

Review

Renal Artery Stenosis - Review Upon Current Diagnosis and Endovascular Treatment in Light of Recent Studies

Dana-Oliviana Geavlete¹, Carmen Beladan^{1,2}, Magda-Ruxandra Zaharia^{2,3}, Alice Brînzea², Dan Deleanu¹, Ionel A. Checheriță^{2,4}, Bogdan A. Popescu^{1,2}, Carmen Ginghină^{1,2}

¹Cardiology Department, "Prof. Dr. C.C Iliescu" Emergency Institute for Cardiovascular Diseases, Bucharest

²"Carol Davila" University of Medicine and Pharmacy, Bucharest

³Department of Internal Medicine - "Saint John" Clinical Emergency Hospital, Bucharest

⁴Department of Nefrology and Dialysis - "Saint John" Clinical Emergency Hospital, Bucharest

REZUMAT

Stenoza de arteră renală - diagnosticul actual și tratamentul endovascular în lumina ultimelor studii

Stenoza de arteră renală este recunoscută drept o cauză importantă de hipertensiune arterială secundară și disfuncție renală. Ateroscleroza reprezintă etiologia principală a stenozei de arteră renală în peste 90% din cazuri. Prognosticul acestor pacienți este deseori nefavorabil prin asocierea de comorbidități importante la vârstnici, natura progresivă a bolii conducând în cele din urmă la insuficiență renală și evenimente cardiovasculare importante. În ciuda interesului global pentru această patologie, rezultatele recente ale studiilor randomizate nu au reușit să demonstreze un beneficiu clar al revascularizării renale cu implantare de stent din perspectiva prezervării funcției renale și al controlului valorilor tensionale. Identificarea și tratamentul precoce al stenozei de arteră renală sunt importante, dar rolul cheie în managementul acestei patologii este reprezentat de selecția adecvată a pacienților care ar beneficia cel mai mult în urma terapiei intervenționale de revascularizare renală. Devin astfel necesare atât o înțelegere mai bună a recomandărilor prezente cât și individualizarea fiecărui caz de stenoză de arteră renală pentru a determina deopotrivă rolul și momentul tratamentului medical și respectiv intervențional. Lucrarea prezintă își propune să summarizeze datele actuale din literatură și să sublinieze cele mai relevante aspecte și recomandări în această patologie din perspectiva celor două alternative terapeutice mai sus menționate.

Cuvinte cheie: stenoza de arteră renală, stenoza aterosclerotică de arteră renală, hipertensiunea renovasculară

ABSTRACT

Renal artery stenosis (RAS) is a recognized cause of renal impairment and secondary hypertension. Being associated with important co-morbidities in elderly patients, its progressive condition might lead to serious

Corresponding author:

Dana-Oliviana Geavlete, MD

"Prof. Dr. C.C Iliescu" Emergency Institute for Cardiovascular Diseases, Bucharest, Romania
Sos. Fundeni 258, sector 2, zip code 022328

e-mail: oliviana_m@yahoo.com

consequences (end stage renal failure and cardiovascular events), usually offering a worse prognosis. Despite the great interest in the field, recently emerged results from randomized trials were unable to demonstrate a clear benefit of renal artery stenting with regard to controlled hypertension and most importantly, renal function preservation. Due to major limitations and inconclusive outcomes, the uncertain clinical attitude resulting from unclear indications can often worsen RAS prognosis. Early identification and treatment in this pathology is important, but the key role in managing these patients is the proper selection of those who would benefit the most from percutaneous renal revascularization. Therefore, it becomes imperative to gain a better understanding of the presently acknowledged recommendations and to individualize every RAS patient in order to determine the correct role and timing for both medical treatment and revascularization therapy. The current paper aims to review the currently available literature data on this subject and to highlight the most relevant aspects and recommendations for RAS management regarding medical treatment and interventional revascularization.

Key words: renal artery stenosis, atherosclerotic renal artery stenosis, renovascular hypertension

INTRODUCTION

Renal artery stenosis represents the main cause of secondary hypertension and, due to its progressive profile, leads to end-stage renal disease and important cardiovascular events (1). Despite the large number of trials in this particular field of interest, RAS therapy remains a complex challenge for clinicians with regard to interventional revascularization, eventually resulting in renal function preservation, improved blood pressure control (BP) and prevention of adverse cardiovascular events in selected patients (2).

In fact, the matter of debate is represented by the proper selection of patients which would benefit the most from renal revascularization with stent implantation, while also taking into account the outcomes of the recently emerging large clinical trials that were unable to confirm the clear benefits of endovascular therapy.

Since the importance of this pathology is quite clear, as RAS is associated with an increased risk of cardiovascular events (stroke, myocardial infarction) and a higher mortality rate (3) an objective perspective upon pathology, current guideline recommendations and specific conditions associating RAS is needed.

Definition and etiology

Renal artery stenosis is defined as the narrowing (over 50% of the luminal diameter) of the main renal artery or its branches. It can affect one of the main renal arteries (unilateral RAS), both of them (bilateral RAS) as well as the contra-lateral renal

artery in a solitary functioning kidney.

The main cause of RAS is represented by atherosclerosis (over 90% of cases), affecting mainly the elderly patients and causing refractory hypertension and renal dysfunction leading to renal insufficiency and increased cardiovascular risks (4, 5).

Another condition generating RAS is the fibromuscular dysplasia (FMD) which is encountered in less than 10% of the cases, causing refractory hypertension predominantly in young women. FMD constitutes a group of non-atherosclerotic, non-inflammatory conditions that affect the renal artery, while interventional balloon angioplasty seems to provide the best results from the perspectives of controlled hypertension and preserved renal function.

Other rare diseases causing RAS include vasculites, neurofibromatosis, renal arterial aneurysm, arterio-venous fistula, systemic emboli of iatrogenic origin, aortic dissection, congenital bands and extrinsic compressions of the renal artery due to the vicinity of various tumor formations (Fig. 1, 2) (6).

Prevalence

Atherosclerotic (ATS) RAS is strongly associated with the traditional cardiovascular risk factors such as age, dyslipidemia, diabetes mellitus, hypertension and the presence of generalized ATS. Among the hypertensive population, RAS is encountered with a frequency of about 5-10%, although much higher rates were reported in selected patients (7).

RAS was discovered in more than 25% of the dialyzed patients with end-stage renal disease and up to 50% in cases in which ATS affects other vascular territories (8, 9).



Figure 1. Renal arteriography: (a) Intimal type FMD – 90% stenosis of the right renal artery in the distal segment; (b) Medial fibro-dysplasia – irregular type FMD, right renal artery stenosis (85%) emphasizing the specific “string of beads” appearance

Coronary artery disease (CAD) is most frequently associated with RAS, the prevalence in patients undergoing cardiac catheterization ranging between 24–34% (10, 11). Additionally, the presence of RAS was emphasized to independently double the risk of death in symptomatic patients with coronary artery disease.

Other vascular beds affected by ATS were documented as displaying a strong relationship with the presence of RAS (a frequency rate of 20-50% in peripheral artery disease (PAD) patients and of 31% in carotid artery stenosis (CAS) cases) (6, 12).

Pathophysiology

The mechanisms responsible for renovascular hypertension are quite complex, as the kidney has a key role in blood pressure regulation.

Unilateral significant RAS leads to reduced renal perfusion and consequently elevated renin release from the kidney perfused by the respective stenotic artery. The production of angiotensin II is subsequently increased and promotes aldosterone release from the renal cortex which increases peripheral vascular resistance, sodium retention, extracellular volume and cardiac output (13).

This is mainly referred to as “renin-dependent” hyper-tension, vasoconstriction being the result of high levels of renin and angiotensin II (14).

One important aspect of the unilateral involvement is that the renin-angiotensin-aldosterone system (RAAS) returns to baseline levels over time



Figure 2. Aortography: Bilateral renal artery stenosis in a patient with aortic coarctation

and the normal kidney is able to compensate natriuresis. However, the transiently stimulated RAAS leads to impaired vasoactive responses affecting both kidneys as well as the systemic micro-circulation. This condition can lead towards irreversible renal parenchymal changes or modifications in the arterial wall (such as the development of atherosclerosis). Most importantly, the effect of revascularization upon these particular mechanisms remains questionable so far, and may partly explain the heterogeneity of data emerged from the current trials (15-17).

Bilateral progressive RAS or solitary functioning kidney RAS implies an elevated renin secretion by both kidneys, subsequently affecting diuresis. Hypertension is maintained due to the aldosterone effect on water and sodium retention resulting in intravascular volume expansion.

Besides RAAS, other mechanisms such as endothelial dysfunction, oxidative stress, ischemic injury of the hypo-perfused kidney or hypertensive end-organ damage to the contra-lateral kidney may contribute to the pathogenesis of hypertension. The activation of the sympathetic nervous system also has a very important role in renovascular hypertension (3).

The complex interplay between several hypertensive mechanisms may explain the failure so far in predicting the revascularization outcome in RAS patients (18).

Clinical profile

The RAS clinical profile ranges from asymptomatic (“incidentally” discovered condition) to end-stage renal failure and adverse cardiovascular events.

Usually, hypertension and renal insufficiency induced by RAS are “silent” until the end-stage of the organ damage process. Therefore, a more suitable functional classification of RAS was proposed with regard to the clinical consequences of the disease. So, stage I and II refer to existing RAS but without clinical manifestations: grade I – normal blood pressure; grade II – medically controlled hypertension and normal renal function. Moreover, there are no demonstrated positive effects of the revascularization approach for these two categories of patients. Grade III refers to RAS associating evidence suggesting abnormal renal function, medically refractory hypertension and volume overload. This represents the situation in which renal revascularization should be considered (19).

The RAS specific clinical spectrum includes accelerated, resistant or malignant hypertension, unexplained renal impairment or hypotrophic kidney, sudden unaccounted for flash pulmonary edema or renal dysfunction, multi-vessel coronary artery disease and peripheral artery disease, refractory angina and congestive cardiac failure without a defined cause (6, 20).

Hypertensive patients with unexplained recurrent pulmonary edema form the main high-risk group for this pathology, usually presenting with bilateral RAS

or RAS in a solitary functioning kidney. Such cases exhibit worsened prognostic with significantly lower 4-years survival rates when compared to unilateral RAS (47% versus 59%, respectively) (19).

Within this special category of patients, an accurate and early diagnosis is of utmost importance, as interventional revascularization is susceptible to offer good clinical outcomes.

Diagnosis of renal artery stenosis

The physical examination provides rather few specific elements indicating RAS (the presence of hypertension, abdominal bruits or co-existence of ATS in other vascular beds). Therefore, a high clinical suspicion index based on personal history, physical and laboratory findings is mandatory in order to be able to make a step forward and to consider the use of specific imaging tools aimed to establish the diagnosis.

Many sensitive screening tests are available as part of the RAS diagnostic armamentarium, based either on the physiologic or anatomic parameters.

The general consensus is that non-invasive investigation methods should be applied in cases of high RAS clinical suspicion (in accordance with the current guidelines, clinical predictive factors and screening presentation scenarios are available) (6, 20).

Doppler ultrasound (DUS) is the most commonly used clinical tool and it is able to provide both physiologic and anatomic information (degree and location of the stenosis process, obstruction, renal compression or aortic aneurysm). The 82% sensitivity and 90% specificity makes DUS a valuable screening tool, but the difficulty in establishing the degree of stenosis (50 to 69% and respectively over 70% stenosis) limits its applicability (21).

Renal flow velocity provides useful information concerning the functional significance of the stenosis and the impact on renal perfusion. From this point of view, a peak systolic velocity (PSV) over 180 cm/s as well as a velocity ratio between the renal artery and the aorta above 3.5 is considered as reliably indicating the presence of significant RAS. Moreover, a renal resistance index (RI) (the ratio between PSV and end-diastolic velocity within the renal parenchyma at the level of cortical blood vessels) can identify RAS patients which may benefit from stent revascularization (RI < 0.8 predicts a favorable outcome after angioplasty) (22, 23).

Another important advantage deemed to be

taken into consideration is represented by the capacity to detect restenosis after percutaneous therapy and surgical bypass, an ability which the other diagnostic modalities (such as magnetic resonance and computed tomography angiography) do not possess (24-25).

Ultimately, it is the most cost-efficient alternative, while on the other hand, its' accuracy and reproducibility depend on both the operator's skill and the patient's characteristics (bowel gas, abdominal obesity). Current guidelines recommend DUS as first line imaging tool aimed to establish the diagnosis of RAS (Class I evidence level B) (6, 20).

Magnetic resonance angiography (MRA) provides excellent image quality of the renal arteries and surrounding structures while also bringing the advantages of a non-invasive procedure and lack of ionizing radiations. As far as the RAS detection is concerned, the Gadolinium-contrast MRA displayed a 97% sensitivity and a 93% specificity (26).

Among the most attractive features of the method, one must underline the ability to directly visualize the anatomic structures, the accurate assessment of the renal size and the capacity to determine both GRF and renal perfusion function (27-29).

On the other hand, this diagnostic alternative is marked by certain limitations in cases of metallic implants (pacemakers, clips, prosthetics), claustrophobic patients and severe renal impairment (nephrogenic systemic sclerosis gadolinium-induced). Additionally, the overestimation of moderate stenosis and the incapacity of follow-up after stent implantation (due to the presence of artefacts) also affect the MRA efficacy (30).

The presently acknowledged recommendations refer to MRA as the optimal screening method for the diagnosis of RAS in patients with a creatinine clearance higher than 30 mL/min (class I level of evidence B) (6, 20).

Computed tomography angiography (CTA) is another imaging technique that offers good quality images of the anatomy of renal arteries. It benefits from several advantages over MRA such as the ability to assess metallic implants, an improved spatial resolution as well as the capacity to clearly visualize the accessory renal artery. The sensibility in detecting RAS was described as varying between 89-100%, with a specificity of 82-100% (31).

The limitations of the method are represented mainly by radiation exposure and nephrotoxicity of



Figure 3. Abdominal CTA-images.

(a) Right renal artery stenosis with a 10 mm moniliform aspect characteristic for DFM and layered, reduced gauge areas (up to 50%); (b) Right kidney smaller than the left one - bipolar diameter; (c, d). Right renal artery stenosis (90%).

the iodinated contrast medium in renal insufficiency patients. It is predominantly recommended in cases of a creatinine clearance of more than 60 mL/min (class I level of evidence B) (Fig. 3) 6, 20].

Digital subtraction angiography (DSA) remains

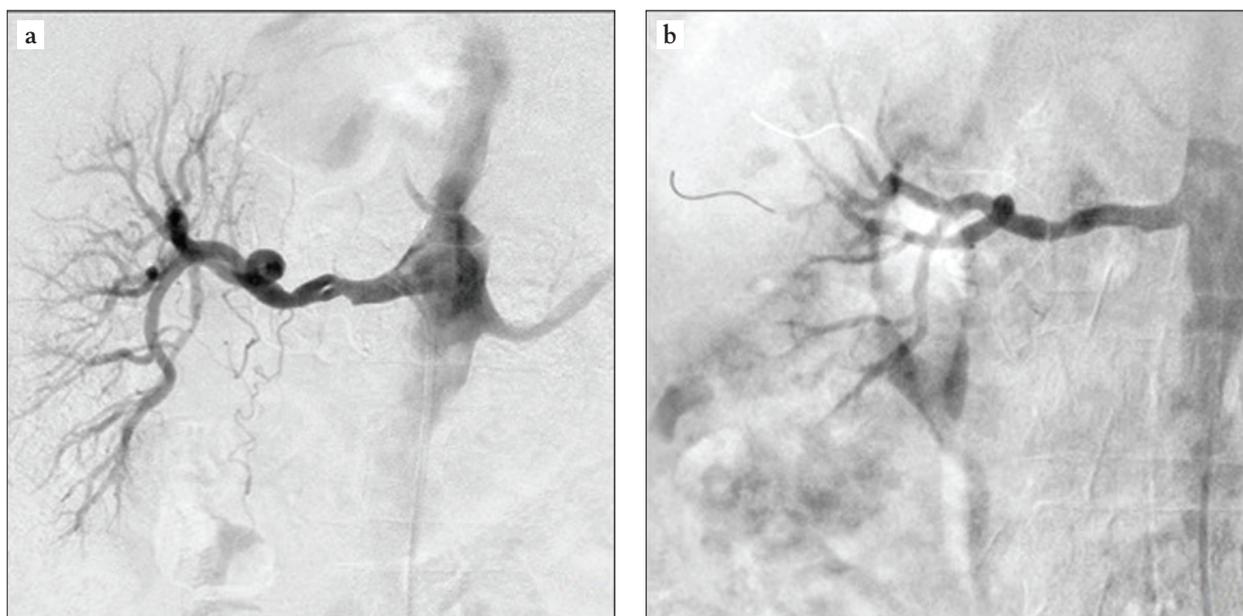


Figure 4. Renal arteriography: Unilateral RAS. Specific aspect of unstable atherosclerotic plaque in the proximal 1/3 segment of the right renal artery (70% stenosis) – atherosclerotic RAS. **(b)** Final result after revascularization – stent placement.

the “gold-standard” for the diagnosis of RAS (both of atherosclerotic and FMD origin) despite the existence of excellent imaging non-invasive tools. It can accurately identify the accessory renal arteries and enjoys a clear visualization of the main renal arteries as well as branch vessels.

The indications for this invasive approach include patients with high clinical index of suspicion and inconclusive non-invasive tests, pre-angioplasty visualization or other angiographic examinations (class I) (6, 20).

Furthermore, given the high prevalence of RAS in patients with CAD, PAD and CAS, non-selective abdominal aortography should be considered at the same time with coronarography or arteriography in patients presenting a high risk of RAS (predictive clinical clues) (19, 32).

Other diagnostic methods such as captopril-renal scintigraphy, selective renal vein – renin measurements, plasma renin activity and the captopril test (the measurement of plasma renin activity after captopril administration) are not recommended anymore as screening tests for RAS (class III) (Fig. 4,5) (6, 20).

Hemodynamically significant renal artery stenosis

Angiographic RAS can be staged as mild (<50%), moderate (50-70%) and severe (>70%),



Figure 5. Aortography – Bilateral significant RAS: Sub-occlusion of the right renal artery in the proximal segment and 80% stenosis of the left renal artery

but this does not define hemodynamically significant stenosis. The only degree of RAS considered as significant (established solely based on angiographic findings without any other confirmation) is constituted by the severe lesion – renal artery stenosis of more than 70% (33).

As far as renal stenting is concerned, only the

significant lesions may be considered. Consequently, moderate stenosis (50%-70%) must be further confirmed and physiological testing should always be performed. The current expert consensus mentions a resting trans-lesional mean pressure gradient over 10 mmHg, a hyperemic peak systolic pressure gradient larger than 20 mmHg or a renal fractional flow reserve (FFR) ≤ 0.8 as determinant parameters for significant hemodynamic severity (33-35).

Treatment

The treatment of atherosclerotic RAS is evolving and many controversies aroused concerning medical therapy alone or combined with stent revascularization, thus frequently making the decision of the clinician rather difficult. Although the medical treatment armamentarium is able to provide a certain degree of efficacy in controlling blood pressure, renal dysfunction may however display a worsening evolution over time (36).

Medical therapy

The main goals should be focused on blood pressure control, renal function preservation, reducing progression of the existing stenosis and lowering the cardiovascular events. Optimal medical therapy must primarily address cardiovascular risk factors (anti-platelet therapy, lipid-lowering treatment, smoking cessation and glycemic control).

Statins were demonstrated to be useful in reducing the progression of RAS lesions, sometimes also producing a partial regression of the atherosclerotic burden (37). The use of statins in RAS patients was also noticed to achieve a lower progression towards renal impairment as well as a reduced mortality rate (38).

Currently proposed strategies include angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), calcium channel blockers (CCB) and beta-blockers.

Anti-hypertensive drugs are effective in controlling BP, slowing the progression of the renal disease and reducing cardiovascular morbidity and mortality (39-41).

ACE inhibitors seem to constitute the proper solution for lowering BP in RAS patients, although caution must be taken into consideration with regard to renal function (a decline in GFR could be precipitated by the reduction of glomerular capillary hydrostatic pressure – reversible effect).

RAAS blockade is mainly well tolerated in RAS

cases, while the GFR reduction ($\geq 30\%$) or the elevation of creatinine serum levels by more than 0.5 mg/dL can also indicate the need of a revascularization procedure (6).

The therapy with ACE inhibitors was described as associated with lower risks of death, myocardial infarction and stroke, as well as reduced rates of death, hospitalization and dialysis initiation in a large series of RAS patients (3).

Renal angioplasty

Balloon angioplasty was highlighted by the published data as the best treatment for DFM, providing positive long-term outcomes (reduction of BP values up to normal values) as well as low restenosis rates (42, 43). Unlike DFM, revascularization in atherosclerotic RAS patients is a debatable subject, making the clinical decision often difficult.

Balloon angioplasty was the first to be considered in atherosclerotic RAS. A meta-analysis of three initial studies comparing balloon angioplasty with medical treatment (EMMA - Essai Multicentrique Medicaments vs. Angioplastie, Scottish and Newcastle Renal Artery Stenosis trial and DRASTIC – Dutch Renal Artery Stenosis Intervention Cooperative) concluded that endovascular therapy improved both the systolic as well as diastolic BP in atherosclerotic RAS patients and should be therefore taken into consideration (44).

Soon, the 1 year follow-up discovered that simple percutaneous renal artery angioplasty (PTRA) was associated with an important risk of restenosis (50%), consequently making the method in question seem unable to provide the expected benefits. Afterwards, the renal artery stent implantation replaced PTRA, as it was characterized by a significantly lower restenosis rate (18.8%), better hypertension control and renal function preservation (45, 46).

Despite the initially favorable results and technical successes, large prospective randomized clinical trials investigating the role of combined medical and renal stenting therapy when compared to medical treatment alone failed to demonstrate the clear benefits of the interventional approach in RAS patients from the perspectives of adverse cardiovascular events and renal function preservation. Therefore, several important studies for this field of interest will be described in the following paragraphs, together with their published outcomes.

STAR (Stent Placement in Patients with Athero-

sclerotic Renal Artery Stenosis and Impaired Renal Function) was a randomized clinical trial which evaluated the efficacy and safety of stent placement in RAS patients presenting impaired renal function. The primary endpoint was represented by the eventual decrease of at least 20% in creatinine clearance. A total of 140 patients with a RAS degree over 50% and renal failure (creatinine clearance < 80 mL/min/1.73 m²) were randomly assigned to stent placement with medication or to medication alone (47).

The primary endpoint was reached in 16% of the cases in the stent placement study arm versus 22% in the medically managed series. The conclusion was that renal angioplasty with stent placement has no clear effect on the progression of renal dysfunction, while on the other hand being associated with severe procedural complications. The limitations of the study were considerable, thus diminishing the significance of the definitive conclusion.

ASTRAL (Angioplasty and Stenting for Renal Artery Lesions) included 808 RAS patients and ultimately found no relevant evidence regarding the clinical benefits of revascularization (48).

Both studies highlighted the hypothesis that revascularization in unselected RAS patients (involving uncertain hemodynamically significant stenosis, controlled hypertension and normal renal function) has no well established benefit.

The debate continued with regard to the best treatment management in high-risk patients, a particular category that could benefit the most from interventional stent placement (unfortunately excluded from the initial trials).

The most recently published prospective, randomized, non-blinded, multicenter trial was CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions). The study failed to show any significant difference in terms of adverse cardiovascular and renal events between the two study arms (renal artery stent-treated plus medical therapy versus medical treatment alone) (49).

Although the trial was well conducted, some patients with no significant stenosis (< 60%) were included. Also, many of the screened patients were not eventually enrolled and only few cases reached the 5-year follow-up (otherwise a main clinical endpoint). Moreover, less than 20% of the enrolled patients had congestive heart failure (the only recommended class I criteria for revascularization), meaning that the study results are not actually that

representative and therefore cannot be truly generalized.

Besides, CORAL did not evaluate cases of failed medical treatment, thus making many of these patients not eligible for inclusion in the study.

Selecting patients for endovascular revascularization

Some specific issues in selecting patients undergoing renal artery angioplasty need to be considered: the extent of large and small vessels disease, progression rate of the stenosis, the potential to develop renal insufficiency and related comorbidities (19).

Although renal stenting in significant unilateral RAS seems to improve renal function or at least to stabilize it, the most important benefits of the revascularization approach are encountered in cases of bilateral RAS involvement or solitary kidney. These cases constitute the highest risk category of patients, suffering the worse prognostic outcomes (50, 51).

The best approach in a RAS patient is to distinguish between renal ischemia and renal nephropathy in order to be able to predict the revascularization outcome.

In order to reduce renal stenting in unsuitable categories of RAS patients and to identify the cohort that would benefit the most, a new classification was described in 2009 by Safian and Madder, separating patients according to the presence of ischemia and nephropathy.

This classification includes patients with normal (type 1) and abnormal (type 2) kidney parenchyma and with normal (type A) and abnormal (type B) renal perfusion.

It is important to note that, according to the available literature, type 1A should not be revascularized due to the lack of ischemia. The category enjoying most of the benefits subsequent to renal angioplasty would definitively be the type 1B – minimal or no nephropathy but strong evidence of renal ischemia. Also, the worse choice in considering revascularization would be constituted by type 2A – absence of renal ischemia and advanced nephropathy (52).

Certain predictors were proposed while aiming to assess the benefits of stent revascularization, but their predictive value had not been consistently confirmed so far.

Baseline eGFR < 40 mL/min/1.73m² was initially showed to be an independent predictor of

absent BP improvement, although several following reports confirmed that patients presenting lower eGFR did also benefit from renal stenting (53).

Furthermore, regarding the follow-up, a recent study even stated that eGFR is not actually an appropriate mean of evaluation after a renal stenting intervention due to its rather poor sensitivity in detecting changes of the (125) I-iothalamate GFR (54).

Proteinuria ≥ 1 g/24 h represents a good indication of nephropathy and was associated with a poor outcome after renal stenting (55).

Renal length of 10-12 cm constitutes a potentially favorable outcome. A value under 6 cm is a sign of irreversible renal atrophy and these patients should not be considered for angioplasty.

Renal arteriogram may also be useful in predicting the possible reversible renal dysfunction after revascularization. Normal cortical blood flow indicates reversibility while, on the other hand, the poor cortical blood flow along with diffuse intrarenal arteriolar disease suggests the presence of advanced nephropathy (52).

RI provided by DUS was another marker deemed worthy of consideration. RI < 0.8 predicts BP and renal function improvement after angioplasty, but there is evidence that patients presenting high RI might also display good outcomes from revascularization (despite the idea that a high value indicates a parenchymal disease) (56).

Fractional flow rate (FFR) and hyperemic systolic gradient (HSG) were proposed for the hemodynamic assessment of stenosis while aiming to predict the revascularization outcomes. From this point of view, a FFR value under 0.8 was associated with significant BP improvement subsequent to renal stenting (35).

In the same way, HSG > 21 mmHg (intra-renal papaverine) displayed the highest prediction value with regard to the revascularization benefit by comparison to the other invasive methods of evaluating the degree of stenosis (57).

Brain natriuretic peptide (BNP) levels were reported as a potential marker for the presence of significant stenosis. A level higher than 80 pg/mL predicted improved outcomes in BP control secondary to renal stenting (58).

Current recommendations of revascularization

Both the American and the European guidelines in this field of interest underlined the idea that the decision of revascularization should take into

consideration the individual characteristics of each patient (prognosis, renal function, associated comorbidities and BP control).

The general consensus is that renal artery stenting should be performed in RAS patients presenting sudden, unexplained "flash pulmonary edema" or recurrent CHF (the only established class I recommendation).

In order to preserve kidney function and to reduce the adverse cardiovascular events, patients with resistant/accelerated/malignant (multidrug resistant – 3 classes of antihypertensive medication including diuretics) hypertension, unexplained hypertension in unilateral small kidney or intolerance to medication represent the candidates that benefit from the revascularization approach (Class II evidence level A).

RAS cases involving unstable angina or progressive chronic kidney disease with bilateral or solitary kidney should also be considered as viable candidates for renal artery stenting (Class II evidence level A) (6, 20).

Additionally, a recent report from The Society for Cardiovascular Angiography and Interventions (SCAI) mentioned that renal stenting in anatomically challenging or high-risk lesions (such as early bifurcation, small vessels, severe concentric calcification, severe aortic atheroma, mural thrombus and unstable plaque) is worth considering despite the lack of conclusive data. The therapeutic management of such patients should be based on both their individual profile as well as the technical skills of the operator. Only in this manner may a proper balance between the risks and benefits of active therapy may be obtained while aggressively treating the cardiovascular risk factors (33).

CONCLUSIONS

While waiting for prospective trials to demonstrate the clear role of renal artery stent placement in RAS cases, clinicians must take into consideration the individual profile of every patient in order to select the proper treatment alternative.

First of all, medical therapy is mandatory and represents the first line of RAS management. Associated classes of antihypertensive medications administered up to the maximal dosages constitute the best initial approach in the effort to control BP and preserve the renal function.

In cases of failure (such as uncontrolled hyper-

tension, extensive medication and intolerance), endovascular renal stenting should be considered.

Despite the great interest in finding predictors for the success of this technique, neither of the above mentioned parameters is satisfactory or even capable to provide a clear prediction. Consequently, if taken into consideration, they all should be corroborated with individual clinical findings and non-invasive screening tests along with outcomes of the clinically indicated (through case selection) renal angiography.

The high prevalence of RAS in elderly patients, especially presenting complex comorbidities and atherosclerosis, is another important issue concerning renal dysfunction. In such cases, RAS cannot always be responsible for renal impairment, so it is crucial to distinguish between renal ischemia and nephropathy in order to provide a proper selection for applying revascularization.

The relationship between these two entities is the clue in understanding the actual results of the recent trials, as it represents the main ambiguity with regard to renal stenting. At this point, the generally accepted approach is to carefully select patients undergoing renal artery stent implantation based on objective renal ischemia (the assessment of functional significance and severity of RAS), the condition of the kidney (nephropathy) and the organ damage (52).

Besides the actual recommendations, anatomically challenging lesions should be considered for the percutaneous approach based on the above mentioned criteria.

In conclusion, there are certain RAS patients that should undergo renal stenting and neither the ambiguity nor the inaccurate interpretation of the presently published trials should delay the procedure in cases that actually require it. Such undesired situations may lead to premature dialysis and unnecessarily persistent cardiovascular risk.

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Conflict of interest

None declared.

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