

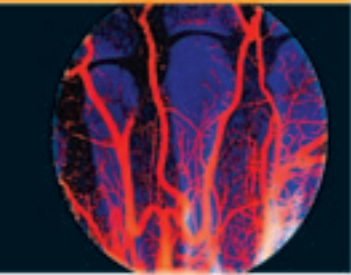
Renovascular hypertension 3: Intervention

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°Abstract

Renovascular hypertension (RHT) caused by renal artery stenosis (RAS) accounts for only 1–5% of all cases of arterial hypertension, but is the leading cause for secondary hypertension. Inadequate control of hypertension by medication and/or progressive renal failure are indications for interventional treatment of RAS. Percutaneous transluminal renal angioplasty (PTRA) is the first-line intervention, while surgical revascularisation is only indicated very selectively. While technical success of PTRA is close to 100%, clinical cure or improvement are observed in only 50–75% of patients. Renal artery stenoses are anatomically divided into ostial lesions, which are primarily treated by stent PTRA, and post-ostial or truncal lesions, which are treated by balloon angioplasty. The restenosis rate for PTRA after 5 years is 30% with a technical success rate for re-interventions close to 100%.

Introduction

In more than 80% of hypertensive patients, the cause of the disease is unknown. Renal artery stenosis (RAS), as the most common cause of secondary arterial hypertension, is responsible for 1–5% of cases.^{1,2} Clinical investigations, including imaging, must be employed to select the subgroup of patients in whom RAS is the cause of hypertension. Once this relation is probable or definitive, indications and treatment options must be reviewed and the expected success rates weighed against the expected complication rates. In patients with renovascular hypertension (RHT), this is an especially important step, because this population has a documented high co-morbidity of other, especially vascular, diseases. This article will discuss the indications for treatment of RAS, the advantages and limitations of the treatment options and finally the technical and clinical success rates.

Prevalence of RAS and renovascular hypertension

Renovascular hypertension is defined as arterial hypertension caused by diseases or abnormalities of the renal arterial circulation. This clinical entity must be distinguished from hypertension caused by renal parenchymal diseases, which mostly have a different cause and therefore require other therapeutic strategies. RHT can be caused by a variety of diseases (e.g. aneurysms, arteriovenous malformation), but RAS is the most frequent cause.

The prevalence of RAS in an unselected population increases with age and reaches approximately 40% in the age group of 75 years and older. However, only a minority of these patients will have hypertension caused by RAS.¹ As a consequence, the presence of RAS in an older hypertensive patient is not necessarily the cause of the disease. Unfortunately, no specific clinical predictors are known to definitely link an RAS with the clinical signs of hypertension. In order to address this issue, clinical data have been compiled from patients with proven RHT to produce a list of criteria that can be used as a clinical selection tool for patients with probable RHT (Table 1). The probability of RAS being the cause of hypertension increases with the number of positive criteria.²

If RHT is suspected, the diagnosis must be confirmed by imaging. The current status of these tests is summarised in an article by Vasbinder *et al.*³ This subject has also been discussed by Professor Sapoval in the previous issue of this journal (Issue 5: Autumn 2004).

Indications for treatment of RAS

The most common cause of RAS is atherosclerosis, which accounts for over 90% of cases.² Fibromuscular dysplasia and other causes of RAS (e.g. lymphoma,

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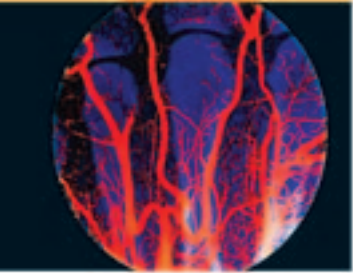


Table 1. Criteria for a higher than average probability for renal artery stenosis in a hypertensive population.

Criteria
Age of onset >50 years
Duration of HT <1 year
Accelerated HT
History of CAD, CVD, PVD
Proteinuria
Abdominal/flank bruit
Chronic renal failure

Modified from Safian RD *et al.*² Abbreviations: HT – hypertension; CAD – coronary artery disease; CVD – cerebrovascular disease; PVD – peripheral vascular disease

radiation exposure) are rare. Fibromuscular dysplasia is typically diagnosed in younger women (<40 years) and is generally treated with balloon angioplasty, resulting in a technical success rate of 95% and a long-term clinical success rate of 65–79%.⁴

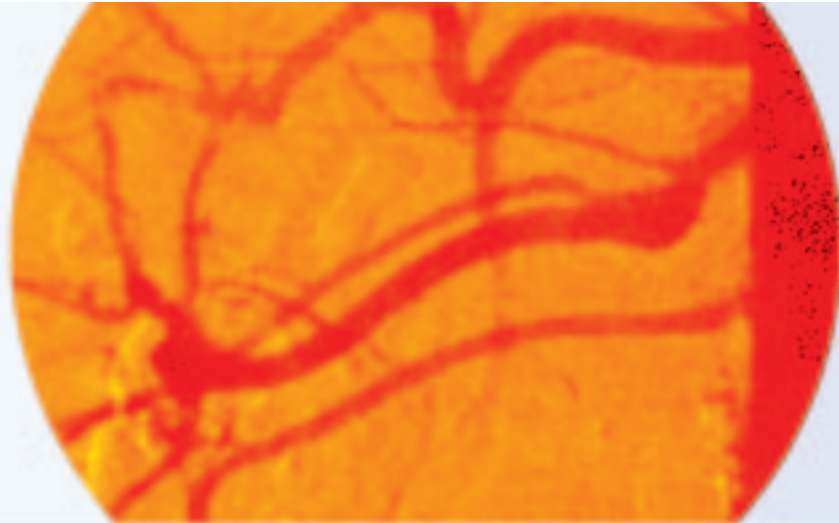
Further discussion will therefore focus on RAS of atherosclerotic origin. Patients with RAS usually suffer from general vascular disease (see Table 1) and while the RAS may not yet impair renal function, the complex nature of RHT may lead to aggravation of coronary artery and/or cerebrovascular disease, with potential deleterious or even lethal sequelae. Confining the interest for didactic reasons only to the renal vasculature, we know that approximately 50% of RAS will progress, and a further 50% of these will cause a deterioration in renal function.² Although this will not be discussed further here, it is important to keep renal failure in mind as a clinical entity, as it cannot be separated from the subject of RAS, and is often part of the decision process for the treatment of RHT.^{5,6}

The lack of controlled randomised studies, the decreased overall survival of multi-morbid patients compared with the general population and the rapid introduction of pharmacotherapy and interventional options have resulted in a lack of evidence to support an accepted algorithm for the treatment of RHT. The fact that the majority of patients with RHT have a high degree of co-morbidity, especially from other vascular diseases, is also an important obstacle for the design of randomised studies. As a result of this high prevalence of co-morbidities, the complication rates of various treatment options also strongly influence the decision process for an individual patient.

It is widely accepted that a patient whose RHT is well controlled with pharmacotherapy is unlikely to benefit from interventional treatment of an RAS.^{7–9} This group comprises the vast majority of patients with RHT. An invasive procedure can only be recommended if renal function deteriorates, which in some cases can be caused by progression of RAS and side-effects of hypertensive medication, or if the RHT is not controllable by two agents.^{7–9,10}

Interventions for RAS

As in all vascular regions, endovascular and surgical options are available to treat RAS. While technical and clinical success rates are similar for both types of treatment, the significantly higher morbidity and mortality of surgical procedures are evident (Table 2).^{8,11,12} In a large series, the calculated death ratio for surgery *versus* endovascular therapy was 1.69.¹¹ Improvement and miniaturisation of endovascular devices improved the technical outcome and also seem to decrease procedure-related complications.¹³ Surgical re-vascularisation for RAS is currently not the



first option, and is by general agreement reserved for selected cases or treatment of endovascular complications that cannot be corrected via the transluminal route.^{8,11,12} In patients with planned abdominal aortic surgery, the risk of an additional renal re-vascularisation probably outweighs the risk for a separate endovascular procedure, so that in these patients a renal artery bypass may be carried out during aortic surgery.¹⁴

Before indicating percutaneous transluminal renal angioplasty (PTRA), one has to be aware of the limited success rates, which are similar for all types of interventions and which differ considerably from those in other vascular areas. Reports from the literature show cure rates for RHT between 7% and 25%, improvement rates from 34% to 76% and failure rates from 25% to 50%.^{9,10,15,16}

clinical evidence, the RAS is not linked to the arterial hypertension, result in the relatively high clinical failure rate, even with the development of very refined endovascular techniques with formidable success rates.¹³

The prevention of microembolisation using transluminal protection was recommended by some study groups, but no current evidence suggests an improved outcome as a result of the use of these devices.¹⁷

Two studies^{18,19} have shown that a resistance index (RI) of >0.8 is a reliable predictor of clinical failure in interventional treatment of RAS.

Despite this evidence, this prognostic factor is not yet generally accepted. In the future, this should be more readily included in the work-up for RHT to prevent unnecessary interventions. In another large study, normal renal parenchymal thickness, high baseline

Table 2. Perioperative morbidity (major and minor complications) and mortality for PTRA and surgical bypass procedures.

	PTRA	Surgical bypass
Perioperative mortality	0.7–2%	2.4–9%
Overall morbidity	Up to 13%	Up to 38%

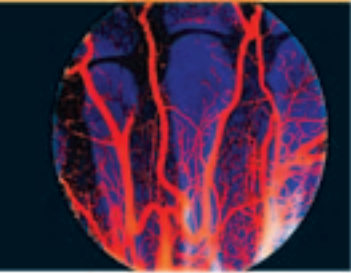
Data compiled from references 8,11,16,20. PTRA – percutaneous renal angioplasty

The cumulative complete and partial clinical success rates of not more than two-thirds of patients compared with technical success rates of 98–100%^{9,15,16} show that the treatment of RAS is not just a mechanical procedure. The damage of renal parenchyma by RHT, the chance of microembolisation during the procedure and the possibility that, despite the presence of strong

mean blood pressure and female sex were shown to be independent predictors of a favourable clinical outcome.⁹ In carrying out PTRA, two treatment options are available: balloon or stent angioplasty. Stent angioplasty requires the implantation of a foreign body into the vasculature and even though prices and hospital costs vary between countries and hospitals,

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stents increase the costs of the procedure considerably.²⁰ The potential complications of an intravascular foreign body, although rare, as well as the economic impact mean that this approach should be restricted to patients where a proven benefit has been shown.

While general complication rates of balloon- and stent-PTRA do not differ significantly, the four-year patency rates for ostial stenoses after stent-PTRA are 80% *versus* 34% after balloon angioplasty (Table 3).^{15,21} As a result of the statistically significant difference in favour of stents, ostial RAS is an accepted indication for primary stent-PTRA (Figure 1). Post-ostial (or truncal) stenoses should be treated primarily by balloon-PTRA. Only if the final haemodynamic result is unsatisfactory (residual stenosis >30%, pressure gradient >15 mmHg, or a significant dissection) is stent implantation warranted.¹⁵ The use of intravascular ultrasound to document technical success after PTRA is a costly procedure, and its usefulness is not proven.²²

Endovascular procedures in the renal arteries have 3–5 year restenosis rates of between 15% and 30%.^{10,16,23,24}

In one study, restenosis was associated with a history of smoking and a vessel diameter of ≤ 4 mm.²⁴ In-stent restenoses are readily treated with balloon angioplasty and only 10% need additional stent PTRA.²³ Reported primary assisted patency rates are close to 100%;^{16,23} the clinical success rate after re-intervention, if reported at all, is in the same range as that of primary procedures.²³ The evaluation of brachytherapy for prevention of renal artery restenosis has not led to conclusive results.²⁵

An analysis from a study group in the Netherlands has generally questioned the usefulness of PTRA in the treatment of RHT after randomising patients for medical and interventional treatment.²⁶ This study, however, received much criticism, because a large number of patients from the 'medical' group needed PTRA for declining renal function and therefore had a much shorter follow-up than the 'angioplasty' group.

However, the debate around this study demonstrates that RAS, RHT and renal function are often combined clinical findings,^{2,27} and their various combinations will always influence therapeutic decisions.

Table 3. Four-year primary patency after angioplasty for renal artery stenosis dependent on location of stenosis and type of procedure.

	Ostial	Truncal
Stent-PTRA	80%	72%
Balloon-PTRA	34%	65%
p-value	0.002	NS

Data taken from Baumgartner *et al.*¹⁵; NS – not significant.

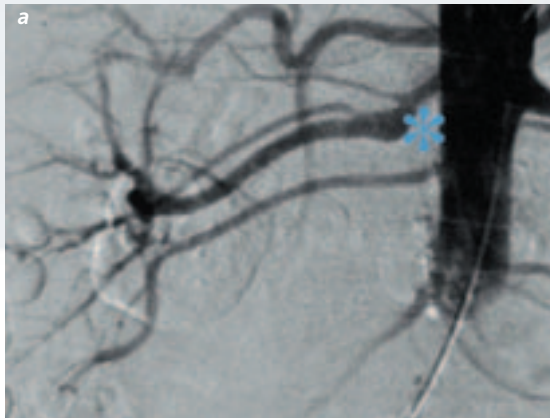
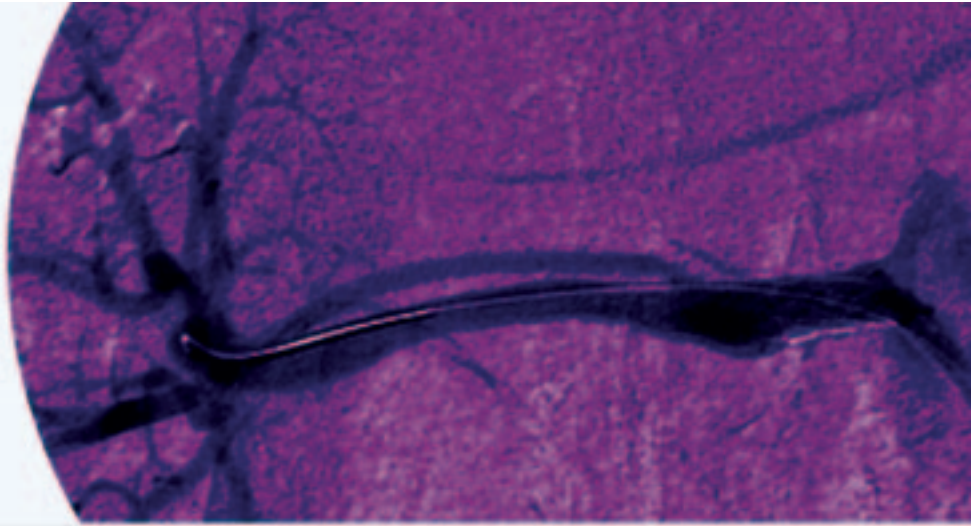
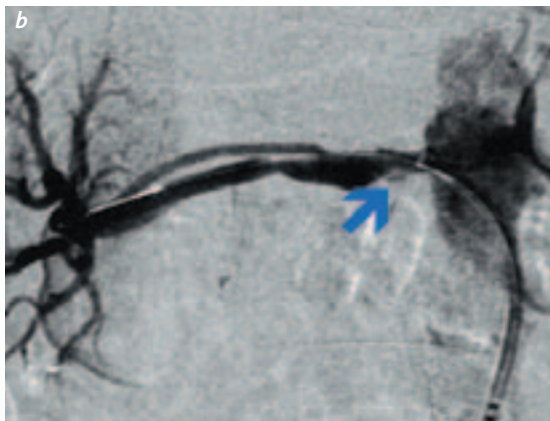


Figure 1. (a) Abdominal aortogram in a patient with renovascular hypertension, two right-sided renal arteries and an ostial stenosis of the dominant vessel (*); (b) insufficient result after balloon angioplasty of the ostial stenosis with a discrete subintimal crack (arrow) and some peripheral spasm; (c) excellent morphological result after implantation of a balloon-expandable Palmaz stent.



Key Learning

- Arterial hypertension has a high prevalence in the general population
- Renal arterial stenosis (RAS) has a prevalence increasing with age and the presence of general vascular disease
- RAS is not necessarily the cause of arterial hypertension
- Renovascular hypertension (RHT) is rare (1–5% of all hypertensive patients)
- Endovascular procedures are the treatment of choice for RHT; surgery is reserved for selected indications or complications
- Ostial stenoses are treated with primary stent placement, post-ostial stenoses primarily with balloon angioplasty; technical success is close to 100%
- As a rule of thumb, $\leq 25\%$ of patients will be cured, 50% will improve, and 25% will remain unchanged or have deteriorating renal function

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