 2006. Thirty-eight (7.9%) had a follow-up period <1 year (death, 15; graft loss, 19; lost from follow-up, 4) and were excluded. All of the patients transplanted in our unit have a protocol Doppler examination 4 months after transplant and at each annual transplant birthday. Twenty patients did not have the two protocol examinations. Four hundred twenty-five stable, renal transplant recipients with transplant duration of at least 12 months and two ultrasound doppler evaluation at 4 months and 1 year after transplant were included in the study.

All of the patients had received induction therapy rabbit anti-thymocytes globulins (either thymoglobulin, genzyme, or fresenius; Fresenius Biotech GMBH, Gräfelfing, Germany) or monoclonal anti-CD25 antibody (anti-CD25 mab; Novartis, Basel, Switzerland). They received the same maintenance immunosuppressive treatment including cyclosporine (June 1993 to July

2001) or tacrolimus (August 2001 to December 2006), azathioprine (June 1993 to October 2000) or mycophenolate mofetil (November 2000 to December 2006), and steroids.

Baseline Pretransplant Evaluation

Age, gender, diabetes, hypertension, smoking habit, and a history of cardiovascular events were analyzed as covariates. Dialysis mode (none, hemodialysis, or peritoneal dialysis) and its duration before transplantation were also recorded.

Immunological and nonimmunological risk factors for graft loss such as pretransplant panel reactive antibodies (0 *versus* positive panel reactive antibodies at any level) and transplant number (first *versus*second or more) were analyzed as covariates.

Data concerning relevant donors (age, serum creatinine level, and collapses during reanimation) were collected. Information on kidney transplant (cold ischemia and human leukocyte antigen compatibility status) was also gathered.

The cumulative dose of steroids at 1 year after transplant, the use of calcineurin inhibitors, and the use of tacrolimus *versus* cyclosporine were considered potential covariates.

One-Year Posttransplant Evaluation

All patients had a clinical and biologic evaluation 1 year after transplant. Body mass index (BMI) was calculated (weight/[height]^2) at transplant and 1 year after transplant. Subjects were categorized as current smokers or nonsmokers. BP was measured using a semiautomatic device, based on an oscillometric method with the patients in a sitting position after having rested for >5 minutes. Pulse pressure (systolic BP – diastolic BP) was calculated as well as mean arterial pressure (diastolic BP + 1/3[systolic BP − diastolic BP]). Anti-hypertensive drugs were assessed for each patient. Hypertension was defined by a BP ≥135/85 mmHg or medication. Diabetes and new-onset diabetes after transplantation was defined according to the 2003 international consensus guidelines on diabetes mellitus in transplantation (12). Serum creatinine concentration and urinary protein excretion were measured. Creatinine clearance was calculated using the Gault-Cockcroft formula. DGF was defined by the need of at least one dialysis after transplantation. Only biopsy-proven acute rejections were considered. Biopsy was considered in any case of serum creatinine increase without other evident causes (obstacle, graft artery stenosis). Diagnosis of cytomegalovirus (CMV) disease required the presence of viral replication and treatment by ganciclovir.

Ultrasonographic Determination of RI

Either an Acuson or Sequoia ultrasound machine (Siemens) with a 3.5-MHz curved-array multifrequency transducer was used. The B-mode measurements were performed at the same time as the Doppler measurement of the resistance index. Intrarenal Doppler signals were obtained from three representative proximal segmental arteries. We controlled all our data by retrospective inspection of the original color mode images and the Doppler flow curves. The

peak velocity (V_{max}) and the minimal diastolic velocity (V_{min}) were determined. The renal interlobal and segmental arterial resistance index was calculated as $100 \times [1 - (V_{min}/V_{max})]$, and the results from the three measurements were averaged.

To rule out renal artery stenosis in the transplant, the course of the renal artery was determined with color-flow imaging. Stenosis was suspected if a segment of the vessel showed color-flow disturbance. Patients with renal artery stenosis were excluded.

Doppler examinations were performed by two investigators. Nevertheless, each of the two Doppler examinations (4 and 12 months) performed in a same patient were done by the same investigator. This way, interindividual operator variations could not explain intraindividual variations in the patients.

All Doppler examinations were done in stable patients.

Statistical Analyses

The results are expressed as mean ± SD. The median and range are given for variables where distribution is not normal. First, univariate analyses were carried out to examine the relationship between RI, $\Delta RI_{4\rightarrow12}$(variation in RI between months 4 and 12) and a number of potential independent variables. Among the latter, covariates to enter multivariate analyses were selected as follows:

- Continuous variables were tested using *t* test or Mann-Whitney's nonparametric test.
- Categorical variables were tested using Pearson's χ^2 or Fisher's exact test.
- Multivariate regression analysis was performed to determine the factors associated with RI and $\Delta RI_{4\rightarrow12}$

We calculated both positive and negative predictive values of different thresholds of $\Delta RI_{4\rightarrow12}$ for the subsequent occurrence of graft loss. A receiver operating characteristics curve was performed to determine the relevance of $\Delta RI_{4\rightarrow12}$ to predict graft loss. The best threshold was the $\Delta RI_{4\rightarrow12}$ corresponding to the higher value of the equation: sensitivity + specificity – 1 (Youden index). This threshold was chosen for further analysis.

Second, univariate analyses were carried out to examine the relationship between graft loss and a number of potential independent variables including RI and ΔRI. Using log rank tests on Kaplan-Meier nonparametric estimates of graft loss distribution, we selected first variables with $P \leq 0.20$. The selected variables were included into a Cox proportional hazards model, and a backward stepwise selection process was performed—this time at a classical $\alpha = 0.05$. The number of years of follow-up was calculated from the date of the 1-year post-transplant ultrasonography until the date of the first event (graft loss) or the last documented visit in our outpatient unit. RI was split into two classes (<0.68 and ≥ 0.68 [median value]). Changes in RI between the first determinations 4 months after transplant (RI_{4m}) and the second one, 1 year after transplant (RI_{12m}), were calculated for each patient. The variation in RI ($\Delta RI_{4\rightarrow12}$) was calculated

as ($RI_{12m} - RI_{4m}/RI_{4m}$). $\Delta RI_{4\rightarrow12}$ was split into two categories (<10 and ≥10%) according to sensitivity/specificity analysis.

Age (<50 or >50 years), creatinine clearance (<50 and ≥50 ml/min), C-reactive protein (<3 and ≥3 mg/L [median value]), and urinary protein excretion (<0.5 and ≥0.5 g/d) were split into two classes.

Results are expressed as hazard ratio (HR) and 95% confidence interval (CI), with a *P* value testing the null hypothesis: HR = 1. Therefore, when $P < 0.05$, HR is significantly different from 1: either >1 (*i.e.,* risk of graft loss is increased) or <1 (*i.e.,* risk of graft loss is decreased). Assumptions of Cox models (log-linearity, proportionality of risk in time) were met in this analysis.

Go to:

Results

Study Population

The cohort of 425 patients was followed for a mean duration of 7.2 ± 5.7 years. The characteristics of the study population are depicted in Table 1.

Table 1.

Characteristics of the study population (mean, thresholds used to categorize patients, percent of patients in the category previously defined)

Variables	Mean ± SD	Category	Percent
Age (years)	47 ± 13	≥50	42
BMI at transplant (kg/m²)	23.8 ± 4.3	≥26	23
BMI at 1-year after transplant (kg/m²)	24.7 ± 4.7	≥26	32
Mean increase in B.M.I. (kg)	4.4 ± 8.5	>5%	45
Creatinine clearance (ml/min)[a]	53.6 ± 17.2	<50	46
Urinary protein excretion (g/day)	0.36 ± 0.62	>0.5 g/d	21
Positive PRA (%)	9.6		
First transplant (%)	81.1		
Acute rejection (%)[b]	19.8		
CMV disease (%)[b]	21.7		
DGF (%)	13.9		
Diabetes (%)	18		

Variables	Mean ± SD	Category	Percent
Gender (% male)	67		
Hypertension (%)[a]	83		
Current smokers (%)[a]	24		

Open in a separate window

BMI, body mass index; PRA, panel reactive antibodies; CMV, cytomegalovirus; DGF, delayed graft function.
[a]At 1-year after transplant.
[b]During the first year after transplant.

All of the patients were followed in our unit weekly the first 2 months and then according to clinical status. In the late post-transplant course, the patients were referred to our unit at least twice a year.

Eighty-four patients (19.8%) experienced at least one episode of biopsy-proven acute rejection. Only two patients were treated for acute rejection without allograft biopsy confirming the diagnosis. These patients were not considered as having had acute rejection.

Intrarenal RI

The mean RI 1 year after transplant was 0.67 ± 0.08 (median value, 0.68; range, 0.50 to 0.94; Table 2). Mean RI values did no significantly vary between the 4th and 12th months after transplant.

Table 2.

Resistance index and ΔRI

	$\Delta RI_{4\rightarrow12}$	RI_{4m}	RI_{12m}
Mean (SD)	2% (8)	0.67 (0.08)	0.67 (0.07)
Median (range)	1% (−23 to 40%)	0.68 (0.44 to 0.87)	0.68 (0.50 to 0.94)
$n \geq 10\%$ (%)	95 (22%)		

Open in a separate window

$\Delta RI_{4\rightarrow12}$, variation in RI between 4 and 12 months after transplant; RI_{4m}, RI 4 months after transplant; RI_{12m}, RI 12 months after transplant.

In univariate analysis, RI was associated with recipient age, recipient's history of cardiovascular disease, the occurrence of CMV disease in the first year after transplant, creatinine clearance, and urinary protein excretion. The multivariate analysis showed that intrarenal RI depends only on recipient age ($P = 0.005$), recipient's history of cardiovascular disease ($P = 0.012$), and the occurrence of CMV disease in the first year after transplant ($P = 0.009$). None of the donor characteristics correlated with RI. There was no difference in RI or $\Delta RI_{4\rightarrow12}$ between patients

under cyclosporine and those under tacrolimus. Moreover, RI and $\Delta RI_{4\rightarrow12}$ were similar in patients receiving or not receiving angiotensin receptor blockers or angiotensin converting enzyme inhibitors 1 year after transplant.

Mean percent of change in RI was 2 ± 8% (Table 2). Nevertheless, we observed great individual variations (from −23 to +40%). Table 3 depicts sensitivity, specificity, and both positive and negative predictive values of different $\Delta RI_{4\rightarrow12}$ thresholds for the later occurrence of graft loss. The area under the receiver operator characteristics curve was 0.75 (Figure 1).

Table 3.

Resistance indices (RI_{12m}) and variations in resistance indices ($\Delta RI_{4\rightarrow12}$) in different categories of patients

	RI_{12m}			**$\Delta RI_{4\rightarrow12}$ (%)**		
	No	**Yes**	***P***	**No**	**Yes**	***P***
Age > 50 years	0.64 ± 0.07	0.72 ± 0.08	<0.0001	2 ± 10	2 ± 9	0.677
Male gender	0.68 ± 0.09	0.66 ± 0.07	0.024	1 ± 9	2 ± 10	0.474
Past history of CVD	0.66 ± 0.07	0.7 ± 0.1	<0.0001	2 ± 10	2 ± 9	0.665
Smoking habit	0.67 ± 0.07	0.66 ± 0.1	0.556	2 ± 10	1 ± 9	0.536
Hypertension	0.68 ± 0.07	0.67 ± 0.08	0.569	5 ± 9	2 ± 9	0.229
Diabetes	0.66 ± 0.07	0.69 ± 0.07	0.061	2 ± 10	2 ± 9	0.783
Creatinine clearance <50 ml/min	0.67 ± 0.07	0.66 ± 0.07	0.479	1 ± 10	2 ± 10	0.328
U.P.E. ≥ 0.5 g/day	0.66 ± 0.07	0.68 ± 0.09	0.076	1 ± 10	4 ± 11	0.143
CMV disease	0.66 ± 0.07	0.69 ± 0.08	0.003	2 ± 10	2 ± 10	0.486
Acute rejection	0.67 ± 0.08	0.66 ± 0.07	0.338	2 ± 10	1 ± 10	0.534
Donor age >42 years	0.67 ± 0.07	0.68 ± 0.09	0.211	2 ± 10	2 ± 9	0.712
Donor creatinine >100 μM	0.67 ± 0.08	0.67 ± 0.08	0.561	1 ± 10	2 ± 9	0.483
Cold ischemia time >20 h	0.67 ± 0.07	0.67 ± 0.07	0.423	2 ± 10	1 ± 10	0.553

Open in a separate window

RI_{12m}, RI 12 months after transplant; $\Delta RI_{4\rightarrow12}$, variation in RI between 4 and 12 months after transplant; CVD, cardiovascular disease; U.P.E., urinary protein excretion; CMV, cytomegalovirus.

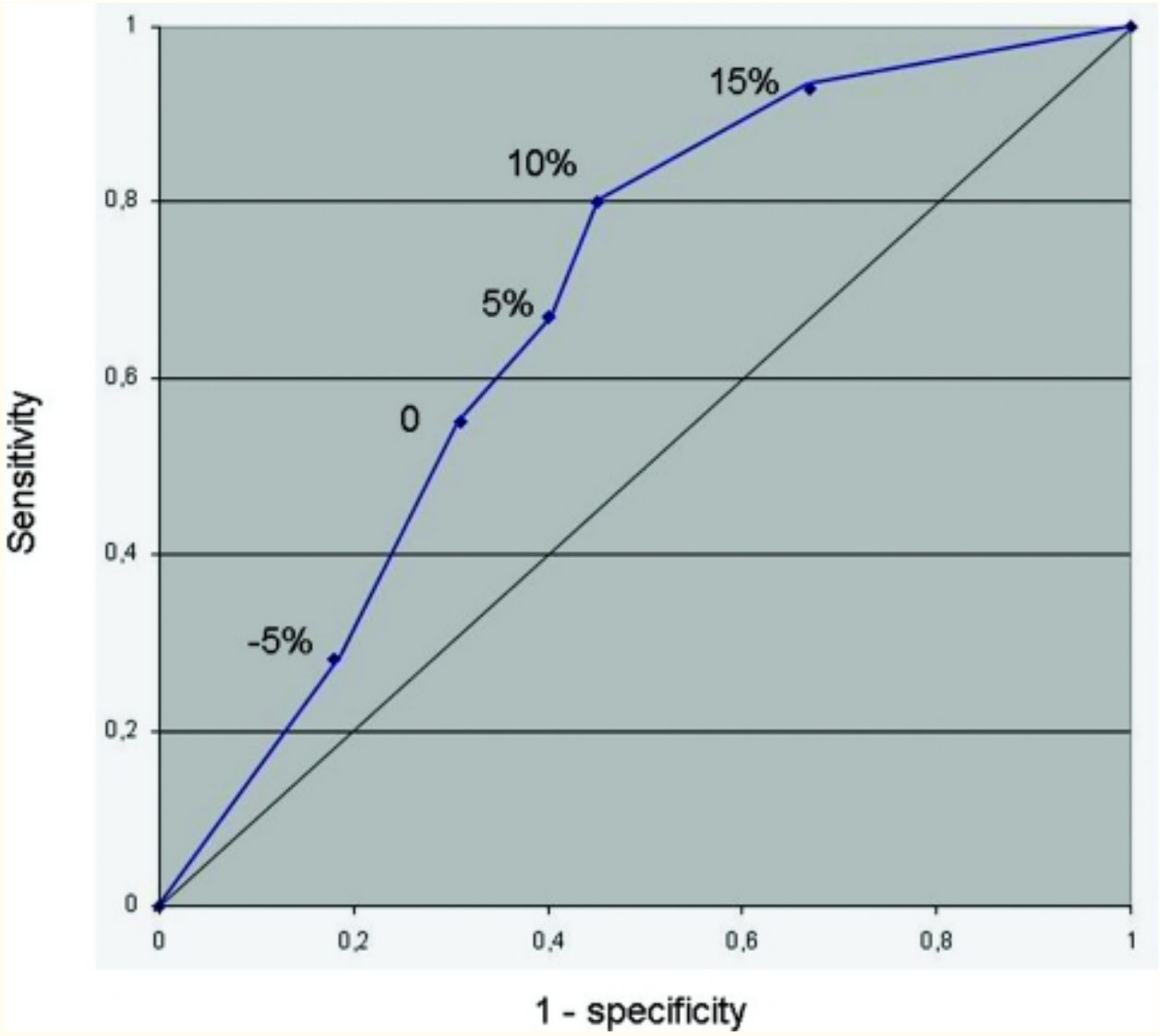

Figure 1.
Association of sensitivity and specificity for different $\Delta RI_{4\rightarrow12}$ values using the receiver operating characteristics curve. The receiver operating characteristics curve was obtained as described in the Patients and Methods section.

A $\Delta RI_{4\rightarrow12} \geq 10\%$ had the best sensitivity and specificity. Therefore, this threshold was chosen for further analysis. Positive predictive values were low for all values of $\Delta RI_{4\rightarrow12}$.

Ninety-five patients (22.3%) had an increase in RI ≥10% between the fourth month and the first year after transplant. These patients with and without a significant increase in RI did not differ for any parameters except for changes in BMI in the first year after transplant (Table 4). Mean variation in BMI was 0.3 ± 7% in patients without $\Delta RI_{4\rightarrow12}$ <10% and 3.8 ± 7% in those with a significant increase in RI ($P = 0.019$). We observed a significant correlation between ΔBMI and $\Delta RI_{4\rightarrow12}$ ($r = 0.20$; $P = 0.018$).

Table 4.

Sensitivity, specificity, positive and negative predictive values, and Youden index for different $\Delta RI_{4\rightarrow12}$ thresholds

$\Delta RI_{4\rightarrow12}$	Sensitivity	Specificity	PPV	NPV	Youden Index
−5%	0.25	0.82	0.1	0.93	0.07
0	0.54	0.71	0.13	0.92	0.25
5%	0.63	0.65	0.16	0.92	0.28
10%	0.86	0.59	0.25	0.91	0.45
15%	0.93	0.34	0.32	0.89	0.27

Open in a separate window

$\Delta RI_{4\rightarrow12}$, variation in RI between 4 and 12 months after transplant; PPV, positive predictive value; NPV, negative predictive value; Youden index, sensitivity + specificity − 1.

RI were also measured 3 and 5 years after transplant. RI remained stable in patients with $\Delta RI_{4\rightarrow12}$ <10% (0.69 ± 0.07 and 0.70 ± 0.08 at 3 and 5 years after transplant, respectively). In contrast, RI increased until 3 years after transplant in patients with $\Delta RI_{4\rightarrow12}$ ≥10% (0.74 ± 0.07 *versus* 0.72 ± 0.07; $P = 0.023$).

Graft Loss (Death Censored)

Fifty-five patients (12.9%) lost their graft during follow-up. The annual rate of graft loss was higher in patients with an increase in RI ≥10% (3.5 *versus* 1.3%; $P = 0.004$; Figure 2).

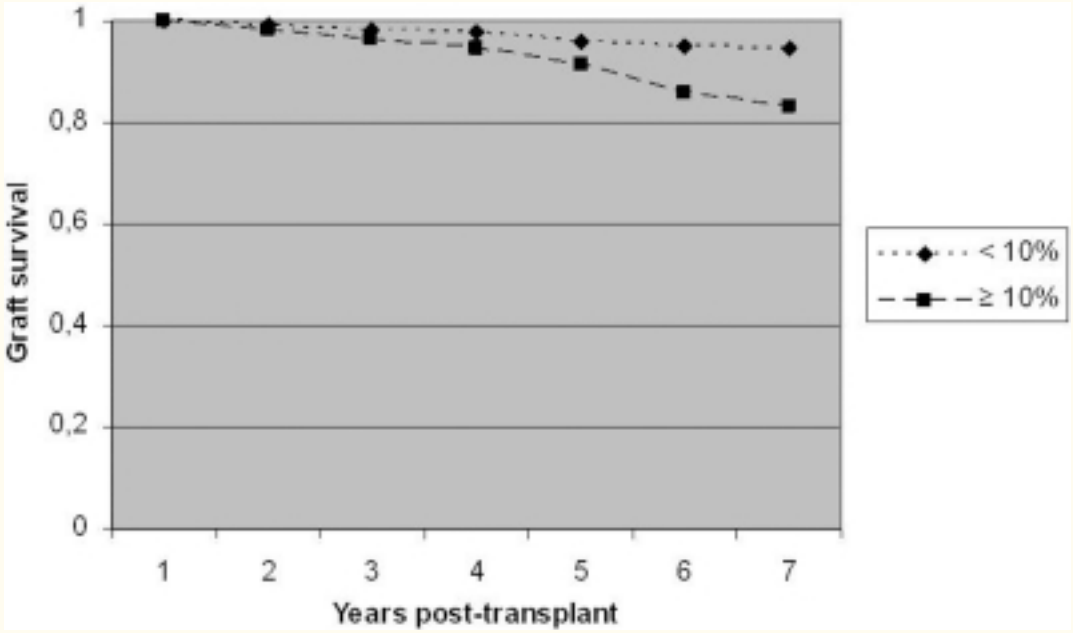

Figure 2.

Death-censored graft survival according to changes in resistance index.

In univariate analysis, low creatinine clearance 1 year after transplant ($P < 0.001$), high urinary protein excretion 1 year after transplant ($P = 0.006$), delayed graft function ($P < 0.001$), acute rejection in the first year after transplant ($P = 0.001$), DGF ($P = 0.039$), an increase in BMI ≥5% ($P = 0.023$), and an increase in RI ≥10% ($P = 0.004$) were associated with graft loss. One-year post-transplant RI was not predictive of graft loss.

Immunosuppressive drugs did not influence graft survival (cyclosporine *versus* tacrolimus, azathioprine *versus* mycophenolate mofetil, anti-thymocytes globulins *versus* anti-CD25 mab).

In multivariate analysis, low creatinine clearance 1 year after transplant (HR, 1.83; 95% CI, 1.19 to 3.22; $P = 0.017$), an increase in RI ≥10% (HR, 6.21; 95% CI, 1.99 to 22.15; $P = 0.002$), and a history of acute rejection (HR, 3.42; 95% CI, 1.41 to 9.67; $P = 0.008$) were independent risk factors for graft loss (Table 5).

Table 5.

Cox model: Hazard ratio estimates for AE and 95% confidence intervals

Variable	Category	Hazard Ratio	95% Confidence Intervals	*P*
Creatinine clearance ml/min	≥50	1	—	—
	<50	1.83	[1.19; 3.22]	0.017
$DRI_{4\rightarrow12} \geq 10\%$	No	1		
	Yes	6.21	[1.99; 22.15]	0.002
Acute rejection	No	1	—	—
	Yes	3.42	[1.41; 9.67]	0.008

Open in a separate window

$\Delta RI_{4\rightarrow12}$, variation in RI between 4 and 12 months after transplant.

When entered into the model as a continuous variable, the percent of change in RI ($\Delta RI_{4\rightarrow12}$) was found to be an independent risk factor for graft loss (HR, 1.11; 95% CI, 1.05 to 1.14 for each increase of 1% of RI; $P = 0.009$).

Changes in RI did not predict death or death-uncensored graft loss.

Go to:

Discussion

Our study showed an increased rate of graft loss in patients with a substantial increase in intrarenal RI in the first year after transplant. More precisely, patients with a 1-year post-transplant increase in RI of >10% showed a six-fold increase in risk of graft loss. However, RI, which primarily depends on recipient-related vascular status rather than on graft function, is not predictive of graft outcomes. Therefore, our study suggests that only comparisons of RI over time can help physicians to detect early graft dysfunction.

Previous studies have reported a correlation between age, vascular compliance, and intragraft RI (10). We also observed that RIs mainly depend on recipient's vascular compliance. Both age and a history of cardiovascular disease correlated with RI. In contrast, neither graft function nor donor characteristics were predictive of RI. Interestingly, we found CMV disease to be associated with RI. CMV is implicated in vascular complications through endothelial dysfunction. In heart transplant patients, CMV infection episodes are associated with impaired coronary endothelial function (13). Moreover, Fearon *et al.* (14) reported that CMV seropositivity and the lack of prophylaxis against CMV correlate with negative remodeling of coronary arteries. Finally, both animal models and epidemiologic studies suggest a role for CMV in atherogenesis (15–17). Concordant with these data, CMV may contribute to endothelial dysfunction and vascular aging in renal transplant patients.

The predictive value of RI for subsequent graft loss is controversial. Some authors found elevated RI to be predictive of graft loss (8,9). Radermacher *et al.* (8) reported that renal arterial RI >0.8 at least 3 months after transplantation was predictive of a combined endpoint including a decrease of 50% or more in creatinine clearance, allograft failure, or death. In this study, 20% of the patients had an RI of 80% or more, which is an unexpectedly high rate of elevated RI. In our study, only 3.3 and 5.4% of the patients had RI ≥80% at 4 and 12 months after transplant, respectively. Concordant with our results is the fact that the median RI was 63% in a study by Saracino *et al.* (9). This value is even lower than in our study. Thus, we believe that a very high cut-off, if predictive of graft loss, is probably not relevant because it selects a small subset of patients. Moreover, some other studies did not confirm these results (10,11). It should be noted that RI did not depend on either donor characteristics or past transplant events. Because RI seems to mainly reflect recipient vasculature, we think that a single measure of RI is not relevant to appreciate current intragraft process and predict transplant course.

The major finding of our study is that changes in RI, rather than RI *per se*, are predictive of graft loss. Because only intraindividual comparisons are of clinical use, RI should be determined as baseline values in each patient for long-term follow-up. Nevertheless, for a continuous variable used as a predictive factor, defining thresholds is mandatory for clinical practice. Thresholds should have both good positive and negative predictive values to help physicians in patient management. We found a variation in RI ≥10% to be the best threshold for subsequent graft loss. A significant change in RI could be an indicator for histologic evaluation and/or therapeutic intervention. Thus, Doppler RIs may be an early marker of intragraft vascular damage.

We recently reported that weight gain in the first year after transplant is a risk factor for graft loss (18). Interestingly, we showed here that changes in RI may at least in part depend on weight gain. Obesity is associated with afferent arteriolar dilation and glomerular capillary hypertension,

which could lead to glomerulosclerosis (19). Hall *et al.* (20) suggested that, in response to the reduced Na excretion capacity acting at sites proximal to macula densa in obesity, reduced NaCl delivery to the macula densa site induces afferent vasoconstriction and renin release to produce compensatory glomerular hyperfiltration, thereby restoring normal distal delivery. Hyperinsulinemia could further interact with elevated intrarenal angiotensin II levels to augment angiotensin II–dependent contraction of glomerular mesangial cells (21). Together, these mechanisms could account for the association between weight variations and RI changes.

There are some limitations to our work. Our study design implied the inclusion of renal transplant recipients with at least 1-year graft survival. A survival bias is possible, and the conclusions of this study might not be applicable to short-term graft survival. Association does not obligatory preclude causality, and one can suspect RI to be an effect of graft failure rather than a cause. Moreover, we cannot exclude the sample size of our cohort to be too small to detect an independent effect of other parameters. Finally, Doppler examinations were performed by two different investigators. Nevertheless, each of the two Doppler examinations performed in the same patient was done by the same investigator. This way, we minimized interindividual operator variability.

A significant increase in RI during the first year after transplant is a powerful predictor of death-censored graft loss. Because a single determination of RI does not predict graft outcome, longitudinal survey of RI seems mandatory. Future studies should examine whether histologic evaluation and/or therapeutic intervention based on RI modifications could prolong graft survival.

Go to:

Disclosures

None.

Go to:

Footnotes

Published online ahead of print. Publication date available at www.cjasn.org.

Go to:

References

1. *Annual Report of the U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients. Transplant Data 1994–2003*, Rockville,

MD, Health Resources and Services Administration, Division of Transplantation, 2004 [Google Scholar]
2. Jevnikar AM, Mannon RB: Late kidney allograft loss: What we know about it, and what we can do about it. *Clin J Am Soc Nephrol* 3: S56–S67, 2008 [PMC free article] [PubMed] [Google Scholar]
3. Bosmans JL, Ysebaert DK, Verpooten GA: Chronic allograft nephropathy: What have we learned from protocol biopsies? *Transplantation* 85: S38–S44, 2008 [PubMed] [Google Scholar]
4. Hariharan S, Johnson CP, Bresnahan BA, Taranto SE, McIntosh MJ, Stablein D: Improved graft survival after renal transplantation in the United States, 1988 to 1996. *N Engl J Med* 342: 605–612, 1999 [PubMed] [Google Scholar]
5. Shoskes DA, Cecka JM: Deleterious effects of delayed graft function in deceased renal transplant recipients independent of acute rejection. *Transplantation* 66: 1697–1701, 1998 [PubMed] [Google Scholar]
6. Bosmans JL, Ysebaert DK, Verpooten GA: Chronic allograft nephropathy: What have we learned from protocol biopsies? *Transplantation* 85: S38–S41, 2008 [PubMed] [Google Scholar]
7. Mengel M, Gwinner W, Schwarz A, Bajeski R, Franz I, Brücker V, Becker T, Neipp M, Klempnauer J, Haller H, Kreipe H: Infiltrates in protocol biopsies from renal allografts. *Am J Transplant* 7: 356–365, 2007 [PubMed] [Google Scholar]
8. Radermacher J, Mengel M, Ellis S, Stuht S, Hiss M, Schwarz A, Eisenberger U, Burg M, Luft FC, Gwinner W, Haller H: The renal arterial resistance index and renal allograft survival. *N Engl J Med* 349: 115–124, 2003 [PubMed] [Google Scholar]
9. Saracino A, Santarsia G, Latorraca A, Gaudiano V: Early assessment of renal resistance index after kidney transplant can help predict long-term renal function. *Nephrol Dial Transplant* 21: 2916–2920, 2006 [PubMed] [Google Scholar]
10. Krumme B, Grotz W, Kirste G, Schollmeyer P, Rump LC: Determinants of intrarenal Doppler indices in stable renal allografts. *J Am Soc Nephrol* 8: 813–816, 1997 [PubMed] [Google Scholar]
11. Chiang YJ, Chu SH, Chuang CK, Chen HW, Chou CC, Chen Y, Wu CT: Resistive index cannot predict transplant kidney function. *Transplant Proc* 35: 94–95, 2003 [PubMed] [Google Scholar]
12. Davidson J, Wilknson A, Dantal J, Dotta F, Haller H, Hernández D, Kasiske BL, Kiberd B, Krentz A, Legendre C, Marchetti P, Markell M, van der Woude FJ, Wheeler DC: New-onset diabetes after transplantation: 2003 International consensus guidelines. *Transplantation* 75[10 Suppl]: SS3, 2003 [PubMed] [Google Scholar]
13. Petrakopoulou P, Kübrich M, Pehlivanli S, Reichart B, von Scheidt W, Weis M: Cytomegalovirus infection in heart transplant recipients is associated with impaired endothelial function. *Circulation* 110[Suppl 1]: II207–II212, 2004 [PubMed] [Google Scholar]
14. Potena L, Hirohata A, Sakurai R, Yamasaki M, Luikart H, Lee J, Vana ML, Cooke JP, Mosarski ES, Yeung AC, Valantine HA: Changes in coronary endothelial dimensions

early after cardiac transplantation. *Transplantation* 83: 700–705, 2007 [PubMed] [Google Scholar]
15. Hsich E, Zhou YF, Paigen B, Johnson TM, Burnett MS, Epstein SE: Cytomegalovirus infection increases development of atherosclerosis in apolipoprotein-E knockout mice. *Atherosclerosis* 156: 23–28, 2001 [PubMed] [Google Scholar]
16. Nerheim PL, Meier JL, Vasef MA, Li WG, Hu L, Rice JB, Gavrila D, Richenbacher WE, Weintraub NL: Enhanced cytomegalovirus infection in atherosclerotic human blood vessels. *Am J Pathol* 164: 589–600, 2004 [PMC free article][PubMed] [Google Scholar]
17. Adam E, Melnick JL, DeBakey ME: Cytomegalovirus infection and atherosclerosis. *Cent Eur J Public Health* 5: 99–106, 1997 [PubMed] [Google Scholar]
18. Ducloux D, Kazory A, Simula-Faivre D, Chalopin JM: One-year post-transplant weight gain is a risk factor for graft loss. *Am J Transplant* 5: 2922–2928, 2005 [PubMed] [Google Scholar]
19. Chagnac A, Weinstein T, Korzets A, Ramadan E, Hirsch J, Gafter U: Glomerular hemodynamics in severe obesity. *Am J Physiol Renal Physiol* 278: F817–F822, 2000 [PubMed] [Google Scholar]
20. Hall JE, Henegar JR, Dwyer TM, Liu J, Da Silva AA, Kuo JJ, Tallam L: Is obesity a major cause of chronic kidney disease? *Adv Ren Replace Ther* 11: 41–54, 2004 [PubMed] [Google Scholar]
21. Kreisberg JI: Insulin requirement for contraction of cultured rat glomerular mesangial cells in response to angiotensin II: Possible role for insulin in modulating glomerular hemodynamics. *Proc Natl Acad Sci USA* 79: 4190–4192, 1982 [PMC free article] [PubMed] [Google Scholar]