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Pattern recognition of loss of early systolic peak by Doppler ultrasound has a low sensitivity for the detection of renal artery stenosis

CT Postma[1], PJ Bijlstra[1], G Rosenbusch[2] and Th Thien[1]
[1]*Department of Medicine, Division of General Internal Medicine; and* [2]*Department of Diagnostic Radiology, University Hospital, 6500 HB Nijmegen, The Netherlands*

In a group of 57 hypertensive patients seen in the outpatient department, the authors did a prospective study to the value of pattern recognition of changes in early systolic peak by Doppler ultrasound (DU) in the examination of renal arteries, as compared with intra-arterial digital subtraction angiography. In five patients (8.7%) DU resulted in technical failure, in one because of the inability to hold breath long enough, in one because the Doppler signals from one part of the kidney were unclear and in three because overlying adipose tissue hindered the examination. Among the remaining 52 patients, 13 had unilateral and six bilateral stenoses greater than 50% of the luminal surface on angiography. By DU 10 patients with a stenosis were identified, one of which was a false positive result. Of the remaining nine, six patients had a unilateral stenosis and three a bilateral stenosis that was identified as unilateral by ultrasound. Therefore, none of the bilateral stenosis was identified as such by DU. Thus, for the detection of renal artery stenoses greater than 50% visual waveform analysis of DU signals has a sensitivity of 47% and a specificity of 97%. The conclusion is therefore that the DU procedure employed in this study has a limited value in the examination of the renal arteries of hypertensive patients with the aim to detect renal arterial stenosis.

Keywords: Doppler ultrasound; renal artery stenosis; diagnosis; secondary hypertension

Introduction

Renovascular disease is one of the most common causes of reversible, secondary hypertension.[1] The prevalence ranges from 0.5% to 5% but can be as high as 9.8% among hypertensive patients over 60 years of age,[2] and because of the potential curable nature its detection is important.[3,4] Also, the medical treatment of hypertension in these patients may lead to irreversible loss of renal function.[5]

In the light of the rather low prevalence, a non-invasive screening procedure for this condition should be preferred. The non-invasive procedures examined so far have however, not shown enough reliability to be used in clinical practice.[1-4]

Since the improvement of the Doppler ultrasound (DU) technique it is possible to examine deep-lying abdominal vessels in this way.[6] The clinical potential of this method in also detecting renal artery stenosis (RAS) has been reported.[7-10] Some studies concluded that it was a reliable way to detect RAS among hypertensive patients,[9,10] although conclusions of more recent research about this subject were less optimistic.[11-13] These reports gave sensitivities as low as 0%, and specificities of 37–50%. Also in 31–42% of the patients the renal artery was not sufficiently visualised to obtain an accurate Doppler signal,[11-13] the latter mainly due to obesity or overlying bowel gas.

In contrast to the methods employed to study the renal arteries directly, the procedures to study the main renal artery indirectly via the segmental arteries reported much higher technical success rates and sensitivities in the detection of renal artery stenosis.[14] The major advantage of such procedures is that it is not necessary to get a direct image of the renal arteries. The signals from the segmental arteries have to be studied and these are much easier to locate than the signals from the exact site of a stenosis in a main renal artery. Because of the presence of a stenosis proximal to where the Doppler signal is recorded, changes in the pattern of the reproduction of the systolic peak blood flow velocity will appear. Several sophisticated calculations of changes in the systolic waveform parameters like pulsatility index and acceleration time have been studied.[14-17] However, the visual interpretation in changes of the peak systolic wave patterns were reported to be an accurate parameter to detect a stenosis.[14] The recognition of these changes is the basis of the DU examination procedure of the renal vasculature that we have used in the present prospective study in hypertensive patients in the outpatient clinic.

Correspondence: CT Postma, Department of Medicine, University Hospital, PO Box 9101, 6500 HB Nijmegen, The Netherlands
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Patients and methods

This prospective study was done in the outpatient clinic of our tertiary referral hospital. The patients included were hypertensive subjects in whom the physicians that treated them deemed it necessary to make an intra-arterial digital subtraction angiography (DSA). Hypertension was diagnosed if at three consecutive outpatient visits a subject had a supine diastolic blood pressure (DBP) over 90 mm Hg measured by sphygmomanometer. The indications for a DSA were grounded on suspicion of the presence of secondary hypertension. In most cases this was based upon the presence of a baseline untreated DBP over 110 mm Hg or a treatment resistant hypertension characterised by a supine DBP over 95 mm Hg despite adequate drug treatment, or a documented onset of high blood pressure before the age of 25 or over the age of 45 years.

After explanation of the study the patients gave their informed consent. All procedures were done as out-clinic examinations, including the DSA. Of the included patients clinical and biochemical data were analysed. Among the biochemical data was their supine baseline plasma renin activity (PRA), after 2 weeks of cessation of antihypertensive medication, and the stimulated PRA, drawn 1 h after the administration of 50 mg of captopril. After the DSA procedure the patients remained in the outpatient clinic for at least 8 h to make sure that no complications had developed.

The DSA was done using the Seldinger technique with a 5F catheter. A colour duplex real-time system was used with a 3.5 MHz sector transducer for imaging and 3.0 MHz for Doppler (Toshiba, Sonolayer Phased Array Scanner SSA-270 A; Toshiba Corp, Tokyo, Japan). The patients were in supine position. When necessary they were placed in left lateral or right lateral position. When optimally audible and visible the Doppler spectra from the segmental arteries of the upper and lower poles, at the periphery of the renal sinus were recorded. The evaluation of the examination consisted of the visual interpretation of the early systolic peak (ESP) of the Doppler signal representing renal blood flow in the renal arteries draining on the investigated segmental arteries.[14]

Stavros *et al* describe three types of waveform that result from different degrees of narrowing of the renal artery. The first is the normal waveform in case of a stenosis of less than 59%. A waveform consistent with a stenosis of 60–79% and one as a result of a stenosis greater than 80%.[14] We regarded a stenosis significant if the luminal surface was narrowed for more than 50%. A difference between 50 and 59% of luminal narrowing on angiography is not consistent. The inter- and intra-observer agreement on stenosis in ranges of 10% are very low.[18] So, we do not consider a difference between 50 and 59% as realistic. The same applies for 70 and 80%.[18] Therefore, we made no distinction in degrees of stenosis, only whether or not a significant stenosis was present. As a consequence we also used one interpretation of the waveform morphology. A normal flow was defined by a systolic upstroke with a single slope and acute angle of the first peak, followed by a second mid-systolic peak. A waveform consistent with stenosis was considered when the systolic upstroke ended with an obtuse angle, or showed a smooth (more or less) round contour of the peak with loss of the midsystolic through.[14]

The DSA and DU were done within 3 weeks of each other. Usually the ultrasound was done first but on some occasions it was the DSA. The ultrasound operators were unaware of the patients' medical history and they were also unaware whether or not the patients had a stenosis, if angiography had been done before the ultrasound examination. The results of the Doppler ultrasound examinations were interpreted by experienced radiologists who were unaware of the clinical histories of the patients and of the outcome of the DSA had it been done prior to the Doppler ultrasound.

Results

Included in the study were 25 male and 32 female patients. In five patients (9%) the Doppler ultrasound resulted in technical failure, due three times to inadequate signals caused by overlying adipose tissue. The body mass indexes (BMI) of these three patients were 31, 36 and 39 kg/m^2 respectively. In one patient no adequate signal could be obtained in one of the segmental parts so the examination was judged incomplete; one patient could not hold her breath long enough to permit a successful procedure. In the remaining 52 patients, with 104 kidneys, adequate signals for interpretation could be obtained, the average examination time per patient was around 45 min.

The clinical data of these patients are shown in Table 1 with the differences between patients with and without a stenosis. Those with a stenosis had a significantly lower creatinine clearance as compared with those without a stenosis (Table 1). Systolic blood pressure (SBP) and stimulated PRA, were significantly higher in the patients with a stenosis (Table 1). Among the 52 patients 13 had a unilateral stenosis and six a bilateral stenosis greater than 50% of luminal surface on DSA. The pathology of the stenosis, as judged by angiography, was atherosclerosis in 13 and fibromuscular dysplasia in six. Of the 13 unilateral stenoses six were identified by Doppler ultrasound. Of the six patients with bilateral stenosis Doppler ultrasound detected a unilateral stenosis in three of them. Although only one stenosis was recognised by Doppler ultrasound, they were regarded as a true positive result because the patients were identified as having renal arterial stenosis (Table 2).

By Doppler ultrasound one stenosis was observed that was not seen on DSA (Table 2). The overall sensitivity of Doppler ultrasound for patients with a stenosis was therefore 47% and the specificity 97% (Table 2). If recognition of only one stenosis in a patient with bilateral stenoses was regarded false negative then sensitivity would be 32%.

Table 1 Characteristics of patients with an adequate examination on Doppler ultrasound

	All patients	*No stenosis*	*Stenosis*
Sex: male/female	24/28	13/20	11/8
Age (years)	51.0 (13.5)	49.6 (13.4)	53.7 (13.6)
Body mass index (kg/m²)	26.4 (5.0)	26.9 (5.2)	25.5 (4.7)
Creatinine clearance (ml/min)	87 (42)	95 (45)*	73 (34)
SBP (mm Hg)	179 (28)	172 (26)*	191 (29)
DBP (mm Hg)	105 (14)	102 (13)	109 (15)
Baseline PRA (nmol/L/h)	4.1 (8.4)	1.5 (1.6)	9.8 (13.6)
Stimulated PRA (nmol/L/h)	9.9 (18.1)	3.7 (6.4)*	23.8 (27.1)

Figures given are means and figures in brackets, one standard deviation.
*Indicates significant difference $P < 0.05$.
Stimulated PRA means measured 60 min after administration of an oral dose of 50 mg of captopril.

Table 2 Results of the detection of renal arterial stenosis by Doppler ultrasound of renal arteries compared with angiography (arterial digital subtraction angiography)

	DSA[a]	*Doppler ultrasound*[a]
Unilateral stenosis >50%	13	6
Bilateral stenoses >50%	6	3 (identified as unilateral)
False positive	—	1
No significant stenosis	33	42

[a]Numbers of patients.
Operating characteristics of Doppler ultrasound in the detection of renal arterial stenosis: Sensitivity 47%; Specificity 97%.

Discussion

A sensitive non-invasive test to detect the presence of RAS in hypertensive patients would be a very practical clinical tool. DU is potentially a very valuable procedure in this respect. However, former studies to the clinical value of DU gave disappointing results.[11-13] The examination of the main renal arteries is a very difficult and time consuming procedure. In particular the high number of technical failures, the low detection rate of accessory renal arteries and the low sensitivities indicated that the studied procedures were unfit to be used for screening purposes among the general hypertensive population.[11-13] But in some groups of patients, especially those with a low BMI, or an easily accessible kidney as in renal transplant recipients, better results of DU in the detection of RAS were reported.[17-19] These studies also showed that although the values and variations of sensitivity and specificity were strongly dependent on the applicated cut-off points of the Doppler parameters, sensitivity did not exceed 70%.[17]

By applying recognition of waveform changes of early systolic peak obtained from the segmental arteries in the DU examination, the technical failure rate of the procedure can be lowered dramatically. In the present study we had a technical failure rate of 9% which is much lower than that reported in the literature, and the rate of 25% found in a previous study, in which among other parameters, flow changes in the main renal arteries were used.[13] The detection of accessory renal arteries is also an important shortcoming in the DU technique in studying the main renal arteries. If the Doppler signals are recorded from segmental arteries that are located downstream from a stenosed vessel, including accessory vessels, it should be possible in theory, to detect such a stenosis by changes in the systolic velocity wave pattern. However, as we had no patients with a stenosis in an accessory artery we can not conclude whether or not this method allows detection of stenoses in accessory renal arteries. A recent study that did include accessory renal arteries reported a very low accuracy for DU in detecting renal artery stenosis, and a total absence of the ability to detect arterial stenosis in segmental and accessory arteries.[20]

The most important characteristic of the DU technique we studied is its sensitivity in the recognition of patients with renal artery stenosis. The sensitivity established was 47% and the specificity 97%. So, half of the patients with a stenosis in this study would have gone undiagnosed had we relied upon Doppler ultrasound.

In this study the test sensitivity in patients with bilateral stenoses was even worse. The cause of this might be in the different mechanisms that are involved in the concomitant high blood pressure (BP). The opinion is that in unilateral stenosis, at least in some stages, angiotensin II plays an important part while in bilateral stenosis an important factor in the sustentation of the high BP is sodium retention. Although the changes in systolic waveform morphology in the case of renal artery stenosis are influenced by many factors, it might be that the changes in arterial compliance brought about by angiotensin II are different from those caused by sodium retention, and that the difference in sensitivity of detecting unilateral and bilateral stenosis can be found in these different mechanisms.

An important aspect of the technique of analysis of waveform features, apart from its low sensitivity, is the low inter-observer agreement in the visual judgement of these waveforms.[21] This is the more important as other more objective DU measures such as acceleration time and peak systolic velocity were even less reliable in separating stenotic from non-stenostic renal arteries.[20]

A recent study using Doppler tardus waveforms for the identification of renal artery stenosis, showed that in six patients with a moderate stenosis the waveforms were not classified as abnormal, but were recognised as abnormal 1 h after the administration of captopril.[22] The authors explained this by speculating that a high angiotensin II concentration causes raised intrarenal vascular resistance which obscures the loss of the end-systolic pressure (ESP) and that the angiotensin-converting enzyme (ACE) inhibitor, by lowering intrarenal vascular resistance and increasing compliance, by inhibiting angiotensin II formation, makes the loss of the ESP visible.[22] The detection of renal artery stenosis by renal scintigraphy also relies upon high angiotensin II levels in the affected kidney influenced by ACE inhibition. But the sensitivity of renal scintigraphy does not rise above 75%.[23] So ACE inhibitor enhanced DU should be studied further, including the aforementioned problem of the low inter-observer agreement in the visual judgement of DU waveforms, before its true value can be inferred. The factors that are involved in the transduction of the BP curves into the flow changes in the renal arteries distant to a stenosis are so numerous and variable that it is not easy to understand that only by changing angiotensin II levels could it lead to consistent and unequivocal changes.[24]

Another option by which the DU results might be improved is the use of ultrasound contrast enhancement with galactose-based microparticle suspensions.[25] Many DU techniques have been studied in an attempt to find a reliable non-invasive procedure to examine the renal vasculature. With the development of intrarenal investigation techniques like the one we employed in the present study much seemed to have been gained. However, as is illustrated by the present results and literature up to now, DU is in general not reliable enough to permit its use as a screening procedure for RAS.[24] In particular, patients with a low BMI can be examined reliably in this way, but there remains a strong influence on the results of the institution where the DU is performed.

We conclude that the DU pattern recognition of the loss of early systolic peak in segmental renal arteries is not sensitive enough to be used in clinical practice for the detection of main renal artery stenosis in an unselected hypertensive population.

References

1 Mann SJ, Pickering TG. Detection of renovascular hypertension. State of the art. 1992. *Ann Intern Med* 1992; **117**: 845–853.
2 Anderson GH Jr, Blakeman N, Streeten DHP. Prediction of renovascular hypertension. Comparison of clinical diagnostic indices. *Am J Hypertens* 1988; **1**: 301–304.
3 Novick AC *et al*. Diminished operative morbidity and mortality in renal revascularisation. *JAMA* 1981; **246**: 749–753.
4 Sos TA *et al*. Percutaneous transluminal renal angioplasty in renovascular hypertension due to atheroma or fibromuscular dysplasia. *N Engl J Med* 1988; **309**: 274–279.
5 Postma CT *et al*. Occlusion of stenosed renal arteries – relation to medical treatment. *J Hum Hypertens* 1989; **3**: 185–190.
6 Greene ER *et al*. Noninvasive characterisation of renal artery blood flow. *Kidney Int* 1981; **20**: 523–529.
7 Avasthi PS, Voyles WF, Greene ER. Noninvasive diagnosis of renal artery stenosis by echo-Doppler velocimetry. *Kidney Int* 1984; **25**: 824–829.
8 Dubbins PA. Renal artery stenosis: Duplex Doppler evaluation. *Br J Radiol* 1986; **59**: 225–229.
9 Handa N *et al*. A new accurate and non-invasive screening method for renovascular hypertension: the renal artery Doppler technique. *J Hypertens* 1988; **6** (Suppl 4): S458–S460.
10 Robertson R, Murphy A, Dubbins PA. Renal artery stenosis: the use of duplex ultrasound as a screening technique. *Br J Radiol* 1988; **61**: 196–201.
11 Berland LL, Koslin DB, Routh WD, Keller FS. Renal artery stenosis: prospective evaluation of diagnosis with color duplex US compared with angiography. *Radiology* 1990; **174**: 421–423.
12 Desberg AI *et al*. Renal artery stenosis: evaluation with color Doppler flow imaging. *Radiology* 1990; **177**: 749–753.
13 Postma CT *et al*. Doppler ultrasound in the detection of renal artery stenosis in hypertensive patients. *Br J Radiol* 1992; **65**: 857–860.
14 Stavros AT *et al*. Segmental stenosis of the renal artery: pattern recognition of tardus and parvus abnormalities with duplex sonography. *Radiology* 1992; **184**: 487–492.
15 Bardelli M, Jensen G, Volkmann R, Aurell M. Non-invasive ultrasound assessment of renal artery stenosis by means of the Gosling pulatility index. *J Hypertens* 1992; **10**: 985–989.
16 Hansen KJ *et al*. Renal duplex sonography: evaluation of clinical utility. *J Vasc Surg* 1990; **12**: 227–236.
17 Saarinen O, Salmela K, Edgren J. Doppler ultrasound in the diagnosis of renal transplant artery stenosis – value of resistive index. *Acta Radiol* 1994; **35**: 586–589.
18 Schrey G *et al*. Interpretation of renal angiography by radiologists. In: Schrey G (ed). *Diagnostic aspects of renovascular hypertension*. (Dissertation). 1995. University Press, Maastricht.
19 Sagalowski AI, McQuitty DM. The assessment and management of renal vascular hypertension after kidney transplantation. *Semin Urol* 1994; **12**: 211–223.
20 Kliewer MA *et al*. Renal artery stenosis: analysis of Doppler waveform parameters and tardus-parvus pattern. *Radiology* 1993; **189**: 779–787.
21 Kliewer MA *et al*. Doppler evaluation of renal artery stenosis: interobserver agreement in the interpretation of waveform morphology. *Am J Radiol* 1994; **162**: 1371–1376.
22 René PC *et al*. Renal artery stenosis: evaluation of Doppler US after inhibition of angiotensin-converting enzyme with captopril. *Radiology* 1995; **196**: 675–679.
23 Prigent A. The diagnosis of renovascular hypertension, the role of captopril renal scintigraphy. *Eur J Nucl Med* 1993; **20**: 625–644.
24 Bude RO, Rubin JM. Detection of renal artery stenosis with Doppler sonography: it is more complicated than originally thought. *Radiology* 1995; **196**: 612–613.
25 Missouris CG *et al*. Non-invasive screening for renal artery stenosis with Doppler ultrasound contrast enhancement. *J Hypertens* 1994; **12** (Suppl 3): S192.