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Advancements in Imaging and Interventional Techniques for Renal Vascular Disease and Hypertension: Addressing Challenges and Exploring Promising Strategies

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ABSTRACT
The management of renal vascular disease and hypertension presents ongoing challenges in clinical practice. However, recent advancements in imaging and interventional techniques, combined with a deeper understanding of renovascular hypertension and irreversible renal damage, offer promising strategies for preserving renal function and controlling blood pressure. In recent years, there has been a notable expansion in the armamentarium of diagnostic imaging modalities and minimally invasive interventions for renal vascular disease. These advancements have enhanced our ability to accurately diagnose and precisely treat various forms of renal artery stenosis and related conditions. Furthermore, a growing appreciation of the intricate pathophysiology underlying renovascular hypertension has shed light on the importance of timely intervention to prevent irreversible renal damage and mitigate the associated cardiovascular risks. Despite these advancements, there remains a paucity of large-scale randomized controlled trials evaluating novel treatment approaches for atherosclerotic renovascular disease. However, the emergence of innovative concepts and tools in the field holds promise for the future. By leveraging insights from smaller-scale trials and ongoing research efforts, clinicians can continue to refine their approaches to managing renal vascular disease and hypertension, ultimately improving outcomes for patients with these challenging conditions.

INTRODUCTION

During the past decade, major advancements in medical therapy, imaging, and renal revascularization have changed the landscape. Hypertension is a condition that is accelerated by atherosclerosis-induced renal artery stenosis (RAS), which might be detected incidentally [1]. There is more controversy and debate surrounding the optimal management of patients with main RAS, despite or perhaps because of these developments [2]. Over 6% of persons over 65 years have RAS with a luminal diameter decrease of at least 60%. As people age and develop coronary artery disease or atherosclerosis, its prevalence increases, and it ranges between 30% and 50% among patients with coronary artery disease [3,4]. In 851 patients with resistant hypertension, renal impairment, flash pulmonary edema, or atherosclerosis, 39% had RAS. As far as kidney failure is concerned, ARAS is unclear. A stenotic renal artery (STAR) can cause kidney failure and hypertension. Even with successful reductions in heart disease deaths, chronic kidney disease remains high, and ARAS is more likely to contribute. [4] Even when silent, ARAS increases cardiovascular disease risk, [5-7] resulting in estimated 16% of deaths annually caused by ARAS. Cardiovascular disease may be caused by increased activity of the sympathetic nervous system and RAAS, as well as by decreased glomerular filtration rates and atherosclerosis elsewhere. ARAS patients' histopathological damage influences renal function outcome. [8,9] The effects of renal arterial hypertension secondary to ARAS are more severe and lead to more target organ injuries and

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a greater decline in renal function than essential hypertension [10] and ARAS.[11] In order to prevent kidney function deterioration, healthcare is essential. According to the AHA Science Advisory [12], early diagnosis and awareness of ARAS are key, although no studies have found benefits of early treatment.

Methodology

It is believed that ARAS and fibromuscular dysplasia (FMD) are two of the most common renal artery diseases. The main renal artery and the peripheral aorta are usually affected by atherosclerosis in 90% of cases (Table 1). 51% of patients with ARAS develop stenosis within five years after diagnosis, with a 5% occlusion rate. Eight of fifty lesions (16%) progressed to occlusion according to the Dutch Renal Artery Stenosis Intervention Cooperative. Only 4 (0.3%) of 1189 cardiac catheterization patients progressed to total occlusion, whereas 133 (11.1%) did.16 ARAS progressed in 119 elderly participants at 1.3%/year but none occluded. The number of patients taking statins and awareness of blood pressure control might decrease the progression rate today. Intima, media, and adventitia of vessels are affected by idiopathic, segmental, non-atherosclerotic fibromuscular dysplasia. FMD can occur incidentally in 5% of normotensives and 16% of hypertensives. [13] The condition is most commonly found in women between the ages of 15 and 49 with normal kidney function. [14] A common dysplastic lesion is medial fibroplasia, characterized by its classic 'string of beads' appearance. There is little information about the natural history of renal FMD. More follow-up studies are needed. 35% of patients progressed.

Table 1: Stenosis and occlusion of the renal arteries

Disease	Prevalence
Renal atherosclerosis	85 – 90%
Diseases associated with fibro muscles	~11%
Occlusion of the renal arteries (thrombosis, embolism, trauma)	3%
Dissection of the aorta with involvement of the renal arteries	2%
Syndrome of the mid-aorta	Rare
Syndrome of anti-phospholipids	Rare

RAS was linked to rare aetiologies such as vasculitis of the large arteries, anti-phospholipid syndrome, and mid-aortic syndrome. There are 26% of people with arteritis who have RAS. Anti-phospholipid antibodies affect all vascular districts. Mid-aortic syndrome occurs in the branches of the aorta. It is 60% likely that you will develop RAS.

Results and discussion

Haemodynamics and anatomical aspects

Identifying vascular lesions non-invasively has never been easier thanks to advances in vascular imaging. It is important to exclude the possibility of severe stenosis before beginning long-term medical treatment. Imaging the aorta and renal arteries with an MR or CT angiography was useful for identifying multiple vessels and estimating the size of the kidneys. An angiography can't provide information on renal flow or pressure distal to the RAS, even if the flow is slow. Despite providing minimal kidney function information, Doppler ultrasound (DUS) provides accurate haemodynamic assessment in competent laboratories. RASs that justify revascu- larization remain undecided. RAS can cause hypertension if it produces a high gradient between afferent arteries and the aorta, resulting in an increase in renin production. 0.014-inch pressure wire measurements may be more accurate, but they are more expensive. In humans, 0.9 aortorenal artery pressure gradient = 25 mmHg systolic gradient.

Angiograms using conventional catheters

Angiography with intra-arterial digital subtraction detects aneurysmal and occlusive aortic disease associated with RAS, and confirms the diagnosis. It provides high spatial and temporal resolution to visualize arterial disease. Invasive imaging has the advantage of measuring haemodynamic significance directly and treating it immediately. An ARAS is characterized by a 50% diameter stenosis, with a translesional gradient of 20mmHg or 10mmHg by guidelines for renal artery revascularization. Because it is invasive, conventional catheter angiography (CCA) has the greatest risk, including radiation and complications associated with contrast and interventions. It is also the most expensive form of catheter angiography in terms of cost, time, and

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inconvenience. Despite its relatively safety and convenience, drive-by angiography remains questionable. In many cases, patients are revascularized after diagnosis, but it is unclear who will benefit from it. ARAS percutaneous transluminal renal angioplasty. Current criteria define a diameter stenosis. Comparatively to detection of haemodynamic significance with trans-stenotic pressure gradient measurements, 50% of renal angiography releases false positives (Table 2).

Computed tomography

With the advancement of CT technology, small renal arteries can be imaged using spiral multi-detector acquisitions. CTA has 94 and 93% sensitivity and specificity compared to CCA25, but offers enhanced visualization of soft tissue, faster acquisitions, and multiplanar imaging of renal arteries. The risks associated with CTA are similar to those associated with MR angiography (MRA). Furthermore, luminal narrowing may be obscured by calcification, and the technique cannot determine stenosis physiologically.

Magnetic resonance imaging

In comparison to CCA, MRA has 92 and 93.5% sensitivity and specificity without gadolinium and 96 and 93% with gadolinium, respectively, in comparison to CCA. Anatomic images of the renal arteries are created using this noninvasive procedure. MRA often overestimates stenosis, especially with less-advanced machines, because of the variety of pulse sequences available for assessing kidneys without significantly increasing scanning time. Gadolinium-enhanced MRI has recently been linked to nephrogenic systemic fibrosis, affecting between 1 and 6% of dialysis patients with a GFR of 30 mL/min.

Table 2: Quantitative angiography and Doppler-derived parameters (Rate of distal renal to aortic pressure <0.90

	Optimal cut-off value	**Confidence intervals**
Quantitative angiography		
Diameter stenosis.	66%	64 – 75
Minimal luminalDiameter	1.79 mm	1.64 – 2.58
Duplex sonography		
Peak systolic velocity	-326 cm/s	244 – 379
Renal aortic ratio	3.86	2.104 – 4.16

Duplex ultrasound

Due to its noninvasive nature, radiation-free nature, low cost, and lack of contraindications, Doppler ultrasound is an excellent ARAS screening method. Flow velocities and vascular resistance can be measured directly, as well as disease progression serially. There are, however, a number of criteria that are commonly used to describe stenosis in the body. In comparison with trans-stenotic pressure gradients, 60% of RAS may be identified incorrectly (Table 2). Dependence on operators and lack of uniformity are major drawbacks of DUS. One of the most common pitfalls is not visualizing all renal arteries and accessory renal arteries during spectral Doppler tracing. There is a correlation between a velocity of 200–320 cm/s in the main renal artery and 60% RAS angiographically with sensitivity and specificity. Second, the intrarenal interlobar or segmental arteries can be imaged. Others include a delayed systolic peak and retarded acceleration, however less specific, and should be used with caution.

Renin-angiotensin system activation

Hypertension and activation of the RAAS have prompted the development of angiotensin receptor blockers (ARBs) and angiotensin converting enzyme inhibitors (ACE). Untreated, RAAS activation appears transient, maintaining blood pressure through alternative pathways, including oxidative stress and endothelial dysfunction. The release of renin occurs when kidney perfusion pressure is reduced by 10-20%,23 which results in a decrease in luminal cross-section of 70-80%. The release of renin occurs when kidney perfusion pressure is reduced by 10-20%, which results in a decrease in luminal cross-section of 70-80%. The response to captopril is measured by renin sodium profiling, ACE-inhibitors' effects on blood pressure and renal function, and captopril renography. Due to its limited predictive value and inability to visualize the renal vessels directly, captopril renography was losing popularity. It is however capable of assessing kidney function when one side has high-grade stenosis.

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Imaging with tomography

In addition to allowing visualization of the renal artery, tomographic imaging has several potential advantages for ARAS assessment. In addition, they can assess both kidneys simultaneously and individually. They can also provide quantitative assessments of post-stenotic kidney function and haemodynamics in the same session. It has been validated that both CT and MR can be used to assess the flow of blood into the kidneys. A computer tomography was used to assess renal functional reserve, tubular function, and endothelial function. Positron emission tomography is used to assess renal cortical perfusion and metabolic activity. Using BOLD MRI, we can assess renal deoxyhaemoglobin levels and indirectly renal oxygen levels, as a result of ARAS. In normal nephrogram human kidneys, furosemide inhibits tubular transport and oxygen consumption, but not in atrophic kidneys distal to total occlusion. Radiation and contrast agents are not used in this technique. In addition to their high cost and limited availability, tomographic imaging tools provide a wealth of information and are mostly used by large medical centers for research.

Treatment

In patients with ARAS, lowering blood pressure is effective with various treatment regimens, though kidney function may deteriorate. Several studies found that antihypertensive therapy reduced blood pressure, but they found inconsistent results on clinical outcomes. RAAS blockade is tolerated well by a vast majority of patients who have significant haemodynamic effects due to ARAS. However, ACE-inhibitors and ARBs can cause a transient drop in GFR and raise serum creatinine, warranting caution and close monitoring. As a result of RAAS blockade, renal function deteriorates acutely, primarily in patients with heart failure, diuretics, and volume contraction. In order to effectively manage ARAS, cardiovascular risk factors must be aggressively managed. Smoking cessation, maintaining an acceptable glucose level, and lowering lipid levels are all critical.

Revascularization

Although medical and invasive therapies are both capable of reducing blood pressure, revascularization may be more effective when bilateral disease is present. The benefits of aggressive diagnosis and renal revascularization are unknown at the present time. The severity of mortality and morbidity increases in patients treated with medical therapy alone. In the course of revascularization, blood pressure and kidney function improve immediately, but mortality and morbidity may occur. Costs and risks limit the universal application of endovascular and surgical procedures, especially for non-immediate renovascular injuries. Patients with unilateral RAS with a systolic gradient of 21 mmHg had the greatest improvement in hypertension following stenting. There is a difference between angiograms and fractional flow reserves. Although general consensus exists, renal revascularization does not have robust evidence to support it for RAS patients with sudden onset, flash pulmonary edema not associated with acute coronary syndrome, congestive heart failure with preserved left ventricular function, or acute renal oligoanuria. Patients with multidrug-resistant renovascular hypertension or advanced chronic kidney disease (stages 4 - 5) 48 should undergo revascularization. ARAS patients suffering from chronic kidney disease or hypertension as well as severe RAS, however, lack adequate evidence for its use.

Interventional

PTRA with or without stenting is an interventional treatment. Guide catheter techniques include guide wires and balloon catheters as well as pre-mounted stents. It is recommended to take heparin and low-osmolar contrast media before the procedure. Almost all institutions prescribe dual antiplatelet therapy for 28 days. A PTRA is considered to be the best treatment for patients suffering from hypertension or FMD. Patient success is 82 – 100%, but 10 – 11% of stenosis recurs. It is less effective for ARAS due to ostial dissection and elastic recoil, with a 10 – 47% restenosis rate. Endovascular techniques have been enhanced with stents to achieve 100% success rates, residual diameter stenosis of 10%, and restenosis of 11 – 23%. Revascularization remains controversial, however. Since its use is not supported by randomized trials, some recommend serum creatinine elevation before bilateral RAS. The increase of 88 mmol/L in baseline creatinine predicts postoperative renal failure. Presence of a baseline creatinine level of 0.130 mmol/L predicts death after renal stenting.

Medical therapy for atherosclerotic renal artery stenosis and angioplasty

The study compared PTRA to medical treatment, yet was underpowered for mortality, cardiovascular, and renal outcomes. A small number of studies used stents, and the treatments used varied both within and between them. The potential of PTRA for drug sparing in unilateral ARAS had been overestimated. Angioplasty and drug therapy did not differ significantly in DRASTIC. The mortality rates for 21 cohort studies

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involving PTRA along with stenting (PTRAS) that were published and were included in a meta-analysis did not show any unifying pattern. Some studies found that patients who underwent PTRAS were still at an increased cardiovascular disease risk. However, some showed improvement in kidney function compared with medically treated patients. Acute arterial hypertension was cured, improved, and worsened by 4 - 18, 35 - 79, and 0 - 13%. Stent placement reduced NYHA Functional Class in patients with bilateral disease and stenosis of one kidney. A meta-analysis of studies published found that renal revascularization was beneficial for patients with congestive heart failure and pulmonary oedema.

Surgical revascularization

Patients who undergo aortic or nephrectomy surgery, or who have complex disease of the renal arteries, such as aneurysms or failed endovascular procedures, benefit from renal artery surgery. Renal artery bypass grafting, endarterectomy, or hepatic or splenic anastomosis are surgical procedures. Preoperative azotemia, aortic reconstruction, and aortorenal bypass all increase 30-day mortality. Perioperative death is strongly predicted by graft failure, which occurs in 1.4 - 10% of cases. Patients with co-morbidities are more likely to die from surgical revascularization, and endovascular repair has similar outcomes.

Conclusions

There is controversy surrounding revascularization of renal arteries. As a result of the STAR and ASTRAL clinical trials, it is no longer feasible to revise ARAS indiscriminately. It is challenging to identify patients who will respond and intervene early enough to reverse kidney damage. When the kidney function has remained stable for at least six to twelve months, an acceptable medical regimen can control hypertension. To verify anatomically relevant RAS of 70%, a functional measurement of 21 mmHg should be performed. 'Flash' pulmonary oedema unrelated to acute coronary syndrome supports intervention for bilateral stenosis. Revascularization may help control hypertension in ARAS patients, but a cure is rare, so preserving renal function is a better goal. Aortic disease must be present for revascularization. For complicated cases, a renal bypass or surgical revascularization may be appropriate. In spite of revascularization, researchers are investigating ways to improve kidney tissue viability.

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