Review Paper ■

Medical Information on Renal Arterial Stenting

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Abstract. Renal artery stenosis (RAS) is a common pathological condition associated with uncontrolled or refractory hypertension, flash pulmonary edema, and worsening renal function. The high prevalence of RAS in patients with coronary and lower extremity vascular disease has been well established. In a recent study on the practice of "drive-by renal shooting", prevalence of significant RAS was found to be high in patients with suspected coronary atherosclerosis referred for coronary angiography. Another study revealed dramatic increase in volume of renal arterial stenting in the Medicare population. Hence, concerns of over-diagnosis and over-treatment of RAS were raised. However, numerous recent studies demonstrated high success rate of renal artery stent revascularization and its clinical benefits. Aggressive screening and early treatment of RAS are therefore warranted in patients with drug-refractory hypertension and/or worsening renal insufficiency. However, some open issues remain. The paper proposes selection criteria for "drive-by renal shooting" and suggests valid criteria for treating RAS.

Medicinske informacije o ledvičnih arterijskih opornicah

Izvleček. Ledvična aretirjska stenoza (LAS) je dobro znano bolezensko stanje, pogosto pri bolnikih s srčno-žilnimi boleznimi. Novejši študiji sta pokazali na visoko prevalenco LAS pri angiografiji pacientov s sumom koronarne ateroskleroze in dramatičen porast vsatavitev ledvičnih aretirjskih opornic pri zavarovancih Medicare v ZDA. To je vzbudilo skrbo o prepogostem diagnosticiranju in zdravljenju LAS. A druge novejše študije so dokazale uspešnost in koristnost vstavljanja ledvičnih arterijskih opornic. Prispevek povzema odprta vprašanja glede tega ter predlaga merila za presejalne postopke in zdravljenje LAS.

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Is Renal Artery Stenosis (RAS) overdiagnosed?

There are two main causes of RAS, which are fibromascular dysplasia and atherosclerosis. Fibromascular dysplasia causes less than 10% of all RAS and is most often seen in young female patients.[1] However, atherosclerotic RAS is by far the most common etiology of RAS (nearly 90%), especially in old aged male patients.[2] The prevalence of atherosclerotic RAS in an elderly cohort has been reported to be 6.8% in a population-based study using duplex ultrasonography and it also frequently coexists with atherosclerotic disease in other vascular territories; approximately 15 to 23% of CAD, 28-38% of aorto-iliac disease, and 45-59% of lower extremity vascular disease.[3,4] Most of the patients with RAS are asymptomatic due to a large renal reserve of function. The two main clinical manifestations are renovascular hypertension and ischemic nephropathy. Renovascular hypertension is often difficult to control and can aggravate the heart failure and precipitate the unstable angina. In addition, renal ischemia may lead to an end-stage renal failure and high mortality.[5] Although RAS can be diagnosed using non-invasive tests with high sensitivity and specificity such as duplex ultrasonography, computed tomography, and magnetic resonance angiography, renal angiography remains the gold standard for the diagnosis of RAS.[6]

Recently, the rapid technology advancement in percutaneous vascular intervention has achieved a high success and very low complication rate in renal arterial stenting. In addition, because of the silent nature of the disease and the frequent association with atherosclerotic disease in other vascular territories, there has a dramatic increase in the practice of simultaneous selective or non-selective renal angiography in patients undergoing cardiac catheterization in order to screen and diagnose the once ignored and underappreciated problem. This practice has been termed as "drive-by renal shooting". An important clinical study examining the practice of "drive-by renal shooting" was performed. Based on a set of pre-selection criteria (Table 1), 1149 patients meeting at least one selection criterion were selected for the study but only 851 did have renal angiograms. The results showed 36.9% of all patients had angiographically evident renal artery atherosclerosis, 14.3% of patients had stenosis ≥50% in at least one proximal renal artery, 7.3% had severe stenosis ≥70%, 1% had total occlusion and 1.4% had severe bilateral stenosis ≥70% (Table 2).[7] However, the results of this study triggered the concerns from other experts who viewed the practice of drive-by renal shooting as an indiscriminate testing for RAS or fortuitous documentation of lesions, which might lead to proliferation of procedures laden with morbidity, high cost, and mortality.[8]

Is RAS over-treated?

In a recent study based on the Medicare data, the annual volume of percutaneous renal artery interventions (renal artery angioplasty and stent placement) increased rapidly with 2.4 fold from 1996 to 2000, whereas the annual volume of renal artery surgery declined by 45% during the same period (Figure 1). Most growth in percutaneous renal artery revascularization is attributed to increased performance by cardiologists with an increase of 287%. Although interventional radiology and surgery increased the volume by 63% and 153% respectively, the total volume contributed by these 2 specialties was relatively small (Figure 2). This explosive growth in annual procedure volume by cardiologists varied in different regions of U.S., but the highest rate was seen in the Southeast region by 1443% (Figure 3).[9]

Table 1 Selection criteria for renal artery angiography.

Category		Definition
Clinical presentation		
1.	Hipertension	
	Resistant	Systolic BP ≥140 or diastolic BP ≥90 mm Hg while on ≥2 drug classes at ≥2 defined daily doses
	Severe	Systolic BP ≥180 or diastolic BP ≥110 mm Hg regardless of drug therapy
2.	Kidney dysfunction	
	Unexplained	C-G CrCl ≤50 ml/min without clearly established cause
	ACEI-ARB induced	Documented acute renal dysfunction attributable to ACEI or ARB therapy
3.	Acute pulmonary edema	Radiographic grade ≥III and no other recognized cause* and associated with acute hypertension (≥160/100 mm Hg) or chronic hypertension
Risk factors for severe atherosclerosis		
1.	Cerebro-vascular disease	Ischemic or arterial embolic stroke; carotid bruit; causing stenosis ≥50%; or previous carotid revascularization
2.	Severe coronary artery disease	Three territories with ≥60% stenosis; previous revascularization of 3 territories; or left main coronary ≥50% stenosis
3.	Severe atherosclerotic abdominal aortic or lower extremity artery disease	Causing stenosis ≥50% of diameter; documented atherosclerotic aneurysm; previous peripheral or aortic surgery; or intermittent claudication with corroborative physical examination

*e.g., ejection fraction ≤40%, acute myocardial infarction, severe valvular disease; ACEI=angiotensin-converting enzyme inhibitor; ARB=angiotensin receptor blocker; BP=blood pressure; C-G CrCl=Cockcroft-Gault creatinine clearance. Modified from Table 1 in Buller et al. The profile of cardiac patients with RAS. Am Coll Cardiol. 2004;43:1606-1613.

Table 2 Results of renal angiography categorized by severity of RAS.

Severity of RAS	No. (%) of patients*
Any renal arterial disease	309 (37%)
Renal stenosis >50%	120 (14%)
Renal stenosis >70%	61 (7%)
Renal occlusion	8 (1%)

*Of the 1149 patients who met one of the criteria, 851 underwent renal angiograms. Modified from Table 2 in Buller et al. The profile of cardiac patients with RAS. Am Coll Cardiol. 2004;43:1606-1613.

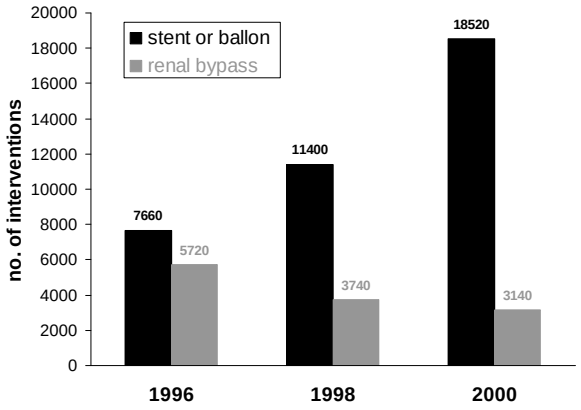

Figure 1 Increase in utilization of percutaneous renal artery interventions by Medicare beneficiaries 1996–2000 (by intervention type). The data are extrapolated from the Medicare population in the USA. Adapted from Murphy TP, Soares G, Kim M, et al. Increase in utilization of percutaneous renal artery interventions by medicare beneficiaries, 1996-2000. Am J Roentgenol. 2004;183(3):561-568.

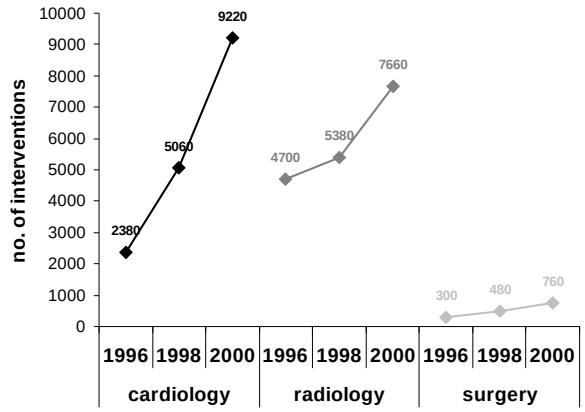

Figure 2 Increase in the total number of percutaneous renal artery interventions by Medicare beneficiaries 1996–2000 (by medical specialty). The data are extrapolated from the Medicare population in the USA.

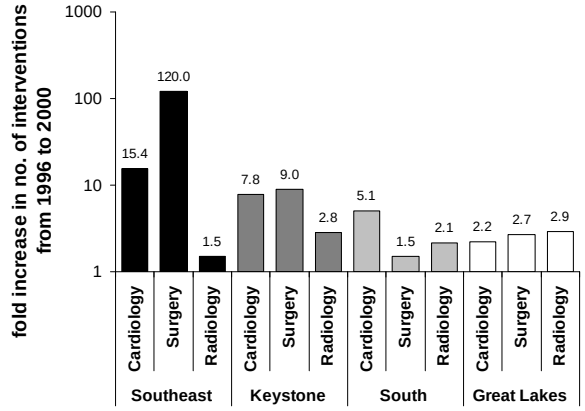

Figure 3 Increase in the total number of percutaneous renal artery interventions by Medicare beneficiaries 1996–2000 (in selected regions, by specialty).

The issues raised by conventional thinking about renal arterial stenting

For years, renal arterial stenting was believed by many to be associated with a high morbidity, mortality, and cost. Furthermore, many experts as well as practicing physicians also believed that there was a lack of data supporting clinical outcome of renal arterial stenting. Therefore, the above-mentioned studies lead to a concern over whether the use of drive-by renal shooting to diagnose RAS is a good practice and whether renal arterial stenting has been over-performed. These arguments against renal arterial stenting suggest medical or conservative therapy as a preferred choice for the treatment of RAS. However, this conventional view may arise mainly from poor understanding of the natural history of RAS and current existing data about clinical efficacy of renal arterial stenting.

Understanding the natural history of atherosclerotic RAS

There were numerous studies examining the natural history of RAS since 1968.[10-22] We would only limit the discussion here on 2 recent most important studies as examples. Caps et al. documented in their prospective study of atherosclerotic RAS progression that overall cumulative incidence of RAS progression was 35% at 3 years and 51% at 5 years. For patients with RAS initially classified as normal, <60% stenosis, and ≥60% stenosis, the 3-year cumulative incidence of RAS progression was 18%, 28% and 49 respectively with an incidence of 6% total occlusion. The risk of RAS progression was the highest among individuals with preexisting high-grade RAS, elevated systolic blood pressure, and diabetes mellitus.[23]

In a prospective study of simultaneous renal angiographies performed in cardiac catheterization laboratory at 2 different times, the incidence of normal renal angiography in the study population decreased from 91% to 75% after a mean period of 2.6±1.6-year follow-up. The disease progression in 1 or more renal arteries was seen in 6% of the patients within 1-year follow-up but it increased to 28% within 6 years.[24] These and many other studies clearly showed the natural history of RAS is undoubtedly progressive over time.

The association of severity of RAS with loss of renal function and size

The single most important impact of progression of RAS is a reduction in the kidney size and function. Along with the progression of severity of RAS, many studies also showed its association with renal atrophy and dysfunction.[25-28] A prospective study showed overall cumulative incidence of renal ischemic atrophy defined by a reduction in renal length of greater than 1 centimeter was 16.2% at a mean of 33 months. For patients with renal arterial stenosis initially classified as normal, <60%, and ≥60%, the 2-year cumulative incidence of renal ischemic atrophy were 5.5%, 11.7% and 20.8% respectively.[29] In addition, it has been estimated that atherosclerotic renal occlusive disease is the primary cause of end-stage renal failure in 5% to 15% of patients over the age of 50 years who begins dialysis each year.[30,31]

The impact of RAS on survival

In a study of 1235 patients undergoing diagnostic cardiac catheterization and abdominal aortography, four-year unadjusted survival for patients with RAS was 65% compared with 86% for patients without significant RAS. Among the factors associated with decreased 4-year survival, i.e., the presence of significant RAS, reduced ejection fraction, elevated serum creatinine, and symptoms of congestive heart failure, significant RAS was a strong independent predictor of 4-year survival in that patient population.[32]

In summary, the nature of progression in atherosclerotic RAS is that renal arteries with higher degree of stenosis progress faster than those with mild or moderate stenosis and this progression leads to a decrease in size and function of kidney and it is associated with a negative impact on the long-term survival without intervention.

Improving success and risk of the renal arterial stenting overtime

The technology of the percutaneous vascular intervention including renal arterial stenting had evolved very rapidly since percutaneous transluminal angioplasty was introduced in 1978. In 1980s, the success rate of balloon angioplasty of renal artery was below 60 to 90% with a complication rate of 5 to 16%.[33-37] Since the introduction of renal arterial stenting in 1990s, the success rate has been reported to be between 90 to 100% with the complication rate of 0 to 4 %.[38-40] Zeller et al. analyzed the impact of technical improvements in stent devices and guiding catheters (i.e. reduced device diameter and increased flexibility) on complication rates associated with percutaneous renal arterial interventions. They concluded that the complication rate of renal arterial intervention of atherosclerotic RAS has been reduced significantly during a 5-year period in parallel with the use of more flexible catheters and pre-mounted lower-profile stents.[41] With continuing refinement of balloon and stent technology, currently, renal arterial stenting is no longer a technically challenging procedure with a success rate of >98% and very low complication rate of <1%.[42-45]

Abundance of existing studies demonstrating the clinical efficacy of renal artery stenting

There were at least 15 studies including more than 1500 patients demonstrating the clinical efficacy of renal arterial stenting.[42, 44-57] Among these studies, some of the more important ones are discussed below.

Improving blood pressure control

Dorros et al. described the impact of renal arterial stenting on blood pressure control in their 4-year prospective follow-up of 145 patients who

underwent Palmaz-Schatz stent revascularization of ≥1 stenotic renal artery. At the 4-years follow-up, the systolic and diastolic blood pressures significantly decreased from (166±26 mmHg) to (148±22 mmHg) and from (86±14 mmHg) to (80±11 mm Hg), respectively. The blood pressure response at 1 year showed that only 1% of patients were cured, 42% were improved, and 54% had no improvement but at 4 years, 2% were cured, 47% were improved and 51% had no improvement.[57]

In another prospective study by Zeller et al., blood pressure (systolic/diastolic/mean) decreased significantly after the intervention from 144/79/102 mmHg at baseline to 132/72/93 mmHg at 6-month follow-up. In 46% of the patients, blood pressure control was improved after mean 34-month follow-up; it remained unchanged in 43% and deteriorated in 11%. The numbers of drugs for blood pressure was also significantly reduced from 3.06±1.17 to 2.76±1.16 after mean follow-up.[58]

Blum et al. also demonstrated the efficacy of renal arterial stenting in 68 patients with ostial RAS after initial unsuccessful balloon angioplasty. At a mean 27-months follow-up, cure of hypertension was seen in 16%, improvement in 62% and no change in 22%.[59]

Stabilizing renal function deterioration or improving renal function

In the study by Dorros et al., serum creatinine level decreased or remained stable in approximately two thirds of all patients received successful renal arterial stenting. For patients with unilateral stenosis, two thirds of patients had improved or stable renal function, whereas one third had progression of their renal dysfunction with an increase in their creatinine by >0.2 mg/dl above baseline. In patients with bilateral stenosis, nearly 75% had stable or improved renal function and only 25% had deterioration of renal function.[57]

In 330 patients after successful renal stenting, Zeller et al. also showed a similar beneficial result with a serum creatinine decreased significantly from 1.45±0.87 to 1.39±0.73 mg/dl in correspondent with an increase of GFR from 59±26 to 62±26 ml/min/1.73 m2 of body surface area over a mean follow-up of 34 months. Serum creatinine decreased ≥10% in 34% of the study patients, remained stable in 39%, and increased at least ≥10% in the rest of patients. Using GFR measure, GFR increased by >10% was noted in 38% of patients, unchanged in 33%, and a decrease >10% in 29%. Furthermore, the study also showed improved or stabilized serum creatinine concentrations in 64% of patients with pre-existing normal renal function, 82% of patients with moderate impairment, and 92% of those with severely impaired renal function, suggesting the more severe the renal dysfunction prior to renal stenting, the more the patients benefited from the intervention.[58]

In another study, Harden et al. also noticed the similar beneficial impact of renal artery stenting on progression of renovasacular renal failure. In their study, 32 patients underwent renal arterial stenting with a 100% success rate. At 6-months follow-up, improvement in renal function measured by >20% decrease in serum creatinine was seen in 34%, stabilized in 34% and worsened in 28% with an overall deceleration in the rate of progression of renal failure in 78% of patients.[53]

In the study of 68 patients by Blum et al., all patients had a stabilized renal function at a mean follow-up of year or months after successful renal stenting.[59]

Improving survival rate

Dorros et al. reported that the cumulative probability of survival was 74±4% at 3 years, with few deaths related to end-stage renal disease. The survival was good in patients with normal baseline function (92±4%), fair in those with mildly impaired renal function (74±7%), and poor in those with elevated baseline creatinine levels (≥2.0 mg/dl) (52±7%). The combination of

impaired renal function and bilateral disease adversely affected the survival in those patients.[57]

In conclusion, there are a large amount of observation studies showing that renal arterial stenting undoubtedly preserves the renal function and improves blood pressure control in a broader spectrum of patients with RAS.

The clinical outcome of medical therapy for significant RAS

Chabova et al. studied the outcomes of atherosclerotic RAS managed medically in 68 patients with high-grade stenosis (>70%) who were followed up for at least 6 months after first angiography. At a follow-up of 38.9±2.8 months, the serum creatinine level rose from 1.4±0.1 to 2.0±0.2 mg/dl and mean blood pressure did not change (157±3/83±2 vs 155±3/79±2 mmHg), but the need for medication increase from 1.6±0.1 to 1.9±0.1 drugs. Four patients (5.8%) eventually underwent renal vascularization for refractory hypertension (1 patient), for progressive stenosis (1 patient), and during aortic reconstruction (2 patients). One additional patient underwent nephrectomy to improve blood pressure control.[60]

In another study of 45 patients with RAS, Soffer et al. used the renal scintigraphy with iothalamate and technetium pentetic acid to measure for total and single kidney glomerular filtration rate (SK-GFR) to compare the effect of renal arterial stenting in Group 1 (n=17) with medical therapy alone in Group 2 (n=28) on SK-GFR. The result of their study remarkably showed that at 14-month follow-up, SK-GFR was increased in Group 1 by 24±8% but it was decreased in Group 2 by 11±5% and the study concluded that renal arterial stenting preserves SK-GFR in patients with RAS, whereas progressive deterioration is observed in medically treated patients.[61]

These two studies clearly showed medical therapy of RAS is associated with continuing decline in renal function and a poor prognosis. Therefore, based on all the up-to-date evidences, renal arterial stenting should be considered as the treatment of choice for significant renal arterial stenosis.

Remaining issues in renal arterial stenting

Indeed, several indeed remain in renal arterial stenting. Even after a successful procedure, 20 to 40% of patients did not improve in blood pressure control and 15 to 20% of patients may have worsening renal function. Therefore, the most important current issues are to identify patients who are most likely to benefit from the procedure and to develop strategies that prevent the worsening renal function after the renal stenting. Currently, there are no useful clinical predictors to select the patients who may respond to the renal stenting procedure. In addition, despite an abundance of data showing the clinical efficacy of renal stenting, there no large scale randomized study to show the benefit of renal stenting over medical therapy although one is now ongoing.

Lack of clinical predictors for outcome of renal arterial stenting

Several clinical parameters had been proposed to be used in predicting the clinical outcome of renal arterial stenting, but none of these were found to be a standard test.

Renal vascular resistance-index: Based on the theory that the structural alteration in smaller renal arteries or arterioles distal to RAS induced by long-standing hypertension leading to a decrease in the intra-renal vascular surface area and increases in the vascular resistance, Radermacher et al. used "renal vascular resistance-index" measured by Duplex Doppler ultrasonography in their prospective study to predict the outcome of renal revascularization in patients with RAS. They concluded that a renal resistance-index value of >80 reliably identifies the patients with RAS in whom the renal

revascularization procedures (renal angioplasty, stenting or surgery) will not improve renal function, blood pressure, or kidney survival but a reversed outcome in patients with a resistance-index of 80 or less.[62]

However, the study by Zeller et al. reported a contradictory result in that the resistance index value before renal arterial stenting did not differentiate patients who had or had not improved renal function and/or better control on blood pressure after stenting.[63]

Serum creatinine and left ventricular function: Zeller et al. also mentioned in their study that elevated serum creatinine and impaired left ventricular function were independent predictors of improved renal function, whereas female sex, preserved parenchymal thickness, and baseline mean arterial blood pressure predicted the improved blood pressure control after successful renal arterial stenting.[63] However, there are no other studies to confirm these findings as yet.

Post-procedural renal dysfunction and its prevention

As mentioned earlier, approximately 15-20% patients have worsening renal function after stenting. The major mechanisms are not clear but are related to the following factors, these are progression of concomitant nephrosclerosis, contrast medium-induced nephrotoxicity, recurrent lesion due to in-stent restenosis and distal atheroembolization. These factors can be minimized by taking preventive measures to reduce the renal injury from the stenting procedures.

To minimize the contrast-induced nephrotoxicity, half-diluted contrast medium, iso-osmolar contrast medium (Iodixanol), oral or intravenous acetylcystine (Mucomyst), hydration with intravenous normal saline and intravenous sodium bicarbonate infusion were shown to reduce the renal dysfunction.[64,65] Effective blood pressure control by anti-hypertensive medications, lowering of blood lipid level by statins and effective control of blood sugar level by insulin and anti-diabetic medications may slow down the progression of concomitant nephrosclerosis.[66,67] To prevent the in-stent restenosis, drug-eluting stents are currently on the clinical trials but Food and Drug Administration.

Distal embolization of debris after percutaneous renal arterial ballooning and stenting are increasingly recognized as major causes of worsening renal function after a successful procedure.[68] Not only balloon dilatation and stent deployment can cause the distal embolization but merely engagement of renal artery with a catheter can produce the embolization. Therefore, the strategies to reduce the distal embolization include careful technique in engaging the renal arteries, down-sizing the guiding and balloon catheter and perhaps more importantly the consideration of using distal protection device.

In a study in which a total of 56 hypertensive patients received a distal protection devices during stenting of 65 renal arteries with >70% stenosis, 38 patients had normal baseline renal function but 13 had moderate, and 5 had severe renal dysfunction. The application of the distal protection devices had 100% technically success without serious complications and visible debris were retrieved in the aspirate in all patients with a mean number of 98.1 ± 60 per procedure and a mean size of 201.2 ± 76.2 μm. At a mean follow-up period of 22.6 ± 17.6 months, systolic and diastolic blood pressure dropped significantly from $169 \pm 15.2/104 \pm 13$ mm Hg to $149.7 \pm 12.5/92.7 \pm 6.7$ mm Hg. In 10 patients, hypertension were cured, 33 improved, and 13 remained unchanged. At 6-month follow-up, renal function did not deteriorate in any patients, whereas 8 patients with baseline renal insufficiency improved after the procedure.[69] These preliminary results showed the feasibility and safety of the distal protection devices during renal stenting and it might possibly prevent the post-procedural deterioration of renal function. Of course, large randomized studies are needed to confirm the benefits of distal protection device.

A proposal to increase the clinical efficacy of drive-by renal shooting and renal arterial stenting

Proper strategies of performing selective "drive-by renal shooting" is of paramount importance to avoid over-diagnosis of the RAS. We propose only to perform "drive-by renal shooting" in patients undergoing cardiac catherization procedure with at lease 2 essential criteria instead of just one criterion as used by the study.[7] First selection criterion is a clinical indication which include at least one of following:

1. drug-resistant hypertension (≥2 drugs) and severe hypertension (systolic BP >180 mm Hg or diastolic BP >110 mmHg),

2. unexplained renal dysfunction (Creatinine clearance <50 cc/min) and Angiotensin Converting Enzyme Inhibitor or Angiotensin Receptor Blocker induced acute renal dysfunction,

3. onset of acute Pulmonary Edema with normal left ventricular function and severe hypertension, but without valvular diseases or clinical factors which aggravate or precipitate the congestive heart failure or unstable angina.

The second criterion is at least one risk factor which is associated with a high probability of a significant RAS. These risk factors include one of the following coexisting conditions (Table 1):

1. patients with severe cerebro-vascular disease,

2. patients with severe coronary artery disease,

3. patients with severe abdominal aortic or peripheral vascular disease.

The approach of using at least these 2 criteria to select patients for "drive-by renal shooting" in cardiac catheterization laboratory not only eliminates the indiscriminative use of this type of practice and increases the yield of diagnosing a significant RAS but also avoid the over-treatment of RAS by providing an indication for treatment.

In addition, defining significant RAS is also very important because it determines the treatment threshold for renal arterial stenting. Although there is no universal consensus on the definition of significant renal stenosis, it is generally accepted that a hemodynamically significant RAS should be at least 50% angiographic stenosis and/or the presence of a significant mean pressure gradient across the lesion (>10mm Hg). A more stringent approach in defining a significant RAS may also avoid over-treatment.

Conclusion

RAS is a well-recognized cause of renal function impairment and secondary hypertension. The natural history of RAS is to progress over time, resulting in renal dysfunction, uncontrolled hypertension and finally leading to an increased mortality. Current data clearly demonstrate the clinical efficacy of renal arterial stenting, which should be considered as the treatment of choice for RAS especially in patients with uncontrolled hypertension and/or renal dysfunction. Careful selection of patients for drive-by renal shooting practice and more stringent criteria to define a significant RAS should avoid over-diagnosis and over-treatment of RAS. The issues remaining in renal arterial stenting are the proper selection of patients who may or may not benefit from the procedure, optimal preventive measures to reduce the post-stenting renal dysfunction including the use of distal protection devices and randomized studies to compare with medical therapy.

References

1. Textor SC. Managing renal arterial disease and hypertension. Curr Opin Cardiol. 2003; 18:260–267.

2. Safian RD, Textor SC. Renal artery stenosis. N Engl J Med. 2001;344:431–442.
3. Edwards MS, Hansen KJ, Craven TE, et al. Association between renovascular disease and prevalent cardiovascular disease in the elderly. A population-based study. Vasc Endovascular Surg. 2004;38:25–35.
4. Plouin PF, Chatellier G, Darne B, et al. Blood pressure outcome of angioplasty in atherosclerotic renal artery stenosis: a randomized trial. Essai Multicentrique Medicaments versus Angioplastie (EMMA) Study Group. Hypertension. 1998;31:823–829.
5. Meaney TF, Dustan HP, McCormack LJ. Natural history of renal arterial disease. Radiology 1968; 91:881-887.
6. Bokhari SW, Faxon DP. Current advances in the diagnosis and treatment of renal artery stenosis. Rev Cardiovasc Med. 2004 ;5(4):204-15.
7. Buller CE, Nogareda JG, Ramanathan K, et al. The profile of cardiac patients with renal artery stenosis. J Am Coll Cardiol. 2004; 43(9):1606-13.
8. Weinrauch LA, D'Elia JA. Renal artery stenosis: "fortuitous diagnosis," problematic therapy. J Am Coll Cardiol. 2004;43(9):1614-6.
9. Murphy TP, Soares G, Kim M, et al. Increase in utilization of percutaneous renal artery interventions by medicare beneficiaries, 1996-2000. Am J Roentgenol. 2004;183(3):561-8.
10. Wollenweber J, Sheps SG, Davis GD. Clinical course of atherosclerotic renovascular disease.Am J Cardiol. 21: 60-71,1968.
11. Meaney TF, Dustan HP, McCormack lJ. Natural history of renal arterial disease. Radiology 91:881-887,1968.
12. Schreiber MJ, Pohl MA, Novick AC. The natural history of atherosclerotic and fibrous renal artery disease. Urol Clin North Am. 11:383-392, 1984.
13. Strandness DE, Jr. Natural history of renal artery stenosis. Am J Kidney Dis 24:630-635, 1994.
14. Caps MT, Perissinotto C, Zierler RE, et al. Prospective study of atherosclerotic disease progression in the renal artery. Circulation 98:2866-2872, 1998.
15. Wollenweber J, Sheps SG, Davis GD. Clinical course of atherosclerotic renovascular disease.Am J Cardiol. 21:60-71, 1968.
16. Schreiber MF, Pohl MA, Novick AC. The natural history of atherosclerotic and fibrous renal artery disease. Urol Clin NorthAm. 11:383-392, 1984.
17. Zierler RE, Bergelin RO, Isaacson JA, Strandness DE Jr. Natural history of atherosclerotic renal artery stenosis: A prospective study with duplex ultrasonography. J Vasc Surg. 19:250-258, 1994.
18. Strandness DE Jr. Natural history of renal artery stenosis.Am J Kidney Dis. 24:630-635, 1994.
19. Crowley JJ, Conlon PJ, Santos RM, et al. Incidence and progression of renal artery stenosis in patients undergoing routine cardiac catherization. Circulation 94:S299A, 1996 (suppl 1) (abstract).
20. Meaney TF, Dustan HP, McCormack J. Natural history of renal arterial disease. Proc Cleve Clin. 881-887, 1968.
21. Dean RH, Kieffer RW, Smith BM, et al. Renovascular hypertension: Anatomic and renal function changes during drug therapy. Arch Surg 116:1408-1415, 1981.
22. Tollefson DFJ, Ernst CB. Natural history of atherosclerotic renal artery stenosis associated with aortic disease. J Vasc Surg. 14:327-331, 1991.
23. Caps MT, Perissinotto C, Zierler RE, et al. Prospective study of atherosclerotic disease progression in the renal artery. Circulation. 1998;98(25):2866-72.
24. Crowley JJ, Santos RM, Peter RH, et al. Progression of renal artery stenosis in patients undergoing cardiac catheterization. Am Heart J. 1998;136(5):913-8.
25. Wollenweber J, Sheps SG, Davis GD. Clinical course of atherosclerotic renovascular disease. Am J Cardiol. 1968;91:60-71.
26. Meaney TF, Dustan HP, McCormack LJ. Natural history of renal artery disease. Radiology 1968;91:881-7.
27. Schreiber MJ, Pohl MA, Novick AC. The natural history of atherosclerotic and fibrous renal artery disease. Urol Clin North Am 1984;11:383-392.
28. Baboola K, Evans C, Moore RII. Incidence of end-stage renal disease in medically treated patients with severe bilateral atherosclerotic renovascular disease. Am J kidney Dis 1998;31:971-977.
29. Caps MT, Zierler RE, Polissar NL, et al. Risk of atrophy in kidneys with atherosclerotic renal artery stenosis. Kidney Int. 1998;53(3):735-42.
30. Kimmer JM, Gennari FJ. Atherosclerotic renovascular disease and progressive renal failure. Ann Intern Med 1993;118:712-9.
31. McNeil EA, Hansen KJ, Canzanello VJ, et al. Prevalence of ischemic nephropathy in patients with renal insufficiency. (abstract) Am Surg 1992;58:485.
32. Conlon PJ, Athirakul K, Kovalik E, et al. Survival in renal vascular disease. J Am Soc Nephrol. 1998;9(2):252-6.

33. Canzanello VJ, Millan VG, Spiegel JE, et al. Percutaneous transluminal renal angioplasty in management of atherosclerotic renovascular hypertension: results in 100 patients. Hypertension. 1989;13(2):163-72.
34. Klinge J, Mali WP, Puijlaert CB, et al. Percutaneous transluminal renal angioplasty: initial and long-term results. Radiology. 1989;171(2):501-6.
35. Puijlaert CB, Klinge J, Mali WP, et al. Results of percutaneous transluminal angioplasty in renal artery stenosis during the period 1978-1986. Ned Tijdschr Geneeskd. 1989;133(8):400-4.
36. Bennicke K, Ladefoged SD, Ulrich I, et al. Results and complications of balloon dilatation of renal artery stenosis in patients with renovascular hypertension. Ugeskr Laeger. 1989;151(9):557-60.
37. Baert AL, Wilms G, Amery A, et al. Percutaneous transluminal renal angioplasty: initial results and long-term follow-up in 202 patients. Cardiovasc Intervent Radiol. 1990;13(1):22-8
38. Fiala LA, Jackson MR, Gillespie DL, et al. Primary stenting of atherosclerotic renal artery ostial stenosis. Ann Vasc Surg. 1998;12(2):128-33.
39. Lim ST, Rosenfield K. Renal Artery Stent Placement: Indications and Results. Curr Interv Cardiol Rep. 2000;2(2):130-139.
40. Leertouwer TC, Gussenhoven EJ, Bosch JL, et al. Stent placement for renal arterial stenosis: where do we stand? A meta-analysis. Radiology. 2000;216(1):78-85.
41. Zeller T, Frank U, Muller C, et al. Technological advances in the design of catheters and devices used in renal artery interventions: impact on complications. J Endovasc Ther. 2003;10(5):1006-14.
42. Sos TA, Pickering TG, Sniderman K, et al. Percutaneous transluminal renal angioplasty in renovascular hypertension due to atheroma or fibromuscular dysplasia. N Engl J Med 1983; 309: 274-279.
43. Henry M, Amor M, Henry I, et al. Stents in the treatment of renal artery stenosis: long term follow-up. J Endovasc Surg 1999; 6: 42-51.
44. Iannone LA, Underwood P, Nath A, et al. Effect of primary balloon expandable renal artery stents on long-term patency, renal function and balloon pressure in hypertension and renal insufficient patients with renal artery stenosis. Cathet Cardiovasc Diagn 1996; 37: 243-250.
45. Von Knorring J, Edgren J, Lepantalo M. Long-term results of percutaneous transluminal angioplasty in renovascular hypertension. Acta Radiol 1996; 37: 36-40.
46. Van de Ven PJG, Kaatee R, Beutler JJ, et al. Arterial stenting and balloon angioplasty in ostial atherosclerotic renovascular disease: a randomized trial. Lancet 1999, 353:282–286.
47. Rodriguez-Lopez JA, Werner A, Ray LI, et al.Renal artery stenosis treated with stent deployment: indications, technique, and outcome for 108 patients. J Vasc Surg 1999, 29:617–624.
48. Henry M, Amor M, Chati Z, et al. First clinical experience with the new AVE "Bridge" stent in the treatment of renal stenoses [abstract]. Circulation 1998, 98: I484–I485.
49. Rocha-Singh K, Mishkel GJ, Katholi RE, et al. Clinical predictors of improved long-term blood pressure control after successful stenting of hypertensive patients with obstructive renal artery atherosclerosis. Cathet Cardiovasc Intervent 1999, 47:167–172.
50. Tuttle KR, Chouinard RF, Webber JT, et al. Treatment of atherosclerotic renal artery stenosis with the intravascular stent. Am J Kidney Dis 1998, 32:611–622.
51. Rundback JH, Gray RJ, Rozenblit G, et al. Renal artery stent placement for the management of ischemic nephropathy. J Vasc Intervent Radiol 1998, 9:413–420.
52. White CJ, Ramee SR, Collins TJ, et al. Renal artery stent placement: utility in lesions difficult to treat with balloon angioplasty. J Am Coll Cardiol 1997, 30:1445–1450.
53. Harden PN, MacLeod, Rodger RSC, et al. Effect of renal-artery stenting on progression of renovascular renal failure. Lancet 1997, 349:1133–36.
54. Henry M, Amor M, Henry I, et al. Stent placement in the renal artery: three-year experience with the Palmaz stent. J Vasc Intervent Radiol 1996, 7:343–350.
55. Hennequin LM, Joffre FG, Rousseau HP, et al. Renal artery stent placement: long-term results with the Wallstent endoprosthesis. Radiology 1994, 191:713–719.
56. Rees CR, Snead D. Results of United States multicenter trial of stents in renal arteries [abstract]. Cardiovasc Intervent Radiol 1994, 17(Suppl 2):S1–S145.
57. Dorros G, Jaff M, Mathiak L, et al. Four-year follow-up of Palmaz-Schatz stent revascularization as treatment for atherosclerotic renal artery stenosis. Circulation. 1998;98(7):642-7.

58. Zeller T, Frank U, Muller C, et al. Stent-supported angioplasty of severe atherosclerotic renal artery stenosis preserves renal function and improves blood pressure control: long-term results from a prospective registry of 456 lesions. J Endovasc Ther. 2004;11(2):95-106.
59. Blum U, Krumme B, Flugel P, et al. Treatment of ostial renal-artery stenoses with vascular endoprostheses after unsuccessful balloon angioplasty. N Engl J Med. 1997;336(7):459-65.
60. Chabova V, Schirger A, Stanson AW, et al. Outcomes of atherosclerotic renal artery stenosis managed without revascularization. Mayo Clin Proc. 2000;75(5):437-44.
61. Soffer D, Pellizzon GG, Lee DT, et al. Renal stenting preserves single kidney glomerular filtration rate compared with medical therapy in patients with renal artery stenosis: a 14-month follow-up. (Abstract). Am J Cardiol. 2002;33H (TCT abstracts/oral).
62. Radermacher J, Chavan A, Bleck J, et al. Use of Doppler ultrasonography to predict the outcome of therapy for renal-artery stenosis. N Engl J Med. 2001;344(6):410-7.
63. Zeller T, Frank U, Muller C, et al. Predictors of improved renal function after percutaneous stent-supported angioplasty of severe atherosclerotic ostial renal artery stenosis. Circulation. 2003;108(18):2244-9.
64. Maeder M, Klein M, Fehr T, Rickli H. Contrast Nephropathy: Review Focusing on Prevention. J Am Coll Cardiol 2004; 44:1763–71
65. Rashid ST, Salman M, Myint F, et al. Prevention of contrast-induced nephropathy in vascular patients undergoing angiography: a randomized controlled trial of intravenous N-acetylcysteine. J Vasc Surg. 2004;40(6): 1136-41.
66. Textor SC. Ischemic nephropathy: where are we now? J Am Soc Nephrol. 2004;15(8): 1974-82.(Review)
67. Mazouz H, Kacso I, Ghazali A, et al. Risk factors of renal failure progression two years prior to dialysis. Clin Nephrol. 1999;51(6):355-66.
68. Krishnamurthi V, Novick AC, Myles JL. Atheroembolic renal disease: effect on morbidity and survival after revascularization for atherosclerotic renal artery stenosis. J Urol. 1999;161(4): 1093-6.
69. Henry M, Henry I, Klonaris C, et al. Renal angioplasty and stenting under protection: the way for the future? Catheter Cardiovasc Interv. 2003;60(3) :299-312.