REVIEW ARTICLE

Pediatric Renovascular Hypertension: Manifestations and Management

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Renovascular hypertension (RVHTN) is an important contributor to secondary etiologies of hypertension in the pediatric population. A delay in diagnosis can be associated with adverse outcomes. The etiologies of renal artery stenosis (RAS) vary from anatomical, inflammatory, genetic syndromes, intra-luminal, external compression and idiopathic. It is a silent disease with isolated hypertension as its primary clinical manifestation. Laboratory values can be notable for electrolyte derangements and renal dysfunction, but are not universally present. The diagnosis requires a high index of clinical suspicion and entails ruling out other secondary causes of hypertension while monitoring for target organ damage. Imaging of individuals with suspected RAS includes: renal ultrasound, computed tomography angiography, magnetic resonance angiography and renal scintigraphy, but angiography continues to be the gold standard. Various factors are used to determine the most appropriate method for ongoing care: anti-hypertensive therapy, with or without radiological or surgical intervention. In all instances, a multi-disciplinary team approach should be used to provide optimal care to these children and adolescents.

Keywords: *Blood pressure, Fibromuscular dysplasia, Renal artery stenosis, Renal imaging*.

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In children and adolescents, renal artery stenosis (RAS) accounts for up to 10% of the secondary causes of hypertension. Glomerular disease and renal parenchymal scarring are responsible for an additional sixty percent [1-3]. RAS is a heterogeneous disease process that includes intrinsic lesions of the renal arteries, extrinsic compressive masses, and intraluminal thrombosis that impede renal blood flow [4].There is an increased risk of developing cardiac and neurologic complications in adulthood (*i.e.* myocardial infarction, stroke) when childhood onset renovascular hypertension (RVHTN) is not adequately managed [5]. There needs to be a high index of clinical suspicion to appropriately diagnose and manage RVHTN in children. Unlike adults where 70-80% of patients have largely non-correctable atherosclerotic lesions, children with RAS often have lesions that are amenable to therapeutic intervention [1]. The protean clinical and laboratory manifestations of RVHTN in children creates a significant challenge in diagnosis that may contribute to chronic kidney disease and target organ damage [5]. Given these difficulties, there is a need for a standardized approach to the diagnosis and management of RVHTN in children and adolescents [6]. In this review, we will examine the clinical findings, diagnostic studies, management, and intervention for pediatric RAS-associated hypertension. This information will hopefully contribute to future standardized recommendations to the approach and management of RVHTN in children and adolescents.

ETIOLOGY

In contrast to adults where the main cause of RAS is from atherosclerosis, the etiologies in the pediatric population vary by disease process and by geography. The major contributor to pediatric RAS in North America and Europe is fibromuscular dysplasia (FMD), as opposed to Takayasu arteritis (TA) in Asia and South Africa [7,8]. The etiologies of RAS in children and adolescents are all summarized in ***Box* I** [7,9].

CLINICAL CLUES

RAS is often a 'silent' diagnosis with many non-specific symptoms. We aim to summarize the most recent findings acknowledging the paucity of clinical features while understanding the concern for complications from long-standing renovascular-associated HTN.

History: The age of the child can be crucial in directing the differential of pediatric RAS. As an infant, there is a higher pre-test probability of having a thrombosis or emboli from a catheter site as opposed to the young child where syndromes and inflammation play a larger role [10]. The odds of detecting a secondary cause of hypertension are inversely proportional to the age of the child, creating an emphasis on early diagnosis [11]. In FMD, the mean age of diagnosis was 8.4 years with a range from 16 days to 17 years [12]. Most children often report non-specific symptoms including headache, and abdominal, and flank pain [12]. In contrast to adults,

Box I Causes of Renal Artery Stenosis in Children and Adolescents

Non-inflammatory
- Fibromuscular dysplasia
- Mid-aortic syndrome

Inflammatory
- Takayasu arteritis
- Kawasaki disease
- Polyarteritis nodosa

Syndromes
- Neurofibromatosis type 1
- Tuberous Sclerosis
- Williams' syndrome
- Marfan's syndrome
- Alagille syndrome
- Turner syndrome
- Congenital rubella

Localized tissue damage
- Trauma
- Radiation

Extra-luminal
- Compression by mass
- Wilms' tumor, Neuroblastoma, Other

Intra-luminal
- Catheter-related thromboembolic disease
- Hypercoagulable states – nephrotic syndrome

Surgical
- Transplant renal artery stenosis

Idiopathic

children may find it difficult to characterize common symptoms associated with hypertension, such as tinnitus or blurry vision [12]. A retrospective study in Israel noted behavioral changes within the 3-12 months prior to diagnosis of RVHTN that included hyperactivity, restlessness, and attention deficits [13]. This creates a conundrum for physicians that are evaluating these patients, as increased blood pressure can be missed or incorrectly diagnosed.

Family history and genetics: When referring to the etiologies of RAS, one of the largest categories include RAS-associated syndromes (***Web Table* I**). Although the discovery of new genes continue to grow, data has shown that approximately 11%-60% of RAS cases are familial [7]. In a cohort of 93 children with RAS and mid-aortic syndrome (MAS) in Canada, 26% had an underlying genetic disease, 24% had an inflammatory process, and 50% were idiopathic [10]. Of the children with genetic conditions, about 40% had neurofibromatosis type 1 (NF-1) and the remaining had William syndrome or Alagille syndrome [10]. Within the FMD registry, there are a significant number of pediatric patients with a family history of FMD in comparison to the adults, supporting a stronger familial genetic inheritance in pediatric FMD-related vascular disease [12,14]. In addition, children and adolescents with underlying genetic or inflammatory syndromes are more likely to have extrarenal vascular involvement including visceral and proximal aortic branches [10].

Blood pressure measurements: The physical examination in children and adolescents with RAS is most often unrevealing, which can cause a delay in diagnosis. The most common finding is of isolated hypertension. It is estimated that 26-70% of renovascular disease presents with hypertension in an otherwise asymptomatic child [15,16]. A report from the Midwest pediatric nephrology consortium in 2010 found no difference in age, weight distribution, or stage of hypertension when trying to differentiate between primary and secondary hypertension [17]. However, children with RAS typically present with stage 2 hypertension [18]. The likelihood of identifying a secondary cause of hypertension such as RAS has been found to be directly related to the degree of blood pressure elevation [11,19].

Other factors that must be taken into consideration include when and how the blood pressure measurements are taken in the clinical setting. Children in the United States start getting blood pressure measurements at the age of three unless they fall into a high-risk category. Unfortunately, some children may be referred with a history of elevated blood pressures after several clinic visits without intervention or evaluation due to the concern of inaccurate readings in an asymptomatic child [7]. Appropriate blood pressure readings are essential, which include the following: (*i*) appropriate cuff size; (*ii*) sitting position; (*iii*) right upper extremity; (*iv*) calm environment; and (*v*) after 3-5 minutes of rest. When the blood pressure is found to be elevated for the first time, four extremity blood pressures are obtained to evaluate for coarctation of the aorta and MAS [9].

Physical examination: Physical findings of RAS-associated syndromes are detailed in ***Web Table* I**. Children with Takayasu arteritis typically have constitutional symptoms and signs secondary to inflammation. This includes arthralgia, skin rashes, abdominal bruits, and absence of pulses [20]. In FMD, bruits can sometimes be heard overlying the epigastrium (7.4%), carotid arteries (7.4%), and flank (7.7%) [12]. For patients with MAS, a mid-abdominal murmur is a classic finding [4].

There is a subset of pediatric patients that present with secondary signs of target organ damage related to hypertension, including neurological (10-15%) and cardiac findings (7%) [4,15]. The neurological symptoms

can range from headache, seizures, stroke, to cranial nerve palsies [7,21]. Bell palsy is the most commonly identified cranial nerve palsy [15]. One study showed that older children are more likely to have cardiac findings of palpitations, murmur, or signs of congestive heart failure, with 10% of them having an underlying syndrome [3,12]. Ocular findings are specific to syndromes such as Alagille, but can be present as a non-specific sign of hypertensive retinopathy [3].

LABORATORY EVALUATION

To evaluate for RVHTN, laboratory and imaging diagnostic tests need to be ordered in a step-wise fashion. An initial basic metabolic panel is appropriate to determine if there are signs of renal dysfunction (azotemia, elevated creatinine) or electrolyte derangements defined by hyponatremia, hypokalemia, and alkalosis suggestive of RAS.

Sodium: There have been a few pediatric cases of unilateral renal artery stenosis that presented with marked hyponatremia. This is termed hypertensive hyponatremic syndrome (HHS) [22]. The hyponatremia is postulated to occur from hyperactivation of the renin-angiotensin-aldosterone system (RAAS) with substantial increase in angiotensin II production directly causing arterial vasoconstriction. This results in a pressure natriuresis from the contralateral kidney that has normal function. The severity of the hyponatremia can be compounded by a reactive secretion of anti-diuretic hormone from the transient volume depletion [22,23].

Potassium: The presence of hypokalemia is rare, but is seen in the setting of unilateral RAS. With decreased perfusion to the affected kidney there is activation of the RAAS system with secondary hyperaldosteronism resulting in hypokalemia due to excessive urinary potassium loss [24]. Ultimately, this can be corrected with either improvement of the renal ischemic state or with blockade of the RAAS.

Creatinine: In unilateral disease, the serum creatinine concentration remains normal through compensation of the healthy kidney. However, monitoring is essential. Bilateral disease can have decreased renal function in the setting of hypoperfusion and can be exacerbated if angiotensin-converting enzyme inhibitors (ACEi) and angiotensin-receptor blockers (ARBs) are initiated [24]. After anti-hypertensive medication is started for BP control in children with RAS, a metabolic panel including creatinine should be checked within 1-2 weeks to ensure that there is no evolving kidney injury.

Urinalysis: With unilateral RAS and prolonged ischemia to a single kidney, there may be compensatory hypertrophy of the contralateral kidney, resulting in glomerular hyperfiltration. This phenomenon combined with chronic activation of the RAAS can lead to proteinuria and glycosuria, biomarkers of sub-clinical damage to an otherwise normal kidney.

Plasma renin activity (PRA): The PRA level is dependent on age, sodium intake, posture, and oscillates in a diurnal pattern. All these factors make a PRA value difficult to interpret. It can also be suppressed in primary essential hypertension in African Americans and various forms of monogenetic hypertension (*e.g.,* Liddle syndrome). Studies have shown normal PRA values in 20%-37% of patients with unilateral RAS [25]. With bilateral RAS, the child is likely to have normal renin and aldosterone levels [1]. This is due to volume-dependent hypertension, after initial RAAS activation and volume retention there is subsequent suppression of renin release [26,27]. Given the low predictive value of PRA, further investigations need to be performed if there is a high index of clinical suspicion for RAS [27].

RADIOLOGICAL IMAGING

There is no single screening, radiological study that can effectively exclude all the causes of RAS in children. There is an ongoing evaluation to identify modalities that are more sensitive and specific in diagnosing RAS (***Table* I**) [7,8,28,29]. This is important from the patient perspective given that the gold standard for the diagnosis of RAS in children and adolescents continues to be the percutaneous angiogram, which is an invasive procedure.

Renal bladder ultrasound (RBUS) with doppler: A RBUS is the appropriate first line of imaging given its advantages (***Table* I**) and the ability to assess for other secondary causes of hypertension including a mass, venous thromboembolism, renal dysplasia, and scarring [30]. It can provide valuable assistance in monitoring progression of RAS after angioplasty by specifically measuring the peak systolic velocity (PSV) and resistive indices of the affected vessel [31]. The many limitations of the doppler US include the difficulty in assessing small vessels, age-dependent cooperation, body habitus and operator proficiency. In children, when compared to angiography, it has a 27% sensitivity as a diagnostic alternative. Although, there are reports of better specificity ranging from 70-100% in both adult and pediatric populations [12,14]. Contrast enhanced ultrasound, a relatively newer modality, has shown improved sensitivity ranging from 79-100% for diagnosis of RAS and may be a better initial screening study [32].

Table I Imaging Modalities for Renal Artery Stenosis

Modalities of imaging	*Advantages*	*Disadvantages*	*Sensitivity*	*Specificiy*
Renal Bladder Ultrasound (RBUS) with Doppler	Easy availability, non-invasive, fast, no radiation, simple, low cost	Operator-dependent, age-dependent cooperation, body habitus, may miss small lesions high false positive and false negative	27-63%	70-100%
Magnetic resonance angiography (MRA)	No radiation, improved image quality	Limited intrarenal vessel visualization, longer study, may require anesthesia, compromised by respiration	62-98%	70-96%
CT angiography (CTA)	Fast, improved image quality, not compromised by respiration	Requires radiation, limited intrarenal vessel visualization	64-100%	62-97%
Renal scintigraphy	Non-invasive, inexpensive	Low predictive probability, reduced accuracy in renal failure, does not visualize the vessels; inconsistent data	59-73%	68-88%
Digital subtraction angiography (DSA)	Detailed imaging of aorta and all branches, can transiation to a therapeutic intervention	Radiation, requires anesthesia	100%	100%

Magnetic resonance angiography (MRA): An MRA provides detailed renal size and blood flow without exposure to radiation [14]. This is an appropriate study to assess the aorta and main renal arteries with limited visualization of intrarenal vessels. In adult studies, MRA's has shown to have a sensitivity of 92-98% and specificity of 70-96% in diagnosis of renovascular disease, particularly for atherosclerotic-associated RAS [33]. Limitations of MRA include its inability to assess involvement of segmental renal vessels. It can exaggerate the degree of narrowing within the main renal artery given lack of adequate spatial resolution compared with a computed tomography angiography [34]. In a pediatric cohort comparing US, MRA, and CTA in 25 patients with FMD, the MRA imaging study demonstrated a sensitivity of 62.5% for RAS detection with 100% specificity [8].

Computed tomography angiography (CTA): A CTA exposes the patient to radiation; however, radiation minimization protocols can be used to reduce this unwanted effect. CTA can depict the renal arteries with its first branches, kidney size, parenchymal wall thinning/scarring, and is not compromised by respiration as opposed to an MRA [29]. The CTA has proven to be the best and fastest alternative to an angiography in detecting RAS and renal artery aneurysms. The sensitivity has been shown to be as high as 84.2% in a pediatric study [8]. It can specifically detect thin webs that can be present in FMD that may be missed on MRA [29]. Within the adult population, it rivals an MRA with a sensitivity range of 64-100% and specificity range of 62-97% [33]. Recent studies show that reconstruction techniques of CTA can reduce noise and improve accuracy of vessel diameter measurements [35,36].

Renal scintigraphy: Renal scintigraphy is a nuclear medicine study that is non-invasive and safe. A radioactive tracer, 99m-technetium-dimercaptosuccinic acid (^{99m} Tc-DMSA) or 99m-Tc-mercaptoacetyl-triglycine (^{99m}Tc-MAG3), is used to assess renal function with administration of an angiotensin-converting-enzyme inhibitor (ACEi). The renogram curve can suggest vessel narrowing by demonstrating time to peak activity and delayed washout. It has a low predictive probability and is an image that does not directly visualize the vessels. The results have continued to be inconsistent and the test has fallen out of favor in comparison to the prior modalities [29].

Renal vein renin sampling: Renal vein renin sampling is an invasive test that entails taking a blood sample from the inferior vena cava and comparing it to samples taken from the main renal veins. This test requires an anesthesiologist, and can be performed in conjunction with a diagnostic angiography *via* a femoral approach. The data allows one to identify the ischemic focus, which can be localized to the specific kidney that is involved. Given that imaging has progressed over the years and that selective renal vein sampling has low sensitivity (74%) and specificity (59%), it is not as commonly used [37]. In adults, the American college of cardiology/ American heart association guidelines no longer recommend using it for detection of RAS [38].

Digital subtraction angiography (DSA): Renal angiography continues to be the gold standard and provides detailed imaging of the aorta and all of its branches. This entails injection of contrast *via* a percutaneous catheter into the aorta and main renal arteries. It is the most invasive out of all the tests, requires radiation exposure, and anesthesia for children and adolescents. The benefit of the angiogram includes the detailed vasculature that highlights occlusion of renal vessels and collateral vessels. It can be transitioned to a therapeutic intervention (angioplasty) or used to provide exact information for next steps in the management of RAS. A retrospective study was performed to evaluate the accuracy of US, MRA, and CTA in comparison to a DSA in 127 children with suspected RAS. The study demonstrated low sensitivities for the former modalities: 63%, 88%, and 80%, respectively [33]. Thus, the DSA remains the cornerstone for accurate diagnosis or exclusion of RAS.

MANAGEMENT OF RAS

Initial Blood Pressure Management

Pre-intervention is directed at blood pressure management with an appropriate antihypertensive agent and controlled reduction. Until bilateral RAS or unilateral RAS to a single kidney is excluded, treatment should be initiated with a vasodilator and/or a beta blocker. Once the former is excluded, an ACEi or ARB can be started. RAAS blockers are relatively contraindicated in critical main RAS and bilateral RAS, but can be used with segmental stenotic lesions [18]. In addition to in-office blood pressure monitoring, 24-hour ambulatory blood pressure monitoring (ABPM) can provide valuable information about control. In a study of 10 children with RAS on antihypertensive treatment with normal in-clinic blood pressure readings only two had adequate control by 24-hour ABPM [39]. ***Fig.* 1** outlines the initial evaluation and management of children with suspected RAS.

Treatment Options

Treatment of RAS includes continuation of medical therapy with no intervention, or intervention through percutaneous transluminal angioplasty (PTA) or surgery. The goal of invasive treatment is to preserve renal function with restoration of renal perfusion, and to aid with blood pressure control [40]. The therapeutic decision algorithm is influenced by the patient anatomy, disease etiology, and clinical expertise of the institution [1].

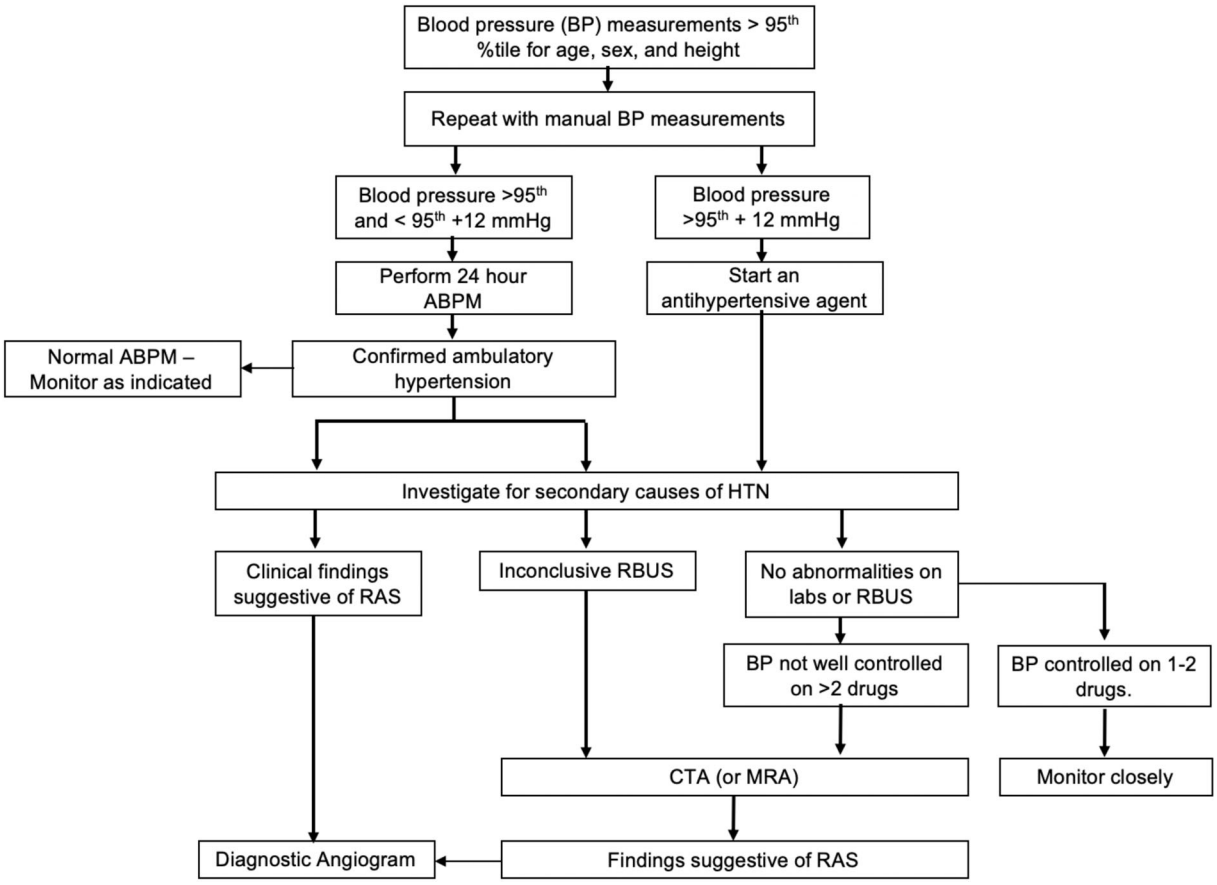
Continuation of Medical Therapy

Continuation of medical therapy includes patients who are still being evaluated for RAS and those who are not eligible for angioplasty or surgical intervention due to unacceptable risk or not technically feasible. In addition, at least half of the children that undergo an interventional radiology or surgical procedure will require continued medical therapy [8]. Patients who are not deemed eligible for intervention tend to have a poorer response to initial medical treatment and will require use of multiple antihypertensive agents from different classes to control their blood pressure. A trial of ACEi or ARB can be used in these patients with careful monitoring of renal function and after discussion about the risks and benefits with the family [7]. Taking a non-invasive approach to the management of blood pressure presents its own set of challenges related to medication adherence and drug side effects [1]. In small children, it may be prudent to wait for the child to complete puberty prior to attempting an intervention, this is particularly true for children with mid-aortic syndrome [41].

Interventional Radiology

Many pediatric centers use PTA as first line therapy for RAS lesions of ≤10 mm, but a surgical approach is appropriate when the RAS is complicated by stenotic lesions >10 mm, multiple stenosed large vessels, or bilateral RAS [42-44]. PTA is performed under general anesthesia with femoral or brachial artery access to introduce a long vascular sheath or a guide wire to the renal arteries. Intra-procedure anticoagulation is performed with heparin. The balloon diameter used for dilation varies with age and vessel size, which can be determined by measuring the adjacent, normal renal artery distal to the post-stenotic dilation or contra-lateral artery [44]. In resistant stenoses, use of the cutting balloon has been most successful in our center (***Fig.* 2** and **3**). Renal artery stenting is another option when there are lesions that show elastic recoil or restenosis after conventional or cutting balloon angioplasty [44]. However, this is controversial, given that the long-term outcome is unknown including in-stent restenosis rates and limitation of future surgeries. In our institution, renal artery stent placement is avoided and is only used in emergent situations as a temporary bridge to surgical repair.

Adult studies have shown that the benefit from a primary angioplasty was as high as 93-98%, and in children cure or improvement is seen in over 50% of cases [3,43]. Complications associated with PTA include arterial spasm, dissection, and perforation of vessel [7]. Patients who have an inadequate response to PTA usually develop worsening hypertension within months post procedure [44].



ABPM: Ambulatory blood pressure monitoring, RBUS: Renal bladder ultrasound; RAS: Renal artery stenosis, MRA: Magnetic resonance angiography, CTA: CT angiography, HTN: Hypertension.

Fig. 1 *An approach to the diagnosis of renal artery stenosis in children and adolescents.*

Surgery

Surgical approaches are primarily used when there is refractory hypertension after angioplasty, conservative medical therapy, or vascular lesions that are not amenable to angioplasty [7,44]. Patients with MAS, long segment stenosis, and aneurysms are best treated with a surgical approach. Surgical procedures include renal artery re-implantation onto an adjacent portion of normal aorta and aorto-renal bypass that uses a conduit of autogenous vessel or prosthetic material to connect the renal artery beyond the stenosis to the aorta. Patch aortoplasty and aortic bypass can be used for MAS [45].

In a published series of children and adolescents, surgical intervention has a cure rate of arterial hypertension in 70-82% and improved blood pressure measurements in 12-27% [41,46]. Cure rates in smaller case series are reported between 36-70% [44-46]. In select cases with a poorly or nonfunctional kidney and unilateral disease, a nephrectomy can be performed that can result in long-term normotension [47].

CONCLUSIONS

RVHTN is an important cause of secondary hypertension in children and adolescents. A heightened clinical suspicion for RAS should be present when blood pressure control is refractory to multiple antihypertensive medications, an abdominal bruit is present, or in the setting of RAS associated syndromes. Medical management includes antihypertensive drug therapies for adequate blood pressue control. Meanwhile, a multi-disciplinary team is essential in providing individualized care, and guidance on interventional radiology/surgical procedures.

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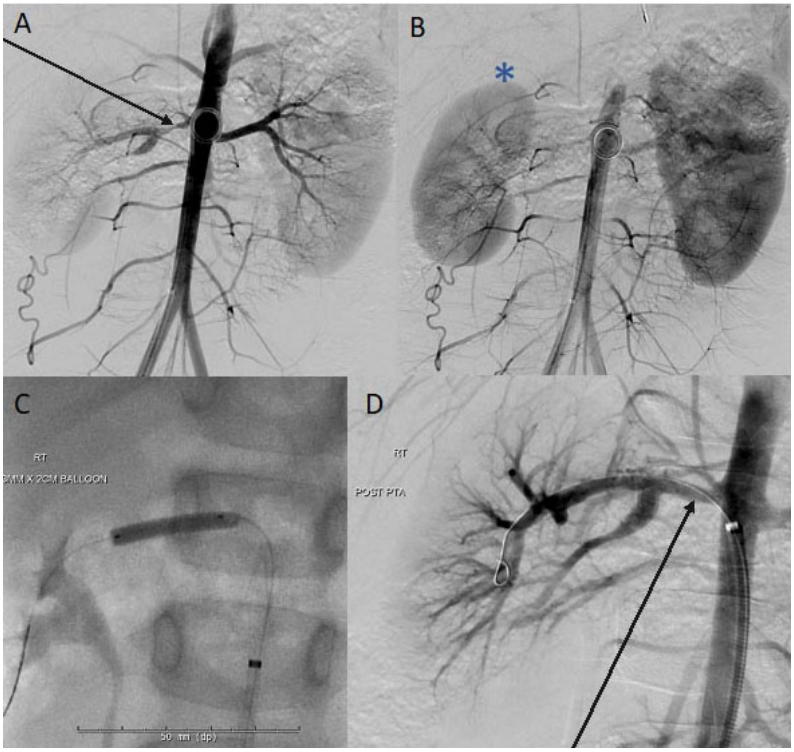

Fig. 2 *(a) and (b): Marked stenosis near the origin of the right main renal artery (arrow) which supplies the upper and mid kidney with diminutive size and delayed perfusion of the right kidney (star) compared to the left; (c) and (d) Panel C and D: Successful, uncomplicated cutting balloon angioplasty of a tight right main renal artery stenosis in a 5-year-old girl with renovascular hypertension. Perfusion to the right kidney normalized on angiography following the angioplasty.*

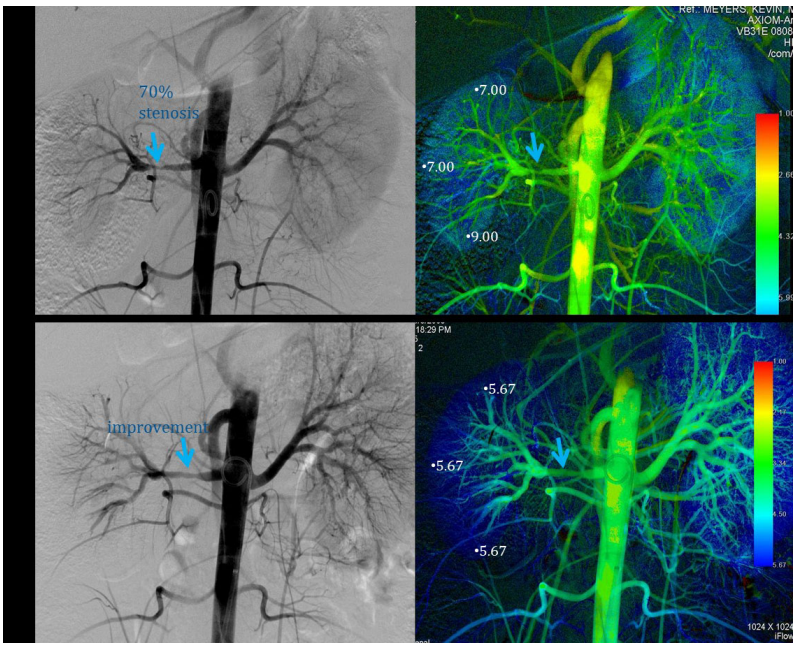

Fig. 3 *Sixteen-year-old female with hypertension and main right renal artery stenosis. Post angioplasty with 4 mm balloon significant improvement is noted in the >70% stenosis with improved time to parenchymal perfusion (TTP) noted on color parametric imaging with the patient now normotensive and off antihypertensive medications.*

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Web Table I Genetic Syndromes Associated with Renal Artery Stenosis in Children and Adolescents

Genetic condition	*Mutation*	*Inheritance*	*Clinical association(s)*	*Renal vascular malformation*
Neurofibromatosis 1	*NF1* gene	AD	Neurofibromas - Café au lait macules, optic glioma, increased risk of tumors - pheochromocytoma, Lisch nodules	RAS, External compression - Wilm tumor
Tuberous sclerosis	TSC1, TSC2	AD	Tubers (glial nodules), seizures, adenoma sebaceum, myocardial rhabdomyomas, shagreen patch, ash-leaf macules	RAS, MAS, renal angiomyolipoma
Turner's syndrome	XO	Non-disjunction	Streak gonads, primary amenorrhea, short stature, webbed neck	Coarctation of aorta, MAS, RAS
Marfan's syndrome	Fibrillin	AD	Arachnodactyly, dissecting aortic aneurysm, ectopic lens, mitral valve prolapse	Aortic aneurysm, renal aneurysm, RAS
Loeys-Dietz syndrome	TGFBR1, TGFBR2, SMD3, TGRB2, TGFB3	AD, sporadic	Aortic aneurysm, aortic dissection, craniosynostosis, pes planus, scoliosis, hypertelorism, bifid uvula	RAS, renal artery aneurysm, coarctation of aorta
Alagille syndrome	JAG1, NOTCH2	AD	Xanthomas, cholestatic liver disease, pulmonic stenosis, broad forehead, deep-set eyes	Coarctation of aorta, RAS
Williams-Beuren syndrome	Deletion of genes in chromosome 7	AD, sporadic	Broad forehead, wide mouth, supravalvular aortic stenosis, developmental delay	MAS, RAS, coarctation of aorta, hypoplasia of the aortic arch
Hereditary Nephropathy, Aneurysms, and Muscle Cramps	COL4A1	AD	Intracranial aneurysms, arterial retinal tortuosity, cataracts, muscle cramps	Cystic compression of renal vessels
Alport syndrome	COL4A3, COL4A4, COL4A5	X-linked (common), AD AR	Sensorineural hearing loss, anterior lenticonus, renal dysfunction	RAS
Idiopathic infantile arterial calcification	ENPP1, ABCC6	AR	Heart failure, respiratory distress, cyanosis	Vaso-occlusive RAS
Autosomal dominant polycystic kidney disease	PKD1, PKD2	AD	Recurrent UTI, kidney stones, heart valve abnormalities, aneurysms	Cystic compression of renal vessels, RAS
Autosomal recessive polycystic kidney disease	PKHD1	AR	Failure to thrive, respiratory failure, enlarged kidneys, oligohydramnios	Cystic compression of renal vessels, RAS

AD: Autosomal Dominant; AR: Autosomal Recessive; RAS: Renal artery stenosis; MAS: Mid-aortic syndrome.