raphy in conditions other than renal artery stenosis where the renin-angiotensin-aldosterone mechanism is active.

In conclusion, we feel that a ^{99m}Tc-MAG3 captopril renal study with MPTT measurements should be performed in high-risk patients with hypertension and chronic renal failure who have a total GFR of greater than 10 ml/min and split renal function of greater than 10%. If abnormal, the result would be consistent with angiotensin II-dependent renovascular dysfunction. If normal, it may indicate a beneficial effect of ACE inhibition on renal function.

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EDITORIAL

Should the Role of Captopril Renography Extend to the Evaluation of Chronic Renal Disease?

The article by Datseris et al. in this issue of the *Journal* (*1*) addresses an important question in the differential diagnosis of renovascular hypertension. It also suggests another potential use for captopril scintigraphy in patients with hypertension and renal disease.

Numerous studies have been reported which evaluate the sensitivity and specificity of captopril renography in renovascular hypertension (*2*). Changes induced in the renogram of a patient with unilateral renovascular disease may be quite dramatic. An otherwise normal-appearing kidney curve may become abnormal after blockade of the renin-angiotensin system by captopril or some other converting enzyme inhibitor. As the baseline renogram curve becomes increasingly abnormal with declining renal function, the changes induced by converting enzyme inhibitors become increasingly unreliable and difficult to interpret (*3*). Among patients with severely reduced renal function, the administration of converting enzyme inhibitors may be of no value at all in the differential diagnosis of essential from renovascular hypertension. This is a significant problem since a large number of patients with renovascular hypertension suffer from a reduction in renal function, either as a consequence of bilateral disease or as a result of long-standing severe hypertension and associated nephrosclerosis. Even in the presence of severe unilateral renal artery stenosis, the captopril renogram may be difficult to interpret.

Hypertension is an invariable consequence of the loss of renal function in patients with chronic renal failure. Therefore, the nephrologist or nuclear medicine physician is faced with two groups of patients who may appear quite similar on the basis of clinical findings, but whose disease has very different etiologies. The problem is further compounded by the high prevalence of secondary renal artery stenosis in hypertensive individuals (*4*). Thus, the patient with significantly impaired renal function and secondary hypertension is not easily differentiated from the patient with primary renovascular disease and secondary impairment of renal function.

A further dilemma is the occurrence of compromised renal function after therapeutic administration of angiotensin-converting enzyme inhibitors to patients with bilateral renal artery stenosis or renal artery stenosis in a solitary kidney. Acute renal failure may occur in these patients because a vital compensatory mechanism to maintain renal function is pharmacologically

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blocked. Although the majority of these cases of acute renal failure are reversible, there have been reports of irreversible disease (*5*).

Datseris et al. have attempted to determine whether renal artery stenosis, renovascular hypertension and chronic renal failure could be differentiated through the use of captopril renography. Their data shed light on the use of captopril renography in identifying patients with reduced renal function and hypertension who might benefit from treatment with angiotensin-converting enzyme inhibitors versus those who might be harmed. This information is of great importance since angiotensin-converting enzyme inhibitors are among the drugs of choice in patients with reduced renal function. In the United States alone it is estimated that hypertension is the basis for renal failure in 25% of patients treated with renal dialysis (*6*).

Datseris et al. categorized patients as high, indeterminate or low probability for renal artery stenosis based on previously published criteria (*7*). In all five patients who had angiography and high probability scans, the presence of renal artery stenosis was confirmed. Two other patients had a high probability scan but were not confirmed by angiography. At this time we do not yet know if these patients had renovascular hypertension. The investigators suggest that these patients did not have the disease, but they do not present adequate data to support their contention that these were likely to be false-positives. The reader should be cautious in reviewing Table 2 of their article which fails to classify five of the high probability studies as angiographically proven renal artery stenosis, but rather lists their clinical diagnoses.

Angiotensin-converting enzyme therapy was initiated in 23 patients in whom there was no evidence of prolongation of the mean parenchymal transit time after captopril and these patients were followed for 6 mo. It is important to note that in none of these patients was there a deterioration of renal function after 6 mo of converting enzyme therapy. Unfortunately, in the patients in whom mean parenchymal transit time was prolonged during the captopril renogram, no converting enzyme inhibitor was administered; therefore leaving unconfirmed the corollary that patients who have an abnormality induced by diagnostic captopril might be harmed by ACE inhibitor therapy. The ethics of the study are such that we may never truly know the answer to this question. A recent publication described 15 cases of converting enzyme inhibitor therapy associated with severe kidney damage (*5*). Thirteen of the 15 patients had increased creatinine levels before converting enzyme inhibitor therapy was begun but were not evaluated further. Nine of the 15 patients subsequently required hemodialysis, four died without recovering renal function and five required dialysis for periods varying from one day to 5 wk. These data do not suggest any danger of a single dose of angiotensin-converting enzyme inhibitor as used in captopril renography, but rather, the need for caution when administering continued therapy in patients with hypertension and reduced renal function. Neither do we know the number of patients who may have had renal artery stenosis in this group since they did not undergo angiography.

The parameter used by Datseris et al. in the evaluation of kidney function was mean parenchymal transit time, which appears to be of value in achieving the investigators' goals. Whether other simpler parameters such as the time to peak of the renogram or 20 or 30 min over peak values would have provided similar data is not presented. The investigators suggest that the t max is not of value. It would have been helpful to have had considerably more quantitative data provided in the report to facilitate a more objective evaluation.

There is still a need for considerable investigation of captopril renography beyond clinical efficacy. Setaro et al. have shown that patients who receive angiotensin-converting enzyme inhibitors as therapy do not have as accurate test results as patients who are not receiving these drugs (*8*). There have been an increasing number of reports that the positive captopril test is highly specific for reversible renovascular hypertension (*9*) rather than renal artery stenosis. Only about 80% of patients who have angioplasty for correction of a renal artery stenosis show an improvement in blood pressure. The positive predictive value of angiography for renovascular hypertension, therefore, is relatively low. The percentage of patients who show an improvement in blood pressure after angioplasty who have had a positive captopril renogram is approximately 90%. The test appears to be much more highly specific for the presence of reversible renovascular hypertension than the so-called "reference standard" renal arteriography.

The current report suggests that even in patients with a significant reduction in renal function, a high probability positive test is strongly suggestive of the presence of renal artery stenosis. Furthermore, we now have data that if the test is negative, the danger of treating the patient's hypertension with an angiotensin converting enzyme inhibitor appears to be minimal.

We still need to know if there is a significant difference in results based on either the choice of radiopharmaceutical or the converting enzyme inhibitor used. The data suggest that these factors are not critical to the performance of captopril renography. Further studies are needed in patients with a wide variety of primary renal diseases and secondary hypertension to determine whether the test is reliable in this situation. Certainly the current investigation suggests this, but this is a very small number of patients from which to draw such far-reaching conclusions.

It remains to be determined which is the best way to interpret these studies. Few data have been published to suggest that any of the quantitative parameters are significantly better than simple qualitative analysis. It may well be that some form of quantitation is desirable. Whether the mean transit time is better than the other parameters still requires further carefully controlled analysis.

The one indisputable conclusion is that captopril renography is an important diagnostic test. It has a role in the differential diagnosis of treatable renovascular hypertension and it may have an even greater and far-reaching role in the evaluation of the safety of angiotensin-converting enzyme inhibitor therapy in patients with reduced renal function and hypertension.

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