EDITORIAL

Captopril Renal Scintigraphy—A Way to Distinguish Functional from Anatomic Renal Artery Stenosis

Since Majd and colleagues first used captopril to enhance the diagnostic value of renal scintigraphy, numerous investigators have attempted to define the place for this test in the evaluation of patients with suspected renovascular hypertension (*1*). Though some groups have not found the test to be sufficiently sensitive or specific, most agree that in properly selected cohorts, carefully done and objectively interpreted, captopril scintigrams are safe and at least as diagnostically accurate as other available techniques (*2–6*).

Two basic types of issues remain. The first are *technical* such as:

1. Which isotope (DTPA or MAG_3) should be used to maximize diagnostic accuracy and minimize time and expense?
2. Should the test be interpreted quantitatively as suggested by Chen et al. or semiquantitatively as recommended by the Working Party on Diagnostic Criteria at a recent consensus conference (*7,8*)?
3. Are both a baseline and post-captopril scintigram necessary and in which order should they be done?

The second are *clinical:*

1. Is captopril scintigraphy most helpful to detect patients likely to have abnormal renal artery anatomy (the *sensitivity* of the test) or to exclude patients likely not to have renal artery stenosis (the *specificity* of the test)?
2. Can captopril scintigraphy predict the outcome of renal vascularization?

The latter question is addressed by Dondi et al. in this issue of the *Journal* (*9*).

We have known for many years that the presence of renal artery stenosis does not establish that the arterial lesions seen are the cause of hypertension in an individual patient (*10–11*). The evidence for this assertion comes from two observations. The first is that many normotensive patients, especially those with diffuse visceral artery atherosclerosis, have identical renal artery atherosclerotic lesions as do hypertensive patients. Second, a sizable proportion of hypertensives with renal artery stenosis do not benefit from technically successful renal artery revascularization, either by surgery or transluminal angioplasty.

Many clinicians have categorized those patients in whom revascularization cures or improves blood pressure as having *renovascular hypertension* or *functional renal artery stenosis*, while those patients who do not benefit are said to have *anatomic renal artery stenosis* (*4*). Clearly, the better we are able to distinguish patients with functional from those with anatomic renal artery stenosis, fewer operations and angioplasties, which are likely to be unsuccessful, will be recommended and we will have a greater success rate in curing or improving hypertensives who are asked to undergo risky and expensive procedures.

The study reported here adds yet more support to earlier data that the renographic response to captopril provides strong evidence that the observed renal artery lesion is functionally significant (*4,12*). Almost all (32 of 33) patients who had a positive captopril scintigram (as defined by the investigators from prior analyses) were cured or improved by revascularization. Five of 18 patients (28%), however, who either had a normal captopril scintigram or did not show any changes when the baseline and captopril scans were compared, also benefited from surgery or angioplasty. Although our group used a different protocol and interpretation of captopril scintigraphy results, we also would have not recommended intervention in 3 of 20 patients (15%) who responded well after a procedure.

These results compare very favorably to the evaluation most commonly used to differentiate functional from anatomic renal artery stenosis, namely the ratio of renal vein renin activities. Though the renal vein renin ratio (RVRR) predicts a good response with significant accuracy, (92% in Rudnick and Maxwell's review), 232 of 342 (65%) of the patients they studied who had surgery despite nonlaterizing RVRRs were either cured or improved by an intervention (*13*). Thus, a lateralizing RVRR predicts a good result, but a nonlateralizing ratio does *not* predict failure. This shortcoming, in addition to the invasive nature of the procedure and the need for precision in doing the assay, has led many centers to abandon RVRR in most patients with renal artery stenosis. Svetkey et al. also showed that neither RVRR after captopril challenge, nor calculation of the Vaughan ratio (renal venous minus arterial renin divided by arterial renin) after captopril, successfully predicted failure of intervention (*14*).

Although the work of Dondi et al. offers promise that the use of renal scintigraphy with captopril may be able to assist the clinician in predicting the success or failure of an intervention, one cannot yet recommend this test with unqualified enthusiasm. The design of this trial excluded the 39% (33/84 patients) initially considered for the study. In this group, there were patients who were technical failures and those whose lesions recurred within 1 mo or who died postoperatively. The exclusion of the very pa-

Received Jul. 21, 1992; accepted Jul. 21, 1992.
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tients who had the worst outcomes casts the test in a much more favorable light than is perhaps appropriate. It is also not clear how useful the results of captopril scintigraphy are in predicting the response in patients with fibromuscular dysplasia (FMD). Two of ten patients with FMD were cured despite negative studies.

Also, the results of Dondi et al. are at variance with the experience of the Yale Vascular Center (*15*). In that paper, which reported on all 45 patients studied and followed for at least 3 mo after intervention, the parameter which best separated those with functional from those with anatomic renal artery stenosis was not a positive scintigram but rather the presence of "captopril-induced changes." When those with a positive scintigram (n = 40) were compared, 4 of 20 patients with captopril-induced changes were cured or improved and only 3 of 20 without captopril-induced changes showed any beneficial response.

Although renovascular hypertension is not a common disease, medical therapy is often unsuccessful in reducing blood pressure and does not prevent progressive ischemic nephropathy and eventual end stage renal disease (*16*). Although we cannot as yet claim that revascularization should be viewed as the best option for patients with renal artery stenosis, there continues to be great potential for the judicious use of renal angioplasty and renal artery surgery to control blood pressure and prevent renal damage in a substantial number of individuals (*17–19*). One of the major limitations for proceeding with angioplasty and also for recommending vascular reconstruction, has been our inability to predict outcome with any reasonable degree of certainty. It would appear from the work of Dondi and others, that captopril scintigraphy offers great promise in this regard. The use of noninvasive test, based on how the kidney actually functions after the inhibition of angiotensin converting enzyme, is a substantial improvement over simply measuring renal vein renin levels. Not only is renal renin production affected by many other physiologic systems, but also the amount of renin in the renal veins may not actually reflect the production of or effects of the local renin angiotensin system.

It is clear, however, that still more needs to be done. We need to evaluate the role of captopril scintigraphy in diagnosing ischemic nephropathy in normotensive patients. We need to evaluate the role of captopril scintigraphy in predicting whether renal revascularization will preserve or improve renal function in the ischemic kidney. And we need to determine how best to analyze and apply the results of this technique. As our population ages and we are faced with a greater number of elderly individuals with significant hypertension, with or without renal insufficiency, it is crucial that we address these questions and define the value of this promising diagnostic test.

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