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Total Renal Artery Occlusion: Recovery of Function After Revascularization

Sandhya Manohar, M.B.B.S¹, Abdurrahman Hamadah, M.D¹, Sandra M. Herrmann, M.D.¹, and Stephen C. Textor, M.D.¹

¹Division of Nephrology and Hypertension, Mayo Clinic, Rochester MN

Abstract

Current trends in managing atherosclerotic renal artery stenosis favor medical therapy, on account of negative results from prospective trials of revascularization, such as CORAL and ASTRAL. One result of this trend has been encountering occasional patients with progressive disease, sometimes leading to total arterial occlusion. Here we illustrate a case of accelerated hypertension with complete renal artery occlusion in which the patient recovered function after surgical bypass and review the clinical approach utilized and the advanced imaging modalities available to us. A high index of suspicion and careful radiological imaging play important roles in selecting patients who may have residual function and may benefit from revascularization. This case illustrates an example whereby restoring renal artery perfusion for carefully selected patients can be life changing, with recovery of kidney function and improved blood pressure, pill burden, and overall quality of life.

Keywords

atherosclerotic renovascular disease (ARVD); hypertension; total renal artery occlusion; revascularization; renal artery stenosis; renal ischemic disease; blood oxygen level-dependent magnetic resonance (BOLD-MR); imaging; case report

Corresponding Author: Stephen C. Textor, stextor@mayo.edu.

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Introduction

Occlusive atherosclerotic renovascular disease (ARVD) is a leading cause of secondary hypertension and renal ischemic disease(1). One of the principal causes of renal arterial occlusion is atherosclerosis. The prevalence of ARVD is estimated to be 6.8% from community-based studies of people aged over 65 years using an ultrasound threshold of elevated peak systolic arterial velocities suggestive of 60% occlusion(2). Some patients with progressive vascular occlusion develop advanced renal failure on that basis and recently concern has been raised for a possible rise in ARVD-related kidney failure (3). Considering that many patients with renovascular disease go undiagnosed, it is difficult to estimate the real incidence of end stage renal disease (ESRD) from ARVD.

We know from the coronary circulation that gradual complete arterial occlusion can occur with preservation of organ viability due to collateral arterial supply (4). Studies utilizing blood oxygen level-dependent magnetic resonance (BOLD-MR) demonstrate that renovascular occlusion of 70–80% ultimately produces demonstrable cortical ischemia (5). This hypoxia can lead to inflammatory changes in the kidney, resulting in fibrosis and subsequent renal dysfunction (6, 7). Salvage of such a hypoxic kidney must be achieved before failure of compensatory mechanisms. We present the case of a 69-year-old patient who developed total occlusion of her left renal artery, underwent a bypass revascularization procedure of the occluded vessel resulting in improvement in blood pressure and recovery of renal function sufficient to be removed from the transplant wait-list.

Case Report

Clinical History and Initial Laboratory data

A 69-year-old Caucasian woman was referred to our Hypertension Clinic for evaluation of accelerated hypertension and kidney dysfunction. She had been diagnosed with hypertension ten years earlier and maintained on a thiazide diuretic with good blood pressure (BP) control. She had no other significant medical conditions. Serum creatinine at that time was 1.4 mg/dl. Six months before presentation, she was hospitalized near home with a hypertensive emergency. Her BP was 250/110 mm Hg associated with a refractory headache, confusion, and creatinine elevation to 2.5 mg/dl. The protein-creatinine ratio was 1.6 g/g. An kidney ultrasound identified probable left renal artery stenosis. An angiogram identified a patent right renal artery, but total occlusion of the left renal artery. No endovascular procedure was possible. Her antihypertensive therapy was intensified with resolution of CNS symptoms. However, BP continued to be labile and difficult to control, and her kidney function progressively deteriorated. She underwent biopsy of the right non-stenotic kidney which showed evidence of severe arteriosclerosis, focal segmental glomerular scarring and mild effacement of podocyte foot process suggestive of secondary focal segmental glomerulosclerosis likely secondary to vascular disease. She came to Mayo Clinic for a second opinion.

Upon presentation to our institution, her BP averaged 165/79 mm Hg despite administration of amlodipine 10 mg daily, carvedilol 12.5 mg daily, clonidine 0.1 mg twice a day, and torsemide 10 mg daily. Initial blood work showed a creatinine of 3.5 mg/dl, plasma renin

activity of 6.3 ng/ml/h, and an aldosterone of 10 ng/dl. Her urinalysis showed no hematuria or cellular elements. She had a proteinuria of 3.5 g/d and a measured creatinine clearance of 13 ml/min/1.73m². She was started on a low dose of losartan, and her other medications were adjusted. She was evaluated and accepted as a transplant candidate. Her blood pressure continued to be difficult to control. The possibility of removal of the left kidney as a “pressor” kidney was considered.

Additional Investigations

An ultrasound of the kidneys with spectral Doppler analysis was performed. The origin of the left renal artery was not well visualized, but dampened, *tardus parvus* Doppler waveforms in the remainder of the left renal artery and the segmental arteries were consistent with the proximal left renal artery occlusion or high-grade stenosis. The right renal artery was widely patent. Remarkably, cortical thickness was relatively preserved in the left kidney, with overall length of 10.1 cm as compared to the right kidney of 12.6 cm. The segmental resistive indices were also normal, at 0.53 (Figure 1 Panel B). A CT Angiogram confirmed the total occlusion of flow in the proximal left renal artery but with visualization of distal vessels and kidney (Figure 1 Panel A).

Renal BOLD-MR imaging was performed before and after intravenous furosemide administration. The BOLD-MR of the left kidney showed elevated cortical R2* suggestive of cortical hypoxia and increased fractional tissue hypoxia (Figure 2) with a modest response to furosemide. Unexpectedly, a nuclear MAG3 renal scan identified the majority of glomerular filtration (57.1%) appeared to derive from the occluded left kidney, while the remaining 42.9% came from the right kidney.

Diagnosis

Accelerated hypertension associated with total left renal artery occlusion with evidence of residual function in a chronically occluded left kidney.

Clinical follow-up

She was evaluated for possible left renal artery revascularization with a focused CT angiogram that confirmed left renal artery occlusion proximally (Figure 1). A viable distal vessel was identified with patency of most intra-renal arterial branches. She underwent a left abdominal aorto-renal bypass using a left non-reversed saphenous vein. At the time of the surgery, her creatinine was 4.8 mg/dl with a BP of 165/82 mm Hg. Two weeks after the surgery, BP was 122/76 mm Hg without losartan and a reduced dose of diuretic, and creatinine had fallen to 2.9 mg/dl with electrolytes within reference ranges. After 3 months, her BP was 108/56 mm Hg with occasional symptoms of dizziness and anti-hypertensive drugs were further reduced to amlodipine 5 mg daily, metoprolol succinate 25 mg daily and torsemide 2.5 mg daily (Figure 3). Her creatinine had stabilized at 2.9 mg/dl, and her proteinuria had fallen to 500 mg/d. After six months, anemia had resolved, appetite improved, and measured GFR was 26 ml/min/1.73m².

Discussion

This case illustrates the complexities experienced by clinicians caring for patients with renovascular disease and progressive renal failure. Substantial observational experience over several decades supports a role for renal revascularization to preserve renal function in a select group of patients (8). However, results from several prospective randomized trials including ASTRAL (Angioplasty and Stenting for Renal Artery Lesions), CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions), and STAR (Stent Placement in Patients With Atherosclerotic Renal Artery Stenosis and Impaired Renal Function) have failed to demonstrate consistent benefits of revascularization in patients with either uncontrolled BP and renal dysfunction (9) (10, 11). Our patient might have met the criteria for inclusion in these studies, but in her case, revascularization resulted not only in better BP control but also led to improved renal function. Her impending need for renal replacement therapy was delayed. This case extends the results of Cherr et al who identified improvement in renal function after revascularization and had improved dialysis-free survival as well in those patients who experienced improved renal function after revascularization (12).

So who are the patients for whom renal function can be salvaged and how do we recognize them? We first need to recognize and diagnose the patients with renovascular disease. Occlusive renal artery disease can clinically manifest in many different ways (Table 1). Our patient presented with accelerated hypertension with neurological symptoms at an older age, despite a history of relatively easy to control hypertension earlier. Patients for whom there is a high degree of suspicion for renovascular disease should proceed with radiological testing for confirmation (Table 2). The answers one would expect from these studies include: presence and severity of the lesion, its precise location and extent within the renal vasculature and most importantly, the status of the kidney at the end of the vessel and its potential for salvage.

Renal ultrasound with Doppler spectral analysis is the most cost-effective non-invasive method for visualizing the renal vasculature. By utilizing a combination of B-mode imaging and Doppler waveforms, stenotic lesions can be reliably detected. The velocity of flow increases as an artery narrows and an increase in velocity is detected by comparing the systolic flow velocity of the renal artery to that in the aorta. A peak systolic velocity above 200 cm/s by ultrasound suggests a stenosis of greater than 60 percent (13). A single measurement of peak systolic velocity has a sensitivity of 85% and specificity of 92%(13). Other useful information obtained from ultrasound is the renal resistive index (RI). This is a ratio of the difference of peak systolic velocity and end-diastolic velocity divided by peak systolic velocity. It is reflective of the degree of intrinsic vascular disease at the segmental artery level. A high resistance to flow here (i.e. RI >0.8) is associated with a worse outcome from revascularization (14). An ultrasound also provides information regarding cortical echogenicity, cortical thickness and overall kidney size. This initial and relatively inexpensive test can give us a wealth of information that can help guide the rest of the workup, but with the caveat that the results are operator- and institution-dependent.

A decrease in blood flow to the kidneys does not necessarily translate to a loss of tissue viability and ischemia. Only 10% of the blood oxygen delivered to the kidney is required for

its metabolic needs. Gloviczki et al have shown that in patients with ARVD a decreased blood flow of up to 35–40% (with moderate stenosis, duplex velocities 384 cm/s) and associated decreased kidney volume is associated with preserved cortical and medullary oxygenation (15) (5). Patients with more severe and advanced vascular occlusion develop evident cortical hypoxia and more severe fractional tissue hypoxia overall, as suggested by the BOLD MR in the case presented (5). But how do we know if our patient has preserved kidney tissue downstream? Some clinical clues are evidence of longstanding damage like small, atrophic kidneys on ultrasound or laboratory evidence of slowly progressive renal dysfunction over years, and/or significant baseline proteinuria (16). The chances of having salvageable kidney tissue in these circumstances are reduced. Muray et al had found that patients with a recent deterioration of renal function had a more favorable outcome after revascularization (17).

For ambiguous cases, additional testing with nuclear MAG3 renal scan and BOLD-MR may be considered. In our patient, the rapid onset of symptoms with preserved kidney size and a MAG3 renogram suggesting that the occluded kidney accounted for the majority of glomerular filtration prompted further studies. BOLD-MR is a non-invasive imaging technique used to assess the kidney's regional oxygenation. It is a type of functional MR that utilizes endogenous deoxygenated hemoglobin as a contrast agent and detects magnetic field disturbances caused by changes in degree of oxygenation of the hemoglobin within kidney tissue. The $R2^*$ score is the magnetic rate of relaxation that correlates positively with deoxyhemoglobin levels (18). A normally perfused kidney would be expected to have a low $R2^*$ score in the cortex and higher $R2^*$ scores in the deeper medullary region, consistent with the known gradient of hypoxia in deep medullary regions. The level of regional deoxyhemoglobin is dependent on many factors, including oxygen consumption related to solute transport in tubules. Furosemide is utilized to partially block tubular transport and is associated with a reduction of medullary $R2^*$ scores.. In our patient, high $R2^*$ scores were seen in the left kidney, demonstrating both reduced blood flow and high degree of oxygen consumption by the under-perfused kidney. The partial response to furosemide suggested, however, that solute transport was still present, and made a case that the kidney retained some meaningful function. The presence of a low $R2^*$ values (suggesting well oxygenated tissue in the right kidney) score needs to be interpreted based on the clinical context. A low $R2^*$ score is seen if there is adequate perfusion and tissue function, but can also be seen if the kidney is 'dead' (non-functioning) as the oxygenated blood would be passing through without oxygen utilization or consumption by atrophic tissue. How best to interpret $R2^*$ in the kidney is still debated. BOLD imaging is available only in select institutions and still requires expert opinion for result interpretation. In our patient, these data were interpreted to indicate that the post-occlusion kidney was severely hypoxic, but still functioned and might be salvageable. Recognizing this window of opportunity of ischemic but recoverable stage is important in selecting the right patients for revascularization.

But extensive testing should not be undertaken if no change in management is clinically feasible. So how do we know if someone really needs revascularization or if medical therapy alone would suffice? This is a difficult question to answer. The balance of morbidity associated with the revascularization procedure needs to be weighed against the morbidity associated with further kidney function decline and a life on dialysis, the neurological and

cardiovascular sequelae of uncontrolled hypertension, and the side effects of the complex regimens needed to maintain reasonable BP control. Cherr et al reviewed their experience with surgical management of ARVD for 477 patients with a mean followup of 56 months. Of these, 12% were cured of their hypertension and 73% had improved BP. Perhaps more importantly 43% had improvement in renal function, defined as a 20% or more increase in eGFR or freedom from dialysis dependence. On follow up, these patients had higher dialysis-free survival. They noted 23 patients that were on dialysis prior to surgery were able to discontinue dialysis after the procedure (12). Misra et al had observed that the patients with high grade proteinuria and advanced CKD (Stage 3B and higher) had a higher risk of progression to dialysis after revascularization with a renal artery stent (16). Our patient had a substantial hypertensive injury to her 'normally perfused' right kidney as well seen as focal segmental glomerulosclerosis on biopsy. We interpreted this as likely from her episode of malignant-phase hypertension. At her age she was quite independent but was at an imminent need for renal replacement therapy, a lifestyle compromise that could potentially be altered with revascularization.

In summary, this case highlights the need for individualized medicine in the care of complex renal patients, particularly in the era of negative trials. Careful review of the timeline of the patient's decline in kidney function combined with information from imaging modalities suggested that the kidney might be salvageable. Our role as nephrologists is crucial in identifying this small cohort of patients that greatly benefit from prompt intervention with a revascularization procedure.

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Figure 1.

Renal imaging. Panel A shows a posterior view CT Angiogram with a total occlusion of flow in the proximal left renal artery with visualization of distal vessels and kidney by angiography suggestive of evidence of preserved distal perfusion. Collaterals cannot be visualized. Panel B is the ultrasound of the left renal artery with spectral Doppler analysis showing a waveform with a delayed upstroke and a dampened tardus parvus.

	Left Kidney: Before surgery		Left Kidney: After surgery	
	A: Pre-Furosemide	B: Post-Furosemide	C: Pre Furosemide	D: Post-Furosemide
Cortical R2*	23	25.2	19.6	21
Total R2*	23.3	24.7	19.2	17.7
% >20	66	70.2	45	33
% >30	22.9	32	7.3	4.3

Figure 2.

Axial images of blood oxygen level dependent MR images of the left kidney. Panel A shows the R2* map of left kidney with high R2* deoxyhemoglobin levels noted even in the cortical area and no significant change after infusion of furosemide (Panel B). The panel C shows lower R2* scores overall after revascularization with expected improvement in R2* scores after furosemide blockade in panel D suggestive of improved oxygenation.

Figure 3.

Trends of serum creatinine (mg/dl) and systolic blood pressure (mm of Hg) from baseline to 3 months after renal revascularization. List of antihypertensive medications at the time of surgery and at the end of 3 months post-surgery are also depicted.

Table 1

The different clinical presentations of occlusive renovascular disease

Clinical Presentation	Comments
New diagnosis of hypertension	Suspect in patients with <ul style="list-style-type: none"> - Presence of abdominal bruit - Age > 55 years - elevation in serum creatinine of >50% after starting ACEi or ARB therapy - Asymmetry of kidney size of >1.5 cm
Acceleration of pre-existing essential hypertension	Presence of atherosclerotic disease elsewhere in body
CKD	Ischemic nephropathy is suspected if presenting with slowly declining GFR with bland urinalysis, minimal proteinuria, a history of difficult to control hypertension and evidence of atherosclerotic disease elsewhere and no other definable alternative cause of renal disease can be given
Worsening of Congestive heart failure	Activation of RAS system with enhanced sodium reabsorption leading to circulatory congestion and failure; these patients present with recurrent episodes of flash pulmonary edema with difficult to control BP.
Stroke	Accelerated rise in BP with target organ injury

RAS= renin angiotensin system; BP= blood pressure; ACEi = angiotensin converting enzyme inhibitor; ARB=Angiotensinogen receptor blocker; CKD., chronic kidney disease; GFR, glomerular filtration rate

Table 2

Radiological tests available for initial diagnosis of renal artery stenosis

Diagnostic Test	Diagnostic Comment
Ultrasound of Kidney with Doppler	<ul style="list-style-type: none"> - Small Kidneys are most likely chronically diseased with low chances of recovery - Preserved Cortical thickness predictive of residual kidney function - A peak systolic velocity > 200 cm/s by ultrasound suggests a stenosis of >60% - Elevated resistive indices of >0.8 indicative of small vessel disease - Preferred initial screening modality
CT Angiography	<ul style="list-style-type: none"> - Higher risk in those with renal dysfunction due to need for iodinated contrast - Preferred if high pretest probability of renal artery stenosis but with negative ultrasound Doppler study
MR Angiography	<ul style="list-style-type: none"> - Risk of nephrogenic systemic fibrosis with gadolinium if GFR <30 ml/min/1.73 m² - sensitivity and specificity of 94% and 96% for detecting significant renal artery stenosis - Newer technique of phase-contrast MR angiography that does not use IV contrast is appealing but not widely available
Renal arteriography	<ul style="list-style-type: none"> - Diagnostic gold standard for confirmation - Invasive procedure

MR, magnetic resonance; CT, computed tomography; GFR, glomerular filtration rate