Magnetic Resonance Angiography and Doppler Scanning for Detecting Atherosclerotic Renal Artery Stenosis

Yee-Yung Ng[1]*, Shu-Huei Shen[2], Hsin-Kai Wang[2], Hsiuo-Shan Tseng[2], Rheun-Chuan Lee[2], Shiao-Chi Wu[3]

[1]Division of Nephrology, Department of Internal Medicine, and [2]Department of Radiology, Taipei Veterans General Hospital, and [3]Institute of Health and Welfare Policy, National Yang-Ming University School of Medicine, Taipei, Taiwan, R.O.C.

Background: Atherosclerotic renal artery stenosis (ARAS) is a progressive but potentially reversible chronic kidney disease. Although the high sensitivity and specificity of renal Doppler scanning (RDS) for ARAS has been reported in western countries, ARAS has not been detected by RDS. This study used magnetic resonance angiography (MRA) to evaluate the sensitivity and specificity of RDS for detecting ARAS among outpatients at a nephrology clinic, and to calculate the degree of underestimation of ARAS by RDS.

Methods: A total of 257 outpatients, aged > 50 years were examined for ARAS by RDS and MRA.

Results: Thirty-seven (14.4%) and 139 (54.1%) of 257 patients had stenosis detected by RDS and MRA, respectively. Among the 220 patients whose RDS results were negative, MRA detected stenosis in 111 (50.45%). Multivariate logistic regression analysis showed that age > 65 years, duration of smoking, coronary artery disease, and serum creatinine levels > 354 μmol/L (4 mg/dL) were significant and independent factors that influenced ARAS in patients with negative results by RDS.

Conclusion: RDS might still be the diagnostic procedure of choice for screening outpatients for ARAS because it is inexpensive, convenient, able to detect severity, and avoids the use of contrast media. When RDS is negative in aged people who have smoked longer than 20 years, with coronary artery disease or serum creatinine > 4 mg/dL, MRA is recommended for further evaluation of ARAS. [*J Chin Med Assoc* 2010;73(6):300–307]

Key Words: Doppler scanning, magnetic resonance angiography, renal artery stenosis

Introduction

Atherosclerotic renal artery stenosis (ARAS) is one of the most common primary diseases of the renal arteries.[1] It can occur alone (isolated anatomical RAS) or in association with hypertension, renal insufficiency (ischemic nephropathy), or both.[2] Echo-color Doppler has emerged as a reliable method for the diagnostic work-up of patients with suspected renovascular stenosis. The prevalence of ARAS ranged from 2.32% in 5,950 hypertensive patients[3] to 6.8% in the elderly population,[4] as determined by renal Doppler scanning (RDS). This prevalence determined by RDS[3,4] was much lower than that reported using cardiac catheterization or aortography (11–42%)[5–7] and autopsy (4–53%).[8–11] This implies that ARAS in many patients is not detected by RDS,[12–14] although the sensitivity and specificity of RDS for ARAS has been reported to range from 63% to 100% and 73% to 100%, respectively.[15,16] These sensitivities and specificities of RDS in patients with ARAS were mainly found in western countries, and not in large groups in Taiwan.

ARAS is a progressive[17,18] but potentially reversible chronic kidney disease.[18–20] The damage to renal function, and its related morbidity and mortality, can be avoided if ARAS is diagnosed and treated early.[20,21] Therefore, it is essential to detect ARAS and initiate medical or interventional therapy early to maintain the renal blood flow above the critical perfusion pressure, to prevent renal ischemic damage.

*Correspondence to: Dr Yee-Yung Ng, Division of Nephrology, Department of Internal Medicine, Taipei Veterans General Hospital, National Yang-Ming University, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, R.O.C.
E-mail: yyng@vghtpe.gov.tw • Received: September 21, 2009 • Accepted: May 25, 2010

This study used magnetic resonance angiography (MRA) to evaluate the sensitivity and specificity of RDS for detecting ARAS among aged patients at a nephrology clinic, and the degree of underestimation of ARAS by RDS.

Methods

Patients

ARAS is a disease of aging. Therefore, we enrolled 257 unselected patients, aged ≥ 50 years, who were visiting the outpatient nephrology clinic of Taipei Veterans General Hospital. Written informed consent was obtained from all patients. This study followed the Declaration of Helsinki, and was approved by the Institutional Research Board. Each patient underwent MRA after RDS and effective renal perfusion tests. Renal angiography is the undisputed gold standard in the diagnostic work-up for renovascular disease; therefore, confirmation by selective renal angiography was encouraged for patients with > 50% renal artery stenosis, as shown by MRA. The diagnosis and severity of ARAS was defined by MRA if selective renal angiography was not performed. Four grades were used to categorize the severity of ARAS: grade 1, < 25% stenosis; grade 2, 26–50%; grade 3, 51–75%; and grade 4, > 75%. Stenosis of > 50% was defined as significant.

Demographic data were collected, including age, sex, body weight and height, and history of smoking and alcohol consumption. Comorbid conditions, including underlying coronary artery disease (CAD), cerebrovascular disease, and diabetes mellitus were also recorded.

Laboratory tests

Blood pressure was measured before RDS. Creatinine clearance (Ccr) and urinary protein excretion were determined after 24-hour urine collection. Serum blood urea nitrogen, creatinine (Scr), cholesterol, uric acid, calcium, phosphate and albumin concentrations were measured by standard laboratory methods. Plasma renin activity, aldosterone and intact parathyroid hormone were measured using radioimmunoassay.

RDS

All RDS was performed by a registered technologist, and the diagnosis was made by a radiologist with extensive experience in ultrasonography. The 257 patients were scanned in the supine position using a multifrequency curved-array transducer (2–5 MHz). Doppler samples were taken from each renal artery and interlobar artery by a bilateral flank approach, while maintaining the angle of insonation at < 60°. The angle of insonation was estimated and combined with the spectral analysis from the Doppler-shifted signal, and the renal artery peak systolic velocity was estimated. In the decubitus position, a B-scan image of each kidney was obtained and kidney length determined. The result of the RDS examination was considered positive for RAS according to the following published criteria: (1) presence of turbulence before and after stenosis, with a color change (confetti phenomenon); (2) maximum flow velocity > 180 cm/sec at stenosis, with concomitant spectral broadening and aliasing (no Doppler signal was obtained from an imaged artery in the case of renal artery occlusion); (3) end-diastolic velocity > 50 cm/sec; (4) post-stenotic drop in velocity; (5) acceleration time > 0.07 seconds and slope of systolic upstroke < 3 m/s^2; or (6) resistance index associated with stenosis or occlusion of the segmental arteries < 0.5.

MRA

MRA was performed with parallel technique (asset number 1.50) using the following parameters: minimum echo time 0.9–1 millisecond; flip angle = 30°; bandwidth = 62.5 kHz; matrix size = 320 × 192; field of view = 35–40 cm; number of excitations = 1; slice thickness = 3.2 mm with zero interpolation; and locations per slab = 36. A standard bolus of 0.1 mmol/kg gadolinium–diethylenetriamine pentaacetic acid was injected into an antecubital vein at a flow rate of 4 mL/sec. The degree of stenosis was determined by reviewing and measuring both coronal raw data and the coronal maximum-intensity projection, expressed as 180° rotational view (5°/frame), and was calculated as the diameter of the stenotic segment divided by the diameter of post-stenotic normal segment. Locations and lengths of stenosis were also measured.

Renal artery angioplasty and renal artery stent

Despite the risks of contrast nephropathy and atheroembolic renal disease, arteriography is considered to be the gold-standard diagnostic test. Twenty-four hours before and after angiography, patients were given hydration,[22] 0.6 g N-acetylcystine[23] and sodium bicarbonate[24] to prevent iodinated contrast-induced nephropathy. A femoral artery approach was used after reviewing the MRA in each case. Aortography was performed first to check the general condition of the abdominal aorta and the renal arteries. Renal arteriograms were then taken for both kidneys and all the renal arteries. A Cobra or RLG catheter was used with a marker wire inside. The diameter and the stenotic segment of the renal artery were measured as

compared with the marker wire. If the stenosis was >50%, percutaneous transluminal angioplasty with a stent was carried out at the same time using a premount balloon-expandable stent. The size of the stent was chosen to be the same as or 10% larger than the normal renal arterial diameter. After introducing an angiosheath, a 6- or 7-Fr guiding catheter was advanced near the renal arterial orifice. The stent was advanced to cross the stricture segment. The position of the stent was checked by injection of contrast medium through the guiding catheter. The stent was then deployed after inflating the pressure gauge. Finally, renal arteriography was performed again, either by the guiding or diagnostic catheter, to check for dissection, bleeding or thrombosis.

Statistical analysis

Statistical analysis was conducted by the χ^2 test, Student's *t* test, Mann–Whitney test and logistic regression using SPSS Version 15.0 (SPSS Inc., Chicago, IL, USA). The variance inflation factor (VIF) was used to measure colinearity among independent variables in multiple regression analysis. The larger the value of VIF, the more troublesome was the variable. Generally, VIF > 10 indicates colinearity among predictor variables. VIF values are easily produced using SPSS (SPSS Inc.). A p value < 0.05 indicated statistical significance.

Results

The mean age and Scr levels of the 257 patients (192 male and 65 female) were 75.49 ± 8.63 years and 2.39 ± 1.42 mg/dL (range, 0.6–1.5 mg/dL), respectively. Thirty-seven (14.4%) and 139 (54.1%) patients were diagnosed with ARAS by RDS and MRA, respectively. Among the 37 patients diagnosed by RDS, 14 stenoses occurred on the right side, 14 on the left, and 9 were bilateral. Among the 139 patients with stenosis diagnosed by MRA, 44 stenoses were found on the right side, 38 on the left, and 57 were bilateral. Ninety-five of 139 (68.3%) patients who were diagnosed with ARAS by MRA were willing to undergo selective renal angiography for confirmation. Twenty-eight of 37 (75.7%) patients whose stenoses were diagnosed by RDS were also shown to have ARAS by MRA. The diagnosis of stenosis made by MRA in 87 of 95 (91.6%) patients was confirmed by selective renal angiography. After eliminating the 8 patients who had negative results by selective renal angiography, there were 186 renal arteries with ARAS in the 131 patients who had true-positive results. This study showed a sensitivity of 20.14%, specificity of 92.37%, and positive predictive value of 75.68%, with an overall accuracy of 53.32% (Table 1). Seventy-nine of 186 (42.5%) renal arteries were considered to have significant (>50%) stenosis (Table 2).

Table 1. Results of atherosclerotic renal artery stenosis categorized by renal Doppler scanning and magnetic resonance angiography

	ARAS proved by MRA	
	Stenosis	Normal
ARAS diagnosed by RDS		
Stenosis	28	9
Normal	111	109
Total	139	118
Sensitivity	20.14% (28/139)	
Specificity	92.37% (109/118)	
PPV	75.68% (28/37)	
NPV	49.55% (109/220)	
Accuracy	53.31% (137/257)	

ARAS = atherosclerotic renal artery stenosis; RDS = renal Doppler scanning; MRA = magnetic resonance angiography; PPV = positive predictive value; NPV = negative predictive value.

Compared with the 126 patients without ARAS, the group of 131 patients with ARAS were older (mean age, 77.17 ± 7.64 *vs.* 73.74 ± 9.27 years, $p = 0.001$) and included a significantly higher number of smokers (65 *vs.* 43, $p = 0.011$) (Table 3). The smokers in the group with ARAS also smoked more (0.49 ± 0.6 *vs.* 0.29 ± 0.52 packs per day, $p = 0.005$) and had smoked longer (21.93 ± 23.99 *vs.* 12.24 ± 20.10 years, $p = 0.001$) than those in the group without ARAS. The number of patients with CAD in the group with ARAS was significantly higher than in the group without ARAS (37 *vs.* 12, $p < 0.001$), as was the Scr level [mean, 2.54 ± 1.53 mg/dL (median, interquartile range, 2, 1.4) *vs.* 2.24 ± 1.28 mg/dL (1.85, 1.4), $p = 0.083$] and the number of patients with Scr level > 4 mg/dL (23 *vs.* 9). The Ccr rate (27.55 ± 12.61 *vs.* 32.83 ± 17.32 mL/min, $p = 0.006$) and the effective renal plasma flow (ERPF) (165.56 ± 64.39 *vs.* 189.85 ± 92.7 mL/min, $p = 0.023$) were significantly lower in the group with ARAS than in that without (Table 3).

Among the 220 patients with negative results from RDS, there were 111 (50.45%) whose ARAS was diagnosed by MRA (Table 4). Compared with the patients with negative MRA results, this group of 111 patients with positive MRA results were older (77.82 ± 6.51 *vs.* 73.84 ± 9.56 years, $p = 0.001$), had more smokers (57 *vs.* 35, $p = 0.002$) who smoked more (0.5 ± 0.59 *vs.* 0.26 ± 0.51 packs per day, $p = 0.001$) and who had done so for longer (22.8 ± 24.16 *vs.* 11.21 ± 20.08 years, $p = 0.001$). The number of patients with CAD (30 *vs.* 11, $p = 0.001$), the average

Table 2. Demographic and clinical characteristics of 257 patients who underwent Doppler scanning and magnetic resonance angiography*

Characteristic	Value
Male	192 (74.4)
Age (yr)	75.49 ± 8.63
Patients with stenosis	131 (51.0)
No. of stenotic arteries	186/514 (36.2)
Grade 1 (right/left)	43 (21/22)
Grade 2 (right/left)	64 (36/28)
Grade 3 (right/left)	35 (14/21)
Grade 4 (right/left)	44 (26/18)
Body weight (kg)	65.29 ± 11.27
Height (cm)	162.32 ± 8.21
Smoking	108 (42.0)
Packs per day	0.39 ± 0.57
Duration (yr)	17.18 ± 22.65
Alcohol consumption	41 (16.0)
Amount (glasses)	0.32 ± 0.92
Duration (yr)	6.16 ± 15.54
Diabetes mellitus	91 (35.4)
Duration (yr)	14.49 ± 9.36
Hypertension	219 (85.2)
Duration (yr)	17.15 ± 12.38
Systolic BP (mmHg)	138.53 ± 18.51
Diastolic BP (mmHg)	74.51 ± 11.38
Previous CAD	49 (19.1)
1 vessel	11 (22.5)
2 vessels	17 (34.7)
3 vessels	21 (42.9)
Previous CVA	29 (11.3)
Renin (3–33 pg/mL)	36.26 ± 45.39
Aldosterone (40–310 pg/mL)	173.09 ± 141.53
Intact PTH (< 50 pg/mL)	96.03 ± 86.56
Albumin (3.7–5.3 g/dL)	3.99 ± 0.47
Calcium (8.4–10.6 mg/dL)	9.09 ± 0.66
Cholesterol (125–240 mg/dL)	167.27 ± 36.05
BUN (19.6–56.0 mmol/L)	90.79 ± 50.87
Uric acid (2.5–7.2 mg/dL)	7.07 ± 1.98
Creatinine (0.6–1.5 mg/dL)	2.39 ± 1.42
Creatinine > 4 mg/dL	32 (12.5)
Potassium (3.4–4.7 mmol/L)	4.28 ± 0.59
Phosphate (2.1–4.7 mg/dL)	3.67 ± 0.90
BMI (kg/m^2)	24.76 ± 3.78
Ccr (mL/min)	30.15 ± 15.31

**Continuous variables are expressed as mean ± standard deviation and categorical data as n (%). The normal ranges of laboratory tests are in parentheses. BP = blood pressure; CAD = coronary artery disease; CVA = cerebrovascular accident; PTH = parathyroid hormone; BUN = blood urea nitrogen; BMI = body mass index; Ccr = creatinine clearance.*

Scr levels [mean, 2.66 ± 1.63 mg/dL (median, interquartile range, 2.1, 1.6) *vs.* 2.19 ± 1.06 mg/dL (1.9, 1.4), $p = 0.04$], and the number of patients with Scr levels > 4 mg/dL (23 *vs.* 6, $p = 0.001$) were significantly higher in the group with results that were negative by RDS but positive by MRA, than the group whose results were negative by both methods. In contrast, Ccr (26.2 ± 11.73 *vs.* 32.5 ± 16.54 mL/min, $p = 0.001$) and ERPF (160 ± 63.59 *vs.* 185.8 ± 86.49 mL/min, $p = 0.018$) were significantly lower in the group whose results were negative by RDS but positive by MRA than in the group whose results were negative by both methods (Table 4). The number of patients with > 75% RAS in the positive RDS group was significantly higher than in the negative RDS group [14/28 (50%) *vs.* 28/111 (25.23%), $p = 0.02$]. In a multivariate logistic regression analysis (Table 5), sex, age > 65 years, smoking duration, CAD, Scr > 4 mg/dL, Ccr and ERPF were included in the final model as significant and independent factors. The variables in this model were [odds ratio (95% confidence interval)]: sex, 1.306 (0.552–3.09), $p = 0.543$; age > 65 years, 5.85 (1.757–19.48), $p = 0.004$; smoking duration > 20 years, 3.095 (1.468–6.526), $p = 0.003$; CAD, 1.521 (1.042–2.22), $p = 0.03$; Scr level > 4 mg/dL, 5.385 (1.518–19.102), $p = 0.009$; Ccr, 1.001 (0.96–1.044), $p = 0.96$; and ERPF, 0.998 (0.99–1.005), $p = 0.524$.

Discussion

Although the most accurate anatomical tests include RDS, MRA and computed tomographic angiography,[25] the latter was not used for this study because of the risk of ionizing radiation and a high incidence of contrast-induced nephropathy,[26] especially for patients with preexisting renal failure.[27] The mean Scr level of 2.39 ± 1.42 mg/dL (normal range, 0.6–1.5 mg/dL) in our patients further supported the decision against using computed tomographic angiography for further evaluation of ARAS after RDS used at the beginning of this study. In contrast, the use of intravenous gadolinium-based contrast media in magnetic resonance imaging has been found not to cause nephropathy in patients with renal insufficiency.[28,29] Although nephrogenic systemic fibrosis related to non-nephrotoxic gadolinium-based contrast media has been reported in some patients with renal failure, factors such as dose of gadolinium and predisposing infection seem to play a role.[29–32] There were no cases of nephrogenic systemic fibrosis in this or our previous study.[29]

For the present study, the number of true-negative results was defined as the total number of patients

Table 3. Demographic and clinical characteristics of 257 patients with and without atherosclerotic renal artery stenosis*

Characteristic	With stenosis ($n=131$)	Without stenosis ($n=126$)	p
Male	104 (79.4)	88 (68.9)	0.086
Age (yr)	77.17 ± 7.64	73.74 ± 9.27	0.001
Body weight (kg)	64.72 ± 10.77	65.86 ± 11.78	0.418
Height (cm)	162.23 ± 7.87	162.41 ± 8.57	0.854
Smoking	65 (51.6)	43 (35.5)	0.015
Packs per day, median (IQR)	0.195 (0–1)	0 (0–0.5)	0.003
Duration (yr), median (IQR)	13.5 (0–50)	0 (0–25)	0.002
Alcohol consumption	18 (14.2)	23 (19.0)	0.312
Amount (glasses)	0.33 ± 1.01	0.31 ± 0.82	0.690
Duration (yr)	5.79 ± 16.02	6.55 ± 15.07	0.940
Diabetes mellitus	45 (34.6)	46 (38.0)	0.601
Duration (yr)	13.70 ± 9.64	15.29 ± 9.11	0.412
Hypertension	112 (86.2)	107 (87.0)	0.856
Duration (yr)	16.40 ± 12.40	17.92 ± 12.37	0.385
Systolic BP (mmHg)	139.62 ± 20.63	137.40 ± 16.07	0.377
Diastolic BP (mmHg)	75.18 ± 11.50	73.81 ± 11.27	0.378
Previous CAD	37 (29.6)	12 (10.0)	< 0.001
Previous CVA	16 (13.0)	13 (10.9)	0.694
Renin (3–33 pg/mL), median (IQR)	21.76 (11.12–51.96)	14.64 (8.48–39.16)	0.112
Aldosterone (40–310 pg/mL)	164.83 ± 144.67	189.00 ± 135.13	0.296
iPTH (< 50 pg/mL), median (IQR)	64.74 (39.02–97.64)	84.5 (56.02–121.0)	0.091
Albumin (3.7–5.3 g/dL)	3.97 ± 0.47	4.02 ± 0.49	0.748
Calcium (8.4–10.6 mg/dL)	9.03 ± 0.58	9.16 ± 0.76	0.252
Cholesterol (125–240 mg/dL)	165.24 ± 34.14	170.37 ± 38.84	0.454
BUN (19.6–56.0 mmol/L)	103.28 ± 55.66	92.07 ± 44.85	0.08
Uric acid (2.5–7.2 mg/dL)	7.25 ± 1.95	6.84 ± 2.00	0.294
Cr (0.6–1.5 mg/dL), median (IQR)	2 (1.6–3.0)	1.85 (1.4–2.8)	0.083
Cr > 4 mg/dL	23 (17.6)	9 (7.1)	0.014
Potassium (3.4–4.7 mmol/L)	4.30 ± 0.62	4.26 ± 0.55	0.659
Phosphate (2.1–4.7 mg/dL)	3.65 ± 0.98	3.71 ± 0.74	0.679
BMI (kg/m^2)	24.59 ± 3.7	24.93 ± 3.87	0.470
Ccr (mL/min), median (IQR)	27.56 (18.86–32.83)	29.84 (19.26–41.41)	0.031

**Continuous variables are expressed as mean ± standard deviation and categorical data as n (%). Median with IQR, and Mann–Whitney test were used for the non-normally distributed data. IQR = interquartile range; BP = blood pressure; CAD = coronary artery disease; CVA = cerebrovascular accident; iPTH = intact parathyroid hormone; BUN = blood urea nitrogen; Cr = creatinine; BMI = body mass index; Ccr = creatinine clearance.*

minus the number of true-positive results (i.e. 257–139 = 118). This study showed that the sensitivity, specificity, and positive predictive value of RDS for ARAS in outpatients were 20.14% (28/139), 92.37% (109/118) and 75.68% (28/37), respectively (Table 1). One hundred and eleven of the 220 (50.45%) patients who had negative results by RDS had a diagnosis of ARAS made by contrast-enhanced MRA. Specifically, stenosis was found in 154 of the 222 (69.37%) renal arteries of these 111 patients, and significant stenosis (> 50%) was found in 60 (38.96%) (Table 4). The superior results obtained using MRA suggest that MRA significantly reduces interobserver variability and offers reliable and reproducible grading of RAS based on stenosis morphology and hemodynamic changes.[33] The high proportion (80%, 111/139) of ARAS cases missed by RDS in the present study might be partially related to a high technical failure rate and operator dependence.[34] Doppler flow volume measurements require the calculation of vessel diameter, which can

Table 4. Demographic and clinical characteristics of 220 patients with negative Doppler scanning results*

Characteristic	Patients with MRA(–) ($n=109$)	Patients with MRA(+) ($n=111$)†	p
Male	78 (71.6)	88 (79.3)	0.211
Age (yr)	73.84 ± 9.56	77.82 ± 6.51	0.001
No. of stenotic arteries	0/218	154/222 (69.37)	
Grade 1 (right/left)	0	25 (14/11)	
Grade 2 (right/left)	0	69 (34/35)	
Grade 3 (right/left)	0	24 (12/12)	
Grade 4 (right/left)	0	36 (19/17)	
Body weight (kg)	66.22 ± 11.46	65.19 ± 10.89	0.499
Height (cm)	162.57 ± 8.20	162.24 ± 8.36	0.772
Smoking	34 (32.1)	57 (53.5)	0.002
Packs per day, median (IQR)	0 (0–0.5)	0.33 (0–1)	< 0.001
Duration (yr), median (IQR)	0 (0–16.25)	20 (0–50)	0.001
Alcohol consumption	19 (17.9)	17 (15.7)	0.717
Amount (glasses)	0.27 ± 0.75	0.34 ± 0.95	0.557
Duration (yr)	5.87 ± 14.31	7.04 ± 17.7	0.671
Diabetes mellitus	39 (37.1)	42 (38.5)	0.888
Duration (yr)	15.91 ± 9.47	13.54 ± 9.42	0.275
Hypertension	90 (84.9)	94 (85. 5)	0.910
Duration (yr)	17.75 ± 12.82	17.59 ± 12.17	0.984
Systolic BP (mmHg)	136.20 ± 16.22	140 ± 19.03	0.125
Diastolic BP (mmHg)	73.35 ± 11.84	74.6 ± 10.58	0.441
Previous CAD	11 (10.5)	30 (28.0)	0.002
Previous CVA	8 (7.8)	17 (16.0)	0.087
Renin (3–33 pg/mL), median (IQR)	17.39 (9.31–39.92)	22.17 (11.35–51.96)	0.2
Aldosterone (40–310 pg/mL)	190.00 ± 147.20	168.00 ± 115.20	0.346
iPTH (< 50 pg/mL), median (IQR)	82.29 (59.6–117.75)	76.47 (49.51–114.0)	0.451
Albumin (3.7–5.3 g/dL)	3.99 ± 0.48	3.99 ± 0.43	0.957
Calcium (8.4–10.6 mg/dL)	9.16 ± 0.75	9.06 ± 0.58	0.399
Cholesterol (125–240 mg/dL)	168.80 ± 39.65	163.00 ± 34.16	0.384
BUN (19.6–56.0 mmol/L)	91.90 ± 44.37	104.48 ± 53.56	0.06
Uric acid (2.5–7.2 mg/dL)	6.91 ± 2.09	7.16 ± 1.94	0.443
Cr (0.6–1.5 mg/dL), median (IQR)	1.9 (1.4–2.8)	2.1 (1.6–3.2)	0.04
Cr > 4 mg/dL	6 (5.5)	23 (20.7)	0.001
Potassium (3.4–4.7 mmol/L)	4.26 ± 0.55	4.27 ± 0.65	0.850
Phosphate (2.1–4.7 mg/dL)	3.75 ± 0.77	3.66 ± 0.95	0.594
BMI (kg/m^2)	25.02 ± 3.79	24.78 ± 3.78	0.643
Ccr (mL/min), median (IQR)	29.75 (19.30–41.30)	27.09 (18.07–32.51)	0.011

**Continuous variables are expressed as mean ± standard deviation and categorical data as n (%); †8 of 111 MRA positive patients were proven to have no renal artery stenosis by selective angiography. Median with IQR, and Mann–Whitney test were used for the non-normally distributed data. MRA = magnetic resonance angiography; IQR = interquartile range; BP = blood pressure; CAD = coronary artery disease; CVA = cerebrovascular accident; iPTH = intact parathyroid hormone; BUN = blood urea nitrogen; Cr = creatinine; BMI = body mass index; Ccr = creatinine clearance.*

introduce considerable error. In contrast, RDS demands optimal sonographic test conditions and is limited by patient obesity and intestinal gas overlying the area of interest.[35] The large variability in duplex results among different laboratories has been attributed to differences in the type of ultrasound machine, the transducer, and the operator. Laboratory-specific rather than published duplex criteria have been suggested for the assessment of carotid and renal artery stenosis.[36–38] RDS also has been reported to be sufficiently sensitive

Table 5. Multivariate logistic regression analysis of factors that influence atherosclerotic renal artery stenosis in 220 patients with negative results by Doppler scanning*

	OR	95% CI	*p*
Sex (female)	1.306	0.552–3.090	0.543
Age > 65 yr†	5.850	1.757–19.480	0.004
Smoking > 20 yr†	3.095	1.468–6.526	0.003
Coronary artery disease	1.521	1.042–2.220	0.030
Creatinine > 4 mg/dL (354.4 μmol/L)†	5.385	1.518–19.102	0.009
Creatinine clearance	1.001	0.960–1.044	0.960
Effective renal perfusion	0.998	0.990–1.005	0.524
Constant	0.107		0.040

**All the variance inflation factor values in this analysis were < 4; †cut-off values for age, smoking duration and creatinine were calculated by receiver operating characteristic curves before logistic regression. OR = odds ratio; CI = confidence interval.*

for detection of high-grade RAS.[39] The severity of most RDS-undiagnosed cases (154 of 222 renal arteries) of ARAS was < 50% in the present study, and the number of patients with > 75% RAS in the positive RDS group was significantly higher than in the negative RDS group (50% *vs.* 25.23%, $p = 0.02$), which also supports the results of Zeller et al.[39] Overall, the above limitations might account for the large variability in sensitivity and accuracy in the use of RDS for the assessment of ARAS in the present and a previous study.[12] This could also explain why only 138 of 5,950 (2.32%) patients with hypertension received a diagnoses of significant RAS using RDS in the study of Radermacher et al.[3] However, RDS is relatively inexpensive and convenient, has severity detection ability, and avoids the use of contrast media. These clear advantages, combined with the high specificity (92.37%) and reasonable positive predictive value (75.68%) demonstrated in the present study, suggest that RDS might still be the diagnostic procedure of choice for screening outpatients for ARAS. However, the 95 subjects with > 50% RAS by MRA, which was confirmed through renal artery angioplasty for diagnosis and treatment, were not randomized. Therefore, the high concordance rate of angioplasty and MRA needs further evaluation.

Although a body mass index of < 25 kg/m^2 has been reported as a predisposing factor for ARAS,[40] it was not apparent in our study; this might be related to the leaner, Asian population included in this study. In our study, cases with CAD, increased age, impaired renal function and a history of smoking had a significantly higher likelihood of being diagnosed with ARAS. In a multivariate logistic regression analysis (Table 5), age > 65 years, smoking duration, CAD and Scr > 4 mg/dL were significant and independent factors for ARAS in the negative RDS but positive MRA patients. These factors reflect risk factors for generalized vascular disease,[41–45] therefore, it is appropriate to recommend MRA for those deemed to be at high risk for vascular disease, in circumstances when RAS is considered likely on a clinical basis.

In conclusion, RDS might still be the diagnostic procedure of choice for screening outpatients for ARAS. It is inexpensive and convenient, offers severity detection, and avoids the use of contrast media. When RDS is negative in aged people who have smoked for > 20 years, with CAD or Scr > 4 mg/dL, MRA is recommended for further evaluation of ARAS.

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References

1. Krumme B, Donauer J. Atherosclerotic renal artery stenosis and reconstruction. *Kidney Int* 2006;37:1184–90.
2. Safian RD, Textor S. Renal-artery stenosis. *N Engl J Med* 2001; 344:431–42.
3. Radermacher J, Chavan A, Bleck J, Vitzthum A, Stoess B, Gebel MJ, Galanski M, et al. Use of Doppler ultrasonography to predict the outcome of therapy for renal artery stenosis. *N Engl J Med* 2001;344:410–7.
4. Hansen KJ, Edwards MS, Craven TE, Craven TE, Cherr GS, Jackson SA, Appel RG, et al. Prevalence of renovascular disease in the elderly: a population based study. *J Vasc Surg* 2002;36: 443–51.

5. Wilms G, Marchal G, Peene P, Baert AL. The angiographic incidence of renal artery stenosis in the arteriosclerotic population *Eur J Radiol* 1990;10:195–7.
6. Jean WJ, al-Bitar I, Zwicke DL, Port SC, Schmidt DH, Bajwa TK. High incidence of renal artery stenosis in patients with coronary artery disease. *Cathet Cardiol Diagn* 1994;32:8–10.
7. Zoccali C, Mallamaci F, Finocchiaro P. Atherosclerotic renal artery stenosis: epidemiology, cardiovascular outcomes, and clinical prediction rules. *J Am Soc Nephrol* 2002;13:S179–83.
8. Iglesias JI, Hamburger RJ, Feldman L, Kaufman JS. The natural history of incidental renal artery stenosis in patients with aortoiliac vascular disease. *Am J Med* 2000;109:642–7.
9. Schwartz CJ, White TA. Stenosis of the renal artery: an unselected necropsy study. *BMJ* 1964;2:1415–21.
10. Uzu T, Inoue T, Fujii T, Nakamura S, Inenaga T, Yutani C, Kimura G. Prevalence and predictors of renal artery stenosis in patients with myocardial infarction. *Am J Kidney Dis* 1997;29:733–8.
11. Sawicki PT, Kaiser S, Heinemann L, Frenzel H, Berger M. Prevalence of renal artery stenosis in diabetes mellitus: an autopsy study. *J Intern Med* 1991;229:489–92.
12. Berland LL, Koslin DB, Routh WD, Keller FS. Renal artery stenosis: prospective evaluation of diagnosis with color duplex US compared with angiography. *Radiology* 1990;174:421–3.
13. Desberg AL, Paushter DM, Lammert GK, Hale JC, Troy RB, Novick AC, Nally JV, et al. Renal artery stenosis: evaluation with color Doppler flow imaging. *Radiology* 1990;177:749–53.
14. Postma CT, van Aalen J, de Boo T, Rosenbusch G, Thien T. Doppler ultrasound scanning in the detection of renal artery stenosis in hypertensive patients. *Br J Radiol* 1992;65:857–60.
15. Spies KP, Fobbe F, El-Bedewi M, Wolf KJ, Distler A, Schulte KL. Color-coded duplex sonography for noninvasive diagnosis and grading of renal artery stenosis. *Am J Hypertens* 1995;8:1222–31.
16. Olin JW, Piedmonte MR, Young JR, DeAnna S, Grubb M, Childs MB. The utility of duplex ultrasound scanning of the renal arteries for diagnosing significant renal artery stenosis. *Ann Intern Med* 1995;122:833–8.
17. Zierler RE, Bergelin RO, Isaacson JA, Strandness DE Jr. Natural history of atherosclerotic renal artery stenosis: a prospective study with duplex ultrasonography. *J Vasc Surg* 1994;19:250–8.
18. Levin A, Linas S, Luft FC, Chapman AB, Textor S; ASN HTN Advisory Group. Controversies in renal artery stenosis: a review by the American Society of Nephrology Advisory Group on Hypertension. *Am J Nephrol* 2007;27:212–20.
19. Khong TK, Missouris CG, Belli AM, MacGregor GA. Regression of atherosclerotic renal artery stenosis with aggressive lipid lowering therapy. *J Hum Hypertens* 2001;15:431–3.
20. Wang F, Wang M, Liu YC, Wang HY. The changing etiology and therapeutic situation of atherosclerotic renal artery stenosis. *Nat Med J Chin* 2005;85:2762–6.
21. Dorros G, Jaff M, Mathiak L, Dorros II, Lowe A, Murphy K, He T. Four-year follow up of Palmaz-Schatz stent revascularization as treatment for atherosclerotic renal artery stenosis. *Circulation* 1998;98:642–7.
22. Erley CM. Does hydration prevent radiocontrast-induced acute renal failure? *Nephrol Dial Transplant* 1999;14:1064–6.
23. Fishbane S, Durham JH, Marzo K, Rudnick M. N-acetylcysteine in the prevention of radiocontrast-induced nephropathy. *J Am Soc Nephrol* 2004;15:251–60.
24. Merten GJ, Burgess WP, Gray LV, Holleman JH, Roush TS, Kowalchuk GJ, Bersin RM, et al. Prevention of contrast-induced nephropathy with sodium bicarbonate: a randomized controlled trial. *JAMA* 2004;291:2328–34.
25. Vasbinder GB, Nelemans PJ, Kessels AG, Kroon AA, Maki JH, Leiner T, Beek FJ, et al. Renal Artery Diagnostic Imaging Study in Hypertension (RADISH Study Group). Accuracy of computed tomographic angiography and magnetic resonance angiography for diagnosing renal artery stenosis. *Ann Intern Med* 2004;141:674–82.
26. Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. *Am J Kidney Dis* 2002;39:930–6.
27. Bartholomew BA, Harjai KJ, Dukkipati S, Boura JA, Yerkey MW, Glazier S, Grines CL, et al. Impact of nephropathy after percutaneous coronary intervention and a method for risk stratification. *Am J Cardiol* 2004;93:1515–9.
28. Prince MR, Arnoldus C, Frisoli JF. Nephrotoxicity of high-dose gadolinium compared to iodinated contrast. *J Magn Reson Imaging* 1996;6:162–6.
29. Ng YY, Lee RC, Shen SH, Kirk GA. Gadolinium associated nephrogenic systemic fibrosis: double dose, not single dose. *AJR Am J Roentgenol* 2007;188:w582.
30. Golding LP, Provenzale JM. Nephrogenic systemic fibrosis: possible association with a predisposing infection. *AJR Am J Roentgenol* 2008;190:1069–75.
31. Reilly RF. Risk for nephrogenic systemic fibrosis with gadoteridol (ProHance) in patients who are on long-term hemodialysis. *Clin J Am Soc Nephrol* 2008;3:747–51.
32. Chrysochou C, Buckley DL, Dark P, Cowie A, Kalra PA. Gadolinium-enhanced magnetic resonance imaging for renovascular disease and nephrogenic systemic fibrosis: critical review of the literature and UK experience. *J Magn Reson Imaging* 2009;29:887–94.
33. Schoenberg SO, Knopp MV, Londy F, Krishnan S, Zuna I, Lang N, Essig M, et al. Morphologic and functional magnetic resonance imaging of renal artery stenosis: a multireader tricenter study. *J Am Soc Nephrol* 2002;13:158–69.
34. White CJ, Olin JW. Diagnosis and management of atherosclerotic renal artery stenosis: improving patient selection and outcomes. *Nat Clin Pract Cardiovasc Med* 2009;3:176–90.
35. Pedersen EB. New tools in diagnosing renal artery stenosis. *Kidney Int* 2000;57:2657–77.
36. Bakker J, Beutler JJ, Elgersma OEH, de Lange EE, de Kort GAP, Beek FJA. Duplex ultrasonography in assessing restenosis of renal artery stents. *Cardiovasc Intervent Radiol* 1999;22:475–80.
37. Kuntz KM, Polak JF, Whittemore AD, Skillman JJ, Kent C. Duplex ultrasound criteria for the identification of carotid stenosis should be laboratory specific. *Stroke* 1997;28:597–602.
38. Alexandrov AV, Vital D, Brodie DS, Hamilton P, Grotta JC. Grading carotid stenosis with ultrasound: an interlaboratory comparison. *Stroke* 1997;28:1208–10.
39. Zeller T, Bonvini RF, Sixt S. Color-coded duplex ultrasound for diagnosis of renal artery stenosis and as follow-up examination after revascularization. *Cath Cardiovasc Intervent* 2008;71:995–9.
40. Krijnen P, van Jaarsveld BC, Steyerberg EW, Man in 't Veld AJ, Schalekamp MA, Habbema JD. A clinical prediction rule for renal artery stenosis. *Ann Intern Med* 1998;129:705–11.
41. Valentine RJ, Clagett P, Miller GL, Myers SI, Martin JD, Chervu A. The coronary risk of unsuspected renal artery stenosis. *J Vasc Surg* 1993;18:433–40.
42. Orth SR. Smoking and the kidney. *J Am Soc Nephrol* 2002;13:1663–72.
43. Shurrab AE, Mamtora H, D'Donoghue D, Waldek S, Kalra PA. Increasing the diagnostic yield of renal angiography for the diagnosis of atheromatous renovascular disease. *Br J Radiol* 2001;74:213–8.
44. MacDowall P, Kalra PA, O'Donoghue DJ, Waldek S, Mamtora H, Brown K. Risk of morbidity from renovascular disease in elderly patients with congestive cardiac failure. *Lancet* 1998;352:13–6.
45. Louie J, Isaacson JA, Zierler RE, Bergelin RO, Strandness DE Jr. Prevalence of carotid and lower extremity arterial disease in patients with renal artery stenosis. *Am J Hypertens* 1994;7:436–9.