ORIGINAL INVESTIGATION

The Place of Renal Scintigraphy in the Diagnosis of Renal Artery Stenosis

Fifteen Years of Clinical Experience

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Background: Renal scintigraphy with radiolabeled pentetic acid (diethylenetriamine pentaacetic acid [DTPA]) or, more recently, mertiatide (mercaptoacetyltriglycine [MAG_3]), with or without captopril challenge, is widely recommended as a diagnostic test for renal artery stenosis.

Objectives: To address (1) whether the diagnostic accuracy has been improved by the use of captopril and the introduction of mertiatide and (2) whether a renal scan that shows abnormalities is a useful criterion to select patients for renal arteriography.

Patients and Methods: A standard diagnostic protocol, using both scintigraphy and arteriography, was followed in 505 consecutive high-risk hypertensive patients who were evaluated for renovascular hypertension at the University Hospital Dijkzigt, Rotterdam, the Netherlands, from 1978 to 1992.

Results: Renal artery stenosis (≥50%) was present in 263 patients. When the single-kidney fractional uptake was used as a diagnostic criterion, a specificity of 0.90 was obtained at a cutoff value of 35% for the worst kidney in scintigraphy using pentetic acid without captopril challenge (n=225) and at a cutoff value of 37% after captopril challenge (n=280). This was associated with sensitivity levels of 0.65 and 0.68, respectively. The difference between the uptake of pentetic acid with and without captopril challenge in the 85 patients who were studied under both circumstances was no more accurate as a predictor of renal artery stenosis. In the 93 patients who were studied with mertiatide as well as with pentetic acid, both after captopril challenge, the diagnostic accuracy was no better with mertiatide than with pentetic acid; mertiatide failed to offer any advantage not only when the single-kidney fractional uptake was used as a criterion, but also with the use of other scintigraphic parameters (eg, time to peak, time to pyelum, overall shape of renographic curve, and kidney size).

Conclusions: The diagnostic accuracy of renal scintigraphy has not been improved by the introduction of mertiatide or by the use of captopril. The usefulness of scintigraphy as a diagnostic test for the presence of renal artery stenosis remains questionable. The physician will always confront either a substantial number of arteriograms that do not show abnormalities when renal scintigraphy is omitted as a screening step or a substantial number of missed diagnoses when a renal scan that shows abnormalities is used as a prerequisite for arteriography.

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THE PLACE of renal scintigraphy in the diagnosis of renovascular hypertension has been hotly debated. Scintigraphy is thought to be the most reliable noninvasive procedure currently available for predicting the presence of a clinically significant renal artery stenosis.[1-10] A renal scan that shows abnormalities is therefore used as the basis for selecting hypertensive patients who will require further diagnostic workup with renal arteriography. Clinical experience, however, shows that the predictive value of renal scintigraphy is highly variable, and it depends on the selection of patients, on the criteria by which the renal scans are analyzed, and on the radiopharmaceutical that is used.[8,11-13] In addition, many clinicians believe that in a patient with severe drug-resistant hypertension, particularly when this condition is associated with signs of generalized atherosclerosis, arteriography is warranted irrespective of whether the renal scan shows abnormalities.

During the past 15 years, all patients who were evaluated for renovascular hypertension at our hypertension center underwent both renal scintigraphy and arteriography. Most of these patients had been referred because of severe hypertension that was difficult to treat; some were referred because their hypertension was associated with generalized atherosclerosis or with an abdominal bruit. Our stan-

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PATIENTS AND METHODS

This study comprised 505 consecutive high-risk hypertensive patients who were referred to the University Hospital Dijkzigt, Rotterdam, the Netherlands, from 1978 to 1992 for evaluation of possible renovascular hypertension. All patients underwent renal scintigraphy and arteriography according to a standard protocol. The reasons for referral were 1 or more of the following conditions: (1) refractory hypertension (diastolic blood pressure ≥95 mm Hg while receiving 3 antihypertensive drugs); (2) severe hypertension (diastolic blood pressure ≥110 mm Hg that was associated with signs of generalized atherosclerotic disease [coronary heart disease and/or intermittent claudication]); (3) severe hypertension before reaching the age of 40 years; (4) the presence of an abdominal bruit; or (5) a rise in the serum creatinine level of 20 μmol/L or greater (≥0.23 mg/dL) during treatment with an ACE inhibitor. The majority of patients had refractory hypertension. None of the patients exhibited evidence of endocrine or renal parenchymal disease. The results of urinalysis and the levels of serum electrolytes, thyrotropin (thyroid-stimulating hormone), and plasma catecholamines were normal; the plasma cortisol level showed adequate overnight suppression after dexamethasone. The serum creatinine level was greater than 106 μmol/L (>1.2 mg/dL) in 239 patients and greater than 221 μmol/L (>2.5 mg/dL) in 27 patients.

Our analysis encompassed the following 4 study groups (**Figure 1**): group 1, scintigraphy using pentetic acid without captopril (n=182); group 2, scintigraphy using pentetic acid both without captopril and following a challenge with 50 mg of captopril at 2 to 8 weeks later (n=85); group 3, scintigraphy using pentetic acid after a challenge with 50 mg of captopril (n=145); and group 4, scintigraphy using pentetic acid and mertiatide, performed 2 to 8 weeks apart, both after captopril challenge (n=93).

SCINTIGRAPHIC PROCEDURES AND DATA ANALYSIS

In patients who were receiving long-term ACE inhibitor treatment, the ACE inhibitor was withheld for at least 24 hours before scintigraphy was performed. Patients who underwent scintigraphy with captopril challenge received 50 mg of captopril orally at 1 hour before the examination. To ensure adequate absorption of captopril, patients were required to fast during the 4 hours preceding scintigraphy. Sufficient hydration was guaranteed by the oral administration of 0.5 L of tap water. Blood pressure was measured with an automatic device (Accutorr 1A and 3, Datascope, Datascope Corp, Montvale, NJ) before administration of captopril and every 5 to 10 minutes for 2 hours after administration of captopril.

Scintigraphy was performed with the patient in a supine position, and the detector was placed posteriorly. After intravenous administration of ^{99m}Tc–pentetic acid or ^{99m}Tc-mertiatide, data were collected in 10-second frames during a 20-minute period, and sequential analog images were obtained every minute. Regions of interest were delineated by the computer, and an area for background correction was placed between the kidneys.[14] The single-kidney contribution to the total renal uptake of the radionuclide, measured during the second minute after injection, was expressed as a percentage of the net total of 2-kidney counts (single-kidney fractional uptake). The kidney with the lowest uptake was considered to be the kidney that was most likely to be affected.

In the patients who were studied with both pentetic acid and mertiatide renography, the following criteria other than the single-kidney fractional uptake of radionuclide were also analyzed[6,14-16]: (1) visual assessment of kidney size (normal or small); (2) time until activity appeared in the renal pelvis, determined by visual evaluation of the 1-minute sequential images by the nuclear radiologist (time to pyelum); (3) time-to-peak activity (T_{max} [ie, the time until the maximal amplitude of the renogram was reached]); (4) the overall pattern of the renographic curve; and (5) interpretation by the nuclear radiologist (suspect or not suspect). The receiver operating characteristic (ROC) curves were generated for various parameters of scintigraphy.[17]

Arteriography was performed via the femoral approach. In the vast majority of patients, aortography with the digital subtraction technique resulted in adequate visualization of the renal arteries and their main branches. In cases of doubt about the patency of the renal artery, a selective ostial injection of a radiocontrast medium was given. A stenosis was considered to be significant when the diameter of the arterial lumen was reduced by 50% or more. In patients with bilateral renal artery stenosis, the kidney with the most severe stenosis on the arteriogram was referred to as the affected kidney. In the same session in which arteriography was performed, the effective renal plasma flow and glomerular filtration rate (GFR) were determined with the continuous infusion method using iodohippurate sodium I 131 (Hippuran I 131) and thalamate iodine I 125 and measuring radioactivity in plasma at the steady state.[18]

STATISTICAL ANALYSES

Data are presented as mean±SD or as the medians and ranges, unless stated otherwise. Comparisons of variables with a binomial distribution were made using the χ^2 test. Comparisons of variables with a normal distribution were made using the Student *t* test and 1-way analysis of variance, and comparisons of variables with a skewed distribution were made using the Mann-Whitney *U* test and the Kruskal-Wallis test. Differences in diagnostic performance between scintigraphy using pentetic acid with and without captopril challenge and between scintigraphy using pentetic acid and mertiatide were assessed by comparing the areas under the ROC curves.[19] Two-tailed *P* values less than .05 were considered to indicate statistical significance.

dard practice of always performing arteriography after scintigraphy remained constant during this 15-year period, although the methods that were used to prepare patients for scintigraphy and the scintigraphic procedures were modified in accordance with prevailing recommendations. From 1978 to 1983, technetium Tc 99m–labeled pentetic acid (diethylenetriamine pentaacetic acid [DTPA]) was used for renal scintigraphy. From 1983 to 1990, the angiotensin-converting enzyme (ACE) inhibitor captopril was administered to enhance the diagnos-