Review Article

Advances in noninvasive methods for functional evaluation of renovascular disease

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Abstract

As the number of patients with newly diagnosed renal artery stenosis increases, so has the number of percutaneous transluminal renal-artery angioplasties in the last few years. Deciding the preferred treatment in the clinical setting is fraught with difficulties related to many factors, and there is limited evidence to support angioplasty/stent for any indication. These considerations emphasize the urgent need for improved noninvasive assessment of kidney function in patients with vascular disease. This review will attempt to summarize the available techniques that may potentially be used for measurement of renal function in this context. J Am Soc Hypertens 2009;3(1): 42–51. © 2009 American Society of Hypertension. All rights reserved.

Keywords: Renal; stenosis; hypertension; ultrasonography.

Introduction

The increase in aging populations has been associated with a rise in the incidence and diagnosis of renovascular disease. Elderly patients with atherosclerotic renovascular disease may have renin-dependent hypertension, a hemodynamically insignificant stenosis with coexisting essential hypertension or both simultaneously. However, in approximately 10% of patients with renal artery stenosis (RAS) due to atherosclerotic disease, blood pressure (BP) values are within the normal range.\textsuperscript{1} Aged patients are more prone to complications during and after revascularization compared to younger subjects.\textsuperscript{2,3} As the number of patients with newly diagnosed RAS increases, so has the number of percutaneous transluminal renal-artery angioplasties with or without stenting (PTRA/S) in the last few years: 7,660 procedures were performed in the year 1996 and 18,520 in 2000.\textsuperscript{4,5}

The American College of Cardiology and the American Heart Association have issued clinical guidelines for the management of RAS. A detailed assessment by the Agency for Healthcare Research and Quality issued a report in 2006 showing that deciding the preferred treatment is fraught with difficulties related to many factors and that there is limited evidence to support PTRA/S for any indication.\textsuperscript{6} The report calls for a systematic evaluation of the role of renal revascularization procedures, kidney dysfunction, and the concomitant diseases.

Data gathered so far show that roughly 25% to 30% of the patients with chronic azotemic renovascular disease submitted to PTRA/S have a consistent benefit from treatment, 45% to 50% stabilize without further deterioration and 20% to 25% show a detrimental effect on their renal function status.\textsuperscript{3} This fact has led the Centers for Medicare and Medicaid Services (CMS) to reconsider the National Coverage Decision (NCD) for treating RAS with balloon angioplasty and/or stenting. A final judgment on this issue remains pending. The uncertainty of benefit from revascularization in atherosclerotic lesions is reflected in the commitment to undertake prospective, randomized treatment trials comparing medical therapy to medical therapy combined with endovascular revascularization. The National Institutes of Health have funded a multicenter study: Cardiovascular Outcomes with Renal Atherosclerotic Lesions (CORAL), in order to evaluate clinical outcomes of more than 1,000 patients treated with medical therapy compared...
will have results from the randomized treatment comparison finished recruitment phase and is in its follow-up stages. We have results from the randomized treatment comparison by the spring of 2008, but data presented so far have been shown inconclusive. A Dutch study, The benefit of STent placement and BP and lipid-lowering for the prevention of progression of renal dysfunction caused by Atherosclerotic ostial stenosis of the Renal artery (STAR), recruited 140 patients and finished follow-up period but results are pending.

Expenditures for the MEDICARE ESRD program are expected to more than double in the next 10 years and surpass 28 billion dollars annually by 2010. If renal stenting proves unnecessary, a cost estimated in 1.7 billion dollars will be saved. These considerations emphasize the urgent need for improved noninvasive assessment of kidney function in patients with vascular disease. This review will attempt to summarize the available techniques that may potentially be used for measurement of renal function in this context. These have been chosen based on a careful review of available literature (Table).

Problems in the Clinical Evaluation of RVH Inherent to the Pathological Physiology of the Disease

For years the diagnosis, evaluation of renal function, and the treatment of renovascular hypertension (RVH) has been a subject of intense debate. Many of these uncertainties are due to the lack of information about changes in intrarenal hemodynamics, glomerular filtration rate (GFR), and proximal and distal function in both the stenotic (ST-) and in the contralateral kidney (CONT-KD), or alternatively for both kidneys if they are affected by vascular disease. Most current methods used to evaluate renal function are not readily applicable in renovascular disease. For example, individual renal clearances cannot be performed in these conditions because of the mixture of urine from both kidneys in the bladder. Split renal function studies obtained by independent catheterization of both ureters carry a risk of pyelonephritis. Intuitively, having accurate information about individual renal function should improve prediction of the success of any therapeutic intervention. Unilateral renovascular disease appears to have different stages that may affect the success of therapy. De Bruyne et al define the severity of the vascular disease required to activate the release of renin by measuring pressure gradients between the aorta and the renal artery distal to the stenosis. This is an invasive technique that needs further validation, but up to this date there are no means to know if the stenosis is affecting renal hemodynamics. In cases with a stenosis of the renal artery where the increase in mean arterial pressure is sufficient to restore renal blood flow (RBF), renal angioplasty can improve renal function of the ST-KD while protecting the CONT-KD against the effects of hypertension. However, cases of hemodynamically significant stenosis in which hypertension maintains only part of RBF and the impairment of total renal function is compensated by a hypertrophy of the CONT-KD require more extensive consideration. In this case, restoration of RBF in the ST-KD can be limited by interstitial fibrosis and deterioration of distal tubular function, and lowering BP could impair renal function in the CONT-KD in which hypertrophy requires high levels of perfusion pressure. How much of the decreased renal function can be restored in the ST-KD or the extent to which the fall in BP will revert the hyperplasia of the CONT-KD cannot be accurately evaluated at the present time because of the lack of suitable imaging methods or “markers.” From these considerations an important goal for renovascular research is to develop tools to assess renal function and hemodynamic changes that may result from revascularization of the ST-KD.

Noninvasive Assessment Studies

Renal Doppler Ultrasonography

Cheap and widely available, renal ultrasonography is established as a useful tool for measuring blood velocity but its potential role in predicting benefit from renal revascularization is controversial. No simple correlation has been found between the degree of stenosis and the response to renal angioplasty with this method.

Parameters like peak systolic flow velocity >200 cm/s or a renal aortic flow velocity ratio >3.5 are highly sensitive in terms of detecting RAS; however, the specificity detecting a hemodynamically relevant RAS is low and lacks reliability for prediction.

Another ultrasonographic parameter, the vascular resistance index (RI), has been proposed as an adequate predicting tool. RI is calculated from the maximum systolic velocity (V_max) and minimum diastolic velocity (V_min) from a Doppler spectrum with the following formula: RI = (1 - (V_min/V_max)), and it has been proposed as a functional equivalent of structurally altered vasculature. Radermacher et al reported that RI values of ≥ 0.8 strongly suggest that a revascularization procedure might prove futile and even harmful due to a worsening in creatinine clearance and mean BP measurements, so that patients with these RI values should not be submitted to an intervention and must be treated medically. Other studies have not shown similar results and suggest that patients with RI ≥ 0.8 should not be excluded from angioplasty unilaterally. These differences may have been due to methodological issues such as placement of stents instead of balloon dilatation, and many factors affecting RI interpretation such as the extent of
stenosis, distensibility/stiffness of the vascular system, acute swelling of the kidney in patients with renal obstruction, hemolytic uremic syndrome, and transplant rejection. Location of intrarenal Doppler placement and nonrenal factors such as tachy-bradycardia, arrhythmias, and aortic valve insufficiency may also play a role in affecting RI. However, further studies are required in order to clarify if this subset of patients should not be treated invasively but medically based on this method alone. On the other hand, there has been a degree of uncertainty regarding the conduct to be adopted with patients having RI values below 0.8. In this group, RI values obtained by ultrasonography have shown 91% to 94% sensitivity and low 31% to 53% specificity in predicting improvement of hypertension after RAS treatment.

Considering the data gathered so far, it can be said that RI values measured with renal ultrasonography alone cannot be recommended to avoid exposure to an invasive procedure such as PTRA/S in the group of patients with RI ≥ 0.8. In the group with RI < 0.8, this method should not be used as the sole selection criteria neither to decide nor exclude patients from a revascularization procedure.

Renal Scintigraphy

Increased renin secretion from the stenotic kidney is a major pathogenetic factor in the development of hypertension in renovascular disease. When captopril is administered to a patient with RVH, an inhibition of the conversion of renin to angiotensin ensues, causing a fall in GFR of the stenotic kidney secondary to a decreased resistance in postglomerular arteries. This suppression in GFR can be detected scintigraphically and is the rationale of its use in RVH diagnosis. However, the role of this method in predicting outcome after revascularization has been debated amidst contradictory results.

Its usage for the detection of RVH has been taking place for years although now is rarely used as a primary tool, having been displaced by morphological methods with well known advantages such as ultrasonography, magnetic resonance angiography, or computed tomographic (CT) angiography. Comparatively, renal scintigraphy is less accurate in cases of renal insufficiency, bilateral stenosis, and unilateral stenosis with single-kidney. It is safe, but has numerous pitfalls, which lead to false interpretations such as dehydration, hypotension, full bladder impairing drainage and also requires that the patient should interrupt ingestion of angiotensin-converting enzyme inhibitors and diuretics 3 to 5 days prior to the procedure. Calcium antagonists may cause false-positive results.

In the midst of these features, the value of this method in identifying patients who will benefit from revascularization looks somber. Some studies failed to find a correlation and concluded that the method was not useful in selecting patients for angioplasty, while others have shown a positive association with variable ranges of specificity (62% to 100%; mean, 78%) and sensitivity (84% to 100%; mean, 92%). Renal scintigraphy provides no information of the functionality beyond the glomerulus, shedding no light on variables such as tissue oxygenation or tubular dynamics. Without these parameters, the ability to predict restoration of the ST-KD function and reversal of CONT-KD hypertrophy after revascularization seems meager.

CT

CT technique uses x-rays for the evaluation of the relationship between arterial, tissue, and venous enhancement after the administration of an intravenous iodine-based contrast material.

Perfusion CTs detect changes in the attenuation of this contrast material which are proportional to its concentration, so that repeated rapid scans acquired at the same location allow determination of time-attenuation curves, which, in turn, may be analyzed to obtain a perfusion value. In the kidney, the administered contrast material is neither secreted nor reabsorbed in the tubules and, therefore, behaves like inulin. Images detect an extravascular flow of contrast media along the renal tubules after leaving the bloodstream. In order to enable reliable measurements of renal hemodynamics, mathematical models have been developed that reliably discriminate renal vascular and tubular flow.

CT offers accurate, reproducible, simultaneous, and non-invasive quantification of single-kidney volume, perfusion, GFR, and segmental tubular function which are difficult to obtain by other methods and may be potentially used to predict outcome after PTRA/S in patients with RVH. However, during more than 30 years renal perfusion measurements were largely confined to research studies that have not yet seen a clinical application. This may be due to the limitations imposed by the use of contrast medium that involved high risk of nephrotoxicity and hypersensitivity, and by the effects of radiation.

We will attempt to summarize the most promising techniques available up-to-date.

EBCT

Electron-Beam Computed Tomography (EBCT) or ultrafast CT has been proposed for assessment of intrarenal volume and perfusion in RVH. It differs from conventional CT because the x-ray tube is larger than the imaging circle and the high-intensity electron beam current within the vacuum tube is swept electromagnetically, not mechanically, enabling far greater speed, which makes it suitable for the abovementioned purpose. Fast image acquisition is required due to the rapid contrast transit time through the renal circulation. Lerman et al tested this method in animal models of RVH showing that it is reliable and
reproducible in estimating renal hemodynamics and function and that it is applicable not only in physiological conditions but also in pathological models of chronic disease. In 33 human subjects with RVH and well-preserved renal function, this group demonstrated that, in contrast to patients with fibromuscular dysplasia, decreased cortical perfusion in atherosclerotic RAS was not correlated with the degree of stenosis, a fact that underlines once more the importance of assessing kidney function rather than the degree of stenosis in this subgroup of patients and proves that the method is suitable for assessing single-kidney function in humans.

EBCT is very large in size and expensive in comparison to conventional CT, and thus is not readily available everywhere. Newer, faster, more affordable methods like multidetector computed tomography (MDCT) may provide nowadays a better option for clinical application with better temporal and spatial resolution.

**MDCT**

MDCT scanners, also known as multislice, multisection, or multidetector-row CTs have been shown to provide a precise assessment of regional renal perfusion (discriminates cortical and medullary volumes and perfusion rates), tubular dynamics, and glomerular flow rate showing good agreement with previously validated EBCT. These are faster helical devices that enable the acquisition of multiple sections simultaneously by means of a 2-dimensional array of detector elements. They provide versatile scanning sequences with wider availability, and better image quality due to lower noise, higher spatial resolution, and larger number of time points than those obtained with EBCT.

In spite of all these features, there are no published data on the assessment of renal hemodynamics in humans, although some studies are under way which may shed light on the enormous potential of this technique for predicting renal response after revascularization procedure.

**PET**

Positron Emission Tomography (PET) is a modern medical imaging technique which has achieved a high level of technological perfection due to improvements in detector technology, computer hardware, and image processing software. It uses different kinds of short-lived radioactive tracer isotopes which are injected intravenously and provide quantitative measurements of functional parameters with very low risk of nephrotoxicity and hypersensitivity. Hybrid PET/CT systems are also in use which merge the benefits of the two imaging modalities. Despite being a minimally invasive technique, it does involve low-dose ionizing radiation exposure.

Renal PET functional imaging nowadays is rather limited because for PET and PET-CT studies of the kidney, new disease-specific molecular probes need to be developed, some of which have been compared for clinical application. Fluorodeoxyglucose, which is the tracer used in 95% of PETs to date is not suitable for this purpose due to its renal excretion. Carbon-11-acetate, on the contrary, is one among the naturally occurring molecules that can be labeled with positron-emitting nuclides and is eliminated by the liver making it suitable for renal studies. There is some experience with its use, especially to assess myocardial oxidative metabolism and blood flow, but it has also been applied for the assessment of renal function in animals and humans as well. With this tracer, excellent images of the kidney can be obtained even when there is a markedly reduced RBF, but cortical and medullary areas are not discernible. In addition, it provides accurate estimates of tissue metabolism by measuring acetate turnover in Krebs cycle and quantitative information of renal oxidative metabolism that correlates well with the amounts of filtrated and reabsorbed sodium, processes well-known to affect renal oxygen consumption.

Other interesting areas of research within renal metabolism are angiotension-1 receptors (AT1Rs) which may also be a sensitive probe of renal ischemia taking into account that when hypoxia occurs (as in the case of RAS) there exists an overexpression of AT1Rs in the kidney, a process which suffers regression after sufficient collateral circulation and renal atrophy develops. In dog models of RVH, PET showed that RAS resulted in reduced RBF, reduced AT1R radioligand delivery, but increased radioligand retention proving the above-mentioned receptor overexpression. If the same phenomenon is demonstrated with PET in humans, practitioners will be able to know if the atrophic kidney really needs revascularization and will have vital information of the contralateral kidney as well.

Describing all the tracers used in PET scanning is beyond the scope of this review. However, it should be emphasized that its potential use for assessing tissue hypoxia and apoptosis in single-kidney renovascular disease and obstructive nephropathy might prove very useful in the future, and may play a key role for predicting outcome after renal PTRA/S. New tracers in PET studies need validation for human use, and cost and availability are still barriers for the widespread use of this technique.

**MRI**

Magnetic Resonance Imaging (MRI) uses a magnetic field to align the nuclear magnetization of protons in water and then by means of radiofrequency fields alter the alignment in order to produce computer-generated images of the body. When enhanced with gadolinium contrast agents it provides a noninvasive and accurate evaluation of renal morphology, proximal arterial anatomy, intrarenal hemodynamics, and estimations of single-kidney function in research settings without exposure to ionizing radiation.
However, although originally thought to be non-nephrotoxic, the use of gadolinium-based contrast agents has been reported to be associated with potentially reversible acute tubular cell injury,\textsuperscript{67} anaphylactoid reactions, and nephrogenic systemic fibrosis.\textsuperscript{68,69} Some techniques are being developed with potential to predict outcome after renal revascularization in RAS.

**BOLD-MRI**

This technique is based on the properties of deoxyhemoglobin, which is an endogenous occurring paramagnetic substance susceptible to being quantified by magnetic resonance imaging. This novel MRI method detects signal variance based on changes in the oxygen levels within the hemoglobin molecule, and therefore pO₂ values within the bloodstream.\textsuperscript{70} The limitations are use of an electromagnetic field, moderate cost and availability, and some confounders such as hematocrit, blood flow, and volume parameters and changes in the hemoglobin-O₂ dissociation curve produced by pH variations and temperature which have to be taken into consideration as they might alter the so-called blood oxygen-level dependent magnetic resonance imaging (BOLD-MRI) or BOLD-MRI readings.\textsuperscript{71} Several investigators in different medical specialties are trying to use the BOLD-MRI technique for clinical applications. Myocardial ischemia,\textsuperscript{72} transplant rejection,\textsuperscript{73} tumor hypoxia,\textsuperscript{74} neurological and psychiatric disorders,\textsuperscript{75} and RVH are some of the subjects under study to quote a few.

In the kidney, the local oxygen tension reflects the balance between oxygen delivery and consumption in viable cells and tissue, with oxygen tension values that differ between the cortical and medullary segments, as renal medulla operates normally with lower pO₂ values than the cortex (10 to 20 mm Hg inner medulla, 40 to 50 mm Hg outer cortex).\textsuperscript{76}

Energy-spending processes which account for most of the oxygen consumption within the kidney are mainly due to sodium reabsorption by the renal tubules (82% to 97%) and in a lesser extent (3% to 18%) to basal metabolic demands that remains after suppressing tubular Na load and thereby tubular reabsorption, as it happens in the nonfiltering kidney.\textsuperscript{77,78} An important consideration to understand the application of BOLD-MRI is that O₂ utilization differs in different tubular segments. It is approximately 27% in the proximal tubules which reabsorbed 67% of the filtered Na. In contrast O₂ consumption reaches 67% in the thick ascending segment of the Henle’s loop (TAHL) although this segment reabsorbs 25% of the filtered Na.\textsuperscript{79,80} Such differences are most likely due to the fact that Na reabsorption in the proximal tubules is isosmotic, while in the TAHIL is against an osmotic gradient and is depending on active participation of a cotransporter called Na, K, 2 Cl. This cotransporter is inhibited by furosemide. Brezis et al\textsuperscript{81}

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**Table**

Summary of methods for functional assessment of renal vascular disease: general features

<table>
<thead>
<tr>
<th>Method</th>
<th>Measures</th>
<th>Potential to Predict Outcome After PTRA/S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doppler ultrasonography</td>
<td>Vascular resistance index</td>
<td>High sensitivity, low specificity ≥ 0.8 high risk Affected by many renal and nonrenal factors</td>
</tr>
<tr>
<td>Renal scintigraphy</td>
<td>Vascular response to captopril</td>
<td>Low sensitivity and specificity; not accurate in renal failure, unilateral stenosis with single kidney and bilateral stenosis Numerous pitfalls such as dehydration, hypotension, impaired bladder drainage</td>
</tr>
<tr>
<td>EBCT/MDCT</td>
<td>RBF, GFR, tubular flux, renal volume Cortico-medullary ratio</td>
<td>Accurate dynamic assessment Single-kidney image</td>
</tr>
<tr>
<td>PET</td>
<td>Tissue O₂ metabolism (with C11-acetate) Renal ischemia (with AT1Rs)</td>
<td>Quantitative, dynamic information Single-kidney image No human studies available</td>
</tr>
<tr>
<td>BOLD-MRI</td>
<td>Changes in deoxyhemoglobin levels in outer medulla during furosemide</td>
<td>Estimates distal Na reabsorption Human studies available Good correlation with invasive pO₂ measurements Single-kidney image</td>
</tr>
<tr>
<td>3-D MRI + radioisotopic GFR</td>
<td>Renal morphological features combined with single-kidney GFR</td>
<td>High parenchymal volume; single-kidney GFR ratio proposed as “hybernating parenchyma”; hypothesis not validated yet</td>
</tr>
<tr>
<td>BNP</td>
<td>Blood BNP levels</td>
<td>Potentially affected by many factors other than RAS</td>
</tr>
</tbody>
</table>

BOLD-MRI, blood oxygen-level dependent magnetic resonance imaging; BNP, B-type natriuretic peptide; EBCT, electron-beam computed tomography; GFR, glomerular filtration rate; MDCT, multidetector computed tomography; PET, positron emission tomography; PTRA/S, percutaneous transluminal renal-artery angioplasties with or without stenting; RBF, renal blood flow; 3-D MRI, 3-dimensional magnetic resonance imaging.

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46
found in experimental animals that furosemide produces a marked increase in O$_2$ concentration in the medulla without affecting O$_2$ concentration in the renal cortex. Consistent with this demonstration Prasad et al. have shown that furosemide induces a significant fall in the intrarenal levels of deoxyhemoglobin in normal kidneys. Consequently the rationale for the use of furosemide suppression of Na transport and O$_2$ consumption in the TAHL is that such an effect is not seen when Na delivery to the TAHL has been significantly decreased. This is assumed to occur in RVH when the fall in GFR is of such a magnitude that the volume of tubular fluid is insufficient to reach the distal nephron. A few animal studies have shown good correlation between BOLD-MRI images and tissue pO$_2$ values obtained by direct in-situ oxygen probes, which encouraged further BOLD-MRI studies that proved that estimating distal function in the ST-KD in RVH with an injection of furosemide is appropriate and suitable for application in humans. Recently, Textor et al. presented for the first time the application of BOLD-MRI in 25 human subjects with vascular compromise from atherosclerotic vascular disease. Whether response to furosemide as an index of distal tubular reabsorption in the assessment of tubular reaction to revascularization by means of MRI using the so-called furosemide-induced suppression of oxygen consumption might be correlated or not with the ability of the kidney to recover after revascularization is a matter that requires further research.

It should be mentioned that the usefulness of BOLD-MRI alone to estimate changes in oxygen blood levels in the renal circulation and/or renal O$_2$ consumption without any other maneuver is debatable. It has been argued that these measurements can be biased by changes in renal tissue pO$_2$ due to renal arteriovenous shunting which has been proved to occur in animal models. Up to this date, the validity of this technique as an indicator of parenchymal oxygenation relies on the assumption that tissue oxygenation varies with blood oxygenation, but further validation is imperative. New functional MRI approaches using extracellular pO$_2$ reporter molecules are under study in order to elucidate this issue.

Three-Dimensional MRI With Radioisotopic Single-Kidney GFR

In this technique the ability of 3-dimensional MRI to produce accurate images and measurements of renal morphology such as parenchymal volume is combined with a standard radioisotopic methodology to assess single-kidney GFR. Although decreases in renal volume, length, cortical, and parenchymal thicknesses are thought to reflect irreversible intrarenal damage, it has been observed in human subjects that a disproportionately high parenchymal volume single-kidney GFR ratio in patients with RAS $\geq$50% is correlated with a “hibernating parenchyma” with potential for recovery after revascularization. However, this hypothesis requires further validation.

Biochemical Markers: BNP

Natriuretic peptides are hormones released from the heart in response to pressure and volume overload. Brain natriuretic peptide (BNP) and N-terminal-proBNP have become important tools as predictors of major cardiovascular events and sudden death in patients with coronary syndromes and congestive heart failure. Silva et al. measured BNP in 27 human subjects with refractory hypertension and angiographic RAS $\geq$70% before and after a renal artery revascularization procedure. The rationale for these measurements were the observation of an angiotensin-2-induced effect on BNP production and release in animals, and the fact that mRNA for both atrial natriuretic peptide and BNP is up-regulated in an animal model after renal artery clipping. Inappropriately high levels of renin and subsequently angiotensin-2 are known to occur in renovascular disease, and according to these findings BNP synthesis and release might theoretically be stimulated in human subjects with RAS.

In this study, patients with medically refractory hypertension and significant RAS presented increased BNP levels and a correlation was found between elevated levels of BNP at baseline (>80 pg/mL) and improvement of clinical hypertension after angioplasty. However, these interesting findings are limited by low statistical power due to a small number of patients, and the lack of a control group with refractory hypertension without RAS. In this setting, it is not possible to determine whether renovascular disease or other potential factors such as old age or atherosclerotic disease in other areas of the vascular tree may have contributed to the elevated BNP levels. Further research is needed in order to clarify these results.

Conclusions

In a global context, detection of renal artery lesions is growing rapidly due to an aging population, along with renal revascularization procedures that carry a rise in annual expenditures for coverage. Understanding the effects of vascular occlusive disease upon kidney function and BP raises major uncertainties. Clinicians have few established criteria for determining which patients are going to benefit from an invasive treatment that carries substantial expense and some risk.

Some facts derived from renal physiology demand the physicians to provide more information about the kidneys before we embark in an invasive intervention, such as the response of the contralateral kidney which is increasing its volume in order to adapt to an atrophic stenotic kidney, the
fact that the degree of RAS does not correlate with the extent of renal damage in the stenotic side, and the lack of information about renal oxygen consumption with the tools used up to this date. Whether these physiological parameters of renal hemodynamics, morphology, and metabolism will help us to determine if renal injury is due to renal artery disease versus intrinsic kidney damage is not clear yet, but more information seems the right approach.

In order to predict outcome after renal revascularization, some promising novel techniques are being developed which may provide a thorough understanding of renal function in a precise and minimally invasive manner, other than the usual parameters used by physicians (eg, creatinine clearance) that do not provide single-kidney information. It seems paramount that these techniques should be able to discriminate physiological parameters in both the stenotic and the contralateral kidney so as to predict outcome on both sides, because they are liable to be damaged after the procedure in a certain extent.

Renal Doppler ultrasonography by means of establishing vascular resistance indexes and captopril scintigraphy have shown controversial results and cannot be used as the only vascular resistance indexes and captopril scintigraphy have shown controversial results and cannot be used as the only vascular resistance indexes and captopril scintigraphy have shown controversial results and cannot be used as the only vascular resistance indexes and captopril scintigraphy have shown controversial results and cannot be used as the only vascular resistance indexes and captopril scintigraphy have shown controversial results and cannot be used as the only vascular resistance indexes and captopril scintigraphy have shown controversial results and cannot be used as the only vascular resistance indexes and captopril scintigraphy have shown controversial results and cannot be used as the only vascular resistance indexes and captopril scintigraphy have shown controversial results and cannot be used as 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