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VASCULAR MEDICINE

CASE REPORT: CLINICAL CASE

Revascularization in a Time After CORAL

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ABSTRACT

Revascularization of renal artery stenosis became less common following randomized controlled trials that failed to demonstrate benefit in low-risk patients. An 88-year-old patient with recurrent acute pulmonary edema and progressive kidney disease in the setting of high-grade renal artery stenosis, a phenotype excluded from these trials, underwent revascularization. (JACC Case Rep. 2024;29:102501) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

An 88-year-old woman presented for the third time in 1 month with recurrent sudden onset shortness of breath and hypoxia. In the emergency department, she had a blood pressure of 181/60 mm Hg, a heart rate of 60 beats/min, a respiratory rate of 23 breaths/min, and an oxygen saturation of 92% on room air, and she required bilevel positive pressure ventilation support. Physical examination was notable for diminished respiratory effort, left-sided jugular venous distention, possible abdominal bruit (faint), palpable dorsalis pedis and radial pulses bilaterally, and no peripheral edema. Carotid bruits were not reported. Laboratory test results demonstrated a serum creatinine level of 2.60 mg/dL, an estimated glomerular filtration rate (eGFR) of 17 mL/min/1.73 m^2, and a pro-B-type natriuretic peptide (proBNP) level of 5,362 pg/mL. Four months before admission, her baseline serum creatinine was 1.70 mg/dL, eGFR was 29 mL/min/1.73 m^2, and proBNP was 3,408 pg/mL. A chest radiograph showed mild pulmonary vascular congestion and a trace right pleural effusion, new findings compared with a chest radiograph obtained 4 days earlier. The patient was admitted for treatment and further work-up of acute pulmonary edema of unknown origin.

TAKE-HOME MESSAGES

- This case highlights the clinical features of patients presenting with hemodynamically significant RAS.
- Renal artery revascularization is appropriate for certain high-risk patients, including those with flash pulmonary edema or progressive CKD and high-grade RAS.

PAST MEDICAL HISTORY

The patient's medical history was significant for long-standing hypertension, hyperlipidemia, coronary artery disease, carotid artery stenosis, heart failure with preserved ejection fraction, atrial fibrillation, prediabetes, and chronic kidney disease (CKD) stage 4. Home antihypertensive medications included the following: amlodipine, 10 mg nightly; carvedilol, 25 mg twice daily; spironolactone, 25 mg daily; torsemide, 20 mg daily; and hydralazine, 25 mg nightly.

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ABBREVIATIONS AND ACRONYMS

CKD = chronic kidney disease

CTA = computed tomography angiography

eGFR = estimated glomerular filtration rate

PAD = peripheral arterial disease

pro-BNP = pro-B-type natriuretic peptide

RAAS = renin-angiotensin-aldosterone system

RAS = renal artery stenosis

She had previously been taking a stable dose of lisinopril, but this drug was discontinued 2 months earlier as a result of progressive renal failure and hyperkalemia.

DIFFERENTIAL DIAGNOSIS

On admission, the cause of this patient's acute pulmonary edema was unclear. Possible causes included an acute exacerbation of chronic heart failure, myocardial ischemia, valvular dysfunction, or renovascular hypertension secondary to renal artery stenosis (RAS).

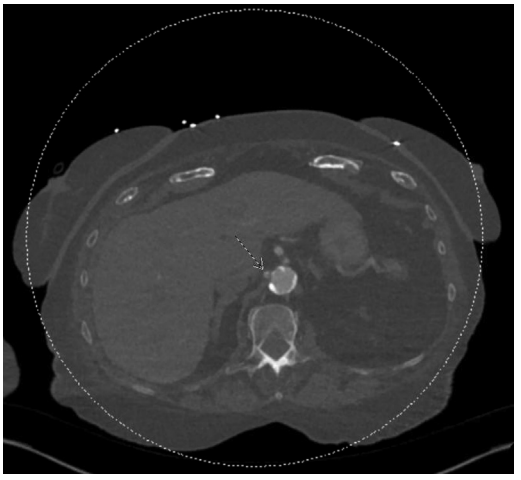
INVESTIGATIONS

Initial cardiac evaluation included a transthoracic echocardiogram, which showed a left ventricular ejection fraction of 76%, mild mitral regurgitation, a severely dilated left atrium, and an elevated left ventricular filling pressure. A nuclear pharmacologic stress test revealed no ischemia or scarring. Renal ultrasound showed moderate left-sided hydronephrosis, an atrophic left kidney, and significant asymmetry in size (right kidney, 9.1 cm; left kidney, 7.5 cm).

MANAGEMENT

Initial management included diuresis with improvement in pulmonary edema, but it was accompanied by further deterioration in renal function and the emergence of uremic symptoms. Although ischemic nephropathy and RAS were considered in the initial differential diagnosis, clinicians did not pursue investigation because it was thought that intervention would be ineffective. The patient was referred for consideration of dialysis and experienced symptomatic improvement with dialysis. However, she was discontent with the prospect of long-term dialysis therapy and wanted to explore the possibility of salvage therapy with renal revascularization. Computed tomography angiography (CTA) of the abdomen and pelvis was obtained and demonstrated severe bilateral RAS, worse on the left, with associated left renal atrophy (**Figures 1 and 2**). Although kidney size was reduced on both sides, measured resistive indices in the right kidney (0.78 in the distal renal artery, 0.70 in the upper pole, 0.72 in the mid-pole, and 0.65 in the hilum) were reassuring. Resistive indices ([peak systolic velocity − end-diastolic velocity] ÷ peak systolic velocity) of <0.8 are associated with less fibrosis and have been shown to be predictive of a favorable response to revascularization.[1] After consideration of potential risks (no improvement, further renal deterioration, bleeding, and arterial dissection) and benefits (better blood pressure control and possible liberation from dialysis), she underwent right renal artery revascularization and placement of a balloon-expandable stent (**Figures 3 and 4**).

FIGURE 1 Computed Tomography Angiography of the Abdomen and Pelvis With Contrast



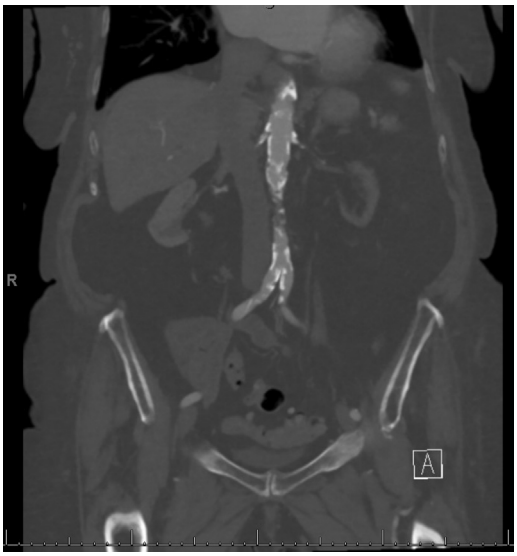
Aortic calcification at the origin of the renal arteries, with the right renal artery indicated by the arrow.

Completion angiography demonstrated significant improvement in right-sided perfusion with excellent flow into the distal renal artery branches (**Figure 5**). She was started on dual antiplatelet therapy with aspirin and clopidogrel. After revascularization, her urine output improved from 245 to 1,740 mL over a 24-hour period, and kidney function improved, allowing dialysis to be discontinued. The patient's kidney function continued to improve from a serum creatinine value of 4.25 mg/dL just before revascularization to a nadir of 1.54 mg/dL within 1 month of discharge.

DISCUSSION

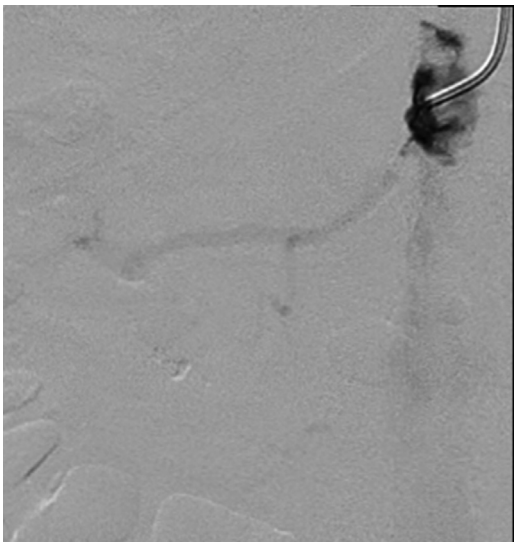
Renal artery stenosis can manifest in several different ways. Common clinical presentations include resistant hypertension despite multiple antihypertensive agents, progressive CKD, acute pulmonary edema, recurrent acute heart failure exacerbations, and intolerance to renin-angiotensin-aldosterone system (RAAS) blockade.[2] Comorbidities strongly associated

FIGURE 2 Computed Tomography Angiography of the Abdomen and Pelvis With Contrast



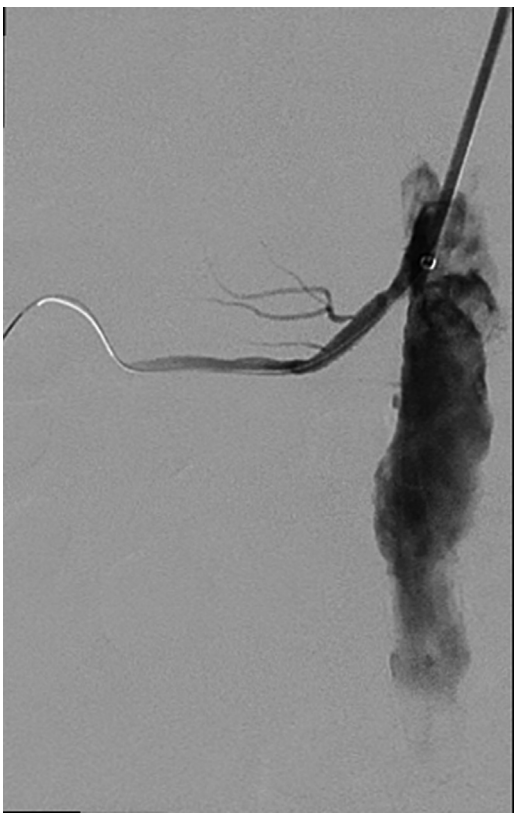
Calcified plaques along the abdominal aorta with involvement of both renal arteries and associated atrophy of the left kidney.

FIGURE 3 Pre-Stenting Angiography



Directed angiography of the right renal artery demonstrating a severely stenosed, heavily diseased, but patent, artery.

FIGURE 4 Post-Stenting Angiography



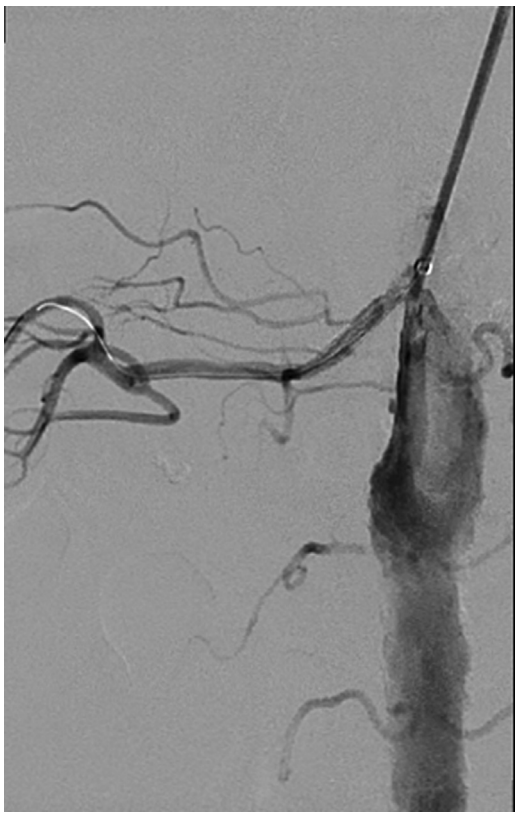
Post-stenting image showing a 6 mm × 19 mm noncovered balloon-expandable stent, demonstrating patency of the proximal renal artery.

with RAS include heart failure and peripheral arterial disease (PAD).[3,4] In epidemiologic studies, 22% to 45% of patients with suspected PAD had radiologic evidence of >50% RAS.[4]

Our case is an example of bilateral RAS manifesting with acute pulmonary edema and progressive CKD. Acute ("flash") pulmonary edema is an accumulation of fluid within the pulmonary interstitium and alveoli over minutes to hours that is caused by increased pulmonary capillary permeability secondary to excessive pulmonary RAAS activity, increased sympathetic activity, and/or impaired nitric oxide synthesis. Acute pulmonary edema is a severe form of acute decompensated heart failure and is often triggered by an acute event, such as a myocardial infarction or hypertensive crisis.[5] The association between bilateral RAS and recurrent episodes of acute pulmonary edema is known as Pickering syndrome. In Pickering syndrome, bilateral RAS causes RAAS activation leading to sodium and water retention, uncontrolled hypertension, left ventricular hypertrophy, progressive renal dysfunction, and altered lung vascular permeability, which predisposes patients to recurrent flash pulmonary edema.[6]

Before the publication of 2 pivotal trials, it was relatively common practice to revascularize RAS. In 2009, the ASTRAL (Angioplasty and Stenting for

FIGURE 5 Post-Stenting Angiography With Distal Flow



Post-stenting angiogram demonstrating excellent flow into the distal right renal artery branches.

TABLE 1 Indications for Renal Artery Revascularization in Patients With RAS

Indication	ACC/AHA/SCAI/SIR/SVM 2018	KDIGO 2022	AHA 2022
Flash pulmonary edema and high-grade RAS[a]	A	A	A
Progressive CKD in high-grade RAS[a] (bilateral or solitary kidney)	A	A	A
AKI secondary to acute renal artery occlusion or high-grade RAS[a]	–	A	–
ACEI or ARB intolerance in high-grade RAS[a]	–	A	–
Kidney transplant with RAS	–	A	–
Resistant hypertension (≥3 medications, 1 of which is a diuretic agent) and high-grade RAS[a]	M	–	M
Progressive CKD and uncontrolled hypertension	–	M	–
Recurrent heart failure and high-grade RAS[a]	M	M	M
Uncontrolled unstable angina despite maximal medical therapy and high-grade RAS[a]	M	–	–
Progressive CKD and unilateral high-grade RAS[a]	M	–	–
Asymptomatic high-grade RAS[a] with viable renal parenchyma	–	M	–
New (<3 mo) dialysis with nonfunctioning but possibly viable kidney	–	M	–

[a]High-grade RAS is defined by ACC/AHA/SCAI/SIR/SVM as RAS ≥70% or 50% to 69% with hemodynamic significance and by KDIGO as RAS >75%.

A = appropriate; ACC = American College of Cardiology; ACEI = angiotensin-converting enzyme inhibitor; AHA = American Heart Association; AKI = acute kidney injury; ARB = angiotensin receptor blocker; KDIGO = Kidney Disease: Improving Global Outcomes; M = may be appropriate; RAS = renal artery stenosis; SCAI = Society for Cardiovascular Angiography and Interventions; SIR = Society of Intervention Radiology; SVM = Society for Vascular Medicine.

Renal Artery Lesions) trial found no significant difference in renal function following revascularization in combination with medical therapy vs medical therapy alone in patients with atherosclerotic renal disease.[7] In 2014, the CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions) trial showed that renal artery stenting had no significant benefit in preventing a primary composite outcome of major cardiovascular or renal events among patients with RAS and hypertension or CKD.[8] In the aftermath of these trials, revascularization of low-risk RAS appropriately became less common. However, both trials had significant limitations. In the ASTRAL trial, 40% of patients had RAS <70%.[7] Participants in the CORAL trial were taking on average 2.1 antihypertensive medications at baseline, >25% of patients had blood pressure already at goal, mean RAS was <75%, and researchers excluded patients who had been hospitalized for heart failure or had experienced a myocardial infarction within the past 30 days.[8] This suggests that high-risk patients, those who may benefit most from revascularization, were not represented in these trials.

Recent consensus guidelines recommend renal artery revascularization for certain high-risk groups (Table 1). Revascularization is appropriate for patients presenting with flash pulmonary edema and high-grade RAS, as well as for patients with progressive CKD in the setting of high-grade RAS. In patients with CKD who are not undergoing dialysis, contrast medium exposure during the procedure may incite dialysis initiation. However, after starting dialysis, the benefits of performing revascularization outweigh this risk. Revascularization may also be appropriate for patients with resistant hypertension or recurrent heart failure and high-grade RAS.[2,9,10] Additional indications are outlined in Table 1.

We present a high-risk patient who underwent renal artery revascularization for RAS and was consequently able to discontinue hemodialysis and avoid future hospitalizations. She presented with acute pulmonary edema and progressive CKD in the setting of high-grade RAS, and thus was an appropriate candidate for renal artery stenting on the basis of current guideline recommendations. If the patient we describe had not undergone revascularization, she would likely still need dialysis, with significant detriment to quality of life, or she could have transitioned to hospice care.

FOLLOW-UP

After 1 year, the patient has remained off dialysis, with a stable eGFR of 33 mL/min/1.73 m^2. She has not

required further hospitalization for acute pulmonary edema.

CONCLUSIONS

Despite the results of the ASTRAL and CORAL trials, renal artery revascularization remains appropriate for select high-risk patients. Failure to revascularize when appropriate can lead to recurrent hospitalization, long-term dialysis dependence, and decreased quality of life.

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KEY WORDS hypertension, stenosis, stents, vascular disease