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Clinical Problems in Renovascular Disease and the Role of Nuclear Medicine

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Although renovascular disease remains defined as a stenosis of the main renal artery or its proximal branches (renal artery stenosis [RAS]), its clinical overview has changed dramatically over the last 15-20 years and its management is more controversial than ever before. The clinical problems, not only diagnosis and treatment but also the relative contribution of different pathophysiological mechanisms involved in the progression of kidney disease, have shifted dramatically. This presentation aims to emphasize the paradigm change revisiting the (recent) past focused on renovascular hypertension (RVH) to the current context of preservation or recovery of threatened renal function in patients with progressive atherosclerotic renovascular disease until its last stage of irreversible "ischemic nephropathy." In the past, the foreground was occupied by RVH, a very rare disease, where the activation of the renin-angiotensin-aldosterone system (RAAS) was supposed to play the major, if not only, role in RVH issues. The retrospective RVH diagnosis was established either on the improvement or, more rarely, on the cure of hypertension after revascularization by, most often, a percutaneous transluminal renal angioplasty with or without a stent placement. At this time, captoptril radionuclide renography was an efficient diagnostic tool, because it was a functional (angiotensin-converting enzyme inhibition), noninvasive test aiming to evidence both the RAAS activation and the lateralization (or asymmetry) of renin secretion by the kidney affected by a "hemodynamically significant" RAS. At present, even if captoptril radionuclide renography could be looked upon as the most efficient (and cost effective in selected high-risk patients) noninvasive, functional test to predict the improvement of hypertension after RAS correction, its clinical usefulness is questioned as the randomized, prospective trials failed to demonstrate any significant benefits (either on blood pressure control or on renal function protection) of the revascularization over current antihypertensive therapy. Today many patients with RVH remain undetected for years because they are treated successfully and at low expense with these new blockers of RAAS. In addition to its well-known role in hemodynamics, angiotensin II promotes activations of profibrogenic and inflammatory factors and cells and stimulates reactive oxygen species generation. The "atherosclerotic milieu" itself plays a role in the loss of renal microvessels and defective angiogenesis. After an "adaptative" phase, ischemia eventually develops and induces hypoxia, the substratum of ischemic nephropathy. Because blood oxygen level–dependent MRI may provide an index of oxygen content in vivo, it may be useful to predict renal function outcome after percutaneous transluminal renal angioplasty. New PET tracers, dedicated to assess RAAS receptors, inflammatory cell infiltrates, angiogenesis, and apoptose, would be tested in this context of atherosclerotic renovascular disease.
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Although the definition of renovascular disease remains unchanged, for example, stenosis of the main renal artery or its proximal branches, its clinical overview has changed dramatically over the last 15-20 years and management remains controversial. Clinical issues relating to diagnosis and treatment and the relative contribution of different pathophysiological mechanisms involved in the progression

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of kidney disease have shifted dramatically. This review aims to emphasize this paradigm change, revisiting the (recent) past focusing on renovascular hypertension (RVH) and current practices, for example, preservation or recovery of threatened renal function in patients with progressive atherosclerotic renovascular disease (ARVD) until last stage of "ischemic nephropathy."[1]

Past: Renal Artery Stenosis as a Cause of Renin-Angiotensin-Aldosterone System Activation Inducing Reversible RVH

In the past, the foreground was occupied by RVH, a very rare disease in the general hypertensive population (< 5%), where the activation of the Renin-Angiotensin-Aldosterone System (RAAS) was supposed to play the major, if not only, role in hypertension genesis. The final diagnosis of RVH was retrospective, established either on the improvement or, more rarely, on the cure of hypertension after revascularization by percutaneous transluminal renal angioplasty (PTRA) with or without stent placement (ostial renal artery stenosis [RAS] especially). Captoptril radionuclide renography (CRR) was thus a very efficient diagnostic tool, because it was a functional (angiotensin-converting enzyme inhibition [ACEI]), noninvasive test aiming to demonstrate both the RAAS activation and the lateralization (or asymmetry) of renin secretion by the kidney affected by a "hemodynamically significant" RAS.[2-5] Figure 1 displays the rationale of this ACE inhibitor showing the decrease in filtration and slowing in tubular transit.

Based on the assumption that such stenotic lesions should be corrected, patients with hypertension with a clinical picture suggesting RVH[6] were included in a 2-step diagnostic strategy. The first step was the "RAS screening" using a noninvasive test, such as duplex Doppler renal ultrasonography, CT arteriography (CTA), or magnetic resonance angiography (MRA), depending on the local experience and expertise. Many patients with hypertension with an "anatomically significant" RAS did not reach the second step because PTRA was considered as "so simple" as compared with surgery for kidney revascularization. The second step consisted of a functional test to demonstrate a cause-effect relationship between RAS and hypertension, for example, establish the diagnosis of RVH diagnosis.

CRR "alone" without a baseline test comparison has been proposed as a "screening test" to reduce the number of unnecessary angiographies and exclude a "hemodynamically significant" RAS. This is by contrast with an "anatomically significant" RAS, the definition of which varies between a 50% and a 70% decrease in arterial lumen area, depending on patient selection in the series screening with CTA and MRA procedures. Three analyses gathering data from 10-14 studies (from 1987-2000) and including over 1200 patients reported an average sensitivity ranging from 85%-90% and a negative predictive value around 90%.[2,3,7]

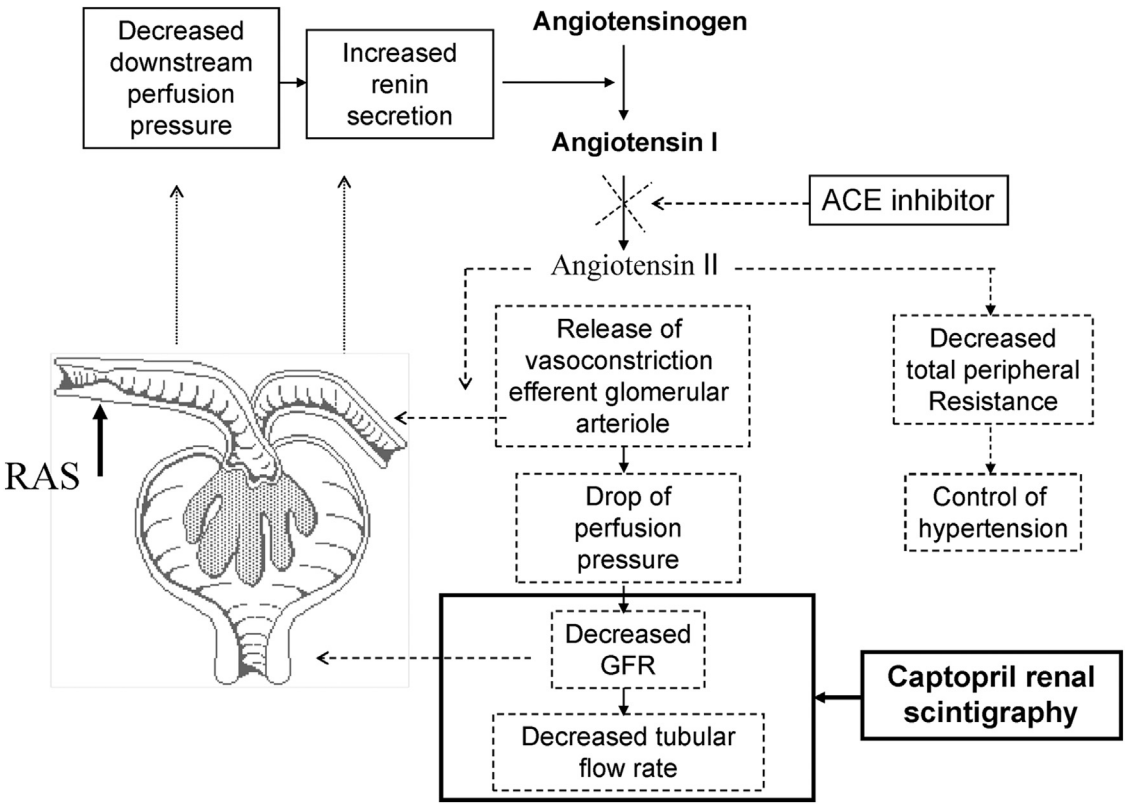

Figure 1 Rationale of the captopril renal scintigraphy showing decreased GFR (ie, early phase of the time-activity curve for totally or partially filtrated tracers) and decreased tubular flow rate (ie, decreased wash out and later phase of time-activity curve for any excreted tracers).