Atherosclerotic renal artery stenosis and reconstruction

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Renal artery stenosis is common especially in patients with generalized atherosclerosis. It is frequently associated with difficult-to-treat hypertension and with renal failure. There is an ongoing debate about the appropriate screening and treatment of atherosclerotic renal artery stenosis. Advances in imaging and interventional devices offer new opportunities, however, clinicians still have to decide individually in every patient to treat or not to treat stenosis with revascularization. This review evaluates the current literature in order to help the physician to find the right decision in this challenging clinical issue.

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Atherosclerosis is the main cause of renal artery stenosis. The lesions mostly occur in ostial segments of the renal artery and represent extension of adjacent aortic atherosclerotic plaque.[1] Renovascular disease may induce renovascular hypertension as well as ischemic nephropathy, an increasingly recognized cause of end-stage renal failure in the US.[2] This article will focus on the management and treatment of patients with atherosclerotic renal artery stenosis (ARAS) rather than on patients with fibromuscular dysplasia, which was recently reviewed in depth.[3]

Despite extensive research there is still a controversy concerning the appropriate treatment of patients with ARAS. Physicians have to balance for their patients the chances of improvement regarding blood pressure and renal function versus risks and costs of intervention. Efforts have focused on finding reliable clinical parameters as well as improved diagnostic techniques for predicting the outcome of ARAS,[4–8] however, ideal solutions have not yet been found. It is of note, that ARAS may occur alone (isolated anatomical renal artery stenosis) or in association with hypertension, renal insufficiency (ischemic nephropathy), or both.[9] Hence screening tests for ARAS as well as interventional procedures have to be discussed in the light of the outcome of renovascular hypertension and ischemic nephropathy.

Additionally it is worth taking in consideration the high cardiovascular mortality of patients with ARAS and its potential pathophysiological background. At present it is uncertain, whether renovascular reconstruction can improve the high mortality of these patients. Patients with ARAS are mainly older than 60 years and frequently suffer from widespread coexistent vascular disease. Five-year-survival has been found to be as low as 45% in patients with bilateral ARAS,[10] decreasing to only 18% in those requiring dialysis therapy.[11]

SCREENING FOR ARAS

In clinical practice it is essential to select patients with a high likelihood of ARAS for the further screening. A clinical score, developed by Krijnen *et al.*,[4] may help in patient selection. However, it is of note, that this score was evaluated in a preselected population with a high probability of ARAS, because only those patients with refractory hypertension or an increase of creatinine after therapy with angiotensin-converting enzyme inhibitors were included into the study.[4] This bias

may have influenced the prevalence of ARAS, evaluated with this score. Nevertheless, it seems useful to rely on several clinical parameters, which increase the likelihood for patients to have ARAS (Table 1). It is of note, that smoking as well as a low body mass index less than 25 kg/m^2 are predisposing factors for ARAS.[4]

Meanwhile several non-invasive tests, such as captopril test, color duplex sonography, captopril scintigraphy, computed tomography angiography, and magnetic resonance (MR) angiography are available, most with excellent accuracy. Intra-arterial angiography including the measurement of the pressure gradient is still the gold standard for the diagnosis of ARAS, however, the diagnostic accuracy of even this invasive procedure is also operator dependent.[12,13] Usually renal arteriography is only indicated, if angioplasty or stenting is intended.

Recently in a meta-analysis Vasbinder *et al.*[6] compared color duplex sonography with other non-invasive tests by analyzing the area under the receiver operator curve of these screening tests. They found computed tomography angiography and MR angiography with higher diagnostic accuracy than color duplex sonography for the diagnosis of ARAS. Captopril scintigraphy and captopril test were less accurate than color duplex sonography in this meta-analysis.

However, diagnostic accuray may be only one of several arguments, which lead the clinician to his favorite screening method. Other criteria may be local availability of the test and personal experience with it, as well as aspects of cost benefit. There are some clear advantages for using color duplex sonography as the first screening test of ARAS. Sonography is an economic test, giving information about the hemodynamic significance of stenosis and avoiding nephrotoxic contrast media. In addition it is useful for the follow-up after renal artery stenting.[14,15] If direct visualization of the renal arteries (Figure 1) is combined with intrarenal scanning of the kidney, both accessible within 30 min of examination time, color duplex sonography has a sensitivity and specificity of 90%, respectively, which is appropiate for a single screening test for ARAS.[16]

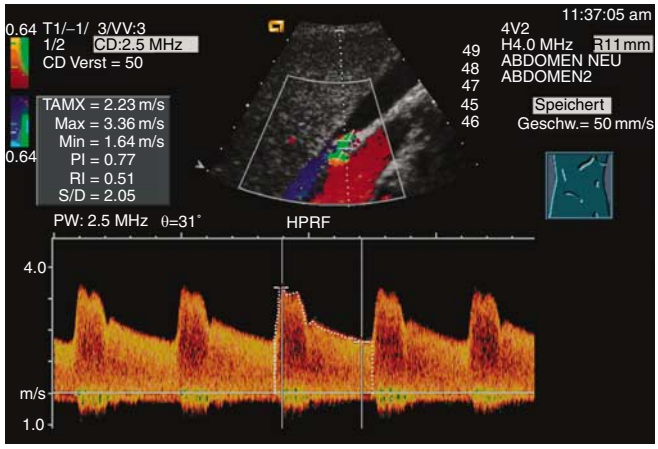

Figure 1 | Color duplex sonography of right-sided ostial renal artery stenosis. High peak systolic velocity of 3.36 m/s is obtained within in the stenosis. The green color indicates high blood flow velocity with turbulences near the stenosis. Low mean resistive index (RI = 47) of the right kidney is an indirect sign of significant stenosis.

Table 1 | Clinical findings compatible with atherosclerotic renal artery stenosis

Hypertension
Abrupt onset of hypertension at or after the age of 50 years
Accelerated or malignant hypertension
Refractory hypertension (not responsive to therapy with $\geqslant$3 drugs)
Renal abnormalities
Unexplained azotemia
Azotemia induced by treatment with an ACE inhibitor
Sonographic length of the kidney $<$8 cm
Other findings
Unexplained congestive heart failure or acute pulmonary edema
Abdominal bruit, flank bruit, or both
Systemic atherosclerotic vascular disease
Severe retinopathy
Current or former smoker
Low body mass index ($<$25 kg/m^2)

ACE, angiotensin-converting enzyme.

Currently, it is at issue whether or not color duplex sonography is useful to predict the outcome of revascularization of ARAS.[17,18] A single study showed a high predictive value of resistive index, obtained in the segmental renal arteries with color duplex sonography,[8] however, subsequent studies could not confirm these results.[19–21]

High operator dependency of color duplex sonography is often felt to argue against this diagnostic tool in the screening for ARAS. This argument, however, is referring to data of the older literature, when high-end sonographic machines with better penetration of the Doppler beam and faster hardware were not available.[22,23] Thus in recent years the success rate of sonographic visualization of the renal arteries has improved owing to further technical improvements as well as owing to broader operator experience.

Additionally it is of note, that other renal imaging techniques, such as computed tomography angiography, and MR angiography, also show substantial operator dependency including the gold standard, as mentioned above.[12,13] Recently Vasbinder *et al.*[24] prospectively assessed the diagnostic validity of computed tomography angiography and MR angiography with two panels of three observers in 356 hypertensive patients who underwent digital subtraction angiography for detection of renal artery stenosis. Moderate interobserver agreement was found, with *K* values ranging from 0.59 to 0.64 for computed tomography angiography and 0.40 to 0.51 for MR angiography.

Owing to the lack of clear evidence in the literature for diagnostic superiority of one technique, the physician, who has to screen patients for ARAS, will choose this technique, he is either performing himself (e.g., color duplex sono-