Renal Atrophy and Arterial Stenosis
A Prospective Study With Duplex Ultrasound

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Abstract
Renal artery disease is an important cause of both renal failure and hypertension. Duplex ultrasound is a reliable noninvasive method for classifying the severity of renal artery lesions and can be repeated to follow the course of the disease over time. The purpose of this study was to determine the changes in kidney size associated with various degrees of renal artery disease. Serial kidney lengths were measured as part of a prospective duplex ultrasound study of patients with renal artery narrowing. Fifty-four patients (22 men, 32 women; mean age, 65.8 years) with 101 renal artery and kidney sides eligible for follow-up were evaluated at 6-month intervals for an average of 14.4 months (range, 4 to 24 months). No kidneys with renal arteries classified as normal or less than 60% diameter stenosis by duplex criteria were found to have a decrease in length of greater than 1 cm during follow-up. In kidneys with a high-grade renal artery stenosis (≥60% diameter reduction), 26% (13 of 49 sides) were found to have a decrease in length of greater than 1 cm. The average decrease in length was 1.9 cm (range, 1.2 to 3.4 cm). By life table analysis, the estimated risk of a decrease in length of greater than 1 cm for kidneys with 60% stenosis or greater was 19% at 1 year. Loss of renal mass, as documented by ultrasound measurement of kidney length, is an important consequence of high-grade renal artery stenosis.

Key Words • hypertension, renovascular • arterial occlusive diseases • renal artery obstruction, renal circulation • ultrasounds

Although renal artery stenosis is regarded as an important cause of secondary hypertension, ischemic renal disease is gaining attention as a cause of end-stage renal failure in the elderly population.1-2 Currently, an estimated 60,000 to 120,000 individuals have ischemic nephropathy in the United States.1 A recent prospective study cites renal artery occlusive disease as the cause of renal failure in 14% of patients older than 50 years who require dialysis.3 The association between an abnormally small kidney and severe renal artery stenosis is believed to represent the end result of progressive renal atrophy from renal artery atherosclerosis.4-5 A kidney length of more than 7 or 8 cm has been used as a parameter favoring revascularization in patients with renal artery stenosis.6-7 In contrast, decreasing kidney size has received little attention in the literature as a parameter for clinical follow-up and is rarely included as an indication for intervention.8

Decreasing kidney size in patients with renal artery stenosis has been reported previously in two retrospective reviews based on arteriography.9-10 A prospective study found decreasing kidney length to be the most common parameter reflecting deterioration of renal function in 41 patients followed on medical treatment.8 A progressive decrease in kidney size may be the earliest and best parameter to follow in patients with renal artery stenosis.11 Ultrasound is an accurate method for determining renal size,12 and duplex ultrasound examination of the renal arteries has been validated as a reliable noninvasive method for evaluating renal artery stenosis.13-17 Routine kidney length measurements are easily incorporated into the renal duplex examination and may provide a useful method for monitoring patients during follow-up. The objective of this study was to determine the changes in kidney length that occur in patients with atherosclerotic renal artery disease and relate these changes to the severity of renal artery stenosis.

Methods
During the period of January 16, 1990, to April 2, 1992, 83 patients were examined as part of a prospective research study on the natural history of renal artery stenosis. These patients were recruited from referrals to the Vascular Diagnostic Service at the University of Washington Medical Center. Patients who had undergone a renal duplex evaluation and who had an abnormal result with a peak systolic velocity of at least 180 cm/s in one or both renal arteries were eligible for inclusion in the natural history study. Informed consent was obtained, with approval from the Human Subjects Review Committee at the University of Washington. After the initial or baseline visit, follow-up evaluations were performed at 6-month intervals.

Patients with only a single renal duplex examination and those who were unwilling or unable to participate in the follow-up protocol were excluded from further analysis (22 patients). Two other patients were excluded because of incomplete examinations that did not allow accurate disease classification. In addition, 2 enrolled patients undergoing successful surgical intervention and 2 patients having a successful percutaneous transluminal balloon angioplasty procedure, as defined by improvement of renal artery stenosis on two successive duplex examinations, were also excluded from this report. One patient was excluded on the basis of a diagnosis of fibromuscular disease based on clinical presentation and the distal site of the stenosis. This left 54 patients with 108 potential renal artery and kidney sides. Two sides with prior nephrectomies, 3 sides with renal artery occlusion, and 1 side

Received April 30, 1993; accepted in revised form December 16, 1993.
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without a baseline renal size measurement were unavailable for analysis. Eight patients had undergone a renal artery balloon angioplasty before recruitment that was unsuccessful by both anatomic and clinical criteria. Although an unsuccessful renal artery angioplasty before or after entry into the study did not necessarily exclude a renal artery from further analysis, we did exclude 2 additional sides in patients who had undergone successful balloon angioplasties as defined by improvement of stenosis on two successive duplex examinations. This left 54 patients with 100 renal artery and kidney sides for analysis.

Among the 54 patients, 22 were men (average age, 66.6 years; range, 46 to 81 years) and 32 were women (average age, 64.2 years; range, 35 to 81 years). The average duration of follow-up was 14.4 months (range, 4 to 24 months). All patients had a history of hypertension. The average number of antihypertensive medications was 1.7 (range, 0 to 4 medications). Atherosclerotic disease in other sites was documented as follows: coronary artery disease in 37%, peripheral vascular disease in 39%, and carotid artery disease in 35% of patients. Analysis of atherosclerotic risk factors revealed diabetes mellitus in 11%, a history of elevated cholesterol in 44%, and a smoking history in 72% of patients.

Patients were examined in the morning after an overnight fast to minimize attenuation of ultrasound transmission by bowel gas. All examinations were done by the same technologist (J.A.I.), using an ATL Ultramark 9 duplex ultrasound scanner (Advanced Technology Laboratories). The technique of renal artery duplex scanning has been described in detail previously. In summary, patients were initially examined in the supine position. With the use of a longitudinal view, the aorta was examined to identify the presence of either aneurysmal or stenotic disease. Aortic velocity was measured at the level of the superior mesenteric artery. The right renal artery origin was then identified in a cross-sectional view of the aorta, and velocities were recorded from the origin and the proximal and middle segments of the artery. Similarly, the origin of the left renal artery was identified, and velocities were recorded from the origin and proximal and middle segments. The angle of insonation for all renal artery velocity measurements was 60° or less.

The degree of renal artery stenosis on each side was determined by duplex scanning according to previously validated criteria based on renal artery peak systolic velocity (PSV) and the ratio of the peak systolic velocity in the renal artery to that found in the adjacent abdominal aorta (renal-aortic ratio, or RAR). These criteria permit classification of renal artery narrowing into four categories: normal, PSV <180 cm/s; less than 60% stenosis, RAR <3.5 and PSV ≥180 cm/s; 60% stenosis or greater, RAR ≥3.5; and occluded, no identifiable renal artery flow signal. The worst disease found among the origin and proximal, middle, and distal renal artery segments defined the disease severity for that side.

At the beginning of our study we realized that kidneys could be viewed from many different approaches: a midline approach with the patient supine, a flank approach with the patient on his or her side, or a posterior approach with the patient prone. Varying kidney length measurements were obtained, depending on which approach was used. To reduce this variability, we acquired the best horizontal kidney image at each follow-up visit when reacquiring the image of the kidney. At the beginning of the study we realized that kidneys could be viewed from many different approaches: a midline approach with the patient supine, a flank approach with the patient on his or her side, or a posterior approach with the patient prone. Varying kidney length measurements were obtained, depending on which approach was used. To reduce this variability, we acquired the best horizontal kidney image at each follow-up visit when reacquiring the image of the kidney. One of our own variability study using healthy subjects, a single observer, and the same duplex scanner, a measurement threshold of greater than 0.7 cm (a value representing 2 SD from the mean) constitutes a significant change in kidney length between examinations. For the purposes of this study, kidney length changes of greater than 1 cm were considered to be significant. The overall change in kidney length was calculated as the length at the baseline visit minus the length at the last follow-up visit. Thus, changes in length for each kidney were determined using the longest possible period of observation.

Data for the renal follow-up study were entered into the PARADOX microcomputer database system (version 3.0, 1988, Borland International) and analyzed using the spss/pc (version 4.0, 1990, SPSS Inc) and bmde (program 1L, 1988, BMDE Statistical Software Inc) statistics packages. Group characteristics are reported as mean±SEM, although the testing for group differences was by the nonparametric Mann-Whitney statistic. Differences in dichotomous classifications between groups were determined using Fisher's exact test.

For 12-month risk estimates, the data were analyzed first by side, assuming statistical independence of sides with regard to changes in renal size. The data were then examined with patients, stratified by baseline disease status, as the unit of analysis to estimate the risk to an individual. Comparisons of survival curves were by the log-rank method.

**Results**

The baseline classification of renal artery stenosis by duplex scan indicated 26 normal renal arteries—25 sides with less than 60% diameter stenosis and 49 sides with 60% diameter stenosis or greater. Disease classification according to patients revealed less than 60% stenosis (bilateral or unilateral) in 13 patients, unilateral 60% stenosis or greater in 33 patients, and bilateral 60% stenosis or greater in the remaining 8 patients. All renal artery lesions involved the origin or proximal segments of the renal arteries. Baseline kidney length measurements were as follows (mean±SD): overall mean, 10.8±0.97 cm (range, 8.8 to 13.7 cm); kidneys with normal renal arteries, 10.8±0.79 cm; kidneys with less than 60% stenosis, 11.2±0.7 cm; and kidneys with 60% renal artery stenosis or greater, 10.7±1.1 cm. There were no statistically significant differences in the average duration of follow-up for sides in the various renal artery disease categories.

Comparing baseline kidney lengths with the lengths at the last follow-up visit, no kidneys with arteries classified as normal or less than 60% stenosis at baseline were found to have a decrease in length of greater than 1 cm. However, 13 kidneys in 12 patients in the 60% stenosis or greater group decreased in length by greater than 1 cm. In these kidneys, the average change in length was −1.9 cm (range, −1.2 to −3.4 cm). The remaining 36 sides with 60% renal artery stenosis or greater showed an average change in length of 0.04 cm (range, −0.83 to 1.30 cm). Fig 1 shows the mean change and 95% confidence interval for kidney length at each follow-up time point according to the renal artery disease classification at the baseline visit. The mean change and 95% confidence interval for kidney length at each follow-up time point for those kidneys with 60% renal artery stenosis or greater are shown in Fig 2, stratified according to whether or not a decrease in length of greater than 1 cm occurred between the baseline and last follow-up visits. Changes in kidney length over time for each kidney that decreased in length by greater than 1 cm are presented in Fig 3. The average rate of decrease in kidney length for those patients with a decrease of 1 cm or greater was 0.15 cm/mo (range, 0.06 to 0.27 cm/mo).
cm/mo). Both renal artery occlusions that occurred during follow-up were associated with corresponding decreases of greater than 1 cm in kidney length.

Analysis by life table shows that for sides with 60% renal artery stenosis or greater the estimated risk of a decrease in length greater than 1 cm during the first 12 months of follow-up was 19%. After 1 year of follow-up, subjects who initially presented with bilateral high-grade renal artery stenoses had approximately three times the risk of developing a smaller kidney than patients presenting with unilateral high-grade stenosis (43% versus 13%, P = .18).

Three patients had a documented increase in kidney length of greater than 1 cm at the time of last follow-up. Two of the three apparent increases did not demonstrate consistent trends of increase in size in all serial measurements. This suggests that the baseline measurement for these cases may have been inaccurate.

Discussion

The feasibility of using duplex ultrasound to characterize renal artery disease has been the topic of some debate. Although a few authors have been unable to apply the technique successfully, others have reported excellent correlations with contrast arteriography. Duplex scanning is also becoming established as an accurate noninvasive method for assessing the results of renal revascularization procedures, including aortorenal bypass, renal endarterectomy, and percutaneous transluminal angioplasty. Studies using arteriography as the gold standard have shown that the overall accuracy of duplex scanning for identifying renal artery disease is in the range of 80% to 96%. One of the main limitations of the current technique is the inability to further classify the degree of stenosis within the category of greater than or equal to 60% (60% to
The observations in the current study expand on this notion by more than 60% are expected to produce a significant drop in pressure and flow in the ipsilateral kidney. 22

Relatively few reports in the literature are concerned with decreasing kidney size in patients with renovascular disease. 6-10. Of the five natural history studies published over the past 23 years, only three have examined this issue. 810 The first of these studies, and the only one with prospective data, was published by Dean et al in 1981. 8 Changes in renal function were analyzed in 41 patients with renovascular hypertension who were followed on medical treatment. A greater than 10% decrease in kidney size was noted on serial intravenous pyelograms in 37% of patients, with a follow-up ranging from 6 to 84 months. This decrease in kidney length was the most common change among renal parameters that eventually led to operative intervention.

The second study, reported by Schreiber et al in 1984,6 retrospectively examined kidney length changes in association with arteriographic progression of renal artery disease. Decrease in kidney size was defined as a difference of greater than 1.5 cm in pole-to-pole measurements on serial roentgenograms. Thirty-seven of 85 patients (44%) with atherosclerotic renal artery disease demonstrated arteriographic disease progression. A decrease in kidney size was also common, occurring in 70% of these 37 patients.

A more recent study was published in 1991 by Tollefson and Ernst,10 who also retrospectively reviewed arteriographic progression of renal artery stenosis. They found renal artery disease progression in 53% of patients, but decreased kidney size was not found more often in patients with progression compared with those without progression. Specific criteria for a significant decrease in kidney length were not defined.

In 1989, Taylor et al14 also found decreases in kidney length by ultrasound in association with renal artery stenosis. Although not strictly a natural history study, a significant decrease in kidney length (mean difference of 1 cm) was found in the subset of 19 renal arteries with 60% stenosis or greater followed without intervention. The observations in the current study expand on this type of prospective data and allow further characterization of this progressive decrease in kidney length. 11

The findings in this report indicate a substantial risk for decrease in renal mass among patients with high-grade renal artery stenosis. This loss of renal mass may have important consequences for overall renal function. Patients with bilateral high-grade renal artery stenoses or high-grade stenosis related to a solitary kidney are at risk for losing a critical amount of renal mass and eventually developing end-stage renal disease. The pertinent questions that follow from this relatively high estimate of risk for loss of renal mass are (1) whether this is an actual decrease in size and (2) how this information should influence the clinical management of these patients.

Factors influencing the reproducibility of length measurements in this study relate primarily to the ultrasound technique used. 12 The examinations were all done by a single technologist using the same ultrasound scanner. In our experience, obtaining an accurate measurement depends on using a consistent approach among patients from visit to visit, obtaining a B-mode image that maximizes kidney length, and using an average of three measurements to represent the final value. Determination of the variability of this examination is also essential for establishing an appropriate threshold for significant changes. The use of 1 cm as the threshold for a significant length difference in this report is based on the variability of kidney length measurements as documented in our own laboratory and is consistent with other studies examining kidney size and variability of measurement. 12

The potential influence of these findings on patient management will depend on whether this type of information should affect the decision to proceed with balloon angioplasty or surgical intervention to increase renal perfusion. A decrease in kidney size seems to be one of the earliest signs of the effects of high-grade renal artery stenosis. 69 However, whether this decrease alone without any other evidence of renal dysfunction warrants intervention remains unsettled, because few reports have addressed the issue of decreasing renal mass as an indication for intervention. Nevertheless, this information may be useful in patients with borderline renal function and either bilateral high-grade renal artery stenoses or a high-grade stenosis with a solitary kidney.

Progression to renal artery occlusion was observed in 2 of 49 sides with 60% stenosis or greater. In both instances, the renal length decreased by greater than 1 cm. Although the other 10 patients who lost renal mass may have had progression of their high-grade stenoses, the current technique of duplex scanning does not
permit further stratification of renal artery narrowing within the category of 60% to 99% stenosis. In addition, loss of renal mass may be secondary to parenchymal changes related to ischemia or arteriolar nephrosclerosis.25 Regardless of the exact cause of the observed changes in renal length, the most important observation may be that kidneys are more likely to decrease in size in the presence of a high-grade renal artery stenosis.

The inclusion of patients with unsuccessful renal artery balloon angioplasties in this study deserves further comment. Because the effect of renal artery stenosis on renal perfusion is related primarily to the degree of narrowing, it was assumed that persistence of a stenotic lesion after attempted angioplasty would have the same effect as an untreated lesion of equal severity. Experience with renal artery duplex scanning after balloon angioplasty has clearly shown that hemodynamic improvement, as documented by the duplex examination, is highly correlated with clinical benefit, whereas persistence of stenosis on duplex scan is associated with clinical failure.21 Thus, the inclusion of unsuccessful angioplasties with persistent renal artery lesions appears to be justified.

In summary, a decrease in length of more than 1 cm was found in 26% of kidneys with high-grade renal artery stenoses. The estimated annual risk of a decrease in kidney length of greater than 1 cm was 19% among all sides with high-grade stenoses, 13% for patients presenting with unilateral high-grade stenosis, and 43% for patients presenting with bilateral high-grade stenoses. Loss of renal mass is an important consequence of renovascular disease, and serial measurements of kidney length by ultrasound may be a useful parameter to follow in patients with high-grade renal artery stenosis. Whether renal revascularization could prevent or slow this decrease in kidney length is worthy of further study.

References
Renal atrophy and arterial stenosis. A prospective study with duplex ultrasound.
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Hypertension. 1994;23:346-350
doi: 10.1161/01.HYP.23.3.346

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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World Wide Web at:
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