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Interest of renal scintigraphy with captopril in the diagnosis of renovascular arterial hypertension

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Abstract **Original Research Article**

Introduction*:** Renal scintigraphy with captopril test of the kidney is a simple, non-invasive functional imaging technique that can be used to demonstrate the role of stenosis in the development of renovascular hypertension (RVH). It also makes it possible to distinguish renal artery stenosis responsible for RVH from stenosis associated with primary arterial hypertension. ***Objective: To illustrate the benefits of renal scintigraphy with captopril test in the diagnosis of RVH. ***Material and Method*:** This was a prospective and descriptive study over a period of 12 months, from 1 March 2016 to 4 March 2017, carried out in the nuclear medicine department of the Institut des Radio Isotopes (IRI) in Niamey. The parameters studied were age, frequency, creatinemia, tracer used, relative perfusion, relative renal function and maximum uptake time. **Results:** We collected 6 cases presenting with either hypertension refractory to well-administered two- or three- therapy, or severe hypertension at the complication stage, or hypertension associated with hypokalaemia or unexplained renal failure or reversible renal failure induced by a conversion enzyme inhibitor. The mean age was 35 years. The age of diagnosis of hypertension ranged from 20 to 28 years. Four patients underwent echodoppler of the renal arteries: unilateral stenosis in patients A, C and F, and bilateral stenosis in patient D. The captopril test was positive in 3 cases, patients A, B and C. ***Conclusion*:** Dynamic renal scintigraphy with captopril testing is a non-invasive, low-radiation diagnostic method for the investigation of renovascular hypertension. It has a triple benefit, including the detection of the most severe arterial stenoses, the prediction of the curability of the stenosis by a revascularisation procedure and, finally, post-treatment follow-up.

Keywords: Renal scintigraphy, kidney, renovascular hypertension (RVH), hypertension.

INTRODUCTION

Dynamic renal scintigraphy with captopril test is a non-invasive, low-irradiant procedure for investigating hypertensive patients with one or more renal artery stenoses. Unlike radiological techniques such as Doppler ultrasound, computed tomography (CT) scans and magnetic resonance imaging (MRI), which only reveal the presence of renal artery stenosis(s), captopril can confirm that renal artery stenosis is the cause of hypertension. But also to predict the recovery or improvement of hypertension after revascularisation by transluminal angioplasty or reconstructive surgery. The aim of our study is to demonstrate the value of captopril-sensitised renal scintigraphy in the diagnosis of renovascular hypertension (RVH).

MATERIAL AND METHODS

This was a prospective and descriptive study over a period of 12 months, from 1 March 2016 to 4 March 2017, carried out in the nuclear medicine department of the Institut des Radio Isotopes (IRI) in Niamey (Niger). Our study population consisted of hypertensive patients seen on an outpatient basis in the nephrology department and the different cardiology departments of the urban commune of Niamey. We selected all consenting patients with: hypertension refractory to well-administered bi- or tritherapy; sudden or accelerated worsening of hypertension; discovery of a lumbar murmur or hypokalaemia; hypertension with progressive unexplained renal failure or reversible renal

failure induced by conversion enzyme inhibitors or any other antihypertensive treatment.

The radiotracer used was 99mTc-MAG3, injected as a pulsed bolus through a catheter placed in the elbow at a dose of 111MBq (3mCi) for basal evaluation and 444MBq (12mCi) for post captopril acquisition. The protocol includes two tests, a basal test and a captopril sensitisation test. Each test comprises 3 phases. Just before launching the first acquisition, the syringe containing the radiotracer to be injected is placed under the scintigraphy in order to measure the initial radioactivity; this stage is called "full syringe". The first acquisition is then launched.

- An initial dynamic acquisition, also known as the "basal test", carried out after injection of the radiotracer.
- The patient ingests 50mg of captopril with a glass of water (after chewing the tablet). Blood pressure is monitored every 15 minutes for 1 hour.
- A second dynamic acquisition or "post captopril acquisition", lasting 30 minutes, is then started after a new injection of radiotracer, in order to assess any effects of captopril. It included the same number of phases as the first acquisition.

The images were interpreted by comparing the data obtained in the basal test before captopril and the data obtained after captopril administration. We adopted the criteria of the European Multicentre Group: relative uptake less than 40% and decreasing by more than 5%, a decrease of more than 5% in renal perfusion, a T max between 2 min and 10 min with an increase of more than 2 min.

RESULTS

The average age was 35. The age of onset of hypertension ranged from 20 to 28 years. A quarter of the patients underwent echodoppler of the renal arteries: unilateral stenosis in patients A, C and F, bilateral stenosis in patient D. The captopril test was positive in 3 cases, patients A, B and C.
The clinical characteristics and scintigraphy results are shown in Tables 1 and 2.

Table 1: General characteristics of patients

	Patient A	**Patient B**	**Patient C**	**Patient D**	**Patient E**	**Patient F**
Age	47years	40years	31 years	19years	45years	50years
Sex	Male	Male	Feminine	Feminine	Feminine	Male
ATCD	-	-	-	-	-	-
Age of onset of hypertension	Since the age of 28	25years	20years	Brutal	3 years	40years
TA	150/110	198/123	151/65	162/98	160/110	150/110
FC	90 bpm	90bpm	65bpm	-	90bpm	90bpm
Headaches, dizziness	non	oui	non	oui	non	non
Créatinine	368µmol/l	287µmol/l	87µmol/l	73µmol/l	203µmol/l	247µmol/l
Echo doppler rénale	RRA Stenosis	--	RRA Stenosis	RRA Stenosis	--	LRA Stenosis

RRA: right renal artery; LRA: left renal artery

Table 2: Results of renal scintigraphy

		left kidney		**right kidney**	
		Before captopril	**After captopril**	**Before captopril**	**After captopril**
Patient A	T max	6mn	10mn	18 sec	7min 28sec
	Relative Perfusion	43.2%	56.8%	56.8%	46.8%
	Relative function	38%	46%	62%	54%
Patient B	T max	1mn40sec	2mn	1mn20	2mn
	Relative Perfusion	45%	58%	55%	41.1%
	Relative function	47%	55.1%	53%	44.9
Patient C	T max	1mn40sec	2mn42sec	1mn40sec	3mn2sec
	Relative Perfusion	52.1%	56.2%	47.9%	44.9%
	Relative function	54.8%	56.2%	45.2%	43.8%
Patient D	T max	1mn54sec	2mn52sec	2mn14sec	4mn12sec
	Relative Perfusion	48.4%	45.6%	51.6%	54.4%
	Relative function	44.2%	45.7%	55.8%	54.3%
Patient E	T max	4mn50sec	3mn34sec	5mn30sec	4min54sec
	Relative Perfusion	42.8%	39.5%	57.2%	60.5%
	Relative function	41.3%	44.1%	58.7%	55.9%
Patient F	T max	3mn16sec	4mn	3mn16sec	3mn40sec
	Relative Perfusion	51.1%	47.8%	48.9%	52.2%
	Relative function	49.4%	48.4%	50.6%	51.6%

Annexes

Patient A

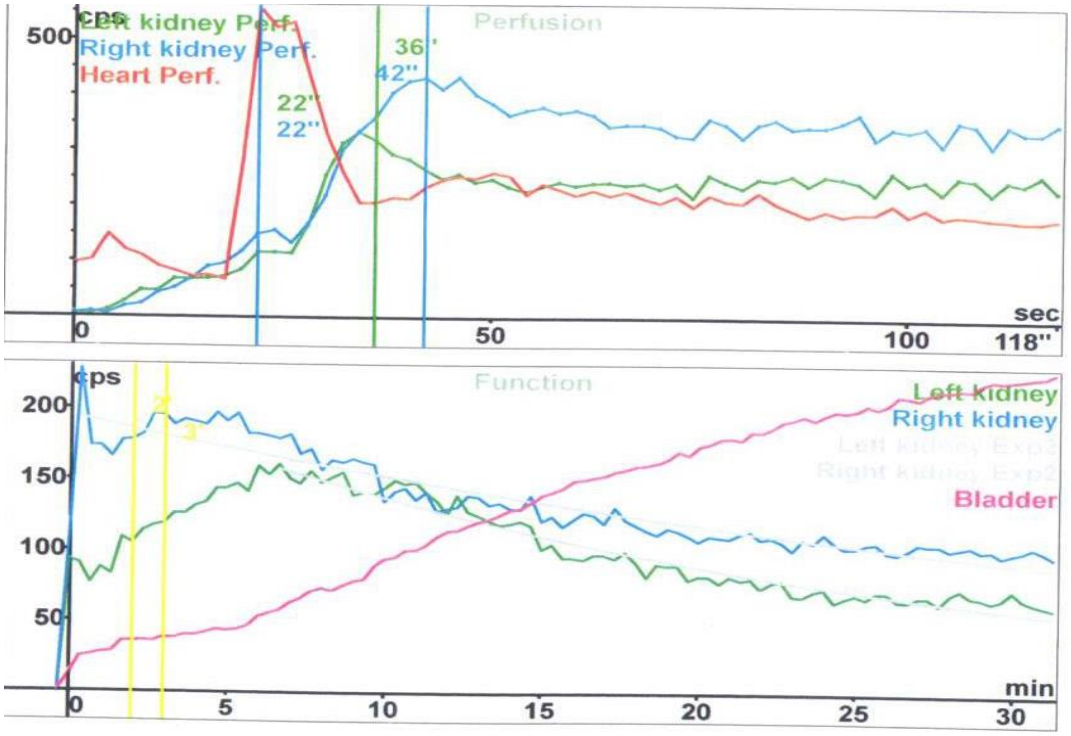

Figure 1: basal renogram in patient A

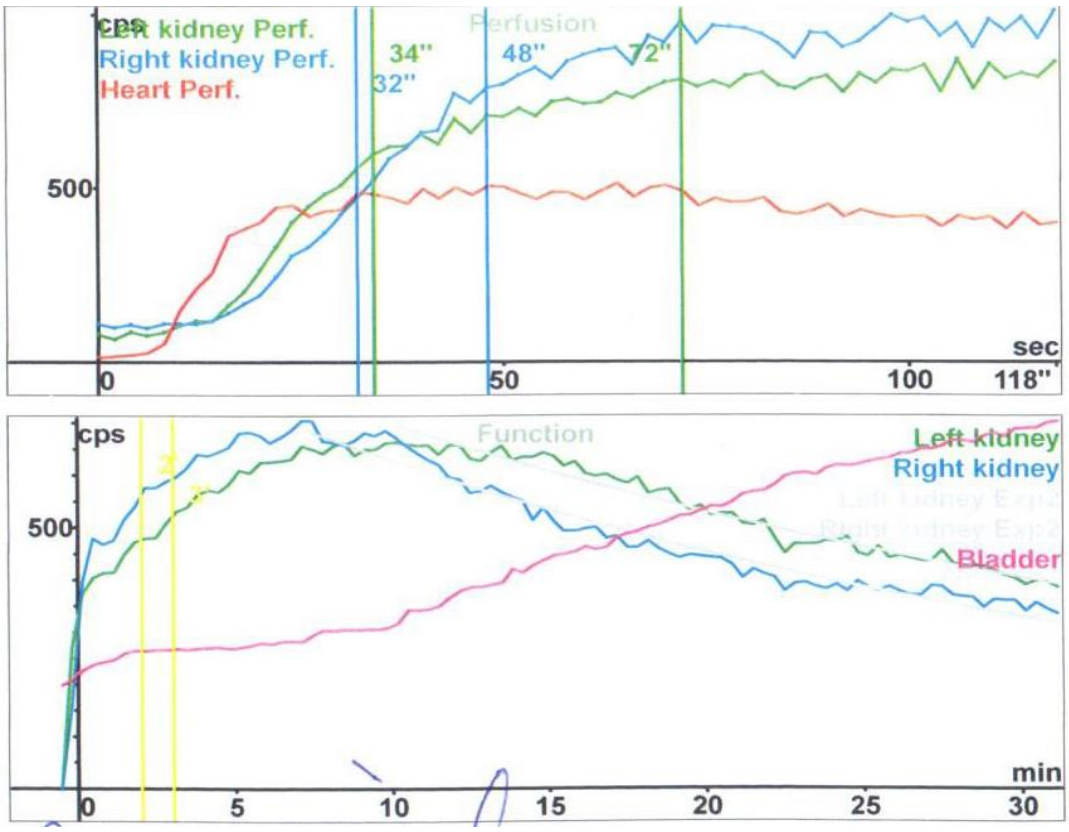

Figure 2: post-captopril renogram in patient A

Patient B

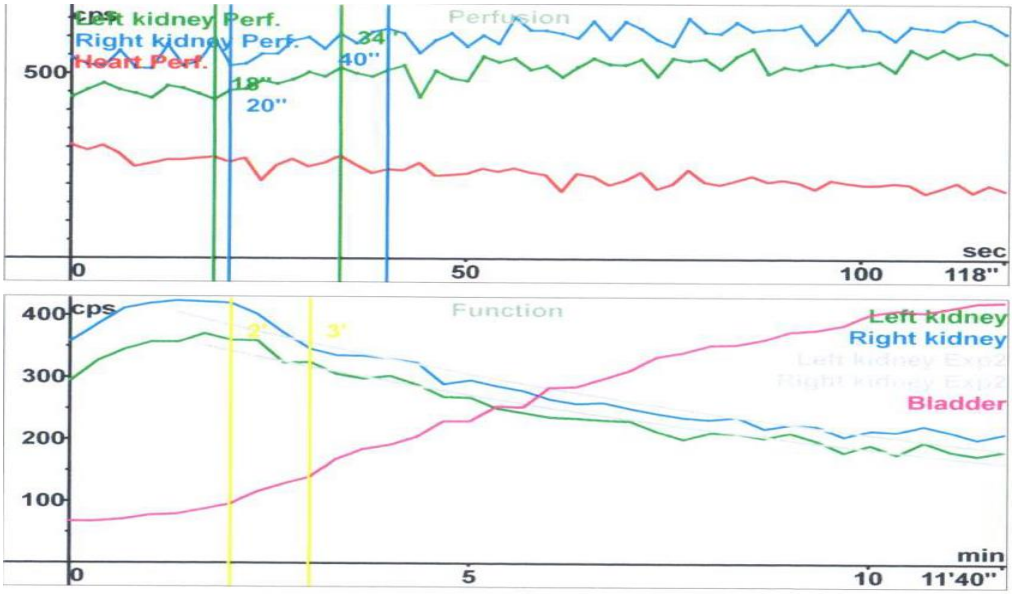

Figure 3: Patient B baseline renogram

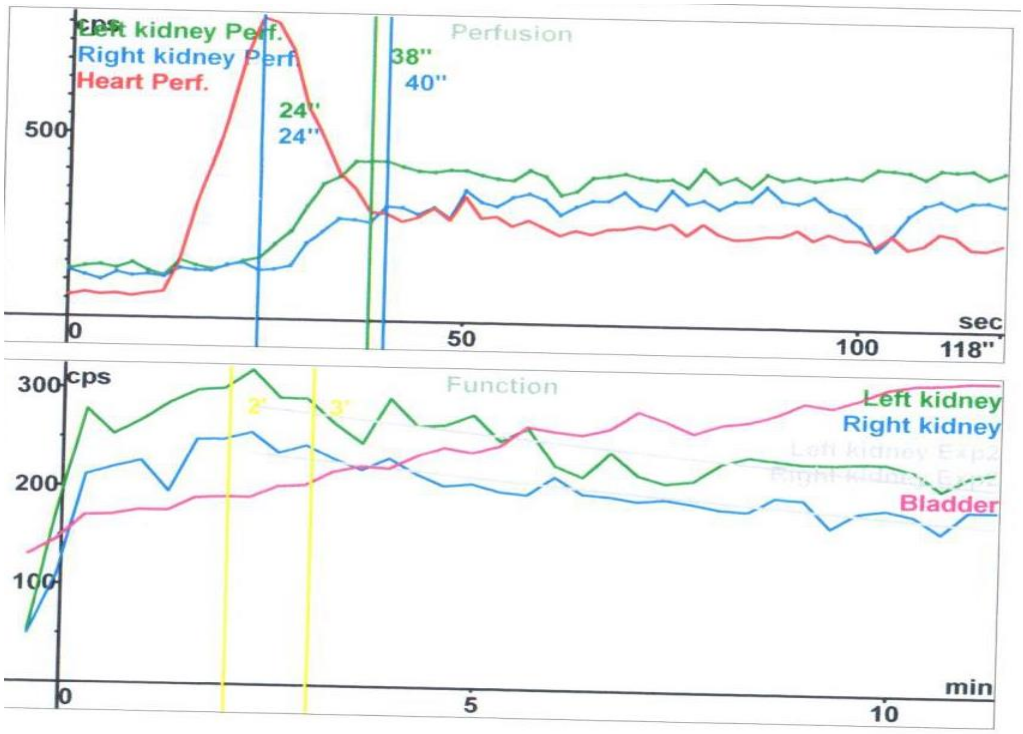

Figure 4: post-captopril renogram of patient B

DISCUSSION

We have a small cohort of patients, but it is interesting because the presentations are varied. This diversity in our 6 patients allows us to classify them into 2 groups according to the results of the renal scan:

- **Group** 1: consisting of 3 patients including patients A, B and C in whom captopril renal scintigraphy was positive.
- **Group** 2: 3 patients including D, E and F who had negative captopril renal scintigraphy.

Group 1

In our cohort, the age of onset of hypertension ranged from 20 to 28 years, which is consistent with the literature according to which, in RVH, hypertension appears in individuals aged under 30 years or over 55 years. [1] Three of the 6 patients in our cohort, or 50%, had a positive renal scintigraphy. This confirms the

facts reported in other studies, in particular the low prevalence of renovascular hypertension. Few prospective studies have been conducted on captopril renal scintigraphy. These include: Gernit screij *et al.,* in 1995 in Holland 28 cases, I. Ghfir *et al.,* in 2007 in morocco only one case, D. Bensellem *et al.,* in 2016 in tunisia 24 cases [2-3 -4]. In our cohort; technetium 99 metatasble labelled mercaptoacetyltriglycine was the only tracer we used.

This result is in conformity with the data in the literature according to which mercaptoacetyltriglycine labelled with metastable technetium 99 is more widely used because it is the best diagnostic agent, particularly in patients with renal failure. [4]. Especially since 2 of our 3 patients had renal failure. 99mTc-Mag3 has a higher renal extraction fraction than 99mTC-DTPA. [5]In our study, we used the following criteria for positivity according to the European Multicentre Group: a decrease of more than 5% in uptake capacity, a two-minute increase in post-captopril Tmax, and a decrease of more than 5% in relative perfusion. However, these criteria are not exactly the same in other reviews of the literature.

- Sandra M.S. Herrmann and Stephen C. Textor in the journal Diagnostic criteria for renovascular disease: where are we now? have suggested the following criteria: a decrease in the percentage of isotope uptake by the affected kidney of less than 40%, the delayed time to maximum isotope uptake is greater than 10-11 min, well above the normal value of 6 min and delayed excretion of the isotope with retention at 25Min or > 20% [6].

- According to the Society of Nuclear Medicine, the various positivity criteria are as follows [7-8]:

¬ Tmax more than 11 min or less than 2 min;

¬ ratio: activity at 20 min/activity at peak, greater than 0.3 or increase of 0.15 after administration of captopril;

¬ relative uptake index of less than 40% or 35% or difference of more than 5% or 10% between the baseline test and the captopril test.

This shows that the criteria for the positivity of captopril renal scintigraphy vary from one school to another. The results of the captopril renal scan in patient C showed a 3% decrease in renal perfusion, which was considered positive even though it did not meet the positivity criteria due to poor centring of the gamma camera, which only centred 2/3 of each kidney. Nevertheless, we retained these results as positive.

Two of our patients, patients A and B in particular, had unilateral renal artery stenosis on Doppler ultrasound, which was 100% consistent with the results of the captopril test scintigraphy. Hence the value of scintigraphy in determining the origin of renovascular hypertension. This is confirmed by the literature, where initial reports in adults suggested that captopril scintigraphy was a good screening method, with sensitivities of 83-93% for the detection of RVH [9-10].

Group 2:

Two of the 3 patients from this group performed a Doppler ultrasound, one of whom (patient D) showed bilateral stenosis of the renal arteries and the other (patient F), stenosis of the left renal artery (less than 50%). In patient D, Doppler ultrasound revealed bilateral stenosis, but renal captopril scintigraphy was inconclusive. Comparative analysis of the semi-quantitative parameters of the isotope curves showed no significant alteration on one side compared with the other. According to the literature, this could be explained by 2 hypotheses: - Among patients with bilateral disease, asymmetry was identified in the more severely affected kidney, but the presence or absence of stenosis in the contralateral kidney could not be reliably identified [11]. This would explain why bilateral stenosis was not found on renal scintigraphy. However, if there was indeed bilateral stenosis, the side with the most stenosis would have been detected on the captopril renal scan, and the results were normal. This shows the limitations of Doppler ultrasound to the detriment of captopril renal scintigraphy. According to the literature, the limits of this technique depend on the skills of the operator, leading to estimates ranging from 60 to 90% [12] hence the value of captopril renal scintigraphy, but this is really limited in the case of bilateral stenosis because it does not allow the less stenotic side to be assessed.

- If there was indeed a stenosis, the fact that renal scintigraphy was unable to objectify it could be explained by the fact that renal artery stenosis can be diagnosed when the diameter narrowing of a main renal artery is >70% [13].

In patient F, Doppler ultrasound showed a unilateral stenosis of less than 50%, but captopril renal scintigraphy revealed nothing. In 2008, the American Heart Association defined significant stenosis as a decrease of at least 60% in the luminal diameter of the renal artery, but renal artery stenosis can be diagnosed when the diameter of a main renal artery narrows by more than 70% [14]. In a selected population of patients with known renal artery atherosclerosis, pre- and post-captopril renograms were highly sensitive (83%) and specific (93%) in detecting unilateral renal stenosis in patients with normal renal function and > 70% stenosis [15]. This would explain why scintigraphy did not show any stenosis. This shows that the positivity of captopril renal scintigraphy is in fact related to the degree of stenosis and that in some patients the degree is not so tight as to cause haemodynamic changes after captopril administration, which could explain why the result was normal on renal scintigraphy as well as in patient E.

CONCLUSION

Dynamic renal scintigraphy with captopril test is a non-invasive, low-irradiating procedure to investigate hypertensive patients with renal arterial stenosis (es).

It has a triple benefit, including screening for the tightest arterial stenoses, prediction of the curability of the stenosis by revascularisation and post-treatment follow-up.

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