Original Article

Angiographic Index for Angioplasty-Treatable Atheromatous Renal Artery Stenosis

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The relative reduction of the lumen diameter by an atheromatous lesion (% diameter reduction) is generally used as an angiographic index for atheromatous renal artery stenosis (ARAS), but its association with the clinical outcome of angioplasty has not been sufficiently evaluated. This study aimed to identify an angiographic index(ices) that can be used to identify angioplasty-treatable ARAS. We evaluated the clinical outcome of angioplasty in 27 patients who had unilateral ARAS without renal insufficiency by assessing the reduction in systemic arterial blood pressure (BP) after angioplasty and examined its association with various angiographic indices. In the receiver operating characteristic analysis for BP reduction, the area under the curve was larger for the absolute value of the lumen diameter at the narrowest part of its constriction (the narrowest diameter), an angiographic index introduced in this study, than for % diameter reduction (0.770 vs. 0.731). At a 3-mm maximum threshold, the narrowest diameter identified cases with BP reduction; the sensitivity/specificity was 0.89/0.75 ($p < 0.001$). Furthermore, the narrowest diameter correlated better than % diameter reduction with hemodynamic indices of ARAS. In conclusion, the narrowest diameter is an angiographic index that can effectively identify angioplasty-treatable ARAS in patients without renal insufficiency. (*Hypertens Res* 2008; 31: 881–885)

Key Words: hypertension, renin angiotensin system, renal ischemia, arteriosclerosis

Introduction

Atheromatous renal artery stenosis (ARAS) is the most common cause of renovascular hypertension (1, 2) and one of the major causes of renal impairment, which can necessitate continuous renal replacement therapy (3, 4). Although angioplasty for ARAS that impairs renal perfusion could reduce systemic arterial blood pressure (BP) and impede the progression of renal impairment, its clinical benefits remain controversial (5, 6). The incidental finding of ARAS without impairment of the renal perfusion in hypertensive patients,

especially in the elderly, is not rare (7, 8). Therefore, it is imperative to appropriately detect ARAS that is treatable by angioplasty (2).

Renal artery angiography is widely used to detect ARAS. ARAS is generally evaluated using the diameter reduction as an index; this parameter, which is expressed as a percentage (% diameter reduction), is calculated as the relative reduction in the lumen diameter by an atheromatous lesion observed on angiography (1, 2). Its use as an index for coronary artery stenosis, a context in which it is well correlated with cardiac perfusion (9–11), is believed to have influenced its use as an index for ARAS. However, the % diameter reduction is

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thought to be less effective for ARAS than for coronary artery stenosis; both its proximal and distal reference diameters which greatly influence the % diameter reduction, are frequently obscure, because ARAS often exists near the orifice of the renal artery and accompanies poststenotic dilatation (12). Consequently, intra- and inter-observer agreement with respect to the estimation of % diameter reduction is poor in ARAS (13, 14).

In contrast to the % diameter reduction, the absolute value of the lumen diameter of the renal artery at the narrowest part of its constriction (the narrowest diameter) is not affected by the value of reference diameters. Therefore, in this study, we introduced the narrowest diameter as an angiographic index for ARAS and evaluated its association with the clinical outcome of angioplasty. Further, we evaluated the association of this index with hemodynamic indices of ARAS.

Methods

Patient Selection

All patients who were referred to our department for suspicion of secondary hypertension between January 1999 and December 2005 were enrolled in this study. Patients were selected for the evaluation by computed tomographic arteriography (CTA) or magnetic resonance arteriography (MRA) if they met all of the following criteria: age ≥ 45 years, at least one of the risk factors of atherosclerosis (smoking, dyslipidemia or diabetes mellitus [DM]), and relatively preserved renal function (a serum creatinine concentration [sCr] < 2.0 mg/dL). Patients suspected of having ARAS based on the CTA and MRA results were further evaluated by selective renal arteriography, and all 27 patients with unilateral ARAS on the main trunk were included in the study. In all patients, ARAS was treated by percutaneous renal artery angioplasty with the insertion of a stainless steel endoprosthesis (Palmaz stent with a diameter of 5–7 mm). The study protocol was approved by the ethics committee of our hospital, and informed consent was obtained from all patients.

Evaluation of the Renal Artery

Angiographic image with ARAS was evaluated as follows. We selected the angiographic view that showed the narrowest diameter of ARAS by tilting the detector. An image of this view was obtained by the digital subtraction method, and the width of the renal artery was measured using distance/stenosis measurement software with auto-calibration on a Siemens MULTISTAR TOP machine (Siemens AG, Munich, Germany). Using the mean width of the first normal segments proximal and distal to the ARAS lesion as the reference width, we calculated the % diameter reduction as follows: $100 \times (1 - \text{width of narrowest part} / \text{the reference width})$ (15). For the ostial lesions, the first proximal normal segment was determined by linearly extending the first normal segment of

Table 1. Baseline Characteristics of Patients and ARAS

Patients	
Number (men/women)	27 (20/7)
Age (years)	59 $\pm$ 7
Weight (kg)	63 $\pm$ 8
Height (m)	1.64 $\pm$ 0.08
BP (mmHg)	133/75 $\pm$ 18/10
sCr (mg/dL)	0.91 $\pm$ 0.26
PRA (ng/mL/h)	6.2 $\pm$ 7.1
ARAS	
Size	
% diameter reduction	56 $\pm$ 15 (13–81)
Narrowest diameter (mm)	2.6 $\pm$ 0.9 (1.1–4.5)
Reference (mm)	5.9 $\pm$ 0.9 (4.5–7.7)
PG	
Systolic (mmHg)	72 $\pm$ 46 (4–173)
Mean (mmHg)	38 $\pm$ 32 (1–105)

BP, systemic arterial blood pressure; sCr, serum creatinine; PRA, plasma renin activity; ARAS, atheromatous renal artery stenosis; PG, pressure gradient across the stenotic lesion. To convert sCr in mg/dL to $\mu\text{mol/L}$, multiply by 88.4. Values expressed as mean $\pm$ SD where appropriate.

the trunk to the orifice. The absolute value of the narrowest diameter was calculated using a catheter for selective renal arteriography as a scaling device.

Measurement of Pressure Gradient across the Stenosis

We measured the pressure gradient across the stenosis (PG) in all the ARAS lesions using end-hole 3-French catheter. The catheter was placed distal to the lesion, and the pressure was recorded while withdrawing the catheter. The post- and pre-stenotic pressures were measured at positions distal and proximal to the ARAS, respectively. The PG was calculated as (pre-stenotic pressure) – (post-stenotic pressure). In all the ARAS lesions, the PG in the systolic phase was decreased to less than 10 mmHg after the angioplasty.

Data Collection

Baseline and postangioplastic information were recorded prior to the angioplasty and at 1–3 months after the angioplasty, respectively. All blood samples were collected under fasting conditions in the morning. The sCr and the plasma renin activity (PRA) were enzymatically measured. The post-angioplastic BP was recorded at the first office visit during 1–3 months after the angioplasty.

For each patient, the total score of the administered antihypertensives was calculated before and after the angioplasty as follows. Each antihypertensive was standardized by dividing the administered dose by its corresponding maximum

Fig. 1. Receiver operating characteristic curves of the narrowest diameter (black line) and % diameter reduction (gray line) for the BP reduction by angioplasty.

approved daily dose. The sum of all the standardized doses was used as the total score. A reduction of BP was defined as 1) a reduction of the total score after the angioplasty with no increase in either the systolic or diastolic pressures or 2) a decrease of post-angioplastic BP of >15 mmHg in the systolic phase and >10 mmHg in the diastolic phase with no change in the total score (6). To minimize the effect of the settings during the office BP readings (16), we performed the conventional office BP readings according to guidelines (15). The self BP monitoring of the pre- and post-angioplastic BP was also performed in all the patients (17), and the reduction of the self-monitored BP was confirmed in the patients with the reduced office BP.

Statistical Analysis

Continuous variables were expressed as the mean $\pm$ SD and compared using Student's *t*-test. Discrete variables were expressed as counts and compared using χ^2 test. Statistical analysis was performed using the Dr SPSS II software package (SPSS, Chicago, USA). Probability values of $p < 0.01$ were considered statistically significant.

Results

The baseline characteristics of the patients enrolled and the ARAS lesions examined in this study are summarized in Table 1. Antihypertensives effectively controlled the baseline BP. Calcium channel blockers were administered to all the patients. In addition, angiotensin-converting-enzyme inhibitors, angiotensin-receptor blockers, α -blockers, β -blockers, and diuretics were administered to 8, 9, 7, 6, and 5 patients,

Table 2. Blood Pressure Changes after Angioplasty

	Total	Reduced	Others	<i>p</i> value
Narrowest diameter				
<3 mm	19	17	2	<0.001
≥ 3 mm	8	2	6	
% diameter reduction				
$\geq 75\%$	2	2	0	0.608
<75%	25	17	8	
($\geq 50\%$ / $<75\%$)	(19)	(15)	(4)	
$\geq 50\%$	21	17	4	0.024
<50%	6	2	4	

Others, no change and deteriorated.

respectively (administration of multiple agents in 18 patients). These medications maintained the mean sCr within the normal range. Approximately half the ARAS lesions (13/27) were ostial.

Using the BP reduction after angioplasty as an indicator of the clinical outcome, we evaluated the association of the narrowest diameter and the % diameter reduction with the clinical outcome. In the receiver operating characteristic (ROC) analysis for BP reduction, the area under the curve (AUC) was larger for the narrowest diameter than for the % diameter reduction (0.770 vs. 0.737) (Fig. 1). At a maximum threshold of 3 mm, the narrowest diameter could be used to detect cases with BP reduction; the sensitivity/specificity was 0.89/0.75 (Table 2). In comparison, the % diameter reduction could not be used to detect these cases with statistical significance; the sensitivity/specificity was 0.89/0.50 and 0.11/1.00 at a minimum threshold of 50% and 75%, respectively.

We next analyzed the correlation between the angiographic indices and the hemodynamic indices of ARAS (Table 3). Both the narrowest diameter and the % diameter reduction showed good correlation with the PG, the generally used hemodynamic index of ARAS (1, 2, 15), and the former correlated better with the PG in both the systolic and mean phases. However, both the angiographic indices showed poor correlation with PRA (normal range: 0.2–2.7 ng/mL/h). Furthermore, in the ROC analysis for the PRA reduction after angioplasty, the AUC of the narrowest diameter and % diameter reduction were also only 0.536 and 0.539, respectively. In addition, independent of the BP reduction after angioplasty, both the PGs showed wide variation. The PG in the systolic phase ranged from 30 to 158 mmHg in the cases with BP reduction and from 4 to 173 mmHg in those without BP reduction, and the PG in the mean phase ranged from 4 to 97 mmHg in the former and from 1 to 105 mmHg in the latter.

Discussion

The results of this study indicate that the narrowest diameter is a better angiographic index than the % diameter reduction for detecting angioplasty-treatable ARAS in patients without

Table 3. Correlation of Angiographic Indices with Hemodynamic Indices

	Narrowest diameter	% diameter reduction
Systolic PG	-0.686 (-0.846 to -0.414)	0.634 (0.335 to 0.817)
<i>p</i> value	<0.001	<0.001
Mean PG	-0.639 (-0.820 to -0.342)	0.570 (0.243 to 0.781)
<i>p</i> value	<0.001	0.002
PRA (ng/mL/h)	-0.317 (-0.622 to 0.072)	0.187 (-0.208 to 0.529)
<i>p</i> value	0.107	0.351

The correlation is expressed by the Pearson's correlation coefficient (95% confidence interval). PG, pressure gradient across the stenotic lesion; Systolic PG, PG in the systolic phase; Mean PG, PG in the mean phase; PRA, plasma renin activity.

renal insufficiency. A narrowest diameter of <3 mm could adequately detect the ARAS lesions that would result in BP reduction after angioplasty, whereas % diameter reductions of $\geq 50\%$ and $\geq 75\%$, the most widely used angiographic indices for "significant" ARAS (1, 2, 15), could not detect them.

The good association between the narrowest diameter and BP reduction after angioplasty was thought to reflect the result that the narrowest diameter is a good indicator of the renal perfusion impairment by ARAS. Corroborating the result of a previous report (18), we confirmed that the narrowest diameter was better correlated with the PG than was the % diameter reduction in both the systolic and mean phases. This is consistent with the hydrodynamic viewpoint that considers the volume and viscosity of fluid; the absolute (the narrowest diameter) rather than the relative (% diameter reduction) lumen diameter influences PG (19). However, the clinical outcome of angioplasty in this study did not depend on the PG at ARAS. The PG in both the systolic and mean phases showed wide variation independent of the BP reduction after angioplasty. However, the micro-catheter used to measure PG in this study could have increased PG, because pressure-measuring devices that obstruct the lumen can artificially increase PG. If PG was measured using a thinner device, such as a pressure wire, the clinical outcome of angioplasty in association with PG might have been different (18).

In addition to PG, the glomerular filtration ratio (GFR) and PRA, which change according to the renal perfusion, could be used as hemodynamic indices (2, 15, 20). A decrease in the renal perfusion decreases GFR and increases PRA, and conversely, an increase in the renal perfusion increases GFR and decreases PRA. Because most of the cases in this study had an estimated GFR of >60 mL/min/1.73 m² before angioplasty, in which range the estimation of GFR is considered to be inaccurate (21), we used PRA as a hemodynamic index. The narrowest diameter had a better correlation with PRA than did the % diameter reduction. However, the correlation still was not good, and the AUC of the ROC analysis for the PRA reduction after angioplasty was also small. The correlation was probably worsened by the effect of the antihypertensive agents on the PRA (22, 23).

An ARAS lesion having a narrowest diameter of ≥ 3 mm is considered not to disturb the renal perfusion independent of

the reference diameter of the renal artery. Because we used the narrowest diameter divided by the reference diameter to calculate the % diameter reduction, the large reference diameter should have increased the % diameter reduction in cases with a narrowest diameter of ≥ 3 mm and % diameter reduction of $\geq 50\%$. The difficulty of defining the reference diameter also causes poor intra- and inter-observer agreement with respect to the estimation of % diameter reduction in ARAS (12–14). These drawbacks make the % diameter reduction inferior to the narrowest diameter, which is not affected by the reference diameter, as an indicator for "significant" ARAS.

The vascular resistance of the smaller arteries distal to ARAS, which reflects the structural alteration of the vasculature, is known to affect the clinical outcome of angioplasty. The parameters obtained by Doppler ultrasonography, such as the resistance index, are generally used to evaluate the vascular resistance (24, 25). The renal function itself is also considered to reflect the vascular resistance of the intrarenal arteries (21). Most cases in this study had an estimated GFR of >60 mL/min/1.73 m² prior to angioplasty. Therefore, we considered that the effect of increased vascular resistance in the intrarenal arteries was negligible, although we did not routinely perform Doppler ultrasonography. Supporting this notion, the resistance index of the intrarenal arteries in all the cases we evaluated was <0.8 , indicating that the structural alteration of the intrarenal arteries was not significant enough to affect the clinical outcome of angioplasty (24). However, evaluation by Doppler ultrasonography should have been performed in all the cases.

CTA and MRA can evaluate the renal arteries less invasively than the conventional catheter arteriography. Recent advances in imaging technologies are enabling the evaluation of renal arteries (especially those of the main trunks) by CTA and MRA with the same accuracy as catheter arteriography (1, 26). Since angioplasty is generally performed on ARAS in the main trunks, CTA and MRA may be used to less invasively identify the angioplasty-treatable ARAS. The narrowest diameter obtained by CTA or MRA might be used as an angiographic index to identify angioplasty-treatable ARAS.

In conclusion, the narrowest diameter is a good angiographic parameter that correlates well with the clinical out-

come of angioplasty for ARAS in patients without renal insufficiency. At a 3-mm maximum threshold, the narrowest diameter can identify the angioplasty-treatable ARAS. However, an important limitation of this study is that the number of patients enrolled was rather small, and the usefulness of the narrowest diameter to identify the angioplasty-treatable ARAS needs to be validated in larger populations including patients with renal insufficiency.

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