Indonesian Journal of Cardiology
Indonesian J Cardiol 2024:45:61-67
pISSN: 2830-3105 / eISSN: 2964-7304
doi: 10.30701/ijc.1687

Case Report

Controlled Resistant Hypertension Following A Successful Renal Artery Stenting: A Rare Case Report in A Developing Country.

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Abstract

Background: Renal artery stenosis (RAS) represents a significant etiological factor in secondary hypertension, where both its identification and therapeutic approach present substantial complexities. This report delineates a case involving a patient afflicted with intractable hypertension, marked by recurrent malignant hypertensive crises, who achieved stabilization following the deployment of renal artery stenting.

Case Illustration: A 36-year-old female patient presented to the cardiovascular clinic for routine management of hypertension, initially diagnosed two years earlier. Despite the commencement of treatment with an angiotensin-converting enzyme inhibitor, her blood pressure remained unmanageable and progressively deteriorated. Upon examination, she was receiving a combination therapy comprising alpha-2 adrenergic agonists, beta-blockers, calcium channel blockers, as well as thiazide and loop diuretics, all of which failed to yield satisfactory control of her hypertensive state. Her blood pressure was recorded at 196/130 mmHg, accompanied by a tachycardia of 112 beats per minute. Clinical assessment revealed cardiomegaly, which was corroborated by a chest radiograph, and echocardiography confirmed the presence of hypertensive heart disease. A comprehensive evaluation for secondary hypertension, including laboratory investigations (complete blood count, electrolytes, creatinine, fasting glucose, lipid profile, urinalysis, thyroid-stimulating hormone, and 24-hour urinary-free cortisol), returned normal findings. However, renal and Doppler ultrasonography suggested the possibility of right renal artery stenosis. Consequently, renal artery angiography was conducted for diagnostic clarification and potential therapeutic intervention. The angiogram demonstrated a normal left renal artery, whereas the right renal artery exhibited a significant 95% stenosis in the proximal segment. An intravascular ultrasound-guided percutaneous transluminal angioplasty was performed on the affected artery, successfully implanting two vascular stents. Remarkable clinical improvement was observed, with the patient's blood pressure becoming manageable within one week, using only a single antihypertensive agent alongside antiplatelet therapy.

Conclusion: The diagnosis and management of resistant hypertension pose considerable challenges, particularly within the context of limited resources. Renal artery angiography, among other investigative modalities, can be instrumental in elucidating the underlying pathology, although its availability may be constrained. This case exemplifies the successful diagnosis and treatment of renal artery stenosis, culminating in the effective control of previously refractory hypertension. Identifying the underlying cause is paramount to providing optimal and tailored therapeutic interventions.

(Indonesian J Cardiol. 2024;45:61-67)

Keywords: *resistant hypertension, renal artery stenosis, renal artery stenting.*

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Background

Secondary hypertension is rare but should become suspicious at a young age. Secondary hypertension must be appropriately diagnosed and treated. Renal artery stenosis is one of many causes of secondary hypertension. Secondary hypertension is an elevated blood pressure that results from an underlying, identifiable, often correctable cause. It is rare to occur because only about 5 to 10 percent of hypertension cases are thought to result from secondary causes.[1] Renal pathologies represent the predominant category among the various etiologies of secondary hypertension, with RAS being the most prevalent. The prevalence of RAS was 24.2% in a population of patients with resistant hypertension. As patients with RAS are often asymptomatic or without severe hypertension, the true prevalence is not known, as cases may go undetected.[2] It is estimated that atherosclerosis accounts for about 70% of all causes of renal artery stenosis in China and 90% in Europe and America.[3]

Percutaneous trans renal arterial stenting (PTRAS) is a modality of revascularization in patients whose RAS is hemodynamically significant (>70% of the diameter of the stenosed renal artery on angiography or a meaningful trans-lesion gradient of >10 mm Hg).[4] A study conducted in China involving 230 patients diagnosed with renal artery stenosis (RAS) demonstrated that PTRAS is an effective intervention for controlling blood pressure and reducing the necessity for multiple antihypertensive medications. Secondary hypertension must be appropriately diagnosed and treated so patients with a secondary form of hypertension might be cured or at least show an improvement in blood pressure control and a reduction of cardiovascular risk.[5] Identifying secondary hypertension in young adults and diagnosing the cause is always challenging in developing countries. The rarity of the case and its complexity make it essential to present this case.

Case Illustration

TA 36-year-old female presented to the cardiovascular polyclinic for a routine evaluation of her hypertension, initially diagnosed two years prior. Her clinical history includes multiple episodes of malignant hypertension, with an absence of symptoms such as weight gain, fatigue, weakness, hirsutism, unintentional weight loss, hair loss, heat intolerance, tremors, fever, prolonged cough, lightheadedness, arthralgia, skin rash, claudication, or Raynaud's phenomenon.

Upon physical examination, the patient appeared mildly ill but remained alert and fully oriented. Blood pressure was measured at all four extremities, yielding values of 196/130 mmHg in the right arm, 194/128 mmHg in the left arm, and systolic readings of 195 mmHg in the right leg and 193 mmHg in the left leg. Radial pulses were noted at 102 beats per minute, regular, with high volume and symmetrical bilaterally. Dorsalis pedis pulses were similarly regular and symmetrical. A cardiac examination revealed normal heart sounds, with no murmurs or gallops detected. Pulmonary auscultation was unremarkable, with no evidence of rales or wheezing. Additionally, no bilateral ankle edema was observed, and the abdomen was free of any palpable pulsatile masses.

The electrocardiogram (ECG) revealed a sinus rhythm with a heart rate of 102 bpm, an axis of -60 degrees, and a normal P wave. The PR interval was measured at 0.12 seconds, with a QRS duration of 0.06 seconds, and no significant ST-T segment alterations were observed. Notably, the S wave amplitude in leads V1/V2 combined with the R wave in leads V5/V6 exceeded 35 mm, indicative of left ventricular hypertrophy (LVH). The ECG findings were consistent with sinus rhythm and evidence of LVH. Laboratory investigations yielded the following results: hemoglobin 13.2 g/dL, hematocrit 39.3 %, leucocyte 8860/uL, platelet 301.000/uL, SGOT 24 U/L, SGPT 15 U/L, ureum 19 mg/dL, creatinine 0.83 mg/dL, random blood glucose 133 mg/dL, and electrolyte levels were in normal ranges. Urinalysis indicated proteinuria (+1) with the absence of erythrocytes. Echocardiography showed concentric LV hypertrophy, normal LV systolic function (LVEF 53%) with normokinetic at rest, normal valves' anatomy and function, low PH probability, and normal RV contractility.

The patient was initially diagnosed with hypertensive heart disease, accompanied by grade 3 hypertension. Initial treatment consisted of Ramipril 10 mg once daily, Amlodipine 10 mg once daily, and Hydrochlorothiazide 12.5 mg once daily. However, upon follow-up one month later, the patient's blood pressure remained inadequately controlled and had increased. Compliance

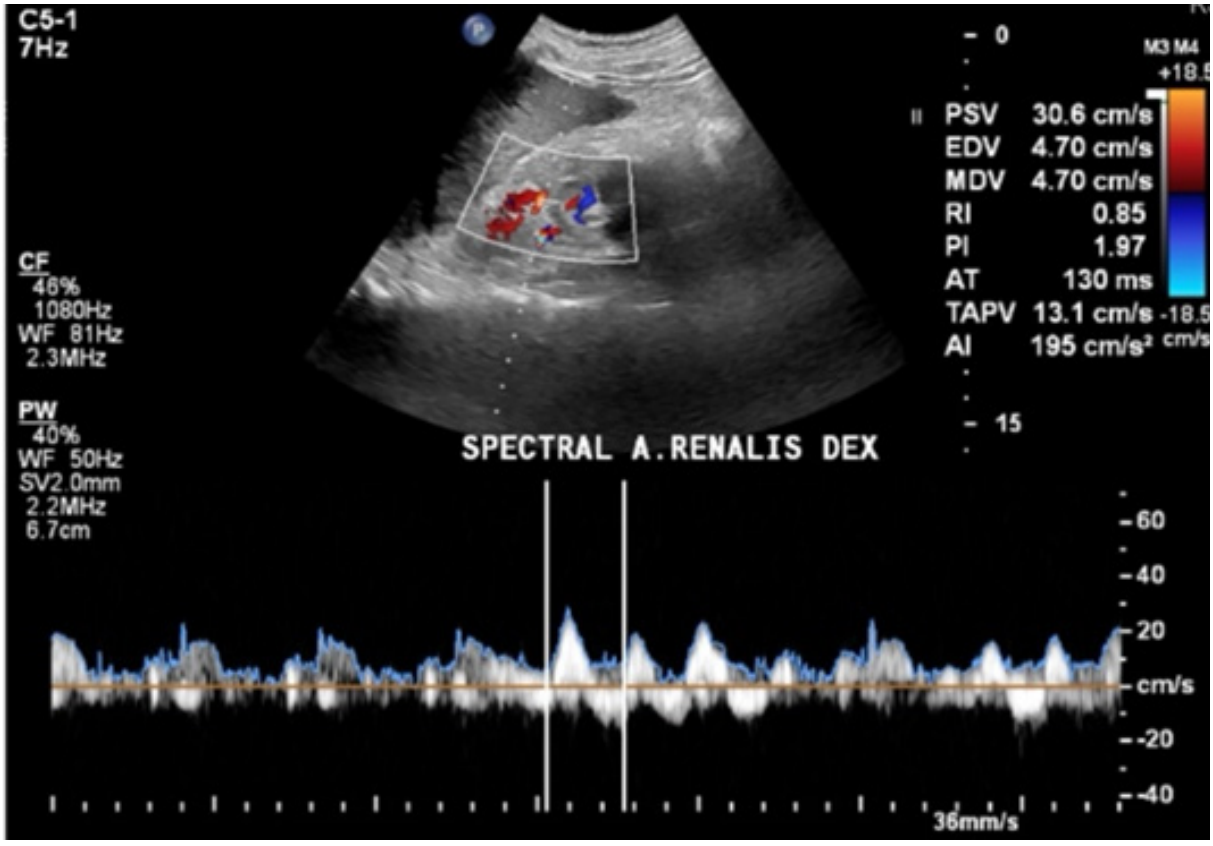

Figure 1. Doppler ultrasound of renal arteries. Intraparenchymal acceleration time (AT) is 130 ms, and the acceleration index (AI) is 195 cm/s^2.

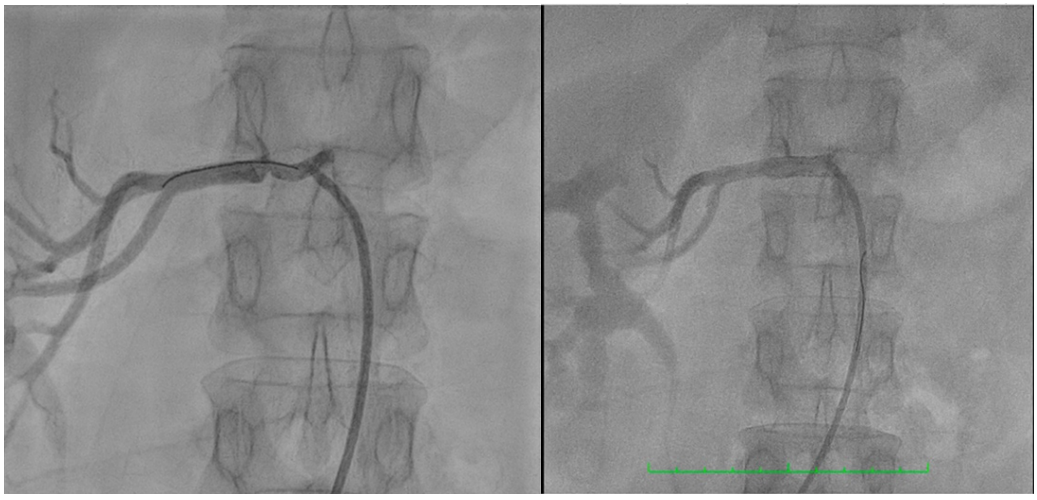

Figure 2. Percutaneous transluminal angiography (PTA) of the right renal artery.
A. Stenosis 95% of the proximal right renal artery (red arrow). B. A stent was successfully placed in the right renal artery.

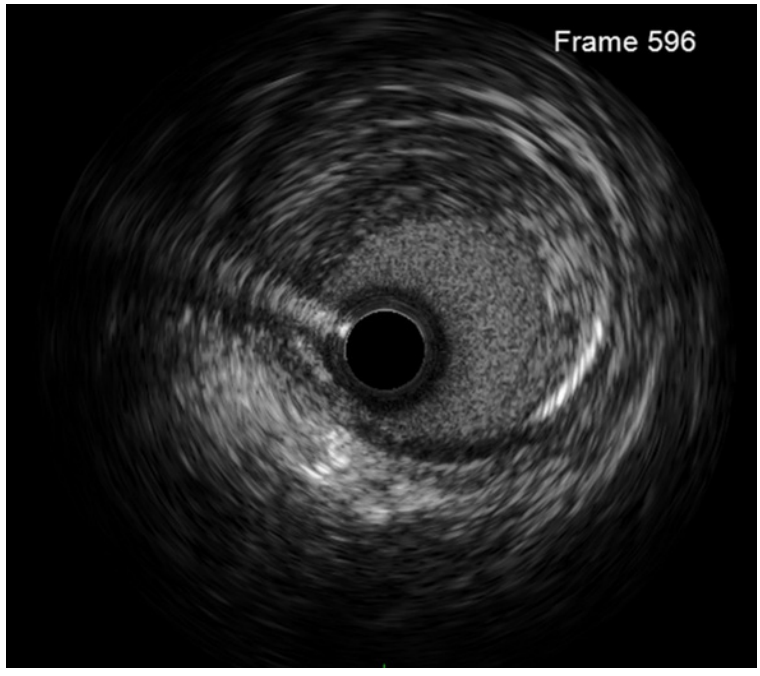

Figure 3. Percutaneous transluminal angiography (PTA) of the right renal artery.
A. Stenosis 95% of the proximal right renal artery (red arrow). B. A stent was successfully placed in the right renal artery.

with the prescribed medication regimen was verified, and the patient was subsequently diagnosed with resistant hypertension. Given the observed escalation in both blood pressure and serum creatinine levels during treatment with an angiotensin-converting enzyme inhibitor (ACEi), the possibility of renal artery stenosis (RAS) as an underlying cause was strongly considered, particularly since RAS is recognized as the most prevalent cause of secondary hypertension. Consequently, renal ultrasound and Doppler ultrasound of the renal arteries were performed. The ACEi was discontinued, and the therapeutic regimen was modified to include Clonidine 0.15 mg once daily, Bisoprolol 5 mg once daily, Amlodipine 10 mg once daily, Hydrochlorothiazide 12.5 mg once daily, and Furosemide 40 mg once daily.

Renal ultrasound and Doppler ultrasound of renal arteries showed normal size and structure of both kidneys, with no evidence of hydronephrosis or calculus. The right renal artery demonstrated increased intraparenchymal acceleration time (AT) and decreased acceleration index (AI).

Percutaneous transluminal angiography (PTA) of the renal artery was performed with right femoral access using a 3.5/6F JR catheter, showing stenosis in 95% of the proximal right renal artery (Figure 1A). The intravascular ultrasound (IVUS) study shows a distal reference diameter of 6 mm, atherofibrotic concentric plaque, and MLA 4 cm^2/ lumen diameter of 2.8 cm. Predilatation scoreflex 3.0/15 mm. Then, it follows the insertion of the Express Vascular SD 7.0/19 mm stent in the right renal artery (Figure 1B). After the procedure, angiography evaluation showed no residual thrombus or dissection.

Figure 2 A. Stenosis 95% of the proximal right renal artery (red arrow). B. A stent was successfully placed in the right renal artery.

On the first day following the renal artery stenting procedure, the patient's blood pressure was recorded at 142/91 mmHg, with no pharmacological intervention, and renal function remained stable. After a 30-day follow-up, the patient was asymptomatic and reported normal blood pressure readings through home monitoring, maintained with a single antihypertensive medication, Amlodipine 10 mg once daily. At the subsequent follow-up two months post-procedure, the patient demonstrated a home blood pressure reading of 122/78 mmHg, with preserved renal function and normal serum electrolyte levels.

Discussion

After confirmed hypertension, the etiology of hypertension must be screened according to history, physical examination, and laboratory tests. Further investigation into a possible secondary etiology in the absence of suggestive signs and symptoms is indicated in resistant hypertension, the onset of hypertension in persons younger than age 20 or older than age 50, a severe or accelerated course of hypertension, worsening of control in a previously stable hypertensive patient, stage 3 hypertension, significant hypertensive target organ damage, lack of family history of hypertension, or specific drug intolerances.[6]

In this case, the patient's blood pressure was recorded at approximately 196/130 mmHg, which is classified as grade 3 hypertension. Despite being on a regimen of five antihypertensive medications, there was no satisfactory reduction in her blood pressure. This lack of therapeutic response strongly indicated the possibility of secondary hypertension. Consequently, further investigations were initiated to ascertain the underlying cause. Secondary hypertension arises from a specific, identifiable cause. It is frequently associated with conditions such as renovascular disease, obstructive sleep apnea (OSA), endocrine disorders (including primary aldosteronism, pheochromocytoma, Cushing's syndrome, and thyroid dysfunction), coarctation of the aorta, genetic predispositions, or the influence of medications and illicit substances. This form of hypertension is observed in approximately 5-15% of all hypertensive cases.[7]

Several investigations have been conducted to elucidate the etiology of secondary hypertension in the diagnostic evaluation. The clinical assessment did not indicate a suspicion of obstructive sleep apnea (OSA), and polysomnography could not be performed due to logistical constraints. Thyroid dysfunction was ruled out based on normal serum levels of FT4 and TSH. Primary aldosteronism could not be definitively excluded due to the inability to measure renin and aldosterone levels. A comprehensive physical examination, complemented by echocardiographic evaluation, excluded coarctation of the aorta. Laboratory tests revealed normal renal function; however, proteinuria in the urinalysis prompted further investigation into possible renovascular abnormalities. Subsequently, a kidney ultrasound was performed, which revealed increased intraparenchymal acceleration time and decreased acceleration index. These findings raised a suspicion of renal artery stenosis (RAS). According to established quantitative criteria for assessing significant RAS, an acceleration time (AT) exceeding 80 milliseconds indicates potentially significant stenosis.[8] Then, to confirm the diagnosis, our patient underwent PTA and found a 95% stenosis of the proximal right renal artery, so the diagnosis was confirmed as renal artery stenosis.

Renal artery stenosis is the narrowing of one or both renal arteries. RAS is a frequent cause of secondary hypertension and affects 1 to 5% of all hypertensive patients. According to some reports, the cause of hypertension is 1% to 10% of the 50 million people in the United States.[9] In Indonesia, renal artery stenosis incidence is still unavailable. Only a few case reports report renal artery stenosis as a cause of secondary hypertension in patients. Renal artery stenosis is still rarely diagnosed with certainty in developing countries such as Indonesia. In Indonesia, not all patients with secondary hypertension are investigated for the etiology, and renal artery angiography is still not widely available in Indonesia as a gold standard for diagnosing RAS.

Some subtypes of renovascular disease include renal artery stenosis, atherosclerotic disease, fibromuscular dysplasia (FMD), and other (less common) causes of renovascular disease. In this case, an atherofibrotic plaque lesion was found on PTA with IVUS guidance, so we suspect that the patient's type of renal artery stenosis is an atherosclerotic disease. In atherosclerosis, the initiator of endothelial injury, although poorly understood, can be dyslipidemia, cigarette smoking, viral infection, immune injury, or increased homocysteine levels. At the lesion site, permeability to low-density lipoprotein (LDL) and macrophage migration increases with endothelial and smooth muscle cell proliferation and the ultimate formation of atherosclerotic plaque. Renal blood flow, which is significantly greater than the perfusion to other organs, along with glomerular capillary hydrostatic pressure, is an essential determinant of the glomerular filtration rate (GFR).[10] In patients with renal artery stenosis, the chronic ischemia produced by the obstruction of renal blood flow leads to adaptive changes in the kidney, including the formation of collateral blood vessels and secretion of renin by the juxtaglomerular apparatus. The renin enzyme has an essential role in maintaining homeostasis in that it

converts angiotensinogen to angiotensin I. Angiotensin I is then converted to angiotensin II with the help of an angiotensin-converting enzyme in the lungs. Angiotensin II is responsible for vasoconstriction and release of aldosterone, which causes sodium and water retention, thus resulting in secondary hypertension or renovascular hypertension.[9,11]

The initial therapy to treat hypertension in patients before diagnosing RAS is an ACE inhibitor. However, the surprising result was that blood pressure increased, and kidney function worsened with increased creatinine value from 0.83 to 1.06. The appointment of ACEi in RAS can oppose hypoperfusion in the kidney. From these data, we can suspect the presence of RAS in patients. After the RAS objection, the ACEi therapy was stopped and replaced with alpha-2-adrenergic agonists, beta-blockers, calcium channel blockers, thiazide, and loop diuretics. However, the patient's blood pressure still could not be overcome even with five oral antihypertensives.

We considered recent onset hypertension, young age, severe and uncontrolled hypertension, and significant stenosis to decide on revascularization. Renal angioplasty with stent placement is a standard treatment option for renovascular hypertension, particularly in the case of atherosclerotic stenosis, with low periprocedural complications and good blood pressure control and renal function results, especially among patients with normal GFR.[12] The first choice of intravascular imaging for PTRA can be IVUS more often than OCT because it is challenging to use OCT for middle to large arteries (vessel diameter ≥5 mm), such as the renal artery.[13] IVUS can provide precise anatomic characterization of the atherosclerotic plaque. IVUS guidance during renal artery stent placement resulted in additional lumen enlargement not considered necessary at angiography. In a series of 363 renal artery interventions, follow-up angiography was available in 102 patients (34%) at an average of 303 days. Larger diameter arteries were associated with a significantly lower incidence of angiographic restenosis. The restenosis rate was 36% for vessels with a reference diameter of less than 4.5 mm compared with 16% in vessels with a reference diameter of 4.5–6 mm (p = 0.068) and 6.5% in vessels with a reference diameter greater than 6 mm (p <0.01). IVUS allows a more accurate way to measure vessel diameter than two-dimensional angiography, allowing the operator to maximize the stent size safely. Visual estimation tends to underestimate the size of the vessel, which can translate to higher rates of ISR.[14]

A critical aspect of revascularization is its capacity to address the fundamental cause of the pathology directly: the stenotic renal artery. It is well-documented in the literature that intervention through revascularization effectively mitigates renal artery stenosis, leading to a diminution in both renin-angiotensin-aldosterone system (RAAS) activity and sympathetic nervous system activity. Several single-center registries of stenting and a recent multicenter registry of stenting for failed balloon angioplasty suggest substantial benefits related primarily to improved blood pressure control. In contrast, the three multicenter trials of PTRA without stenting failed to demonstrate a blood pressure benefit.[15] Renal artery stent placement is standard today and substantially improves technical and long-term clinical outcomes compared with angioplasty alone, especially for ostial stenoses, which comprise 80% of atherosclerotic stenoses. In a meta-analysis of 1322 patients, stent placement had a higher technical success rate and a lower restenosis rate than PTRA (98% versus 77% and 17% versus 26%, respectively; P<0.001) and a higher cure rate for hypertension.16 The clinical outcomes observed following revascularization were highly favorable. On the day following stent placement, the patient's blood pressure measured 142/91 mmHg without pharmacological intervention. At the 30-day follow-up, the patient demonstrated normalized blood pressure on home monitoring while being maintained on a single antihypertensive agent.

Conclusion

TA case of resistant hypertension attributable to RAS has been documented, supported by clinical findings from the patient's history and physical examination, and confirmed through PTA, which is considered the gold standard for diagnosing RAS. This case exemplifies the efficacy of revascularization and demonstrates an excellent outcome. It underscores the necessity of thoroughly investigating the etiology of secondary hypertension in all cases of resistant hypertension. Currently, in Indonesia, the identification of secondary hypertension etiology remains infrequent, largely due to limitations in the availability of definitive diagnostic

examinations for determining the underlying causes of secondary hypertension.

List of Abbreviations

AT	Acceleration Time
AI	Acceleration Index
ACEi	Angiotensin-Converting Enzyme Inhibitor
ECG	Electrocardiogram
FMD	Fibromuscular Dysplasia
GFR	Glomerular Filtration Rate
IVUS	Intravascular Ultrasound
LVH	Left Ventricular Hypertrophy
LDL	Low-Density Lipoprotein
OSA	Obstructive Sleep Apnea
PTA	Percutaneous Transluminal Angiography
PTRAS	Percutaneous Trans Renal Arterial Stenting
RAS	Renal Artery Stenosis
RAAS	Renin-Angiotensin-Aldosterone System

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