Seminars in ROENTGENOLOGY

Diagnosis and Treatment of Renovascular Disease in Children

Premal A. Patel, BSc (Hons), MBBS, MRCS, FRCR,* and Jelena Stojanovic, MD, FRCPCH†

Introduction

As with other forms of endovascular treatments, renovascular intervention has an established role in adults. There is an increasing volume of data supporting its use in children. In particular, it is useful in the diagnosis and management of pediatric hypertension which often has a renovascular cause. The popularity of endovascular techniques to treat angiomylipomas as well as nutcracker syndrome (NS) is growing, and many groups are actively studying the effects of these treatments. In this review, we present diagnostic features of these conditions and discuss their management in particular, the endovascular techniques used by interventional radiology to treat these conditions.

Renovascular Hypertension

Clinical Diagnosis and Pathologies Causing Hypertension

The diagnosis of hypertension in children is usually made incidentally (reported to represent 26%-77% of cases).[1] Blood pressure (BP) is not often measured in children despite the guidelines from the USA and Europe which strongly recommend regular BP screening in children.[2] The recommendations state every child above 3 years of age should have BP measured at each clinical setting,[3] and a recent large study demonstrated 36% of screened children had elevated BP.[4] However, in practice only a third of children attending a hospital appointment have their BP measured.[5] Pediatric hypertension is defined as systolic BP >95th percentile for age, sex, and height.[6] Hypertension is diagnosed on 24-hour ambulatory BP monitoring for children above the age of 5 years. In younger children, at least 2 consecutive sitting BP measurements taken in repeated visits are needed to confirm diagnosis of hypertension. Those should be ideally taken in a relaxed environment, with well-maintained equipment and with a rest period of at least 5 minutes before measurement. Early identification and management of hypertension in childhood is helpful to reduce the risk of cardio- and cerebrovascular events as well as renal damage in the future.[7,8]

Due to lack of routine BP checking in clinical settings and a lack of sufficient information on BP, renovascular hypertension (RVH) is often ignored and/or diagnosed after a considerable time delay by referring physicians. Before obesity became the leading cause, childhood hypertension was secondary to other conditions such as endocrine, neurologic, metabolic but most commonly being renal in origin.[9]

The incidence of pediatric primary hypertension has increased and is now more common than secondary hypertension in children older than 6 years.[10] The chances of detecting a secondary cause of hypertension are inversely proportional to the age at presentation and directly related to the severity of BP elevation (ie, the younger the child at diagnosis and the higher the BP measurement, the more likely a secondary cause will be found to account for the elevated BP).[11] RVH causes 5%-10% of childhood hypertension and is potentially amenable to treatment.[12,13] RVH is characterized as a flow-limiting stenosis in the renal artery system which leads to upregulation of the renin-angiotensin system and subsequently elevated systemic BP. The flow limiting vascular lesion may affect a portion of a kidney or the entire kidney depending on the site of the affected vessel.[1]

While most patients present with an incidental finding of elevated BP, other presenting signs and symptoms include

Abbreviations: ACEi, angiotensin converting enzyme inhibitors; AML, angiomyolipoma; BP, blood pressure; CTA, CT angiogram; DMSA, 99m-technetium-dimercapto-succinic acid; FMD, fibromuscular dysplasia; IR, interventional radiology; MRA, MR angiogram; NF, neurofibromatosis type 1; NS, nutcracker syndrome; RVH, renovascular hypertension; RSDN, endovascular renal sympathetic denervation; TA, Takayasu's arteritis; TS, tuberous sclerosis; US, ultrasound

*Interventional Radiology, Radiology Department, Great Ormond Street Hospital for Children, London, United Kingdom.
†Renal Unit, Great Ormond Street Hospital for Children, London, United Kingdom.

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Address reprint requests to Premal A. Patel, Interventional Radiology, Radiology Department, Great Ormond Street Hospital for Children, London WC1N 3JH, United Kingdom. E-mail: premalpatel@doctors.org.uk

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hypertensive encephalopathy (including headache, visual changes, seizures, mental status changes, tinnitus, intracranial hemorrhage, and facial nerve paralysis), proteinuria/hematuria, fatigue, abdominal bruit, emesis and rarely heart failure (Fig. 1).[1]

RVH can be caused by an isolated or multifocal renal artery stenosis (RAS) most often associated with fibromuscular dysplasia (FMD) and neurofibromatosis type 1 (NF1). Less common etiologies include Williams syndrome, tuberous sclerosis (TS), various vasculitidies (Takayasu aorto-arteritis arteritis, polyarteritis nodosa, Kawasaki disease), prior arterial thrombosis or as a consequence of prior medical interventions such as radiation vasculopathy or

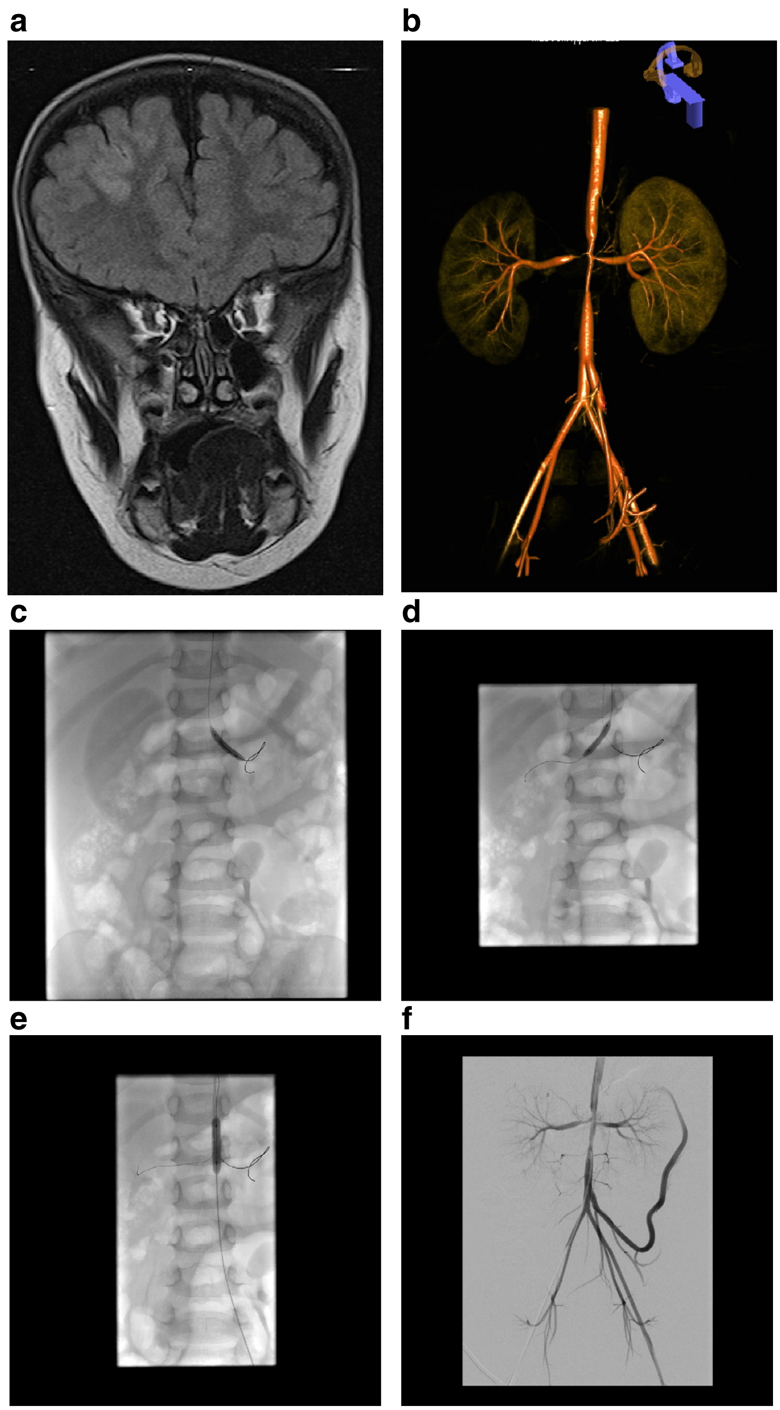

Figure 1 Three years old with symptomatic uncontrolled hypertension. The patient presented to the emergency department with right arm weakness, ataxia, slurred speech. (a) Coronal FLAIR MRI showed infarction involving right frontal cortex. Systolic blood pressure in the upper limb was 240 and 168 in the lower limb. (b) Cone beam CT demonstrated a stenotic aorta with a critical stenosis at the origin of the right renal artery and a severe narrowing of the proximal left renal artery. (c-e) Angioplasty of both renal arteries and the supra-renal aorta was performed. (f) Significant improvement in vessel caliber seen at repeat angiogram (approximately 6 weeks following the initial procedure).

transplant renal artery anastomotic stenosis.[1,14] RAS can also be associated with middle aortic syndrome (MAS). RVH is believed to be familial in 11%-60% of cases, most being consistent with autosomal dominant mode of inheritance with variable penetrance.

FMD

FMD is the most common cause of RAS in children.[15] However, histologic confirmation of the renovascular lesions is very rarely obtained thereby making FMD a diagnosis of exclusion as soon as other typical causes of RAS (such as Takayasu's arteritis (TA) and NF1) are ruled out.[15]

The majority of children in North America and Europe are diagnosed with FMD, and Takayasu arteritis is the predominant diagnosis in Asia and South Africa.[9] TA is an inflammatory condition with no specific diagnostic findings. Additional challenges include the fact that some children might present in "burnt out" phase of TA, making it more similar to FMD.[16]

FMD can affect children of all ages. A large, multicenter, descriptive study of FMD included 1023 patients with 33 pediatric patients who were diagnosed at a mean age of 8.4 ± 4.8 years (range from 16 days to 17 years).[17] The same study reported that 93.9% of the children studied initially presented with the complaints of headaches and/or abdominal pains and were also found to have hypertension. The finding of hypertension prompted further investigation of the renovascular system.

Achieving an accurate diagnosis is important, as FMD may be amenable to endovascular treatment using angioplasty and/or stenting or by more traditional surgical techniques.[15] An analysis of 20 years of local experience of angiography in renovascular disease suggests the pattern of FMD in children is also different to that in adults. FMD in children typically has severe focal narrowing with mild beading and poststenotic aneurysmal dilation. Pediatric FMD more often involves the main renal artery with less involvement of the intrarenal arteries. In adult FMD, the lesions are more commonly bilateral with the diagnostic "beads on a string" appearance.

If untreated, RVH in children can lead to sequelae including retinopathy, chronic renal failure (in up to10%), stroke, encephalopathy, left ventricular hypertrophy, and myocardial infarction.[1,18]

NF1

Besides FMD, neurofibromatosis is the most common cause for RAS in children in western countries.[19] NF1 is an autosomal dominant condition associated with various manifestations including vascular lesions such as RAS, aneurysm formation, and aortic coarctation.[20] The phenotype associated with cafe au lait, neurofibromas, and iris hamartomas is most commonly associated with vascular lesions in children. Apart from RAS, RVH can be due to extrinsic compression of renal arteries by retroperitoneal hamartomas. The preferred treatment option is maximizing antihypertensive medication. However, not uncommonly surgical interventions are needed including ex vivo reconstruction.[21]

Mid-Aortic Syndrome

Mid-aortic syndrome is localized narrowing of the distal thoracic/abdominal aorta which usually involves the renal and visceral arteries.[1] It is estimated at 0.5%-2% of all aortic stenosis are due to MAS. Most MAS are idiopathic (64%) with pathogenesis remaining largely speculative.[22] Ninety one percent of children with mid-aortic syndrome have concomitant RAS.[23] MAS may also lead to severe narrowing of intestinal, iliac, carotid, cerebral, and brachial arteries.[8,9,22-29] A study of 68 angiograms in children with RVH showed that 16% of all had MAS, and this was most commonly associated with NF1.[19] Some MAS patients are likely to need renal transplantation and a recent study on clinical use of 3D printing in children has shown how this new technique can help surgeons when transplanting patients with complex vasculature whilst enhancing surgical planning and operative feasibility in cases which would otherwise be uncertain.[30]

Noninvasive Diagnostic Imaging

Ultrasound

There is significant variability in the way children with hypertension are evaluated and managed.[31] Ultrasound (US) is the most available and widely performed screening investigation; renal US is relatively easy to perform, can be repeated, and cause no deleterious effect to a child. It can detect tumors which can cause hypertension (such as neuroblastoma or pheochromocytoma) and show discrepant renal lengths or other renal pathologies.

US is considered suggestive of renovascular disease when a stenosis can be directly visualized, a parvus et tardus waveform pattern is present, or pathologic age-dependent flow parameters (peak systolic flow greater than 180 or 200 cm/s, acceleration time >80 ms, renal artery to aortic flow velocity ratio >3, and difference in resistive index more than 0.05) are seen.[29,32-34] A significant difference in kidney length (≥1 cm) is regarded as a possible indirect sign of RAS.[29]

Doppler US may be most helpful in older children or children with aortic stenosis.[11,14] Segmental and subsegmental stenoses, involvement of multiple renal arteries, and early branching of the main renal artery are challenges to accurately diagnose by US images alone in small patients.[11] Adult series have reported Doppler US to have a sensitivity of 60%-100 % and specify of 70%-100 % in the detection of RAS.[29] In the authors' experience, this is lower in children. Trautman et al evaluated the accuracy of Doppler US, magnetic resonance angiography (MRA), and computed tomography angiography (CTA) compared to angiography in 127 patients. US, performed in all patients, had a sensitivity of 63% and specificity of 95%.[29] The sensitivity increased to 73% when the diagnostic criteria included ≥1 cm total kidney size discrepancy. While US is reported to be both sensitive and specific, it can miss main renal artery distal and branch vessel stenosis.[33] Trautman et al reported that 65% of 71 missed RAS were located in the main renal artery.[29] Other studies have reported a sensitivity for Doppler US of 65%-88% and specificity of 83%-99%.[11,29,33,35-37] Therefore, the conclusion remains the most common location for missed stenoses on US exams most often involves a segmental renal artery branch.[11]

MR and CT

CTA and MRA can provide detailed anatomic evaluation of the abdominal vascular structures. They are suggestive of renovascular disease when one or more stenosis are directly visualized as a narrowing of the intraluminal diameter or if there is the presence of collateral vessels.[29] They are adequate for diseases of the aorta but for small vessels and in smaller in smaller children they can have limited success.[9,31,38] CTA is usually preferred over MRA due to better resolution of fine vascular anatomy. Another advantage of CTA is that, unlike MRA, it can be performed without sedation or anesthesia. However, pediatric scanning protocols for CT should be carefully optimized to limit radiation dose. Trautman et al demonstrated that CTA performed slightly better than MRA with sensitivities of 88 vs 80% and specificity 81 vs 63%.[29] Five incidences of renovascular disease were missed by CTA in this study. All missed stenoses were in the main renal artery, with an additional stenosis in a branch renal artery in one case. MRA missed the diagnosis of RAS in 10 kidneys, which included lesions in the main renal artery in 6 cases, a main branch artery in 2 cases and a segmental artery in 2 cases.[29] One of the drawbacks of this study was that MRA and CTA studies included in the analysis had been performed prior to referral to the treating pediatric nephrology and interventional radiology service with subsequent heterogeneity in imaging protocols and image quality.

Scintigraphy

Renal scintigraphy with 99m-technetium-dimercapto-succinic acid (DMSA) or 99m-Tc-mercaptoacetyltriglycine pre- and postangiotensin-converting-enzyme inhibitor administration has been considered as a potential method of localizing RAS in children.[9] However, results are inconsistent in children with reported sensitivities of 59%-73% and specificities of 68%-88%.[9,39]

Invasive Diagnostic Imaging

Angiography

Angiography is the gold standard for diagnosis of renovascular disease in children.[9,15,38,40,41] Digital subtraction angiography provides the best spatial and temporal resolution.[29,42] No noninvasive technique is capable of excluding renovascular disease in children.[9,14] In one study 28% of vascular lesions in children with hypertension were only detected by angiography.[38] Children who are thought to have a high probability of renovascular disease should undergo angiography which allows possible endovascular treatment regardless of findings of noninvasive imaging.[9,29,38]

In the authors' institution, the criterion for angiography are poor BP control on 2 or more medications.[9] MRA and CTA are rarely performed in the authors' institution although many children have had this imaging at an outside facility at time of referral. In this carefully selected group, an abnormality will be seen approximately 40% of the time.[9,41,43] Angiography is repeated if there is an increase in BP suggestive of restenosis. Some institutions prefer a less invasive follow-up approach, favoring imaging with grayscale and Doppler US until worsening of symptoms or evidence of end-organ disease merit further cross-sectional imaging or a secondary intervention.[44]

Renal artery lesions may be uni- or bilateral; studies report the incidence of bilateral disease to be 24%-78% of cases.[1,9] When there are bilateral lesions, there are often abnormalities of the aorta and other medium arterial vessels (Fig. 1).[1] Focal arterial stenoses are most common in children.[41] Diffuse narrowings are more likely when there is extrarenal disease, syndromes, or vasculitidies.[1,41] The distribution of lesions in pediatric patients are typically 25% in the main renal arteries, 50% in a second order branches, 12.5% in a third order branches, and 12.5% in accessory renal arteries.[41]

Antihypertensive medications are maintained up to the day of the procedure. BP is managed intraprocedure by anesthesiologist and may require an arterial line to manage and accurately monitor the BP. Diagnostic angiography is usually performed from a femoral approach. A cone beam CT is performed initially with up to 2 mL/kg injected into the aorta over 7 seconds with a 2 second X-ray delay. It is imperative this is done first to limit the amount of contrast within the intravascular system because excretion of contrast into the urinary collecting system will obscure detail of the intra-renal arteries (Figs. 1 and 2). This initial CT provides an assessment of the aorta, evaluates anatomy of the adjacent visceral vessels and any small accessory renal arteries, and is useful in planning catheter selection and vessel measurements for potential balloon angioplasty.

Following the cone beam CT, selective angiography of all renal arteries in frontal and collimated oblique views is performed. In selected cases, the thoracic aorta, cerebral, and abdominal visceral vessels may require imaging. The considerations for imaging these vessels are given in Table 1. Angiography and intervention can usually be performed within the less than 3 mL/kg contrast.[40] However, contrast doses above the suggested maximum 6-8 mL/kg may be necessary when complex anatomy, difficult access, and multiple dilations are necessary. In the authors' experience, there have been no increased rates of contrast induced nephropathy in cases requiring larger contrast doses.[45]

Intravascular Imaging: Optical Coherence Tomography and Intravascular US

Angiography allows only 2-dimensional visualization of the vessel lumen. If abnormal arterial segments are identified on angiography, intravascular pressure measurements may be useful to assess if they are significant. In selected cases, intravascular imaging by intravascular US (IVUS) or optical coherence tomography (OCT) can also be used to assess vessel wall thickness and evaluate aneurysms and the results of angioplasty and/or stenting. The role of IVUS and OCT has not been validated in renovascular intervention in children. However, these high-resolution imaging techniques have been shown, to improve the clinical outcomes of patients undergoing percutaneous coronary intervention where they

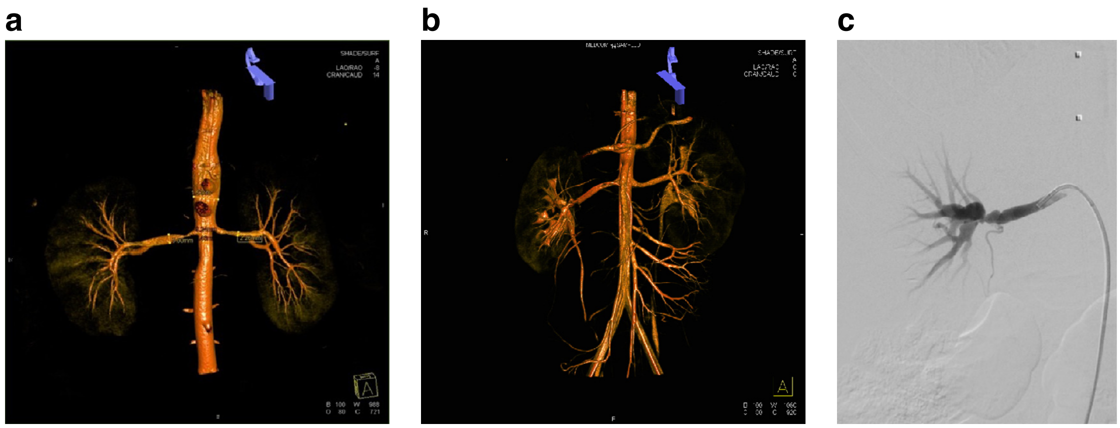

Figure 2 Examples of cone beam CTs performed at the start of a renal angiography procedure. (a) 17-year-old with Takayasu's arteritis showing irregular caliber of the aorta and focal stenosis of the bilateral renal arteries. (b) Eleven years old with stenosis of the right renal artery at a trifurcation at the hilum with poststenotic dilation. There was contrast in the collecting system at the time of the CB-CT therefore vessel details are obscured. The lesion is better seen on the selective angiogram in this case (c).

Table 1 Vessel(s) to consider for assessment by noninvasive and invasive imaging

		Considerations
Renal arteries	main	Is/are there lesions (stenoses/webs/aneurysms) which could be contributing to hypertension?
		Is/are lesion(s) amenable to endovascular treatment
	branch and intra-renal arteries	Is/are the lesion(s) amenable to angioplasty or ethanol ablation?
		Imaging evidence of hypertension sequela?
Aorta	abdominal	Uniform caliber, smooth tapering of the infrarenal aorta?
		Is there stenosis above the renal artery origins?
		If there is occlusion, what vessels are supplying the collateral route?
	thoracic	Is there undiagnosed/untreated coarctation possibly causing hypertension?
Iliac arteries		Is the caliber suitable for auto-transplantation?
Coeliac axis and branches and superior mesenteric artery		Are they involved in the underlying disease process?
		Could they be used for auto-transplantation/other surgery?
		Do they provide collateral supply?
Subclavian and axillary arteries		Are they involved in the underlying disease process?
		Can the left axillary artery be used for access for future interventions?
Carotid and cerebral vessels		Are they involved in the underlying disease process?
		Is there vascular disease which must be treated prior to intervention to drop the blood pressure to reduce the risk of stroke secondary to cerebral hypoperfusion?

have been used to direct appropriate stent sizing, miss; identify acute complications such as dissection and stent malapposition.[46]

Renal Vein Renin Sampling

Renal artery abnormalities detected angiographically are often bilateral or involve small intrarenal branches. In such cases, renal vein renin sampling can help to lateralize or even localize to one part of a kidney, an ischemic focus driving hypertension and help direct selective angiography when lesions are not diagnosed at initial angiography.[47] Renal vein renin sampling is thought to be more useful in children than in adults.[48,49] At the authors' institution, renal vein sampling is performed following angiography under the same general anesthesia if there is not a clear arterial lesion detected.[14,49] Two samples are taken from the infrarenal inferior vena cava and each renal vein with a single sample obtained from the upper, interpole, and lower pole intrarenal tributaries on each side. Renin ratio of greater than 1.5 between the main renal veins is considered significant. A ratio of less than 1.3

between the contralateral renal vein and the infrarenal inferior vena cava supports this.[48,49] There is some evidence that a positive result is predictive of favorable outcome following angioplasty or surgery.[49]

Management

Medical Management

Hypertension in children is initially medically managed. However, despite treatment with multiple antihypertensive drugs, the vast majority will not achieve normalization of their BP.[1,9,24]

Angioplasty

The indication for endovascular treatment is inadequate control of BP or significant adverse effects of the anti-hypertensive regimen.[9] The goal of all treatment in children is restoration of renal perfusion and lifelong preservation of renal function.[1] Endovascular treatment also reduces the need for polypharmacy. It may also have a role in temporizing hypertension in younger patients before surgical repair during puberty.[24] Angioplasty is the most common intervention and can be performed in arteries with mild to severe stenoses. If vessels are completely occluded, they can be recanalized (Fig. 3); endovascular recanalization has been reported be successful in children as small as 3.4 kg.[31]

Angioplasty is usually undertaken from a femoral approach. However, renal arteries sometimes arise at an acute angle from the aorta making an antegrade approach from superior access necessary for intervention. In such cases, the authors use US-guided access into the axillary artery (Fig. 3). This has been demonstrated to be feasible and safe, in children as small as 2.6 kg.[50] However, others have reported successful and safe use of a percutaneous carotid approach.[31] Prior to angioplasty 75-100 IU/kg intravenous heparin is administered to reduce thrombotic complications.[9,51]

Angioplasty equipment designed for use in adult coronary arteries (such as 0.014-inch monorail, low-profile balloons) is ideal for renal arteries in children. The wires are usually J'ed in the kidney to reduce the risk of perforation of small intrarenal vessels. For larger children (>25 kg), as long as the aorta is not so narrow as to prevent the shape from being useful, shaped guiding catheters or sheaths are used.[25] Angioplasty balloon diameter is chosen to be similar to the renal artery proximal to the stenosis because there is often poststenotic dilation (aneurysm) distally. Some centers base the angioplasty balloon size on the minimal arterial lumen diameter.[52] Average balloon to minimum lumen diameter ratio has been reported as 2.4:1 in one study.[52] If the waist is not completely abolished during balloon inflation, a high-pressure balloon may be considered. High pressure balloons are not the first choice as they are stiffer, may cause arterial damage, and can be difficult to track over the wire. The use of drug coated balloons in renal artery angioplasty has been reported; however, there is little evidence to support their use at present.[31]

Following endovascular treatment, the BP can be labile. For this reason, close postoperative monitoring for at least 12 hours is needed after endovascular treatment. At the authors' institution, a day after the surgery all antihypertensive medications the patient was taking before the procedure are usually resumed. Weaning of medication is dependent on the response to endovascular treatment but it is not uncommon that children need continue antihypertensive medication for a monitored time (particularly those with severe findings including multiple stenosed vessels or those with MAS). Twenty four hours BP monitoring 6-8 weeks post-treatment is advised. At the authors' institution, following angioplasty Aspirin (1 mg/kg daily) for 3-6 months to prevent thrombosis in the treated vessels is prescribed. There is little evidence to support this practice; however, a similar protocol has been reported in other series.[8,40]

Cutting Balloon. Cutting balloon angioplasty has a role in lesions resistant to conventional and high-pressure balloon angioplasty. Reports of cutting balloon use are limited, although they have been used with mixed success in some series.[40,53,54] They have been used for high-grade, long stenotic segments and cases of restenosis.[40,55,56] Complications such as dissection and renal artery aneurysm requiring surgical intervention have been reported with cutting balloon angioplasty.[53,54] For this reason, it is recommended that cutting balloon diameter be limited to no more than the normal vessel diameter in the incisional phase. After this, if

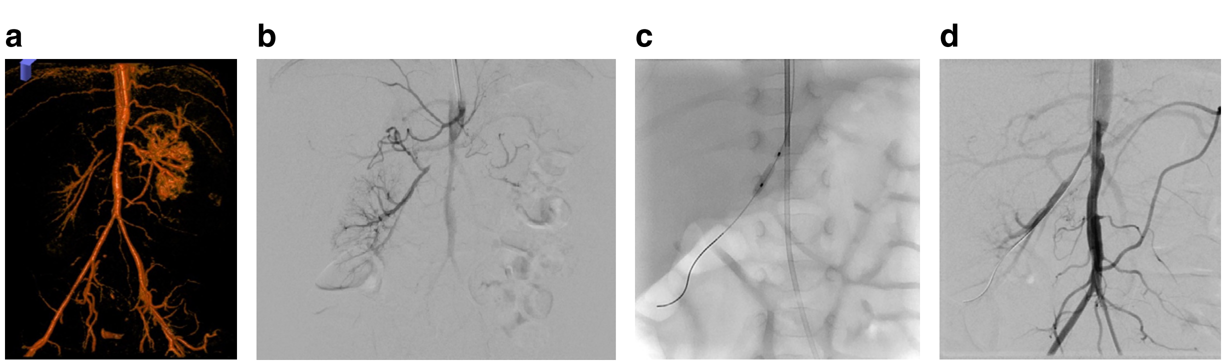

Figure 3 3.4 kg, 5-week-old infant with severe hypertension causing heart failure. (a) CB-CT and (b) digital subtraction angiography showing occlusion of right renal artery. (c) Right upper renal artery angioplasty performed with 2.25 mm high pressure balloon via an axillary approach. (d) Final angiographic appearance following aortic and right upper renal artery angioplasty.

necessary, further dilation can be performed with a conventional balloon.[53] In one study, the cutting balloon to minimum lumen diameter ratio was 1.7:1 compared to 2.4:1 noncutting balloon.[52] Consideration should also be given to performing imaging of the arterial wall (by IVUS or OCT) to help place the cutting balloon in the safest position.[53]

Stenting

Stenting has been reported useful for vessels which show elastic recoil or restenosis after conventional or cutting balloon angioplasty[40] and in some pediatric series has been used as the primary intervention.[52] Use of drug eluting stents in renal arteries in children has also been reported as part of a larger series.[31] Stents are generally avoided in most pediatric interventions because long-term outcomes are unknown. Restenosis after stenting is significantly more common than after angioplasty.[24,25] One study reported restenosis 35.5% of case following stent insertion compared to 17.4% following angioplasty.[25] Stents may also eventually become a fixed stenosis as the child grows. Repeat angioplasty is considered more appropriate than stenting.[25] Stent placement has been used in our institution for severe or recurrent lesions in children and to manage iatrogenic dissection.[24,48] The current data are insufficient to compare outcomes between drug eluting stents, bioabsorbable, and conventional stents; however, it is important to be aware these stents have been used with success at various institutions.[57]

Outcomes Related to Angioplasty and Stenting

A number of retrospective studies reporting outcomes of endovascular intervention for RVH have been published, particularly in the last 10 years (Table 2).[1,8,24,25,31,40,44,52,54,58-61] Overall endovascular treatment is reported to be beneficial in between 48.5% and 100% of patients.[8,24,27,59] Cure, usually defined as normal BP (<95th centile for age, gender, and height) with no antihypertensive medication has been reported in between 18% and 60%.[1,8,24,25,27,29,31,40,44,52,54,59] Improvement, usually defined as BP reduced below 95th percentile while still requiring antihypertensive medications or diastolic BP reduced by more than 15% of preintervention level has been reported in 17%-65%.[1,8,24,25,27,29,31,40,44,52,54,59]

In addition to improvements in BP, endovascular revascularization has been demonstrated to improve renal function. In a study of 30 children with abnormal DMSA scans with reduced uptake or focal lesions with available follow-up, 13 showed improvement, 6 developed a normal DMSA with equal uptake, and 11 had static appearances and 3 had worsening of their scans.[25]

Factors reported to be associated with a hypertension cure or clinical improvement are a single, short-segment stenosis (<10 mm) with residual stenosis <10%-20% after angioplasty.[8,27,40,61] However, these findings are not consistently reported.[54] Severity of stenosis has not been found to predict the clinical result of angioplasty.[40] One study suggests that children below the age of 5 years more often improved or cured compared to children >5 years; however, the difference was not statistically significant.[25] Other studies have found no association with age.[40,54]

Some reports suggest differential efficacy dependent on underlying etiology of RAS, but this is also inconsistent. Improvement in BP was higher in children with mid-aortic syndrome and RAS compared to those with isolated RAS after intervention.[44] Favorable results have also been reported in patients with NF1, likely due to single, short-segment stenosis.[40] Unfortunately, these outcomes are also inconsistent as other reports found decreased effectiveness for NF1 vs FMD and TA.[59,60,62]

A delayed response may be seen after angioplasty.[59,63] This may be related to smooth muscle spasm giving a false impression of residual narrowing on immediate postangioplasty angiogram or retraction of fibrous bands during arterial healing increasing the lumen.[59,63]

It is quite common that the angioplasty needs to be repeated to achieve a full response and sometimes to treat restenosis after an initial good response.[25] In children, dilation causes not just simple stretching of the vessel wall but commonly tearing, flap formation, or dissection.[64] Repeated angioplasty may result in eventual remodeling of the vessel to a larger size.

Reported restenosis rates for balloon angioplasty range from 17% to 41%,[1,8,25,27,52,59,65,66] and repeated angioplasty may be required.[24,25] Time interval between first and second angioplasty procedures varies from 0.4 to 60 months[25]; no significant increase in risk with repeated angioplasty procedures.[54] Restenosis after stenting is significantly more common than after angioplasty occurring in 36%-37%.[24,25]

Hypertension, secondary to transplant RAS occurs in around 5%-20% of children with renal transplants.[67,68] In such patients, angioplasty has been shown to significantly improve BP and graft function[67]; however, there have been reports that this is less successful in strictures distal to the anastomosis.[68]

The wide ranges and disparity of outcomes as well as the paucity of information regarding predictive factors relates to the nature of published studies. Clear guidelines for the diagnosis and management of RVH in children are not defined. The population treated is heterogenous with regards of etiology, response to medications, and vascular involvement. This is reflected in the published studies. Additionally, many of the studies reporting outcomes of endovascular intervention for RVH in children are retrospective, include multimodality treatment including conventional angioplasty, cutting balloon angioplasty, stent placement and surgery and have small patient numbers or covering a long time period (>20 years; Table 1).[1,8,24,31,40,44,52,54,58-61,69] During this time period, standards of care and the tools available to perform endovascular treatment has changed.

Complications. Complications of renal angioplasty include contrast-induced nephropathy, arterial spasm, dissection, and perforation. Complication rates reported in the literature vary from 0% to 43%.[1,54] Arterial spasm is usually self-limiting. Dissection happens often but is not usually hemodynamically significant.[9] When dissections do impede flow, they can be treated by reinflation of the angioplasty balloon to pin back the intimal flap. Therefore, guide wire access should be

Table 2 Summary of studies reporting outcomes of endovascular intervention for renovascular hypertension in the last ten years

Reference and Year Published	Time period	No. pts Included	Age	Intervention	Technical success	Complications	Outcome	Length of Follow Up
Lobek et al, 2018	21 y	39	mean 6.93 (±5.27) y	Angioplasty (17 patients) Primary surgery (10 patients) Medication only (12 patients)	Not reported	None	Angioplasty: 3/17 (18%) cured, 11/17 (65%) improved Surgery: 3/10 (30%) cured, 5/10 (50%) improved Medication alone: 0/12 (0%) cured, 3/12 (75%) improved	mean 52.2 ± 58.4 m
Agrawal et al, 2018	27 y	53	median 4.5 (0–18) y	Endovascular intervention (136) (included angioplasty (aorta/renal arteries, stenting (aorta/renal arteries) thrombectomy (aorta)) Surgery (27)	Not reported	10/136 (7.4%) following endovascular procedures 11/27 (41%) following surgery	Endovascular intervention: significant decline in number of antihypertensive medications & systolic and diastolic BP Surgery: no significant decline	median 3.6 (0.1 - 35.2) y
Rumman et al, 2018	30 y	93	mean 7.0 (±5.4) y	Medication only (28 patients) Invasive management (65 patients): Endovascular (53 patients), Surgery (29 patients, patch grafts, nephrectomy, and aorto-aortic bypass)	Not reported	Endovascular: 13%. Surgery: 31%	Endovascular: Mean BP z-score 1.7 ± 1.6 (compared to 2.4 ± 2.0 preintervention, P = 0.7), Mean number of antihypertensive medications 1.9 ± 1.1 (compared to 1.3 ± 1.0 preintervention, P = 0.06) Surgery: Mean BP z-score 1.9 ± 1.5 (compared to 2.8 ± 2.0 before surgery, P = 0.2), Mean number of antihypertensive medications 1.9 ± 1.1 (compared to 1.2 ± 1.0 pre- intervention, P = 0.01)	median 1.9 (0.4–4.7) y
Alexander et al, 2017	17 y	28	median 8.25 (7 m- 17.3) y	Endovascular intervention (angioplasty/cutting balloon angioplasty), 42 procedures in 28 patients	24/42 (57%) (residual stenosis <30%)	7% major complication 43% minor complication	10/28 (36%) cured 9/28 (32%) improved 9/28 (32%) failed	median 3.8 (1.0 - 9.9) y

Table 2 (*Continued*)

Reference and Year Published	Time period	No. pts Included	Age	Intervention	Technical success	Complications	Outcome	Length of Follow Up
Peco-Antić et al, 2016	13 y	25	mean 10.4 (± 5.2) y	Medication (100%) Angioplasty (23 patients (92%)) Surgery: Renal auto-transplantation (4 patients (16%)), surgical revascularization (3 patients (12%)) and nephrectomy (3 patients (12%)	Not reported	Not reported	10/25 (40%) cured 12/25 (48%) improved 2/25 (8%) remained severely hypertensive	median 3 (0.5 - 13) y
Kari et al, 2015	29 y	78	median 6.5 (0.5 – 17) y	Angioplasty (incl. cutting balloon) (83) Angioplasty and stent (31)	84% success (technical failure defined as unable to pass balloon catheter or unable to dilate vessel with balloon)	13/114 (11.4%) procedures One procedure related death	18/78 (23.1%) cured 31/78 (39.7%) improved	median 3 (0.1–14) y
Zhu et al, 2014	13 y	22	median 9 (3 - 17) y	Angioplasty (34 procedures in 22 patients)	32/34 (94%) (residual stenosis <30%)	2/22 (9%) patients Groin haematoma (1), Temporary elevation in serum creatinine (2)	6/22 (27.3%) cured 10/22 (45.5%) improved	mean 7y 2m (range: 6 m to 13 y 10 m)
Colyer et al, 2014	8 y	12	median 8.2 (1.3 - 19.1) y	Angioplasty (5) Stent (7)	100.00% (angiographic improvement in the minimum luminal diameter)	2/12 (16.7%) patients Stent slippage (1) Stent thrombosis (1)	Minimal luminal diameter increased by 1.2±0.9 mm for all patients. Significant improved blood pressure only in stent group. Restenosis: 40% after angioplasty, 0% after stent.	median 165 (interquartile range: 9.5 - 38.4) m
Srinivasan et al, 2010	11 y	19	median (range) 9.6 (2 - 18)	Angioplasty (incl. cutting balloon)	16 / 19 (84%) patients 29 of 32 (91%) lesions (residual stenosis <30%)	3/19 (15.7%) Renal artery perforation (1) Accelerated hypertension (1) Puncture site haematoma (1)	7/18 (39%) cured 3/18 (17%) improved 8/18 (44%) failure	median 10 (1 – 83) m
Bayrak et al, 2008	15 y	20	mean 12.5 (range: 3 -18) y	Angioplasty (46 procedures on 35 stenotic segments)	29/34 (85%) initially technical success (residual stenosis <50%)	None	12 /20 (60%) Cured 8/20 (40%) Improved	mean 55.7 (range: 4 – 168) m

maintained across the lesion before, during and following angioplasty and the subsequent angiogram; wire access across the lesion allows for balloon reinflation or as a last resort stent placement. Procedure-related deaths are uncommon but have been reported. In the Kari et al series of 114 procedures, there was a procedure-related death secondary to hemorrhage from a graft tear after repeat angioplasty of a synthetic graft.[25] In the setting of arterial rupture and active extravasation, if balloon reinflation or covered stent placement is not possible vascular surgery consultation should be readily available.[40,48] Another rare complication is accelerated or worsening of hypertension following angioplasty.[40,70] Children with underlying cerebrovascular disease are at particular risk of stroke secondary to labile BP which can occur postangioplasty[9] and should be carefully monitored in the immediate postprocedure setting.

Embolization

Embolization was first reported in the 1970s as a method for managing hypertension.[71] Embolization can be considered when diseased subsegmental arteries cannot be treated by angioplasty and open reconstructive surgery is not favorable.[47,72] Embolization is less invasive and results in less tissue loss than nephrectomy or partial nephrectomy. Ethanol is used because it causes severe, irreversible, endothelial injury, which effectively results in infarction of the renin-producing ischemic parenchyma (Fig. 4). Embolization coils are avoided because occlusion of medium-sized arteries will result in recruitment of collateral supply by the ischemic focus with persistent hypertension.[9]

Sympathetic Denervation

Chronic activation of the sympathetic nervous system has an important role in sustained hypertension.[73] Surgical sympathectomy was developed in the 1930s, patients showed a favorable BP response following treatment but it was associated with high surgical morbidity and mortality.[74] Endovascular renal sympathetic denervation (RSDN) was recently developed and early trials (SYMPLICITY HTN-1 and SYMPLICITY HTN-2) suggested it have the potential to offer a nonpharmacologic treatment for resistant hypertension.[74-76] However subsequent trials failed to show a consistent benefit on BP.[77] More recently, 3 new trials (SPYRAL HTN-OFF MED, SPYRAL HTN-ON MED, and RADIANCE-HTN SOLO) have suggested RSDN has a modest benefit on hypertension compared with sham controls.[77-80] In a pediatric setting, RSDN has been reported to have been used in a successfully in a 16-year-old boy for drug resistant postcoarctation repair hypertension,[81] a 6-year-old girl with Turner syndrome, and in drug resistant hypertension.[82] In the latter case, energy delivery was modulated to account for patient size.[82] As evidence grows, RSDN may have a role in pediatric drug-resistant hypertension.

Surgery

In adults, surgery for RAS has been shown to have a higher complication rate and higher early and long term mortality than angioplasty.[83] A meta-analysis including 47 angioplasty studies (1616 patients) and 23 surgery studies (1014 patients) showed that the major complications of surgery were two and a half times higher angioplasty (6% vs 15%).[84] However, in this study, the cure rate of surgery was slightly higher (54%) than that of angioplasty (36%).[84] It is unknown whether these rates remain true in a pediatric population.

Some centers favor surgery as the treatment of choice in children. Open surgical interventions have been reported to have high rates of cure of 70%[26] and 82%[85] and require less re-intervention than endovascular interventions.[86] Some centers argue that surgery is harder after angioplasty due to fibrotic changes affecting the renal artery and have reported poorer surgical outcomes in such cases.[72]

Primary surgical intervention with a goal of managing renovascular disease in a single operation is not typically performed in most centers, including the authors'. This is in regards to the technical challenges in small children. If planning surgery, it may be preferable to wait until full adult growth and adult vascular size is reached.[23] Given the established safety and success of endovascular intervention, adopting a primary endovascular treatment strategy is the

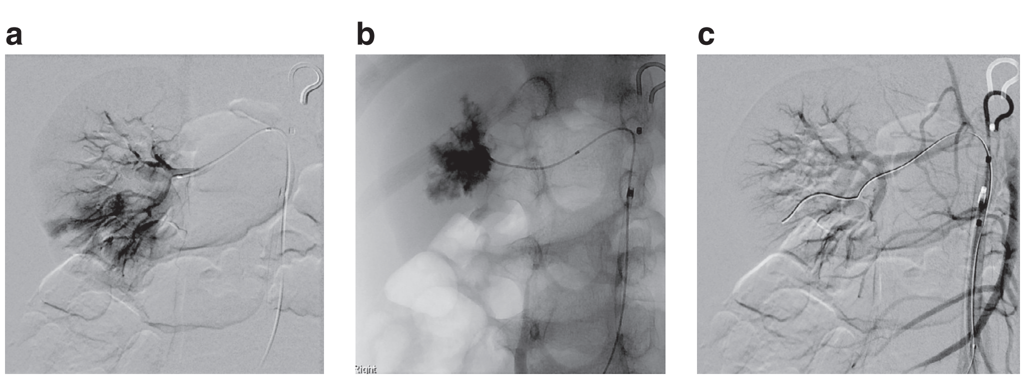

Figure 4 Patient with mid-aortic syndrome who had previously undergone bilateral renal artery angioplasty. Renal vein renin was high in the veins draining the right interpolar region. (a) DSA shows intrarenal branch stenoses. (b) Selective ethanol embolization was performed in these vessels. (c) Postembolization DSA shows persevered flow elsewhere in the kidney.

preferred treatment option, even if repeat interventions will be required.

Angiomyolipoma

Angiomyolipoma (AML) is the most common benign renal neoplasm occurring in 0.1% of males and 0.2% of females without tuberous sclerosis (TS)[87] and in approximately 80% of patients with TS. In patients with TS, the blood vessels supplying AMLs are often dysplastic and this predisposes to formation of intratumor aneurysms.[88] AMLs can be found incidentally or may present with flank pain, hydronephrosis, hematuria, impaired renal function or acute hemorrhage.[88] Growth of AMLs in children can be rapid and unpredictable. Annual radiological imaging is recommended for children >11 years or those with AMLs larger than 2 cm.[89]

Cumulative risk for hemorrhage is approximately 20% for females and 10% for males.[88] This risk of hemorrhage is higher for AMLs associated with TS than in sporadic AMLs. Risk of hemorrhage is also increased for AMLs larger than 4 cm in diameter.[90] Another factor that has been found to correlate with increased rupture and hemorrhage risk is the presence of intra-AML aneurysms >5 mm.[90] The presence of these can only be reliably detected by angiography, although aneurysm formation is thought to be related to AML size.[88] AMLs' should therefore be monitored by noninvasive imaging follow-up if less than 4 cm. Other risks of large AML's include reduction in renal function secondary to infiltration and destruction of normal renal tissue and renal vascular compromise.[88]

Imaging

AMLs are classically hyperechoic with acoustic shadowing due to a combination of fat and blood vessels within the tumor (Fig. 5).[87] Color flow Doppler can assist in detection of aneurysms with the AML. On CT and MRI, AML classically demonstrate macroscopic fat within the tumor (Fig. 5).

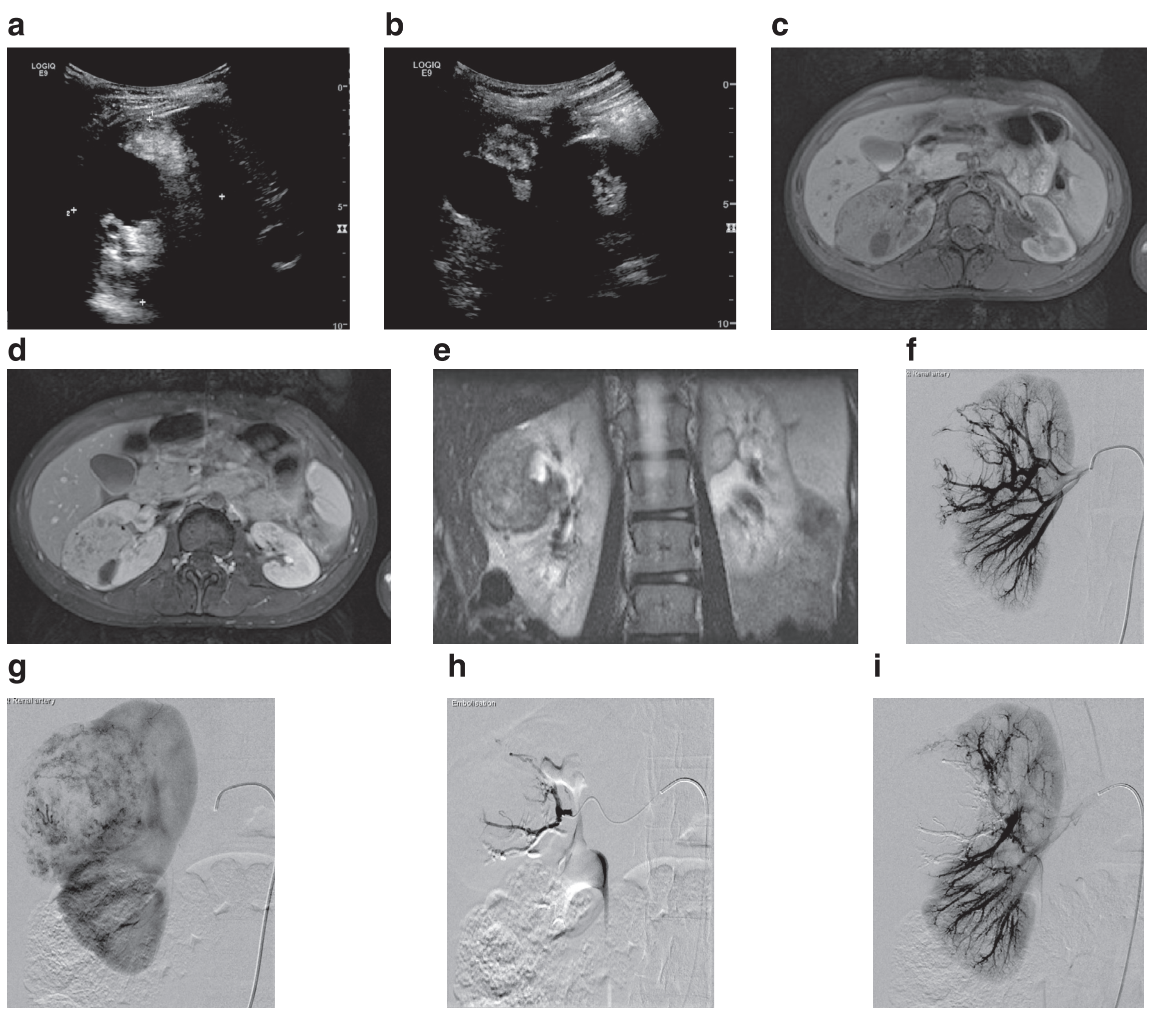

Figure 5 Fifteen years old with right kidney AML. (a, b) Ultrasound images showing right renal hyperechoic mass. (c, d) Axial T1 pre- and postcontrast and (e) coronal T2-weighted MRI showing the mass containing fat. (f) Early and (g) late arterial phase DSA showing abnormal vasculature in the large interpolar AML. (h) Embolization performed with glue mixed with ethiodized oil. (i) Postembolization DSA shows AML devascularization with preserved flow to the rest of the kidney.

However, approximately 5% of AMLs are atypical or fat poor which can make the diagnosis challenging.[91] Angiographically, AML vasculature has long and tortuous vessels with aneurysmal dilations which are easily distinguished from the normal renal vasculature.[87]

Treatment

Traditionally, indication for angiography and embolization of AMLs are acute hemorrhage and AMLs greater than 4 cm.[88,92] The aim of angiography and embolization is to prevent hemorrhage, preserve viable renal tissue, and avoid the reduction in renal function resulting from partial or total nephrectomy.[88] The indication for embolization of asymptomatic AMLs greater than 4 cm in the context of TS is more debatable. Factors to consider when determining necessity of embolization include tumor growth rate, magnitude of the vascular supply, severity of dysplastic vessels and the presence of microaneurysms and/or macroaneurysms.[88,92] When there is flank pain, retroperitoneal hemorrhage, or hematuria, embolization should be performed, regardless of AML size.[93,94]

Embolization has been reported to have been performed successfully with combinations of PVA particles (200-1190 micrometers) and/or coils[88,92] with the goal being cessation of blood flow to the AML.[88] At the authors' institution glue has also been used successfully (Fig. 5). Embolization of renal AMLs is a relatively safe procedure. In addition to the standard risks of any endovascular embolization procedure (such as nontarget embolization), the risks specific to this procedure include risk of damage to functional renal tissue, hypertension (secondary to renal ischemia), formation of renal abscess and postembolization syndrome.[88,94] Postembolization syndrome, manifesting as pain and fever is caused by the inflammatory response to necrotic tissue after embolization. It has been reported to occur in 85%-89% of patients if steps are not taken to prevent/treat it.[92,94] A protocol which has been reported to be successful in reducing postembolization syndrome in 3 of 11 (27%) patients is periprocedural antibiotics and a course of tapering steroids.[92] Four doses of a first-generation cephalosporin are given, starting with the first dose prior to embolization and subsequent oral dosing. Before embolization, 250 mg/m^2 of methylprednisolone (maximum dose 260 mg) is given intravenously. Beginning on the first postoperative day, 2 mg/kg prednisone in 3 divided doses per day for 2 days (maximum dose of 60 mg/d) is given, then every 2 days the prednisone dose is tapered to finish approximately 14 days after embolization. Additionally, acetaminophen may be used every 6 hours if needed for pain.[92]

Following embolization, there is a relatively immediate reduction of the vascular involvement on CT/MRI. In a series of 20 AMLs in 16 patients with TS who were treated with embolization, there was an average reduction in tumor volume by 56%, and the glomerular filtration rate was unchanged.[88] In the short term and intermediate term (23-40 months), repeat hemorrhage events were reported in various studies to occur in 0%-17% of patients.[88,94] Unfortunately, the long-term outcomes of these patients are poorly reported.[88]

Following the results of EXIST 2 study, consensus guidelines now include mammalian target of rapamycin inhibitor for treatment of asymptomatic and growing AMLs. Everolimus has been confirmed to decrease or stabilize the size and number of subependymal giant cell astrocytomas in patients with TS complex.[95] It has also demonstrated significant reduction in renal AML volume compared with placebo in the phase 3 EXIST-2 trial.[96]

A study on long-term use of everolimus clearly demonstrated evidence of efficacy and safety in patents with TS. Although not a primary focus of this study, everolimus caused increasing and sustained reductions in renal AML volume providing evidence for broad clinical impact of systemic treatment with patients with TS. Nearly 95% of patients experienced reduction in the AMLs with more than 80% showing >50% reduction in volume at week 24. Median duration of renal AML response being 42.3 months (95% confidence interval). AML volume continued to decrease over the study period.[97] Recommendations for initiation of treatment with everolimus are at least one, enlarging, asymptomatic AMLs >3 cm in diameter.[91] Based on the recent studies showing effective shrinkage of AMLs in patients on low dose everolimus, it could be anticipated that the need for embolization will be reserved to those with acute bleeding.[98]

Nutcracker Syndrome

Nutcracker syndrome (NS) refers to the symptoms and signs associated with nutcracker phenomenon. Nutcracker phenomenon is the external compression of the left renal vein between the superior mesenteric artery and the aorta (anterior nutcracker). A less common variant is the compression of a retro-aortic left renal vein between the aorta and vertebral body (posterior nutcracker).[99-101] Compression typically is most severe in an upright position.[99] Hematuria is the most common presenting sign. The proposed etiology of hematuria in NS is secondary to venous hypertension and congestion causing rupture of the thin-walled veins into the collecting system.[102] Orthostatic proteinuria, flank and pelvic pain, and gonadal varices can also be present at presentation.[102]

NS is a diagnosis with some controversy. It is generally regarded as a rare diagnosis which should be made after other more common causes of similar symptoms have been excluded.[102] Some authors suggest that it underestimated and under-recognized in children and is in fact the most common cause of isolated hematuria in children without urinary tract infection or proteinuria.[103] Anatomic nutcracker phenomenon is not always associated with clinical symptoms and signs; therefore, it has been suggested as a normal anatomic variant.[102]

Imaging

US is the recommended first-line investigation.[102,103] For detection of left renal vein compression, Doppler US has been reported to have a sensitivity and specificity of 69%-90% and 89%-100%.[104] Between the lateral portion of the left renal vein near the hilum and where it courses between the aorta and the superior mesenteric artery, an anteroposterior diameter ratio >4.2 and peak systolic velocity ratio of >4.2-5.0 is considered a diagnostic criteria.[102,105] The degree of compression on US has been correlated with severity of symptoms at presentation.[106]

The advantage of US is the ability to scan the child supine and erect. Measurements taken with the child erect may correlate better with symptoms than those taken supine.[107] CT and MRI can also be used to demonstrate left renal vein compression. A superior mesenteric artery branching angle of $<35°$ has been proposed as required for the diagnosis of NS.[102] However, in one study the mean was 46° in 205 pediatric abdominal CTs (range of 11°-113°). In that study, using a threshold of 25° would have resulted in 9% of asymptomatic children being defined as abnormal.[108]

Nuclear medicine studies do not usually have a role in diagnosis; however, accumulation ^{99m}Tc-Albumin-Conjugate accumulation in the renal pelvis on scintigraphy has been shown to be useful as an adjunct to US for diagnosis.[109]

Catheter venography and pressure measurements can also be used to identify left renal vein compression. A pressure gradient of $\leq$1mm Hg is considered normal and patients with NS usually have a venous pressure gradient $>$1mm Hg across the area of compression.[102,104] Intravascular US is also useful and can show the exact point where the over-riding vessel causes maximal compression and may overcome some of the difficulties in accurately assessing planar compression of veins with 2-D imaging.[110]

Treatment

Initially a conservative approach to management should be considered if symptoms are mild. In children this allows further growth and increase in the retroperitoneal fat which may improve the superior mesenteric artery branching angle and relieve compression of the left renal vein.[102,104,111] If conservative management fails, endovascular stenting (Fig. 6) and left renal vein transposition and have been used.[111] A systematic review on the management of NS which reviewed 17 references suggest that, due to the rare nature of the condition, paucity of evidence and limited long-term follow up data, a definitive recommendation regarding best management method cannot be made.[102]

Endovascular stenting has shown good results but there are significant limitations such as stent migration (into the right atrium or ventricle).[112,113] A variety of stents have been used throughout the literature since there is not 1 stent that achieves both precise deployment with the strength needed to completely relieve the external compression. In a large series of 61 patients who all underwent endovascular stenting, 97% had symptomatic improvement including resolution of flank pain and hematuria at 6-month follow-up; as well as significantly decreased peak velocity in the aortomesenteric portion, and less severe antero-posterior diameter ratio of the renal hilum and the aortomesenteric portion of the left renal vein compared to presenting on follow-up US evaluation.[114] In a smaller study, 15 patients who underwent stenting remained asymptomatic at 6 years.[104,113] Following stenting for NS, stent migration rate has been reported in an adult series to be more than 6%.[112] Other reported complications include intrastent stenosis, thrombosis, and fracture with resultant vessel occlusion.[104]

Surgical approaches to management include left renal vein transposition, renal auto transplantation, and laparoscopic extravascular stent placement.[102,104] In a small pediatric series of 3 children, open surgical repair with left renal vein transposition has been reported to provide complete resolution of symptoms and hematuria/proteinuria in all patients.[115] Transposition of the left renal vein can be used for anterior and posterior compression and has been reported successful for posterior NS in children as small as 5 years old.[99] However, transposition of the left renal vein is carries with it the morbidity of a long recovery period, potential for adhesion formation, and other risks of major abdominal surgery.

It is well known that orthostatic proteinuria could be associated with NS and could cause massive protein excretion.[116]

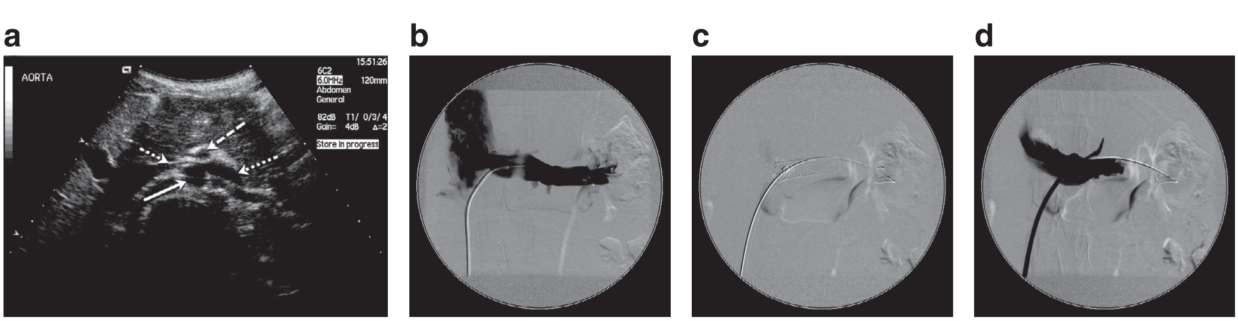

Figure 6 Sixteen years old with left flank pain associated with macroscopic hematuria attacks. (a) Ultrasound suggested compression of the left renal vein (aorta solid arrow, superior mesenteric artery dashed arrow, left renal vein dotted arrow). (b) Venography confirmed, partial obstruction by a band-like compression at the position of the superior mesenteric artery. (c) A 12-mm diameter (40 mm long) Wallstent was deployed in the left renal vein across the narrowed segment. (d) Poststenting venous drainage appeared improved. The patient became asymptomatic postprocedure.

As long-term proteinuria has been accepted as an independent prognostic factor for progression of renal disease,[117,118] some might argue that use of angiotensin converting enzyme inhibitors (ACEi) could reduce effects of proteinuria and slow down progression to chronic kidney disease. Some evidence exists that use of ACEi can improve proteinuria associated with NS.[119] However, there is no consensus for the use of ACEi in NS patients and its use is patient and center dependent.

Conclusion

We have described renovascular interventions in children for hypertension, AML and NS accompanied by the diagnostic features of these conditions. Pediatric interventional radiology has been used successfully to manage all these conditions. Clear guidelines for the diagnosis and management of RVH in children are not defined. This is partly due to heterogeneity of this population in terms of etiology, response to medications, and vascular involvement. Current literature only provides data on small patient cohorts over long time periods. This problem impairs development of reliable evidence for radiological intervention in children more widely and will require novel research methodologies or significant multi-institutional cooperation with standardization of approaches to treatment and pooling of data. Data available suggest that safe and effective interventional radiological management of these conditions can be undertaken with careful case selection, multidisciplinary discussions with pediatric nephrologists and vascular surgeons, and a dedicated pediatric IR team. Similarly based on the small published data available, endovascular interventions for AML and NS in children are safe and effective.

References

1. Lobeck IN, Alhajjat AM, Dupree P, et al: The management of pediatric renovascular hypertension: A single center experience and review of the literature. J Pediatr Surg 53:1825-1831, 2018. https://doi.org/10.1016/j.jpedsurg.2017.12.008
2. Tullus K: To screen or not to screen: For high blood pressure. Pediatr Nephrol Berl Ger 33:81-82, 2018. https://doi.org/10.1007/s00467-017-3808-z
3. Lurbe E, Cifkova R, Cruickshank JK, et al: Management of high blood pressure in children and adolescents: Recommendations of the European Society of Hypertension. J Hypertens 27:1719, 2009. https://doi.org/10.1097/HJH.0b013e32832f4f6b
4. Beacher DR, Chang SZ, Rosen JS, et al: Recognition of elevated blood pressure in an outpatient pediatric tertiary care setting. J Pediatr 166:1233-1239, 2015. https://doi.org/10.1016/j.jpeds.2015.02.006
5. Shapiro DJ, Hersh AL, Cabana MD, et al: Hypertension screening during ambulatory pediatric visits in the United States, 2000-2009. Pediatrics 130:604-610, 2012. https://doi.org/10.1542/peds.2011-3888
6. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 114(Supplement 2):555-576, 2004
7. Bartosh SM, Aronson AJ: Childhood hypertension. An update on etiology, diagnosis, and treatment. Pediatr Clin North Am 46:235-252, 1999
8. Zhu G, He F, Gu Y, et al: Angioplasty for pediatric renovascular hypertension: A 13-year experience. Diagn Interv Radiol 20:285-292, 2014. https://doi.org/10.5152/dir.2014.13208
9. Tullus K, Brennan E, Hamilton G, et al: Renovascular hypertension in children. Lancet Lond Engl 371:1453-1463, 2008. https://doi.org/10.1016/S0140-6736(08)60626-1
10. Gupta-Malhotra M, Banker A, Shete S, et al: Essential hypertension vs. secondary hypertension among children. Am J Hypertens 28:73-80, 2015. https://doi.org/10.1093/ajh/hpu083
11. Dillman JR, Smith EA, Coley BD: Ultrasound imaging of renin-mediated hypertension. Pediatr Radiol 47:1116-1124, 2017. https://doi.org/10.1007/s00247-017-3840-y
12. Gill DG, de Costa BM, Cameron JS, et al: Analysis of 100 children with severe and persistent hypertension. Arch Dis Child 51:951-956, 1976
13. Wyszyńska T, Cichocka E, Wieteska−Klimczak A, et al: A single pediatric center experience with 1025 children with hypertension. Acta Paediatr 81:244-246, 1992. https://doi.org/10.1111/j.1651-2227.1992.tb12213.x
14. Roebuck D: Childhood hypertension: What does the radiologist contribute? Pediatr Radiol 38:501-507, 2008. https://doi.org/10.1007/s00247-008-0838-5
15. Tullus K, Roebuck DJ, McLaren CA, et al: Imaging in the evaluation of renovascular disease. Pediatr Nephrol 25:1049-1056, 2010. https://doi.org/10.1007/s00467-009-1320-9
16. Tullus K, Roebuck DJ: Renovascular hypertension in small children-is it Takayasu arteritis or fibromuscular dysplasia? J Am Soc Hypertens JASH 12:506-508, 2018. https://doi.org/10.1016/j.jash.2018.04.011
17. Green R, Gu X, Kline-Rogers E, et al: Differences between the pediatric and adult presentation of fibromuscular dysplasia: Results from the US Registry. Pediatr Nephrol Berl Ger 31:641-650, 2016. https://doi.org/10.1007/s00467-015-3234-z
18. Burnei G, Burnei A, Hodorogea D, et al: Diagnosis and complications of renovascular hypertension in children: Literature data and clinical observations. J Med Life 2:18-28, 2009
19. Srinivasan A, Krishnamurthy G, Fontalvo-Herazo L, et al: Spectrum of renal findings in pediatric fibromuscular dysplasia and neurofibromatosis type 1. Pediatr Radiol 41:308-316, 2011. https://doi.org/10.1007/s00247-010-1854-9
20. Elias DL, Ricketts RR, Smith RB: Renovascular hypertension complicating neurofibromatosis. Am Surg 51:97-106, 1985
21. Han M, Criado E: Renal artery stenosis and aneurysms associated with neurofibromatosis. J Vasc Surg 41:539-543, 2005. https://doi.org/10.1016/j.jvs.2004.12.021
22. Rumman RK, Nickel C, Matsuda-Abedini M, et al: Disease beyond the arch: A systematic review of middle aortic syndrome in childhood. Am J Hypertens 28:833-846, 2015. https://doi.org/10.1093/ajh/hpu296
23. Sethna CB, Kaplan BS, Cahill AM, et al: Idiopathic mid-aortic syndrome in children. Pediatr Nephrol Berl Ger 23:1135-1142, 2008. https://doi.org/10.1007/s00467-008-0767-4
24. Shroff R, Roebuck DJ, Gordon I, et al: Angioplasty for renovascular hypertension in children: 20-year experience. Pediatrics 118:268-275, 2006. https://doi.org/10.1542/peds.2005-2642
25. Kari JA, Roebuck DJ, McLaren CA, et al: Angioplasty for renovascular hypertension in 78 children. Arch Dis Child 100:474-478, 2015. https://doi.org/10.1136/archdischild-2013-305886
26. Stanley JC, Criado E, Upchurch GR, et al: Pediatric renovascular hypertension: 132 primary and 30 secondary operations in 97 children. J Vasc Surg 44:1219-1228, 2006. https://doi.org/10.1016/j.jvs.2006.08.009. discussion 1228-1229
27. Tyagi S, Kaul UA, Satsangi DK, et al: Percutaneous transluminal angioplasty for renovascular hypertension in children: Initial and long-term results. Pediatrics 99:44-49, 1997
28. Tummolo A, Marks SD, Stadermann M, et al: Mid-aortic syndrome: Long-term outcome of 36 children. Pediatr Nephrol Berl Ger 24:2225-2232, 2009. https://doi.org/10.1007/s00467-009-1242-6
29. Trautmann A, Roebuck DJ, McLaren CA, et al: Non-invasive imaging cannot replace formal angiography in the diagnosis of renovascular hypertension. Pediatr Nephrol Berl Ger 32:495-502, 2017. https://doi.org/10.1007/s00467-016-3501-7

30. Chandak P, Byrne N, Coleman A, et al: Patient-specific 3D printing: A novel technique for complex pediatric renal transplantation. Ann Surg 269:e18-e23, 2019. https://doi.org/10.1097/SLA.0000000000003016
31. Agrawal H, Moodie D, Qureshi AM, et al: Interventions in children with renovascular hypertension: A 27-year retrospective single-center experience. Congenit Heart Dis 2018. https://doi.org/10.1111/chd.12608
32. Conkbayir I, Yücesoy C, Edgüer T, et al: Doppler sonography in renal artery stenosis. An evaluation of intrarenal and extrarenal imaging parameters. Clin Imaging 27:256-260, 2003
33. Brun P, Kchouk H, Mouchet B, et al: Value of Doppler ultrasound for the diagnosis of renal artery stenosis in children. Pediatr Nephrol Berl Ger 11:27-30, 1997
34. Krumme B, Blum U, Schwertfeger E, et al: Diagnosis of renovascular disease by intra- and extrarenal Doppler scanning. Kidney Int 50:1288-1292, 1996. https://doi.org/10.1038/ki.1996.440
35. Castelli E, Tonutti M, Arfelli F, et al: Mammography with synchrotron radiation: First clinical experience with phase-detection technique. Radiology 259:684-694, 2011. https://doi.org/10.1148/radiol.11100745
36. Kchouk H, Brun P, Sentou Y, et al: [Renal stenosis in hypertensive children. Doppler/arteriographic correlation]. J Mal Vasc 22:86-90, 1997
37. Chhadia S, Cohn RA, Vural G, et al: Renal Doppler evaluation in the child with hypertension: A reasonable screening discriminator? Pediatr Radiol 43:1549-1556, 2013. https://doi.org/10.1007/s00247-013-2741-y
38. Louis R, Levy-Erez D, Cahill AM, et al: Imaging studies in pediatric fibromuscular dysplasia (FMD): A single-center experience. Pediatr Nephrol Berl Ger 33:1593-1599, 2018. https://doi.org/10.1007/s00467-018-3983-6
39. Ng CS, de Bruyn R, Gordon I: The investigation of renovascular hypertension in children: The accuracy of radio-isotopes in detecting renovascular disease. Nucl Med Commun 18:1017-1028, 1997
40. Srinivasan A, Krishnamurthy G, Fontalvo-Herazo L, et al: Angioplasty for renal artery stenosis in pediatric patients: An 11-year retrospective experience. J Vasc Interv Radiol JVIR 21:1672-1680, 2010. https://doi.org/10.1016/j.jvir.2010.07.012
41. Vo NJ, Hammelman BD, Racadio JM, et al: Anatomic distribution of renal artery stenosis in children: Implications for imaging. Pediatr Radiol 36:1032-1036, 2006. https://doi.org/10.1007/s00247-006-0253-8
42. Tullus K: Renal artery stenosis: Is angiography still the gold standard in 2011? Pediatr Nephrol Berl Ger 26:833-837, 2011. https://doi.org/10.1007/s00467-010-1757-x
43. Shahdadpuri J, Frank R, Gauthier BG, et al: Yield of renal arteriography in the evaluation of pediatric hypertension. Pediatr Nephrol Berl Ger 14:816-819, 2000
44. Rumman RK, Matsuda-Abedini M, Langlois V, et al: Management and outcomes of childhood renal artery stenosis and middle aortic syndrome. Am J Hypertens 31:687-695, 2018. https://doi.org/10.1093/ajh/hpy014
45. Patel PA, Pass J, McLaren C, et al: Contrast induced nephropathy following high contrast dose angiographic procedures. Pediatr Radiol 44: S113, 2014. https://doi.org/10.1007/s00247-014-2920-5
46. Maehara A, Matsumura M, Ali ZA, et al: IVUS-guided versus OCT-guided coronary stent implantation: A critical appraisal. JACC Cardiovasc Imaging 10:1487-1503, 2017. https://doi.org/10.1016/j.jcmg.2017.09.008
47. Teigen CL, Mitchell SE, Venbrux AC, et al: Segmental renal artery embolization for treatment of pediatric renovascular hypertension. J Vasc Interv Radiol JVIR 3:111-117, 1992
48. McLaren CA, Roebuck DJ: Interventional radiology for renovascular hypertension in children. Tech Vasc Interv Radiol 6:150-157, 2003. https://doi.org/10.1053/j.tvir.2003.10.007
49. Goonasekera CDA, Shah V, Wade AM, et al: The usefulness of renal vein renin studies in hypertensive children: A 25-year experience. Pediatr Nephrol Berl Ger 17:943-949, 2002. https://doi.org/10.1007/s00467-002-0954-7
50. Roebuck DJ, Vendhan K, Barnacle AM, et al: Ultrasound-guided transaxillary access for diagnostic and interventional arteriography in children. J Vasc Interv Radiol 21:842-847, 2010. https://doi.org/10.1016/j.jvir.2010.02.025
51. Heran MKS, Marshalleck F, Temple M, et al: Joint quality improvement guidelines for pediatric arterial access and arteriography: From the societies of interventional radiology and pediatric radiology. J Vasc Interv Radiol 21:32-43, 2010. https://doi.org/10.1016/j.jvir.2009.09.006
52. Colyer JH, Ratnayaka K, Slack MC, et al: Renal artery stenosis in children: Therapeutic percutaneous balloon and stent angioplasty. Pediatr Nephrol Berl Ger 29:1067-1074, 2014. https://doi.org/10.1007/s00467-013-2730-2
53. Towbin RB, Pelchovitz DJ, Baskin KM, et al: Cutting balloon angioplasty in children with resistant renal artery stenosis. J Vasc Interv Radiol 18:663-669, 2007. https://doi.org/10.1016/j.jvir.2007.02.014
54. Alexander A, Richmond L, Geary D, et al: Outcomes of percutaneous transluminal angioplasty for pediatric renovascular hypertension. J Pediatr Surg 52:395-399, 2017. https://doi.org/10.1016/j.jpedsurg.2016.08.011
55. Son JS: Successful cutting balloon angioplasty in a child with resistant renal artery stenosis. BMC Res Notes 8, 2015. https://doi.org/10.1186/s13104-015-1673-z
56. Gumus B, Cevik H, Vuran C, et al: Cutting balloon angioplasty of bilateral renal artery stenosis due to Takayasu arteritis in a 5-year-old child with midterm follow-up. Cardiovasc Intervent Radiol 33:394-397, 2010. https://doi.org/10.1007/s00270-009-9623-6
57. Arce-Santiago M, Rodríguez-Cruz E: Treatment of a recurrent renal artery stenosis and stent fracture using a drug eluting stent in a pediatric patient. CEN Case Rep 5:18-22, 2015. https://doi.org/10.1007/s13730-015-0182-1
58. Peco-Antić A, Stajić N, Krstić Z, et al: Associated extrarenal vascular diseases may complicate the treatment and outcome of renovascular hypertension. Acta Paediatr 105:e35-e41, 2016. https://doi.org/10.1111/apa.13229
59. Bayrak AH, Numan F, Cantaşdemir M, et al: Percutaneous balloon angioplasty of renovascular hypertension in pediatric cases. Acta Chir Belg 108:708-714, 2008
60. Stanley P, Hieshima G, Mehringer M: Percutaneous transluminal angioplasty for pediatric renovascular hypertension. Radiology 153:101-104, 1984. https://doi.org/10.1148/radiology.153.1.6236476
61. Mali WP, Puijlaert CB, Kouwenberg HJ, et al: Percutaneous transluminal renal angioplasty in children and adolescents. Radiology 165:391-394, 1987. https://doi.org/10.1148/radiology.165.2.2958896
62. Fossali E, Signorini E, Intermite RC, et al: Renovascular disease and hypertension in children with neurofibromatosis. Pediatr Nephrol Berl Ger 14:806-810, 2000
63. Gardiner GA, Freedman AM, Shlansky-Goldberg R: Percutaneous transluminal angioplasty: Delayed response in neurofibromatosis. Radiology 169:79-80, 1988. https://doi.org/10.1148/radiology.169.1.2971240
64. Ino T, Kishiro M, Okubo M, et al: Dilatation mechanism of balloon angioplasty in children: Assessment by angiography and intravascular ultrasound. Cardiovasc Intervent Radiol 21:102-108, 1998
65. Sharma S, Thatai D, Saxena A, et al: Renovascular hypertension resulting from nonspecific aortoarteritis in children: Midterm results of percutaneous transluminal renal angioplasty and predictors of restenosis. Am J Roentgenol 166:157-162, 1996. https://doi.org/10.2214/ajr.166.1.8571868
66. Sharma S, Gupta H, Saxena A, et al: Results of renal angioplasty in nonspecific aortoarteritis (Takayasu disease). J Vasc Interv Radiol JVIR 9:429-435, 1998
67. Ghirardo G, De Franceschi M, Vidal E, et al: Transplant renal artery stenosis in children: Risk factors and outcome after endovascular treatment. Pediatr Nephrol Berl Ger 29:461-467, 2014. https://doi.org/10.1007/s00467-013-2681-7
68. Aliabadi H, McLorie GA, Churchill BM, et al: Percutaneous transluminal angioplasty for transplant renal artery stenosis in children. J Urol 143:569-572, 1990. discussion 572-573
69. Serruys PW, Ormiston JA, Onuma Y, et al: A bioabsorbable everolimus-eluting coronary stent system (ABSORB): 2-year outcomes and results from multiple imaging methods. Lancet Lond Engl 373:897-910, 2009. https://doi.org/10.1016/S0140-6736(09)60325-1
70. Larar GN, Treves ST: Accelerated renovascular hypertension following angioplasty. Assessment of therapy by Tc-99m DMSA imaging. Clin Nucl Med 18:278-280, 1993

71. Reuter SR, Pomeroy PR, Chuang VP, et al: Embolic control of hypertension caused by segmental renal artery stenosis. AJR Am J Roentgenol 127:389-392, 1976. https://doi.org/10.2214/ajr.127.3.389
72. Eliason JL, Coleman DM, Criado E, et al: Remedial operations for failed endovascular therapy of 32 renal artery stenoses in 24 children. Pediatr Nephrol Berl Ger 31:809-817, 2016. https://doi.org/10.1007/s00467-015-3275-3
73. Smith PA, Graham LN, Mackintosh AF, et al: Relationship between central sympathetic activity and stages of human hypertension. Am J Hypertens 17:217-222, 2004. https://doi.org/10.1016/j.amjhyper.2003.10.010
74. Stuart S, Patel P: Renal sympathetic denervation for treatment resistant hypertension. In: Jolesz F, Penzkofer T (eds): Current Approaches in Image-Guided Therapy, London, UK: Future Medicine Ltd, 36-48, 2014 http://www.futuremedicine.com/doi/abs/10.2217/fmeb2013.13.142
75. Symplicity HTN-1 Investigators. Catheter-based renal sympathetic denervation for resistant hypertension: Durability of blood pressure reduction out to 24 months. Hypertens 57:911-917, 2011. https://doi.org/10.1161/HYPERTENSIONAHA.110.163014
76. Symplicity HTN-2 InvestigatorsEsler MD, Krum H, et al: Renal sympathetic denervation in patients with treatment-resistant hypertension (the Symplicity HTN-2 Trial): A randomised controlled trial. Lancet Lond Engl 376:1903-1909, 2010. https://doi.org/10.1016/S0140-6736(10)62039-9
77. Wyatt CM, Textor SC: Emerging evidence on renal denervation for the treatment of hypertension. Kidney Int 2018. https://doi.org/10.1016/j.kint.2018.08.002
78. Townsend RR, Mahfoud F, Kandzari DE, et al: Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): A randomised, sham-controlled, proof-of-concept trial. Lancet 390:2160-2170, 2017. https://doi.org/10.1016/S0140-6736(17)32281-X
79. Kandzari DE, Böhm M, Mahfoud F, et al: Effect of renal denervation on blood pressure in the presence of antihypertensive drugs: 6-month efficacy and safety results from the SPYRAL HTN-ON MED proof-of-concept randomised trial. Lancet Lond Engl 391:2346-2355, 2018. https://doi.org/10.1016/S0140-6736(18)30951-6
80. Azizi M, Schmieder RE, Mahfoud F, et al: Endovascular ultrasound renal denervation to treat hypertension (RADIANCE-HTN SOLO): A multicentre, international, single-blind, randomised, sham-controlled trial. Lancet Lond Engl 391:2335-2345, 2018. https://doi.org/10.1016/S0140-6736(18)31082-1
81. Buchhorn R, Ziemer G, Jetter HM, et al: Renal sympathetic denervation for resistant hypertension in a child after aortic coarctation surgery. Int J Cardiol 172:e447-e448, 2014. https://doi.org/10.1016/j.ijcard.2013.12.317
82. Bonanni A, Pasetti F, Ghiggeri GM, et al: Renal denervation for severe hypertension in a small child with Turner syndrome: Miniaturisation of the procedure and results. BMJ Case Rep 2015. https://doi.org/10.1136/bcr-2014-208777, 2015
83. Alhadad A, Ahle M, Ivancev K, et al: Percutaneous transluminal renal angioplasty (PTRA) and surgical revascularisation in renovascular disease—A retrospective comparison of results, complications, and mortality. Eur J Vasc Endovasc Surg Off J Eur Soc Vasc Surg 27:151-156, 2004. https://doi.org/10.1016/j.ejvs.2003.10.009
84. Trinquart L, Mounier-Vehier C, Sapoval M, et al: Efficacy of revascularization for renal artery stenosis caused by fibromuscular dysplasia: A systematic review and meta-analysis. Hypertension 56:525-532, 2010. https://doi.org/10.1161/HYPERTENSIONAHA.110.152918
85. Lacombe M: Surgical treatment of renovascular hypertension in children. Eur J Vasc Endovasc Surg Off J Eur Soc Vasc Surg 41:770-777, 2011. https://doi.org/10.1016/j.ejvs.2011.02.023
86. Porras D, Stein DR, Ferguson MA, et al: Midaortic syndrome: 30 years of experience with medical, endovascular and surgical management. Pediatr Nephrol 28:2023-2033, 2013. https://doi.org/10.1007/s00467-013-2514-8
87. Halpenny D, Snow A, McNeill G, et al: The radiological diagnosis and treatment of renal angiomyolipoma—Current status. Clin Radiol 65:99-108, 2010. https://doi.org/10.1016/j.crad.2009.09.014
88. Williams JM, Racadio JM, Johnson ND, et al: Embolization of renal angiomyolipomata in patients with tuberous sclerosis complex. Am J Kidney Dis 47:95-102, 2006. https://doi.org/10.1053/j.ajkd.2005.09.028
89. Warncke JC, Brodie KE, Grantham EC, et al: Pediatric renal angiomyolipomas in tuberous sclerosis complex. J Urol 197:500-506, 2017. https://doi.org/10.1016/j.juro.2016.09.082
90. Yamakado K, Tanaka N, Nakagawa T, et al: Renal angiomyolipoma: Relationships between tumor size, aneurysm formation, and rupture. Radiology 225:78-82, 2002. https://doi.org/10.1148/radiol.2251011477
91. Buj Pradilla MJ, Martí Ballesté T, Torra R, et al: Recommendations for imaging-based diagnosis and management of renal angiomyolipoma associated with tuberous sclerosis complex. Clin Kidney J 10:728-737, 2017. https://doi.org/10.1093/ckj/sfx094
92. Bissler JJ, Racadio J, Donnelly LF, et al: Reduction of postembolization syndrome after ablation of renal angiomyolipoma. Am J Kidney Dis Off J Natl Kidney Found 39:966-971, 2002. https://doi.org/10.1053/ajkd.2002.32770
93. Golzarian J: Vascular Embolotherapy: A Comprehensive Approach Volume 2 Oncology, Trauma, Gene Therapy, Vascular Malformations, and Neck. Berlin; Heidelberg [u.a.]: Springer, 2006
94. Nelson CP, Sanda MG: Contemporary diagnosis and management of renal angiomyolipoma. J Urol 168(4 Pt 1):1315-1325, 2002. https://doi.org/10.1097/01.ju.0000028200.86216.b2
95. Krueger DA, Northrup H: International Tuberous Sclerosis Complex Consensus Group. Tuberous sclerosis complex surveillance and management: Recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference. Pediatr Neurol 49:255-265, 2013. https://doi.org/10.1016/j.pediatrneurol.2013.08.002
96. Bissler JJ, Kingswood JC, Radzikowska E, et al: Everolimus for angiomyolipoma associated with tuberous sclerosis complex or sporadic lymphangioleiomyomatosis (EXIST-2): A multicentre, randomised, double-blind, placebo-controlled trial. Lancet Lond Engl 381:817-824, 2013. https://doi.org/10.1016/S0140-6736(12)61767-X
97. Franz DN, Belousova E, Sparagana S, et al: Long-term use of everolimus in patients with tuberous sclerosis complex: Final results from the EXIST-1 study. PLoS One 11, 2016. https://doi.org/10.1371/journal.pone.0158476
98. Wei C-C, Tsai J-D, Sheu J-N, et al: Continuous low-dose everolimus shrinkage tuberous sclerosis complex-associated renal angiomyolipoma: A 48-month follow-up study. J Investig Med Off Publ Am Fed Clin Res 2018. https://doi.org/10.1136/jim-2018-000865
99. Quinones-Baldrich WJ: Posterior nutcracker syndrome in a child. J Vasc Surg 61:511, 2015. https://doi.org/10.1016/j.jvs.2013.11.087
100. Kurklinsky AK, Rooke TW: Nutcracker phenomenon and nutcracker syndrome. Mayo Clin Proc 85:552-559, 2010. https://doi.org/10.4065/mcp.2009.0586
101. Park JH, Lee GH, Lee SM, et al: Posterior nutcracker syndrome—A systematic review. VASA Z Gefasskrankheiten 47:23-29, 2018. https://doi.org/10.1024/0301-1526/a000670
102. Velasquez CA, Saeyeldin A, Zafar MA, et al: A systematic review on management of nutcracker syndrome. J Vasc Surg Venous Lymphat Disord 6:271-278, 2018. https://doi.org/10.1016/j.jvsv.2017.11.005
103. Park SJ, Oh JY, Shin JI: Diagnostic value of renal Doppler ultrasonography for detecting nutcracker syndrome in children with recurrent gross hematuria. Clin Pediatr (Phila) 51:1001, 2012. https://doi.org/10.1177/0009922812459071
104. Ananthan K, Onida S, Davies AH: Nutcracker syndrome: An update on current diagnostic criteria and management guidelines. Eur J Vasc Endovasc Surg Off J Eur Soc Vasc Surg 53:886-894, 2017. https://doi.org/10.1016/j.ejvs.2017.02.015
105. Park SJ, Lim JW, Cho B-S, et al: Nutcracker syndrome in children with orthostatic proteinuria: Diagnosis on the basis of Doppler sonography. J Ultrasound Med Off J Am Inst Ultrasound Med 21:39-45, 2002.. quiz 46
106. Nalcacioglu H, Ceyhan Bilgici M, Tekcan D, et al: Nutcracker syndrome in children: Role of Doppler ultrasonographic indices in detecting the pattern of symptoms. J Clin Med 7, 2018. https://doi.org/10.3390/jcm7080214

107. Taktak A, Hakan Demirkan T, Acar B, et al: Clinico-radiological correlation of nutcracker syndrome: A single centre experience. Arch Argent Pediatr 115:165-168, 2017. https://doi.org/10.5546/aap.2017.eng.165
108. Arthurs OJ, Mehta U, Set PA: Nutcracker and SMA syndromes: What is the normal SMA angle in children? Eur J Radiol 81:e854-e861, 2012. https://doi.org/10.1016/j.ejrad.2012.04.010
109. Sugimoto K, Fujita S, Miyazawa T, et al: Pediatric left renal vein entrapment syndrome diagnosed by 99mTc-albumin-conjugate scintigraphy. Nephron Clin Pract 122:122-126, 2012. https://doi.org/10.1159/000350814
110. Gill AE, Ciszak T, Braun H, et al: Intravascular ultrasound versus digital subtraction angiography: Direct comparison of intraluminal diameter measurements in pediatric and adolescent imaging. Pediatr Radiol 47:450-457, 2017. https://doi.org/10.1007/s00247-016-3771-z
111. Erben Y, Gloviczki P, Kalra M, et al: Treatment of nutcracker syndrome with open and endovascular interventions. J Vasc Surg Venous Lymphat Disord 3:389-396, 2015. https://doi.org/10.1016/j.jvsv.2015.04.003
112. Wu Z, Zheng X, He Y, et al: Stent migration after endovascular stenting in patients with nutcracker syndrome. J Vasc Surg Venous Lymphat Disord 4:193-199, 2016. https://doi.org/10.1016/j.jvsv.2015.10.005
113. Zhang H, Li M, Jin W, et al: The left renal entrapment syndrome: Diagnosis and treatment. Ann Vasc Surg 21:198-203, 2007. https://doi.org/10.1016/j.avsg.2006.10.021
114. Chen S, Zhang H, Shi H, et al: Endovascular stenting for treatment of nutcracker syndrome: Report of 61 cases with long-term follow-up. J Urol 186:570-575, 2011. https://doi.org/10.1016/j.juro.2011.03.135
115. Ullery BW, Itoga NK, Mell MW: Transposition of the left renal vein for the treatment of nutcracker syndrome in children: A short-term experience. Ann Vasc Surg 28:1938-e5-8, 2014. https://doi.org/10.1016/j.avsg.2014.07.022
116. Shintaku N, Takahashi Y, Akaishi K, et al: Entrapment of left renal vein in children with orthostatic proteinuria. Pediatr Nephrol Berl Ger 4:324-327, 1990
117. Brandenburg V, Floege J: [Early diagnosis of chronic kidney disease. New insights into creatinine and proteinuria]. Med Klin 101(Suppl 1):158-162, 2006
118. de Jong PE, Brenner BM: From secondary to primary prevention of progressive renal disease: The case for screening for albuminuria. Kidney Int 66:2109-2118, 2004. https://doi.org/10.1111/j.1523-1755.2004.66001.x
119. Ha T-S, Lee E-J: ACE inhibition can improve orthostatic proteinuria associated with nutcracker syndrome. Pediatr Nephrol Berl Ger 21:1765-1768, 2006. https://doi.org/10.1007/s00467-006-0206-3