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Evaluation of duplex ultrasound and captopril renography for detection of renovascular hypertension

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Background. Renovascular hypertension is the most common form of curable secondary hypertension and, if untreated, may lead to end-stage kidney disease. Given that renal function and hypertension may improve after renal angioplasty, it is pertinent to identify patients with renal artery stenosis. The aim of the present study was to evaluate both duplex ultrasound and captopril renography for detection of renal artery stenosis among hypertensive patients.

Methods. To avoid selection bias, all patients referred to our center for evaluation of renovascular hypertension were asked to participate in the study. Patients were examined by intra-renal duplex ultrasound ($N = 121$), measuring pulsatility index and acceleration of the blood flow during early systole. In 98 patients, ^{99m}Tc-DTPA captopril renography was performed in conjunction with duplex ultrasound. Renal angiography was performed in all patients regardless of the results of the noninvasive tests.

Results. The prevalence of renal artery stenosis was 19%. In the 98 patients examined by both duplex ultrasound and captopril renography, sensitivity and positive predictive values for detection of a renal artery stenosis of 50% degree or more were 84 and 76%, respectively, for duplex ultrasound, whereas captopril renography was associated with a sensitivity and positive predictive value of 68% for both (P = NS). Specificity and negative predictive values were 94 and 96%, respectively, for duplex ultrasound, whereas the corresponding values for captopril renography were 92% for both (P = NS). Specificity and negative predictive values were 94 and 96%, respectively, for duplex ultrasound, whereas the corresponding values for captopril renography were 92% for both (P = NS).

Conclusions. Both duplex ultrasound and captopril renography are associated with high specificity and negative predictive values for detection of renal artery stenosis. Sensitivity and positive predictive values are at least as good for duplex ultrasound compared with captopril renography. Given that duplex ultrasound is easier to perform and more cost effective, we propose that it should be the method of first choice when screening for renal artery stenosis in a hypertensive population.

Key words: diagnosing hypertension, renal artery stenosis, noninvasive testing, cardiovascular mortality.

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Renovascular hypertension is the most common form of curable secondary hypertension, constituting 1% or less of patients presenting with hypertension [1]. Renovascular disease that is not always accompanied with hypertension is associated with high cardiovascular mortality [2, 3]. There is also emerging evidence to support renovascular disease as being a common cause of end-stage kidney disease [4]. Given that renal function and hypertension may improve after renal angioplasty, it is pertinent to identify the patients with renal artery stenosis [5, 6].

Renal angiography is necessary for a definite diagnosis of a renal artery stenosis. However, the functional significance of the stenotic lesion cannot be assessed by angiography, and the examination is both invasive and expensive. The noninvasive methods captopril renography and Doppler ultrasound are also utilized for detection of functional renal artery stenosis. There are, however, limitations to both of these latter methods, and at present, it is unclear whether captopril renography or duplex ultrasound should be used as the method of first choice when screening for renal artery stenosis in a population of patients with hypertension.

The present study was undertaken to evaluate prospectively captopril renography and duplex ultrasound examination of the intra-renal arterial circulation for detection of renal artery stenosis. Scanning of the intrarenal arterial circulation detects changes in the velocity profile of the blood flow downstream from the stenotic lesion [7, 8]. By using this method, the success rate is higher compared with direct scanning of the blood flow within the stenotic lesion of the main renal artery, and results could be obtained in almost all patients [7, 9]. When evaluating diagnostic tests, it is crucial to select a study population relevant to the population of patients

to whom the test should be applied in the clinical setting. In addition, all study patients should undergo renal angiography, regardless of the results of the noninvasive tests. If patients are selected for renal angiography on the basis of the results of the noninvasive testing, there is an obvious risk of selection bias and an overestimation of test efficacy. Most previous studies evaluating captopril renography and duplex ultrasound have been carried out in populations of hypertensives with a higher prevalence of renal artery stenosis compared with what prevails in clinical practice [8, 10]. Consequently, the study populations may not have been representative for hypertensives undergoing testing for renovascular hypertension in general. Furthermore, in several studies the inclusion criteria were poorly defined, and some patients had apparently been selected for renal angiography on the basis of the noninvasive test results [8, 10, 11]. There are recent data suggesting that the efficacy of captopril renography in detection of renal artery stenosis is not as good as was initially believed when the test is applied in a large unselected material of hypertensives, referred for evaluation of renovascular hypertension [12].

Hence, in order to avoid selection bias, the present study encompassed all hypertensive patients referred to our clinic for evaluation of renovascular hypertension who were willing to participate. Importantly, renal angiography was carried out in all patients regardless of the results of the noninvasive tests.

METHODS

Subjects

The local ethical committee and the radiation committee at Sahlgrenska University Hospital, Göteborg, Sweden, approved the study, and all subjects gave their consent to participate. The study material comprised patients with hypertension who were referred for investigation of renovascular hypertension. All patients who were referred to the Department of Clinical Physiology, Sahlgrenska University Hospital ($N = 270$), were asked to participate in the study, and 121 (74 males and 47 females) accepted. Their mean age was 54 ± 1 years. The referring physicians were specialists in family practice ($N = 30$) and were hospital-based specialists ($N = 91$), including specialists in cardiology, nephrology, and rheumatology. To mimic the clinical setting, the responsible physician decided whether testing was justified. In Sweden, the following criteria are most commonly used when selecting hypertensive patients for further testing regarding renovascular disease: severe hypertension with target organ damage, absence of family history for hypertension, symptoms of vascular disease elsewhere, or elevation of serum creatinine during treatment with angiotensin-converting enzyme (ACE) inhibitors. Patients with severe renal impairment (serum creatinine ≥200 μmol/L) were excluded. Initially, the study involved an evaluation of duplex ultrasound compared with renal angiography for detection of renal artery stenosis. After six months, there was a change in the clinical testing procedure, and hence, Doppler ultrasound was performed in conjunction with captopril renography in 98 patients.

Clinical examination

All patients who were accepted to participate in the study underwent a clinical examination by a specialist in nephrology, including a comprehensive medical questionnaire and routine serum biochemistry prior to the other investigations.

Duplex ultrasound

All patients were examined by duplex ultrasound prior to the captopril renography and the renal angiography using an Acuson 128 XP (Acuson Corp., Mountain View, CA, USA) equipment. Antihypertensive medication was continued, except for ACE inhibitors and angiotensin II receptor blockers, which were withheld five days prior to the investigation of both captopril renography and duplex ultrasound. Experienced technicians performed the investigation with the patient in the lateral decubitus position. After B-scanning for determination of the kidney size, renal arterial blood flow velocities were localized within the interlobar renal artery using a 3.5 MHz sector probe and color Doppler ultrasound. The pulsed Doppler registered blood flow velocity spectra for at least four to eight seconds with the patient holding breath at the end of a normal expiration. During the examination, at least four measurements in different interlobar arteries, covering the upper pole, the midportion, and the lower pole of each kidney, were registered, and an average value was calculated. The pulsatility index (PI) was calculated according to the formula:

$$\text{PI} = (\text{peak systolic velocity} - \text{end diastolic velocity})/\text{mean velocity during a cardiac cycle}$$

A side-to-side difference of >0.20 was used as a criterion for a renal artery stenosis (lower PI in the stenotic kidney). In addition, acceleration of the blood flow velocity during early systole [13] was measured, and an acceleration of the blood flow <2.3 m/sec^2 was used as a criterion for renal artery stenosis. When planning the present study, we decided that the specificity for a clinically useful diagnostic test should be at least 90% for detection of a renal artery stenosis ≥50% according to renal angiography. Given that this condition was fulfilled, the cut-off values were established retrospectively. Both the PI and the acceleration index were calculated using the software of the ultrasound equipment. Figure

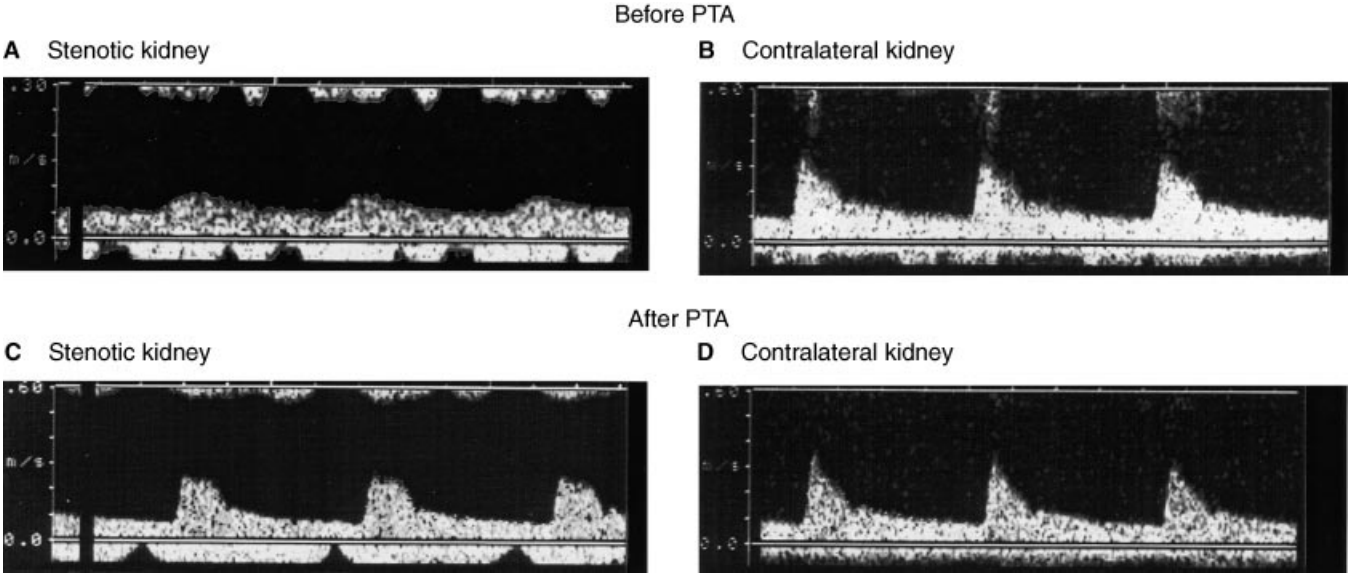

Fig. 1. Doppler velocity spectra registered downstream from the stenotic lesion within the interlobar renal artery in a stenotic (*A* and *C*) and the contralateral kidney (*B* and *D*) before (A and B) and one day after (C and D) percutaneous transluminal angioplasty (PTA). Both acceleration of the blood flow during early systole and the pulsatility index (PI) were reduced within the stenotic kidney compared with the contralateral kidney. After PTA, both acceleration and PI within the stenotic kidney increased.

1 is showing a Doppler velocity spectra registered downstream from the stenotic lesion within the interlobar renal artery in a stenotic and in the contralateral kidney before and one day after percutaneous transluminal angioplasty (PTA).

Renography

Captopril renography was performed on the same occasion as the duplex ultrasound examination prior to renal angiography in 98 patients. The procedure was carried out in accordance with the guidelines given in the consensus report on ACE inhibitor renography for detection of renovascular hypertension [14]. We used a two-day protocol with renography one hour after 50 mg of captopril given orally. Patients with normal findings on captopril renography were not examined further, whereas patients with abnormal captopril renograms were re-examined one to two weeks later without administration of an ACE inhibitor. Patients were hydrated during the hour preceding the investigation by giving 10 mL water per kg body weight by mouth. Antihypertensive medication was continued, except for ACE inhibitors and angiotensin II receptor blockers, which were withheld five days prior to the investigation. Renographic examinations were performed in the supine position with the back of the patient against a large field γ camera (APEX 415, Elscint, Israel) in order to visualize the kidneys and the heart. Ninety-six frames (64×64 pixels) of 10 seconds each were recorded after an intravenous bolus injection of 100 MBq $^{99}Tc^{m}$-DTPA. Time-activity curves for the regions of interest over the kidneys were created. Renograms were corrected for the extrarenal background after normalization for kidney area. Relative function was estimated by means of the uptake index [15]. Cortical renograms were generated using parenchyma regions of interest that excluded activity in the calyces and pelvis. The single kidney glomerular filtration rate was estimated by the uptake index method [15], and cortical mean transit times were calculated according to the matrix method [16]. Two independent physicians, who were blinded with regard to the angiography results, performed evaluation of the renograms.

The renograms were classified according to the consensus report on ACE inhibitor renography [14] in low, intermediate, or high probability for renovascular hypertension. Normal captopril renograms or renograms with slightly prolonged excretion (grade 1 that did not change after ACE inhibition) were considered to represent low probability for renovascular hypertension, provided that the relative uptake exceeded 30% for any kidney [14]. A renogram with relative function of one kidney $\leq$30% or markedly prolonged excretion ($\geq$grade 2) that did not change after renography, a reduction in relative uptake $\geq$5% or a change $\geq$1 renogram grades in cortical renograms (prolonged cortical transit-times) after ACE inhibition renography compared with basal renography were classified as intermediate/high probability. Intermediate- or high-probability renograms were considered diagnostic for significant renal artery stenosis and renovascular hypertension.

Renal angiography

The radiological diagnosis of renal artery stenosis was established by digital renal subtraction angiography us-

ing a Philips DSI machine with a 512 matrix. By the Seldinger technique, a 5F ratchet-shaped pigtail catheter was placed in the aorta, and a 35 mL contrast medium (sodium meglumine ioxaglate 160 mgJ/mL; Guerbet, Roissy Charles de Gaulle Cedex, France) was injected at a speed of 25 mL/s. Three pictures per second were recorded during the arterial phase. Definite documentation was processed on film through a laser converter. The remaining lumen in the stenosis was measured in millimeters down to a minimum of 0.5 mm and given as a fraction of the ordinary lumen of the renal artery. The angiographic pictures were reviewed independently by two radiologists. If disagreement regarding the grading of a renal artery stenosis was found, a third radiologist reviewed the angiographic picture, and the majority made the decision. Radiological significant renal artery stenosis was defined as ≥50% lumen reduction, and a lumen reduction >70% was considered as a severe renal artery stenosis.

Follow-up

Patients with renal artery stenosis who underwent renal angioplasty were followed up to one year after the intervention. The following criteria were used to define a successful outcome one year after intervention based on mean systolic and mean diastolic blood pressure (DBP) measurements on separate days registered with the cuff method during hospital stay: (*1*) A patient was considered cured if renal angioplasty was followed by normotension, defined as mean DBP ≤90 mm Hg without treatment. (*2*) A patient was considered improved if satisfactory blood pressure control (mean DBP ≤95 mm Hg) was maintained with a 50% reduction in antihypertensive treatment index according to Delin, Aurell, and Granerus [17], or with a mean DBP reduction of ≥20 mm Hg with unchanged medication. (*3*) The remaining patients were not successfully treated with renal angioplasty.

Statistical methods

Results are expressed as means ± SEM values. Student's *t*-tests for unpaired observations were used. Parameters not normally distributed were transformed logarithmically before the parametric test. If a non-normal distribution was retained, the Mann–Whitney *U*-test for unpaired comparisons was used. Comparisons of proportions were carried out using cross-tabulation and Fischer's exact test. Sensitivity, specificity, and predictive values were determined using the Four-Fold Table and for comparison of paired proportions, the McNemar's test was used. Statistical significance was defined as $P < 0.05$.

Table 1. Demographic data for patients with renal artery stenosis ≥50% according to angiography and primary hypertensives

	Renal artery stenosis ($N = 23$)	Primary hypertension ($N = 98$)
Systolic blood pressure *mm Hg*	167 ± 6	163 ± 3
Diastolic blood pressure *mm Hg*	88 ± 5	92 ± 1
Serum cholesterol *mmol/L*	6.3 ± 0.4	5.7 ± 0.1
Serum sodium *μmol/L*	139 ± 0.4	139 ± 0.3
Serum potassium *μmol/L*	3.6 ± 0.3[c]	4.0 ± 0.1
Serum creatinine *μmol/L*	103 ± 6	104 ± 2
Treatment		
Beta-blocker treatment %	61	54
Diuretics %	39	36
Calcium channel blocker %	48	61
ACE inhibitor[a] %	48	50
≥3 Antihypertensive drugs %	39	32
Adequate blood pressure control[b] %	65	65
Concomitant diseases		
Coronary heart disease %	35[c]	12
Congestive heart failure %	4	3
Cerebrovascular lesion %	4	4
Intermittent claudication %	26[d]	4
Diabetes mellitus %	17	5
Smoker %	45	30

[a] Or angiotensin II receptor blocker
[b] According to the referring physician
[c,d] Statistical difference, $P < 0.05$ and $P < 0.01$, respectively

RESULTS

Renal artery stenosis ≥50% according to renal angiography was found in 23 patients giving a prevalence of 19% (16% among patients referred by specialists in internal medicine and 36% among patients referred by specialists in family practice, P = NS). In 14 patients, the narrowing of the stenotic lesion was >70%. One patient had a stenosis in a branch of the main renal artery. Two patients had stenosis in accessory renal arteries, and another two patients had bilateral renal artery stenosis. Fibromuscular dysplasia was found in four patients. One patient had a renal artery stenosis caused by an injury of the renal artery after lower abdominal surgery, and 18 patients showed atherosclerotic vascular disease. The prevalence of overt coronary disease (previous myocardial infarction or treatment for angina pectoris) and intermittent claudication were higher in patients with renal artery stenosis compared with primary hypertensives ($P < 0.05$; Table 1), whereas medical treatment, blood pressure control, and renal function did not differ (Table 1). Renal angioplasty with a successful angiographic result was carried out in 19 of 23 patients with renal artery stenosis, and hypertension was cured or improved in 12 of these patients.

An adequate duplex ultrasound examination was achieved in all patients ($N = 121$). The mean size of stenotic kidneys ($N = 25$) was lower compared with nonstenotic kidneys ($N = 217$, 10.1 ± 0.2 vs. 11.4 ± 0.1 cm in nonstenotic kidneys, $P < 0.01$). Both PI and acceleration of the blood flow were higher in nonstenotic

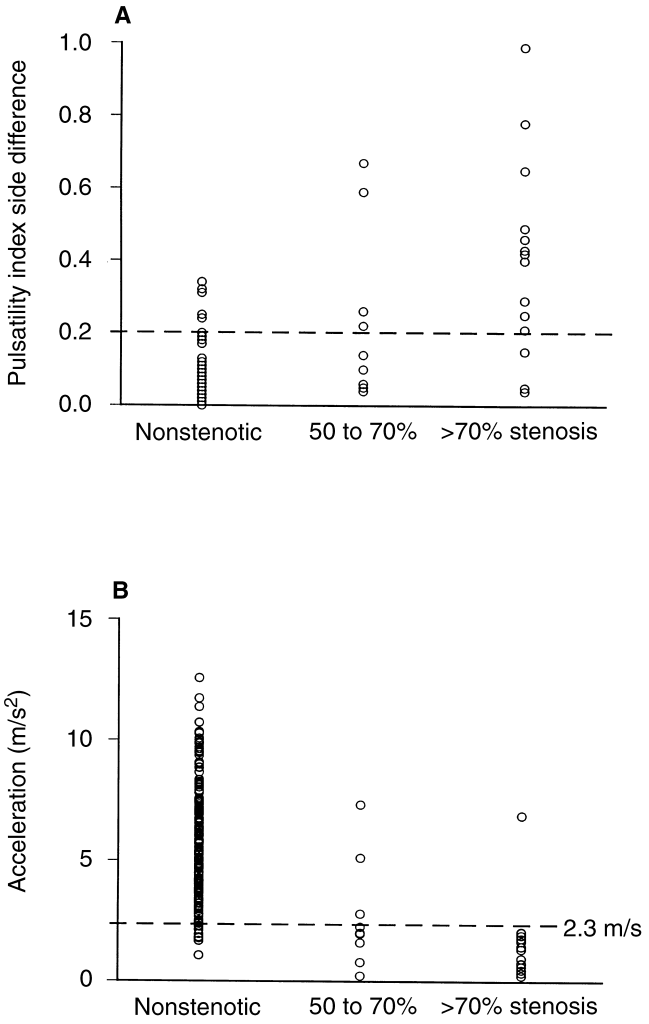

Fig. 2. Graph showing the absolute values for the side-to side difference of interlobar renal arteries in patients with normal (< 50% stenosis) renal angiography (N = 98), 50 to 70% stenosis (N = 9), and >70% stenosis of the renal artery (N = 14). The cut-off values, chosen on the basis of a ≥90% specificity for detection of a renal artery stenosis ≥50 were a PI side difference >0.20 and an acceleration <2.3 m/s^2.

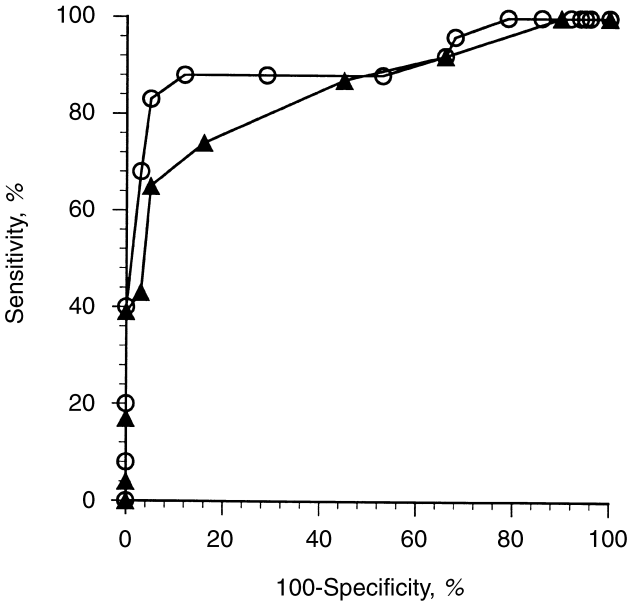

Fig. 3. Receiver operating characteristic (ROC) curves (N = 242 kidneys) showing sensitivity for detection of a renal artery stenosis ≥50% vs. 1-specificity for different acceleration (○) and PI (▲) cut-off values. The area under curve was somewhat larger for acceleration of the blood flow compared with the PI side difference criteria.

Table 2. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of Doppler measurements for detection of renal artery stenosis ≥50% according to renal angiography (N = 121)

	Sensitivity	Specificity	NPV	PPV
		%		
ΔPI	65	95	92	75
Acceleration	83	95	96	79
ΔPI + acceleration	87	92	97	71

A side-to-side difference of the pulsatility index (PI) >0.20 and an acceleration <2.3 m/sec^2 of the velocity during early systole, registered within the interlobar renal arteries were used as criteria for renal artery stenosis. Sensitivity, specificity, NPV, and PPV are calculated as percentages based on the number of stenoses ≥50% in 121 angiographically controlled subjects (23 with RAS ≥ 50%).

kidneys compared with kidneys with a renal artery stenosis (1.10 ± 0.02 and 5.6 ± 0.2 m/s^2 in nonstenotic kidneys vs. 0.96 ± 0.05 and 2.0 ± 0.4 m/s^2 for stenotic kidneys, PI and acceleration, respectively, $P < 0.01$ for both; Fig. 2). Sensitivity for detection of renal artery stenosis ≥50% was somewhat higher for acceleration of the intra-renal blood flow compared with PI, and acceleration correctly identified 13 of 14 patients with renal artery stenosis ≥70% (Table 2). Combination of the two measurements slightly increased sensitivity (Table 2), and 10 of 12 patients with renovascular hypertension, defined as cure or improvement of hypertension after renal angioplasty were correctly identified. The area under the receiver operating curve (ROC) showing sensitivity for detection of a renal artery stenosis ≥50% versus 1-specificity for different acceleration and PI cut-off values was somewhat larger for acceleration of the blood flow compared with the PI side difference criteria (Fig. 3).

In patients undergoing both duplex ultrasound and captopril renography, 19 had a renal artery stenosis of ≥50% according to renal angiography, and 13 had a stenotic lesion >70%. All of these patients were examined after captopril administration, and in 31 patients, a basal examination without prior ACE inhibitor administration was performed one to two weeks after the captopril renography. Stenotic kidneys showed reduced single kidney glomerular filtration rate (22 ± 4 vs. 37 ± 1 mL/min · 1.73 m^2 for nonstenotic kidneys, $P < 0.01$) and prolonged cortical transit times (3.6 ± 0.3 vs. 2.8 ± 0.05

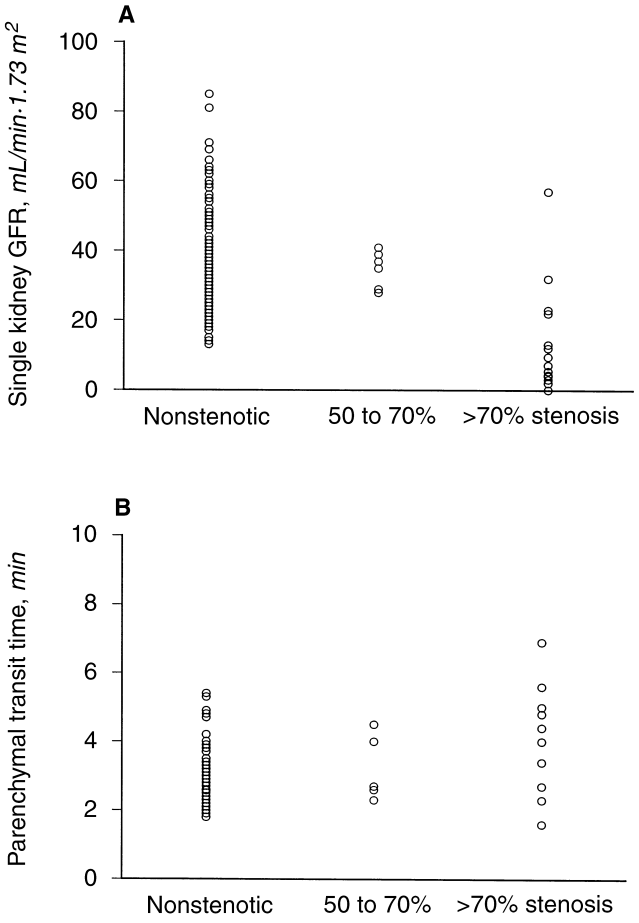

Fig. 4. Graphs showing individual values for (*A*) single kidney glomerular filtration rate (GFR) estimated by γ camera renography after captopril administration using ^{99m}Tc-DTPA and (*B*) cortical mean transit time. Values for patients with normal (<50% stenosis) renal angiography (N = 79), 50 to 70% stenosis (N = 6), and >70% stenosis of the renal artery (N = 13) are shown separately.

min for nonstenotic kidneys, $P < 0.01$; Fig. 4). Specificity and negative predictive values were high for both duplex ultrasound and renography, whereas sensitivity and positive predictive values for detection of a renal artery stenosis ≥50% were somewhat higher (P = NS) for duplex ultrasound compared with renography (Table 3). Renography criteria were positive in five of nine patients with proven renovascular hypertension, whereas Doppler ultrasound correctly identified eight of these patients (P = NS). Sensitivity for detection of renal artery stenosis ≥70% was 85% for renography compared with 92% for ultrasound (P = NS). Combination of the duplex ultrasound and renography methods increased sensitivity for detection of a renal artery stenosis ≥50% from 84 to 89%, whereas 11 of 12 patients with proven renovascular hypertension were correctly identified without changing specificity.

Table 3. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of Doppler measurements and gamma camera renography (DTPA) for detection of renal artery stenosis ≥50% according to renal angiography

	Sensitivity	Specificity	NPV	PPV
		%		
Doppler	84	94	96	76
Renography[a]	68	92	92	68

[a] Renography criteria according to the Consensus Report on ACE Inhibitor Renography [14] and doppler criteria as defined in Table 2 (ΔPI > 0.20 and/or acceleration <2.3 m/s^2). Sensitivity, specificity, NPV. and PPV are calculated as percentages based on the number of stenoses ≥50% in 98 angiographically controlled subjects (19 with RAS = 50%).

DISCUSSION

The prospective design and consequent use of renal angiography in all patients, regardless of the findings of the noninvasive tests, firmly establish high specificity and negative predictive values for both intra-renal duplex ultrasound and captopril renography in the detection of a renal artery stenosis. Moreover, both tests were applied to a study material consisting of all hypertensive patients referred to our center for evaluation of renovascular hypertension who were willing to participate. Thus, the study material was appropriate with regard to the population to which our findings will be referred. Although the sensitivity for detection of renal artery stenosis was somewhat higher for duplex ultrasound compared with captopril renography, there were some patients with renovascular hypertension (defined as cure or improvement of hypertension) in whom both tests failed to correctly identify the renal artery stenosis.

Early studies of duplex ultrasound for detection of renal artery stenosis used the technique of directly measuring the peak velocity within the main renal artery [9]. Although the initial results were impressive, this method was limited by technical failure in 10 to 20% of patients examined. We, as well as others, have used duplex ultrasound examination of the intra-renal arteries for detection of renal artery stenosis [7, 18, 19]. This technique is less time consuming compared with direct scanning of the main renal arteries, and technical failures are uncommon [7, 8]. Recently, Riehl et al reported in 214 hypertensives (53 with renal artery stenosis) a sensitivity of 92% and specificity of 96% for detection of renal artery stenosis >70%, using a reduction in resistive index within the interlobar arteries of stenotic kidneys [20]. Furthermore, Krumme et al reported the results of a prospective study of 135 hypertensives using a combination of intra-renal and extra-renal scanning, and found a sensitivity of 89% and specificity of 92% for detection of a renal artery stenosis ≥50% according to angiography [8]. The authors emphasized the importance of scanning the main renal artery. However, they used only a side-to-side difference in a resistive index, in contrast to

both PI and acceleration of the early systolic velocity used in the present study. Moreover, in their study, some patients were selected on the basis of the Doppler findings, and a high prevalence of renal artery stenosis (65%) was reported, suggesting the possibility of selection bias [8]. Our data suggest that the results of extra-renal duplex scanning could be improved by examination of blood flow velocities within the interlobar renal arteries by means of measuring the PI and acceleration of the blood flow velocity during early systole. Acceleration of the blood flow during early systole was the most valuable measurement for detection of renal artery stenosis in the current study. This observation corroborates with the findings of Burdick et al [21] and Malatino et al [22], who both reported superiority of acceleration over PI as a screening test for renal artery stenosis. The cut-off values for diagnosis of renal artery stenosis by acceleration reported in those studies were higher compared with the present study. We registered velocity spectra within the interlobar renal arteries, whereas Burdick et al and Malatino et al measured acceleration within the distal portion of the main renal artery or within the segmental vessels [21, 22]. In a pilot study (unpublished), we registered velocity spectra both within the segmental and the interlobar renal arteries. The early systolic acceleration within the segmental arteries was somewhat higher compared with acceleration measured within the interlobar renal arteries, whereas PI values did not differ. Thus, differences regarding the cut-off values between the studies mentioned previously in this article and the present could be explained by measuring acceleration within a more distal site of the renal arterial tree in the present study.

For captopril renography, sensitivity was only 68% for detection of a renal artery stenosis ≥50%, whereas specificity and negative predictive values were high. Most studies evaluating captopril renography for detection of renal artery stenosis have reported higher sensitivity values compared to the present study [10, 14, 23]. Considering the high prevalence of renal artery stenosis in most previous studies of captopril renography, one may question whether the study populations were representative for hypertensive patients referred for evaluation of renovascular hypertension in general [10, 14, 23]. In a large series of hypertensives examined by captopril renography, van Jaarsveld et al recently reported a sensitivity of 68% for the detection of renal artery stenosis ≥50% [12]. The sensitivity did not differ whether DTPA or mertiatide (MAG-3) was used. Moreover, in the largest prospective study of captopril renography study, including 380 hypertensive patients, the sensitivity for detection of renal artery stenosis ≥70% was 83% [11]. Collectively, our data concerning sensitivity of captopril renography in detection of renal artery stenosis corroborate with the largest studies that have evaluated captopril renography for the detection of renal artery stenosis [11, 12].

There are few studies that have directly compared duplex ultrasound and captopril renography. By direct scanning of the main renal artery, Miralles et al found a sensitivity of 87% for duplex ultrasound compared with 45% for captopril renography in the detection of a renal artery stenosis ≥50% among hypertensive patients having concomitant aortoiliac disease [24]. Only 16 patients in that study were examined because of clinical suspicion of renovascular hypertension, and the prevalence of renal artery stenosis was high (58%). Pedersen et al reported 75% sensitivity for both intra-renal Doppler ultrasound and captopril renography in the detection of renal artery stenosis ≥50% [25]. In their study, the ultrasound examination was not optimized since the examinations were performed by all doctors at the department, including doctors in training, and only a side-to-side difference in resistive index and kidney size were measured. The study is of importance, however, since selection criteria were appropriate, implying that all patients referred were eligible for inclusion. Hence, renal artery stenosis was found in 28 of 131 hypertensives examined giving a prevalence of 21%, which is comparable to the 19% prevalence found in the present study.

In the patient population examined by both duplex ultrasound and captopril renography ($N = 98$), duplex ultrasound correctly identified 16 of 19 patients with renal artery stenosis. The cost for a duplex ultrasound investigation at our laboratory is $134. Thus, the cost for correctly identifying one patient with renal artery stenosis by duplex ultrasound in the present population of hypertensives was $821. The cost for γ camera renography using ^{99m}Tc-DTPA at our laboratory is $267. In 31 patients, a basal examination without prior ACE inhibitor administration was performed one to two weeks after the captopril renography. Overall, 129 renography examinations were performed to correctly identify 13 of 19 patients with renal artery stenosis, and hence, the cost for identifying one patient with renal artery stenosis by captopril renography was $2649. Since the number of false positives was similar for duplex ultrasound and captopril renography, duplex ultrasound was more cost-effective in identifying patients with renal artery stenosis compared with captopril renography.

Some authors have advocated the use of clinical criteria to identify high-risk patients and to proceed directly to renal angiography [26]. Our results support the usefulness of selecting hypertensive patients for further investigations on the basis of signs of concomitant atherosclerotic vascular disease such as coronary heart disease or peripheral arterial insufficiency. In contrast to what has been proposed by Derkx et al, our results do not support the usefulness of therapy resistant hypertension or elevated serum creatinine (up to 200 μmol/L) when

selecting patients for renal angiography [26]. It is, however, important to point out that duplex ultrasound correctly identified 10 of 12 patients with proven renovascular hypertension, whereas captopril renography only identified 5 of 9 patients. Hence, both methods failed to detect all individuals who improved after renal angioplasty. Consequently, renovascular hypertension may prevail in spite of negative noninvasive test results, and renal angiography should be considered if there is a strong clinical suspicion of secondary hypertension.

Study limitations

Patients with markedly reduced renal function were not included in the present study. This is an important subgroup, considering ischemic nephropathy as a common cause of end-stage kidney disease [4]. The contrast medium used at angiography may further impair renal function and hence, noninvasive methods for detection of renal artery stenosis are especially important for these patients. Unfortunately, there is uncertainty about the efficacy of both captopril renography and duplex ultrasound in this group of patients. There are data indicating that captopril renography may be associated with lower sensitivity and specificity for detection of renal artery stenosis among patients with reduced renal function [11]. Intra-renal duplex examination is often technically difficult in patients with renal failure, but in most cases, it is possible to obtain Doppler signals of good enough quality to permit interpretation. Echocontrast agents that enhance Doppler signals may prove especially valuable in these patients [18]. Preliminary data from our group, regarding echocontrast-enhanced scanning of the intra-renal circulation in patients with renal failure, suggest that sensitivity is comparable to the data of the present study (Johansson, unpublished observations).

Although medication with ACE inhibitors were withheld five days prior to the captopril renography, there are data suggesting that the use of ACE inhibitors may reduce the sensitivity of the captopril renography several months after cessation of the medication [27]. Half of our study population was on chronic treatment with an ACE inhibitor or an angiotensin II receptor blocker, and one may argue that this treatment could have reduced sensitivity of the captopril renography. From a clinical point of view, it is impossible to withhold these antihypertensives for more than five days, and hence, we advocate that captopril renography was evaluated in a relevant setting. On the other hand, ACE inhibitors may improve the diagnostic accuracy of the intra-renal duplex ultrasound examination [28, 29]. Thus, a persisting effect of the ACE inhibitors on the tissue-bound renin-angiotensin system could have improved the sensitivity for diagnosis of renal artery stenosis by duplex ultrasound.

In conclusion, both duplex ultrasound and captopril renography are associated with high specificity and negative predictive values for detection of renal artery stenosis, whereas sensitivity appears higher for duplex ultrasound. Although it is operator dependent, duplex ultrasound is at least as accurate as captopril renography, more cost-effective, and easier to perform since antihypertensive medication could be continued during the examination. Thus, we consider duplex ultrasound the first choice method when screening for renovascular hypertension. Captopril renography is valuable for estimation of split renal function when deciding whether renal angioplasty should be performed.

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