Detection of Renal Artery Stenosis with Doppler Sonography Before and After Administration of Captopril: Value of Early Systolic Rise

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OBJECTIVE. The goal of this study was to assess the value of quantitative and qualitative analysis of the early systolic rise on Doppler waveforms obtained before and after administration of captopril in patients suspected of having renal artery stenosis.

SUBJECTS AND METHODS. Seventy-one hypertensive patients (135 kidneys) were studied with transrenal Doppler sonography. Ninety-six kidneys were studied again after administration of captopril. All patients also underwent renal angiography. All Doppler studies were independently reviewed by two observers. Specific criteria for Doppler waveform patterns that were applied in the detection of renal artery stenosis included acceleration, acceleration time of early systolic rise, differential velocity of systolic rise, and resistive index. These criteria were then correlated with angiography, and receiver operating characteristic curves were generated.

RESULTS. On the basis of waveform pattern recognition, Doppler sonograms obtained before administration of captopril had a sensitivity of 81% and a specificity of 98% for the detection of renal artery stenosis greater than or equal to 50%. Sensitivity of Doppler sonography obtained after administration of captopril was 100%, and specificity was 100%. For renal artery stenosis greater than or equal to 70%, sensitivity was 94% and specificity was 89% before administration of captopril. The area under the receiver operating characteristic curve for the acceleration criterion was significantly larger after administration of captopril (p = .009) for the detection of renal artery stenosis greater than or equal to 50%. After captopril administration, an acceleration threshold value of 440 cm/sec^2 for early systolic rise was associated with a sensitivity of 100% and a specificity of 94% for the detection of renal artery stenosis greater than or equal to 50%.

CONCLUSION. Doppler sonography of the renal arteries performed before administration of captopril appears to be an excellent screening tool in the detection of severe stenosis (≥70%). Administration of captopril improves the detection of renal artery stenosis greater than or equal to 50% with Doppler sonography when observers use both morphologic and quantitative criteria.

The high prevalence of hypertension in the general population and the low percentage (1–5%) of a curable renovascular cause translates into problems in selecting patients for invasive studies and potential revascularization [1]. Much attention has been given in the recent literature to Doppler sonography as a means of detecting renal artery stenosis. Direct evaluation of the proximal renal artery with color Doppler sonography has been disappointing in terms of sensitivity and specificity for renal artery stenosis detection, with a low rate of technical success varying between 58% and 69% because of obesity or overlying bowel gas [2, 3]. Furthermore, this technique has proven to be inadequate for identifying accessory renal arteries, which are present in approximately 20% of patients [2–4]. Encouraging results were initially obtained with the analysis of the Doppler waveform in the intrarenal circulation distal to a potential stenosis using a transrenal approach [5–8]. Because intrarenal arteries are anatomically suitable for Doppler interrogation, technical failures occur in only 0–2% of kidneys studied [5, 7, 8]. The most typical abnormal waveform consists of alterations described as "pulsus tardus et parvus" (a delayed early systolic acceleration with low amplitude peak) described by Kotval [9] as occurring in the carotid artery. Doppler waveform abnormalities included the absence of

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the normal early systolic peak that had been reported as a reliable criterion for the evaluation of renal artery stenosis [7]. Other researchers have reported excellent results using the acceleration index for detecting renal artery stenosis [5, 6, 10]. Unfortunately, these results have been difficult to reproduce, and some have discouraged the use of Doppler sonography as a screening tool for renal artery stenosis [11].

More recent studies have reported new observations concerning Doppler arterial waveform changes distal to a stenosis. In an experimental model, Bude et al. [12] demonstrated that the degree of pulsus tardus increased as the compliance of the poststenotic vessel increased, independent of the transstenotic pressure gradient. These findings are supported by an experimental model developed by Halpern et al. [13] that showed the loss of the early systolic peak of a compliant vessel as being a normal finding. The use of captopril administration has been recently reported to improve the sensitivity of Doppler sonography for detecting renal artery stenosis [14]. The goal of our study was to further assess the value of intrarenal Doppler sonography with and without captopril with morphologic criteria based on the early systolic rise and also to determine quantitative criteria for renal artery stenosis detection.

Subjects and Methods

Study Population

Between March 1994 and June 1996, 71 consecutive hypertensive patients (135 kidneys) underwent Doppler sonography of the renal arteries and renal angiography in our institution to evaluate the possibility of renovascular hypertension. The present study is a continuation of our initial evaluation of Doppler sonography of the renal arteries with captopril, and the study population includes the 31 patients previously reported [14]. Patient selection was based on either of the following clinical criteria: severe hypertension (malignant hypertension, grade 3 or 4 hypertensive retinopathy, hypertensive encephalopathy, or diastolic blood pressure >115 mm Hg); uncontrolled hypertension (systolic blood pressure >160 mm Hg or diastolic blood pressure >95 mm Hg despite maximal doses of three antihypertensive agents); onset of hypertension before 25 years old or after 45 years old; onset of hypertension within the past 2 years; acceleration of hypertension by 15% within the preceding 6 months; or auscultation of an abdominal or flank bruit. The population included 32 males and 39 females who were 16–81 years old (mean age, 61 years). Among these 71 patients, 48 underwent a second Doppler sonographic examination of the renal arteries 1 hr after receiving an oral dose of 25 mg of captopril. Blood pressure monitoring after administration of captopril was abandoned in this study because no significant blood pressure variations were observed in our initial experience. The selection of patients for captopril administration was based on the absence of exclusion criteria for captopril administration: creatinine clearance of less than 40 ml/min (0.67 ml/sec), hyperkalemia (K^+ > 5.5 mEq/l [5.5 mmol/l]), solitary kidney, history of stroke or transient ischemic attack with a carotid bruit, or a history of allergy to captopril or other angiotensin-converting enzyme inhibitors. All patients underwent an angiogram within 3 months of the Doppler examination. The project was readily approved by the Department of Radiology and the ethics committee of our institution.

Doppler Study

The examinations were performed by three operators, all of whom used a Spectra sonography unit (Diasonics, Milpitas, CA) equipped with a 3.5-MHz phased-array sector transducer. Intrarenal arteries were identified by color flow imaging using a posterior oblique approach, and spectral waveforms were obtained at an angle of insonation of less than 60°. In addition, our instrument was set for the smallest velocity scale, the lowest wall filter, and a sweep time of 2 sec. Spectral tracings were obtained from segmental arteries at the superior, mid (anterior and posterior), and inferior portions of the kidney. No time restriction was imposed on the examiners for completion of the examination; the average time for the Doppler examination was approximately 20 min. When Doppler sonography was performed after the administration of captopril, the Doppler examination was repeated 1 hr after an oral dose of 25 mg of captopril based on the recommendations for radionuclide studies [15]. Peak blood concentrations of captopril are reached after 45–60 min, and the elimination half-life of unchanged captopril is approximately 2 hr [16]. The most abnormal (provided that it was reproducible) Doppler tracing was selected by the examiner for each kidney before and after administration of captopril. Each Doppler spectrum obtained was morphologically classified by two independent observers into one of three categories that we predetermined according to our experience (Fig. 1). Type A represents normal tracings with an early systolic peak and a steep linear early systolic rise. Type B includes normal tracings without an early systolic peak but with a steep linear early systolic rise. Type C represents abnormal tracings with a decrease of the early systolic rise.

The reading was performed on the most optimal Doppler spectrum for each kidney by two independent investigators who were unaware of the angiographic results. For each selected spectrum, the resistive index, differential velocity of systolic rise (δv), and acceleration time of systolic rise (t) were measured using electronic calipers, thereby allowing calculation of the acceleration ($a = \delta v / t$).

Angiographic Study

Angiography was performed within 3 months of Doppler sonography using conventional arteriography or digital subtraction angiography. All studies were performed using a femoral artery approach with a 5-French pigtail catheter. Arteriography of the abdominal aorta was performed in a posteroanterior projection with a right posterior oblique projection if necessary. The examinations were sometimes

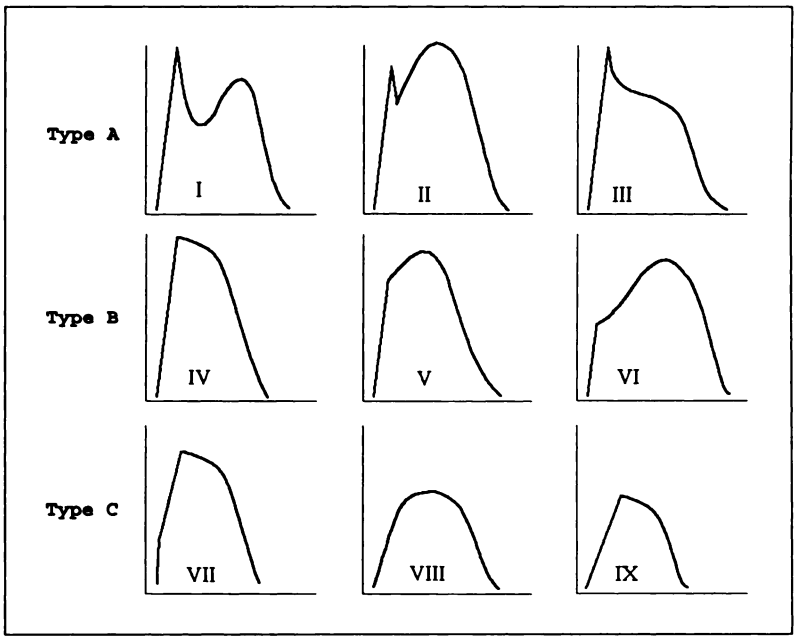

Fig. 1.—Doppler waveform patterns. Types A and B waveforms show normal Doppler spectra. In type A, note peak at end of early rise. In type B, no peak occurs, but rise remains straight. Note that waveform VI is considered normal despite high compliance peak. This type of waveform is most often seen in patients younger than 50 years old. Type C waveforms show abnormal spectra with varying degrees of slowed early rise.

completed with selective renal arteriograms. All angiograms were interpreted by the same staff radiologist. The percentage of diameter reduction was calculated with a precision caliper and a magnifying lens. Renal arteries were classified into one of three categories: severe stenosis group (≥70% diameter reduction), moderate stenosis group (50–69% diameter reduction), and normal group (<50% diameter reduction). In cases of multiple renal arteries, the kidney was classified according to the most stenotic artery. The angiographic studies were interpreted by an investigator who was unaware of the results of the Doppler examination.

Statistical Analysis

Statistical analysis of the data was performed using SPSS/PC+ (SPSS, Chicago, IL) and BMDP (BMDP Statistical Software, Los Angeles, CA) statistical software packages. A statistically significant difference was considered to exist at a p value of less than or equal to .05 for all tests performed.

We correlated the distribution of the angiographic stenoses with the Doppler findings according to their distribution among the three morphologic spectral groups in the population of 135 kidneys studied without captopril administration and in the population of 96 kidneys studied before and after administration of captopril. Pooling of types A and B constitute the normal Doppler group and type C, the positive Doppler group. Sensitivity and specificity values for the detection of renal artery stenosis greater than or equal to 50% and renal artery stenosis greater than or equal to 70% based on pattern recognition were calculated for each population group.

To test the interobserver agreement on the application of morphologic Doppler criteria, a kappa coefficient was calculated for each population group. Receiver operating characteristic (ROC) curves were generated for the early systolic acceleration, the acceleration time in the population of 135 kidneys studied without captopril, and in the population of 96 kidneys studied before and after administration of captopril. The area under the curve was calculated and the results were compared using the z test of Hanley and McNeil [17]. To give guidelines to the readers, threshold values were computed for each variable; these threshold values were chosen to obtain the best overall accuracy while maximizing the sensitivity. In the group of renal artery stenosis greater than or equal to 50%, the mean values for the acceleration, the acceleration time, the differential velocity, and the resistive index were compared before and after the administration of captopril using a two-way analysis of variance for repeated measures.

Results

Table 1 summarizes the qualitative and quantitative analysis of the Doppler sonography data for the precaptopril group of 135 kidneys. Table 2 summarizes those analyses of the Doppler sonography data for the pre- and postcaptopril group of 96 kidneys. All Doppler examinations were technically successful for all patients in both groups, for a technical success rate of 100%.

TABLE 1 Doppler Sonography of 135 Kidneys Before Administration of Captopril

Analysis	Renal Artery Stenosis	
	≥50%	≥70%
Morphologic		
Sensitivity (%)	81	94
Specificity (%)	98	89
Area under ROC curve		
Acceleration (cm/sec^2)	.876	.914
Acceleration time (sec)	.870	.870
Velocity ratio (cm/sec)	.709	.772
Resistive index (%)	.542	.570

Note.—ROC = receiver operating characteristic.

TABLE 2 Doppler Sonography of 96 Kidneys Before and After Administration of Captopril for Detecting Renal Artery Stenosis[a]

Analysis	Captopril	
	Before	After
Morphologic		
Sensitivity (%)	81	100
Specificity (%)	99	100
Area under ROC curve		
Acceleration (cm/sec^2)	.883	.984
Acceleration time (sec)	.901	.967
Velocity ratio (cm/sec)	.629	.688
Resistive index (%)	.531	.547

Note.—ROC = receiver operating characteristic.
[a] ≥50%.

Pattern Recognition

Precaptopril population.—One hundred thirty-five kidneys were studied in this group. Among the 135 kidneys, 87 had no significant stenosis of their renal arteries, 16 had a moderate (50–69%) stenosis, and 32 had a severe (≥70%) stenosis. The correlation of Doppler sonography with angiography based on pattern recognition of the waveform for the detection of renal artery stenosis greater than or equal to 50% and renal artery stenosis greater than or equal to 70% is detailed in Table 1. For the detection of renal artery stenosis greater than or equal to 50%, Doppler sonography obtained a sensitivity of 81%, a specificity of 98%, a positive predictive value of 90%, and a negative predictive value of 99%. For the detection of severe (≥70%) renal artery stenosis, Doppler sonography had a sensitivity of 94%, a specificity of 89%, a positive predictive value of 73%, and a negative predictive value of 98%. If we consider the detection of moderate (50–69%) stenosis exclusively, sensitivity was 56% and specificity was 99%. Overall, the interobserver agreement for the recognition of all Doppler waveforms in the precaptopril group based on their classification into normal (types A and B) and abnormal (type C) was $\kappa = .96$.

Pre- and postcaptopril population.—Table 2 summarizes the Doppler sonography results correlated with the angiographic findings in this group of 96 kidneys with 70 normal arteries, 11 moderate (50–69%) renal artery stenoses, and 15 severe (≥70%) renal artery stenoses. On the basis of morphologic criteria, Doppler sonography before the administration of captopril obtained a sensitivity of 81% and a specificity of 99% for the detection of renal artery stenosis greater than or equal to 50%, whereas Doppler sonography after the administration of captopril obtained a sensitivity of 100% and a specificity of 100%, with a significant difference between the test performance for studies before and after the administration of captopril ($p = .031$, one-tailed test). A one-tailed test was justified here because our goal was to verify that captopril could improve the performance of Doppler sonography for detecting renal artery stenosis. In these conditions, similar results for the Doppler revelation of renal artery stenosis before and after the administration of captopril would be sufficient to prove captopril useless. Only one stenotic accessory artery was present in this series in the severe (≥70%) category. The stenotic accessory artery was detected with Doppler studies both before and after the administration of captopril. In this population group, of the 11 moderate (50–69%) renal artery stenoses, seven (64%) were detected with Doppler sonography before the administration of captopril and 11 (100%) after the administration of captopril.

In the normal (<50%) artery group, one kidney was falsely classified as abnormal with Doppler sonography before the administration of captopril but was correctly diagnosed after the administration of captopril. Among the nonstenotic kidneys, 13 had type B waveforms (normal without systolic peak) before the administration of captopril, 11 of which changed to type A configuration (with systolic peak) after the administration of captopril (Table 3). The interobserver agreement in the pre- and postcaptopril population was $\kappa = .95$.

TABLE 3 Distribution of Doppler Waveform Patterns Before and After Administration of Captopril in 70 Kidneys Without Renal Artery Stenosis

Type of Doppler Sonography	Waveform Pattern		
	Type A	Type B	Type C
Before captopril	56	13	1
After captopril	68	2	0

Quantitative Analysis

Precaptopril population.—Pertinent values are summarized in Table 1 for this group of 135 kidneys examined without captopril administration. For the detection of renal artery stenosis greater than or equal to 50%, the acceleration threshold was determined at 473.64 cm/sec^2 for a sensitivity of 81% and a specificity of 90%. The area under the ROC curve was .876. Similarly, the threshold value for the acceleration time was decided at 0.05 sec for a sensitivity of 75% and a specificity of 91%. The area under the ROC curve was .870.

For the detection of renal artery stenosis greater than or equal to 70%, an acceleration threshold of 390 cm/sec^2 determined a sensitivity of 91% and a specificity of 86%, with an ROC curve area of .914 (Fig. 2). For the same category of stenosis, an acceleration time threshold of 0.08 sec yielded a sensitivity of 84% and a specificity of 91%, with an ROC curve area of .870. A differential velocity threshold of 21.8 cm/sec determined a sensitivity of 75% and a specificity of 71%, with an ROC curve area of .772; a resistive index threshold of 63% determined a sensitivity of 50% and a specificity of 72%, with an ROC curve area of .570.

Pre- and postcaptopril population.—The following results are based on the 96 kidneys that were studied before and after the administration of captopril. For each quantitative criterion, the average measurement for the stenotic group (≥50%) was calculated before and after administration of captopril (Table 4). A statistically significant variation occurred of the average acceleration (p = .01), acceleration time (p = .02), and resistive index (p = .018) for the renal artery stenosis group after the administration of captopril. The average differential velocity of systolic rise did not change significantly.

An acceleration threshold of 390 cm/sec^2 determined a sensitivity of 77% and a specificity of 93% for the detection of renal artery stenosis greater than or equal to 50% before the administration of captopril. The area under the ROC curve was .8836 (Fig. 3). In comparison, after the administration of captopril, an acceleration threshold of 440 cm/sec^2 was associated with a sensitivity of 100% and a specificity of 94% for the detection of renal artery stenosis greater than or equal to 50%. The area under the ROC curve was substantially improved to .9847 (Fig. 4). This improvement after the administration of captopril was highly significant (p = .009). For the detection of renal artery stenosis greater than or equal to 70%, the areas under the ROC curve before and after the administration of captopril were not significantly different (p = .39).

An identical analysis was performed with the acceleration time for the renal artery stenosis group (≥50%). The area under the ROC curve before administration of captopril was .901. Before administration of captopril, Doppler sonography resulted in a sensitivity of 77% and specificity of 97%, for a threshold value of 0.065 sec. After the administration of captopril, a threshold value of 0.095 sec determined a sensitivity of 81% and a specificity of 97%. The area under the ROC curve after administration of captopril was .9666. However, the improvement of the area under the ROC curve after the administration of captopril was not statistically significant (p = .06).

For the detection of renal artery stenosis greater than or equal to 50% before the administration of captopril, a differential velocity threshold of 29.5 cm/sec determined a sensitivity of 61% and a specificity of 56%, with an ROC curve area of .629; and a resistive index threshold of 68% determined a sensitivity of 58% and a specificity of 43% with an ROC curve area of .531. After captopril, a differential velocity threshold of 28 cm/sec yielded a sensitivity of 65% and a specificity of 62%, with an ROC curve area of .688; and a resistive index threshold of 69% determined a sensitivity of 54% and a specificity of 55%, with a ROC curve area of .547.

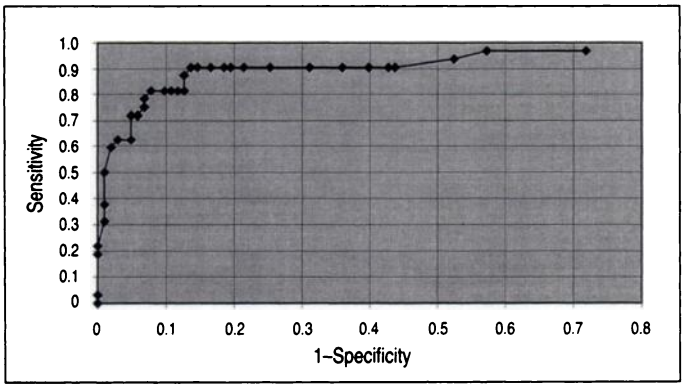

Fig. 2.—Receiver operating characteristic (ROC) curve for acceleration measured with Doppler sonography performed without administration of captopril in 135 kidneys with renal artery stenosis that equals or exceeds 70% diameter reduction. Area under ROC curve is large (.914) and specificity remains acceptable for high sensitivity values.

Discussion

Analysis of the intrarenal Doppler waveform for renal artery stenosis detection is still controversial. Waveform alteration in the presence of renal artery stenosis was initially attributed to the transstenotic pressure drop created by the stenosis [6, 10]. More recently, two Doppler studies [12, 13] conducted in experimental models showed that waveform alterations are produced by complex interactions between poststenotic compliance and resistance to flow. Halpern et al. [13] showed that the systolic portion of the waveform is made of two components, an early peak and a late compliance peak. These components can be affected separately, but it is suggested that the early peak reflects the transmitted pulsation. This information is important for the understanding and the selection of Doppler criteria for renal artery stenosis detection. This information also implies that the early systolic rise is a determinant component of the Doppler spectrum for detecting renal artery stenosis, which supports our criteria selection.

The waveform pattern approach that we used was based on the analysis of the early systolic upstroke. Our results confirm that the absence of an early systolic peak is not an indicator of renal artery stenosis as previously suggested in the literature [11, 13]. Our mor-

phologic classification differs from the criteria described by others. In the classification used by Kliewer et al. [18], a waveform is considered to be abnormal or equivocal when an abrupt change is seen at the end of the early systolic rise, forming an obtuse angle and rising above the early upstroke. Conversely, we consider only the early rise to be significant regardless of the later compliance peak (type B). Abnormal waveforms are determined by a slowed early systolic acceleration, the emphasis being on the most initial portion of the rise and not on the summit of the wave (type C). This approach allowed us to obtain an excellent angiographic correlation.

Among the population of 135 kidneys studied without captopril administration, we obtained a high sensitivity for the detection of severe (≥70%) renal artery stenosis with an acceptable false-positive rate for a screening test and an excellent interpretation reproducibility. The detection of moderate renal artery stenosis remains problematic, but the clinical significance of such moderate stenoses is still uncertain.

We also obtained satisfactory results with quantitative criteria, particularly the acceleration. This measurement represents the slope of the early systolic upstroke. Conflicting results have been reported in the literature concerning quantitative criteria. Several authors have used an acceleration index with success [5, 6, 10]. However, discouraging results were obtained by Kliewer et al. [11] using the systolic acceleration. These results may be explained by the method of measurement, specifically in defining the end point of the systolic acceleration. In the work by Kliewer et al., the systolic acceleration ends at the first systolic peak. Conversely, our definition of the early systolic acceleration is independent of the systolic peak. In type B waveforms, an early systolic peak is not present. In this category, tracings V and VI (Fig. 1) are considered normal, and the systolic peak is part of the late compliance peak. On the basis of our definition, we found the acceleration to be a helpful measurement for the diagnosis of renal artery stenosis, especially with the determination of threshold values, leading to a sensitivity of 81% for the detection of renal artery stenosis greater than or equal to 50% and a sensitivity of 91% for the detection of renal artery stenosis greater than or equal to 70%.

TABLE 4 Average Values of Variables Measured with Doppler Sonography Performed Before and After Administration of Captopril in 26 Kidneys with Renal Artery Stenosis[a]

Variable	Before Captopril	After Captopril	p
Acceleration (cm/sec^2)	324.88	211.98	.010
Acceleration time (sec)	0.118	0.144	.021
Resistive index (%)	69.46	66.41	.018
Velocity ratio (cm/sec)	26.42	25.34	.541

[a] ≥50%.

Consequently, Doppler sonography of the intrarenal circulation may be a valuable tool for the detection of renal artery stenosis (particularly ≥70%) using morphologic or quantitative criteria. The conflicting results found in the literature could be explained largely by the different interpretations of the systolic acceleration as well as disagreements concerning morphologic criteria.

Recently, the value of intrarenal Doppler sonography has been seriously challenged by van der Hulst et al. [19]. In this study, Doppler measurements were obtained with endovascular flow wires at the site of the stenosis and in the distal intrarenal circulation. Those authors were quick to conclude that intrarenal Doppler sonography evaluation has no diagnostic value and that duplex Doppler sonography is not a suitable screening test for renal artery stenosis. However, their definition of renal artery stenosis was based on invasive pressure gradients and not on angiographic measurement. In addition, the value of pressure gradients in their study can be questioned because the measurement of these gradients implies the presence of a catheter inside the artery, which further reduces the effective cross-sectional area of the residual lumen. Furthermore, the validity of the Doppler spectrum obtained with endovascular flow wires has not been established. The intrarenal vascular bed is prone to catheter-induced spasm, which could easily alter the Doppler data.

Few data are available on captopril-induced alterations of the renal Doppler signal. Pretolesi et al. [20] documented significant increases of peak systolic and diastolic intrarenal blood flow velocities with Doppler sonography after oral administration of captopril in normotensive patients. René et al. [14] reported an increased sensitivity of Doppler

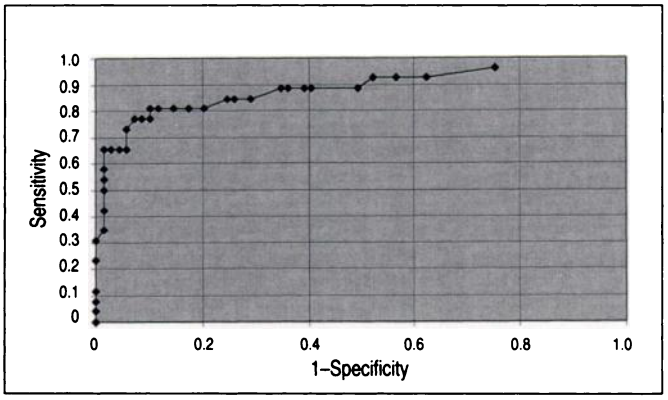

Fig. 3.—Receiver operating characteristic (ROC) curve for acceleration measured with Doppler sonography performed before administration of captopril in 96 kidneys with renal artery stenosis that equals or exceeds 50% diameter reduction. Area under ROC curve measures .8836.

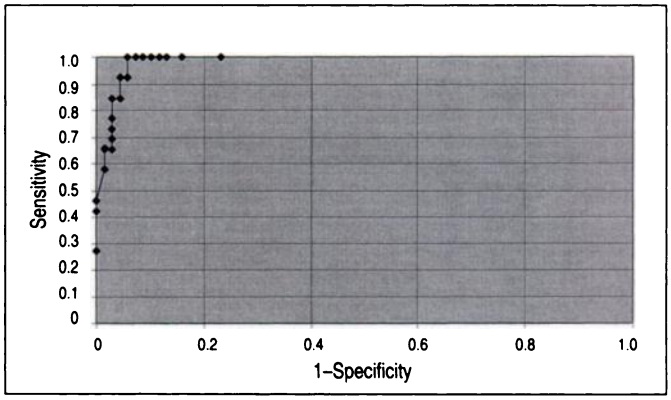

Fig. 4.—Receiver operating characteristic (ROC) curve for acceleration measured with Doppler sonography performed after administration of captopril in 96 kidneys with renal artery stenosis equal to or exceeding 50% diameter reduction. Area under ROC curve measures .9847, which is significantly greater (p = .009) than that under curve for sonography performed before administration of captopril (.8836).

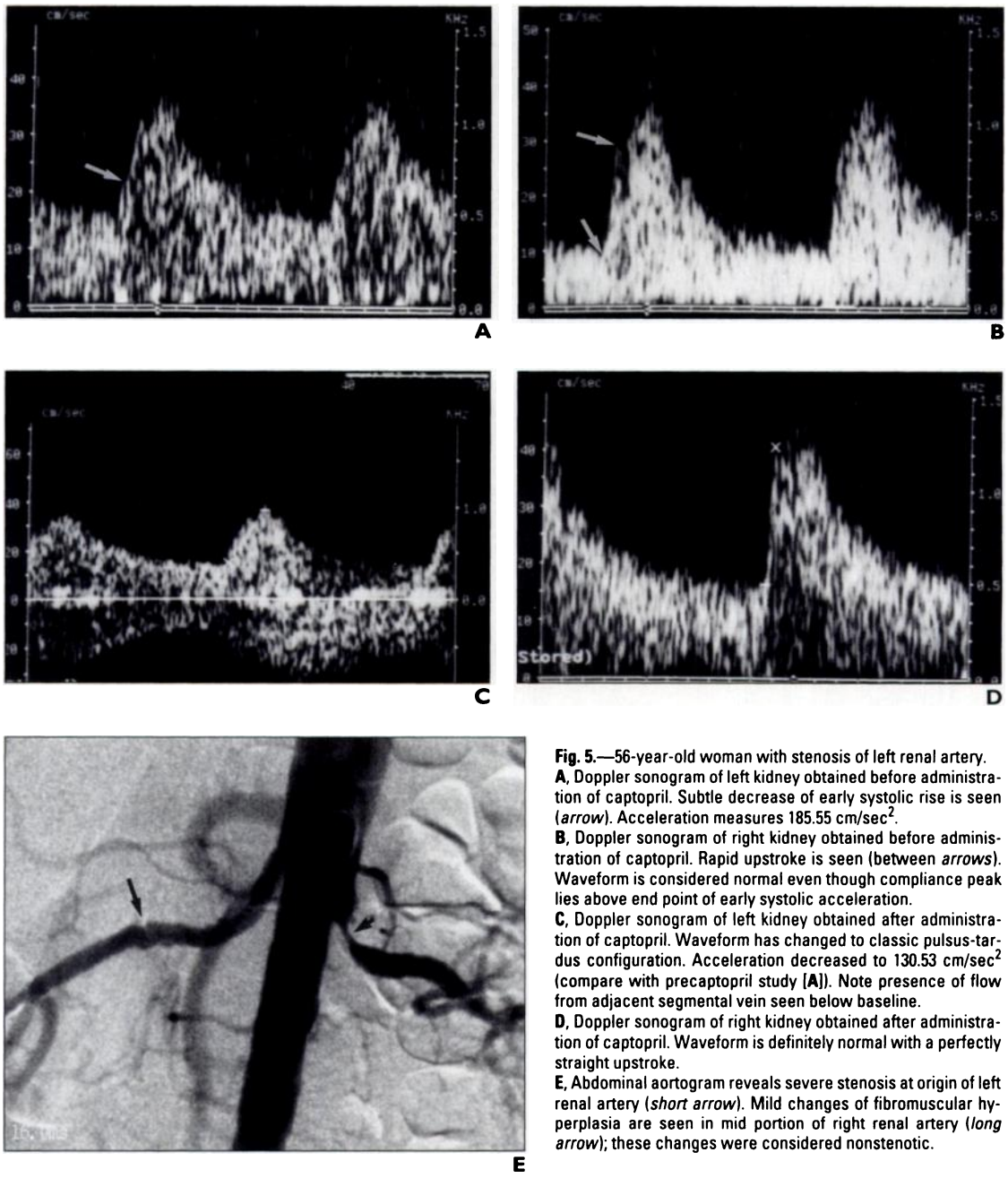

Fig. 5.—56-year-old woman with stenosis of left renal artery.
A, Doppler sonogram of left kidney obtained before administration of captopril. Subtle decrease of early systolic rise is seen (*arrow*). Acceleration measures 185.55 cm/sec^2.
B, Doppler sonogram of right kidney obtained before administration of captopril. Rapid upstroke is seen (between *arrows*). Waveform is considered normal even though compliance peak lies above end point of early systolic acceleration.
C, Doppler sonogram of left kidney obtained after administration of captopril. Waveform has changed to classic pulsus-tardus configuration. Acceleration decreased to 130.53 cm/sec^2 (compare with precaptopril study [**A**]). Note presence of flow from adjacent segmental vein seen below baseline.
D, Doppler sonogram of right kidney obtained after administration of captopril. Waveform is definitely normal with a perfectly straight upstroke.
E, Abdominal aortogram reveals severe stenosis at origin of left renal artery (*short arrow*). Mild changes of fibromuscular hyperplasia are seen in mid portion of right renal artery (*long arrow*); these changes were considered nonstenotic.

sonography for the detection of renal artery stenosis after administration of captopril based on morphologic criteria and showed that captopril could induce or enhance the pulsus tardus phenomenon distal to a renal artery stenosis.

However, the physiologic explanation of these captopril-induced waveform changes is still unclear. Two mechanisms are possible: Captopril directly increases the compliance of the arterial wall [21], and captopril decreases the intrarenal vascular resistance by inhibiting the vasoconstrictive effect of angiotensin II [22–24]. This last mechanism was questioned by Bude et al. [4]. These researchers used an analogy with a resistance–capacitance electrical circuit in which they stated that a drop in resistance should decrease the resistance–capacitance product and increase waveform pulsatility. Because captopril lowers the peripheral vascular resistance in the kidney, Bude et al. concluded that captopril should increase waveform pulsatility and lower the degree of pulsus tardus. These researchers also stated that this theory is opposite to the observations of the initial work by René et al. [14] that captopril increases the degree of pulsus tardus distal to a renal artery stenosis. However, it is unclear in this electric circuit analogy whether the resistance represents the proximal stenosis or the resistance of the renal vascular bed. If the resistance component of the resistance–capacitance product represents the proximal stenosis as Bude et al. [12] state in their original article, then we agree that a reduction of the degree of proximal stenosis will lower the degree of pulsus tardus. We also believe that lowering the peripheral renal vascular resistance in a model in which a proximal stenosis is present will have the opposite effect and will increase the pulsus tardus. Captopril-induced pulsus tardus distal to a renal artery

stenosis is analogous to the poststenotic waveform dampening that takes place in the lower extremities after exercise-induced vasodilatation of the peripheral vessels. This theory is supported by the results of the present study in which a significant decrease of the mean resistive index is observed after the administration of captopril in the renal artery stenosis group. However, we also agree that captopril should increase the pulsatility of the Doppler waveform in a nonstenotic artery. This theory is also supported by the results of the present study in that most type B waveforms changed to type A waveforms after administration of captopril in our nonstenotic group. Unfortunately, no researchers using an experimental model have been able to verify this hypothesis. Halpern et al. [13] used a clamp that could theoretically reproduce variations of the peripheral vascular resistance in their flow model. However, these variations were used to alter the compliance of the system and not to study the effects of the peripheral resistance on the Doppler spectrum.

Because we observed no significant variation of the systemic blood pressure in our initial experience, we do not believe that captopril-induced hypotension can be retained as a mechanism for the explanation of the increased sensitivity of Doppler sonography for renal artery stenosis detection.

Our study has documented the physiologic effects of captopril on the Doppler spectrum not only by showing morphologic waveform changes but also by demonstrating significant variations of the acceleration, acceleration time, and resistive index distal to a renal artery stenosis (Fig. 5). Also, potentially useful acceleration threshold values have been determined before and after administration of captopril for renal artery stenosis detection.

Although our results are encouraging, some limitations of our work must be considered. Because the population studied is selected and because some patients referred from outside hospitals may have been screened for renal artery stenosis with other diagnostic studies, the accuracy of the technique might be overestimated. Also, all the Doppler examinations were performed by investigators who had extensive experience with renal Doppler examinations. Therefore, the reproducibility of our results remains uncertain. Lastly, we cannot comment on the specific performance of intrarenal Doppler sonography for the evaluation of accessory renal arteries because only one stenotic accessory artery was encountered in our series. We must emphasize that Doppler interrogation of the intrarenal arteries was performed in all portions of the kidneys studied, and therefore a stenotic accessory artery can be detected using our technique by identifying an abnormal Doppler signal in the corresponding portion of the kidney without the need for identifying the artery.

In conclusion, on the basis of our criteria and definition of the early systolic rise, excellent results may be obtained with a high level of interobserver agreement for the interpretation of Doppler patterns. Captopril enhances the Doppler sonography revelation of renal artery stenosis with both morphologic and quantitative criteria. The administration of captopril could be warranted in the presence of a normal Doppler sonogram when the clinical concern of finding a renal artery stenosis is high.

Acknowledgment

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References

1. Detection, evaluation, and treatment of renovascular hypertension: final report—Working Group on Renovascular Hypertension. *Arch Intern Med* **1987**;147:820–829
2. Berland LL, Koslin DB, Routh WD, Keller FS. Renal artery stenosis: prospective evaluation of diagnosis with color duplex US compared with angiography. *Radiology* **1990**;174:421–423
3. Desberg AL, Paushter DM, Lammert GK, et al. Renal artery stenosis: evaluation with color Doppler flow imaging. *Radiology* **1990**;177:749–753
4. Bude RO, Rubin JM. Detection of renal artery stenosis with Doppler sonography: it is more complicated than originally thought. *Radiology* **1995**;196:612–613
5. Handa N, Komada T. Efficacy of echo-Doppler examination for the evaluation of renovascular disease. *Ultrasound Med Biol* **1988**;14:1–5
6. Patriquin H, Lafortune M, Jaquier JC, et al. Stenosis of the renal artery: assessment of slowed systole in the downstream circulation with Doppler sonography. *Radiology* **1992**;184:479–485
7. Stavros AT, Parker SH, Yakes WF, et al. Segmental stenosis of the renal artery: pattern recognition of tardus and parvus abnormalities with duplex sonography. *Radiology* **1992**;184:487–492
8. Schwerk WB, Restrepo IK, Stellwaag M, Klose KJ, Schade-Brittinger C. Renal artery stenosis: grading with image-directed Doppler US evaluation of renal resistive index. *Radiology* **1994**; 190:785–790
9. Kotval PS. Doppler waveform parvus and tardus: a sign of proximal flow obstruction. *J Ultrasound Med* **1989**;8:435–440
10. Lafortune M, Patriquin H, Demeule E, et al. Renal arterial stenosis: slowed systole in the downstream circulation: experimental study in dogs. *Radiology* **1992**;184:475–478
11. Kliewer MA, Tupler RH, Carroll BA, et al. Renal artery stenosis: analysis of Doppler waveform parameters and tardus-parvus pattern. *Radiology* **1993**;189:779–787
12. Bude RO, Rubin JM, Platt JF, Fechner KP, Adler RS. Pulsus tardus: its cause and potential limitations in detection of arterial stenosis. *Radiology* **1994**;190:779–784
13. Halpern EJ, Deane CR, Needleman L, Merton DA, East SA. Normal renal artery spectral Doppler waveform: a closer look. *Radiology* **1995**;196: 667–673
14. René PC, Oliva VL, Bui BT, et al. Renal artery stenosis: evaluation of Doppler US after inhibition of angiotensin-converting enzyme with captopril. *Radiology* **1995**;196:675–679
15. Blaufox MD, Dubovsky EV, Hilson AJW, Taylor A Jr, de Zeeuw R. Report of the Working Party Group on determining the radionuclide of choice. *Am J Hypertens* **1991**;4:747S–748S
16. Duchin KL, McKinstry DN, Cohen AI, Migdalof BH. Pharmacokinetics of captopril in healthy subjects and in patients with cardiovascular diseases. *Clin Pharmacokinet* **1988**;14:241–259
17. Hanley JA, McNeil BJ. A method of comparing the areas under the ROC curves derived from the same cases. *Radiology* **1981**;148:839–843
18. Kliewer MA, Tupler RH, Hertzberg BS, et al. Doppler evaluation of renal artery stenosis: interobserver agreement in the interpretation of waveform morphology. *AJR* **1994**;162:1371–1376
19. van der Hulst VPM, van Baalen J, Kool LS, et al. Renal artery stenosis: endovascular flow wire study for validation of Doppler US. *Radiology* **1996**;200:165–168
20. Pretolesi F, Derchi LE, Crespi G, Biggi E, Saffioti S, Pontremoli R. Variazioni del flusso renale indotte da captopril: valutazione mediante eco Doppler. *Arch Ital Urol Nefrol Androl* **1991**;63:81–83
21. Safar ME, Laurent SL, Bouthier JD, London GM, Mimran AR. Effect of converting enzyme inhibitors on hypertensive large arteries in humans. *J Hypertens* **1986**;4:82–87
22. Nally JV, Black HR. State-of-the-art review: captopril renography—pathophysiological considerations and clinical observations. *Semin Nucl Med* **1992**;22:85–97
23. Nally JV. Renal physiology of renal artery stenosis: implications for captopril-stimulated renography. *Am J Hypertens* **1991**;4:669S–674S
24. Carmines PK, Morrison TK, Navar LG. Angiotensin II effects on microvascular diameters of in vitro blood-perfused juxtamedullary nephrons. *Am J Physiol* **1986**;251:F610–F616