Peer Review File

Article information: https://dx.doi.org/10.21037/tp-23-215

Reviewer A

Comment 1: *I would be curious to know what happened to the 1 patient w/ NF-1 follow PTA.*

Reply 1: Thank you for your comment. As the only patient diagnosed with NF-1 in this study, his course of disease is indeed remarkable. Restenosis occurred 10 months after first PTA and then treated with stenting implantation. In-stent restenosis (ISR) occurred 8 months later. PTRA was then performed for the ISR lesion, and no stenosis was present at last follow-up. The SBPR and DBPR in the NF-1 patient were controlled to 0.89 and 0.85 under 2 antihypertensive drugs at the last follow-up. We added related content (see Page 10, line 193-196).

Changes in the text:

The remaining restenosis lesion was seen in the NF-1 patient in 10 months after the first PTA and then treated with stent implantation. In-stent restenosis (ISR) occurred 8 months later. (see Page 10, line 193-196)

Reviewer B

Comment 1:

Why were only patients with >60 % stenosis on DSA included. What happened to the patients with <60 % stenosis. Were intravascular pressure measurements performed?

Reply 1:

Thank you for your comment.

Due to the small number of the patients, there has been no consensus on the threshold of intervention for the severity of pediatric renal artery stenosis. Some literature suggests intervention as long as stenosis occurs (*Lee Y, Lim YS, Lee ST, Cho H. Pediatric renovascular hypertension: Treatment outcome according to underlying disease. Pediatr Int. 2018 Mar;60(3):264-269. doi: 10.1111/ped.13491. Epub 2018 Feb 26. PMID: 29281158.*), while some literature suggests intervention only if stenosis ≥ 70% (*Zhu G, He F, Gu Y, Yu H, Chen B, Hu Z, Liang W, Wang Z. Angioplasty for pediatric renovascular hypertension: a 13-year experience. Diagn Interv Radiol. 2014 May-Jun;20(3):285-92. doi: 10.5152/dir.2014.13208. PMID: 24675165; PMCID: PMC4463347.*). According to the latest review, "angioplasty is the most common intervention and can be performed even in small children in vessels with mild to severe stenoses" (*Patel PA, Cahill AM. Renovascular hypertension in children. CVIR Endovasc. 2021 Jan 7;4(1):10. doi: 10.1186/s42155-*

020-00176-5. PMID: 33411105; PMCID: PMC7790992.). Based on experiences with adult RAS, revascularization was only considered for children with hemodynamically severe stenosis in our center. Also referring to previous research, PTRA was performed only in children with stenosis ≥ 60% (*Guo J, Wu S, Zhang F, Zhang C, Gu Y, Guo L. Long-term outcomes of angioplasty for pediatric renovascular hypertension: A single-center experience. Vascular. Epub 2021 Nov 30.*). We added related content (Page 12, line 235-236).

For hypertension children with mild renal artery stenosis, careful follow-up was insisted, monitoring ultrasonic image of renal artery, RAAS system (renin-aldosterone) and medical therapy to gain well BP control. We added related content (Page 12, line 236-238).

Translesional pressure gradient is very helpful in identifying hemodynamically RAS. However, translesional pressure gradient for children is not regularly performed in our center. On the one hand, pressure gradients across stenosis were not measured because of the small size of the pediatric vasculature. On the other hand, pressure wire is costly and only partly covered by health insurance based on local policies. We added related content (Page 7, line 114-115).

Changes in the text:
Based on the previous literature standards and multidisciplinary team decision, PTRA was performed in pediatric patients with stenosis ≥60% in our center (1,19). (Page 12, line 235-236)

For hypertension children with mild renal artery stenosis, careful follow-up was insisted, monitoring ultrasonic image of renal artery, renin-angiotensin-aldosterone system and medical therapy to gain well BP control. (Page 12, line 236-238)

Intravascular pressure measurements were not performed mainly due to the small size of the pediatric vasculature. (Page 7, line 114-115)

Comment 2:
Line 114 on - severe residual stenosis requiring bailout stent was considered 50% however technical success is considered residual stenosis <30%. The stented patients should be considered technically unsuccessful angioplasty. It may be a 'cleaner' data set if the stented patients are removed (3).
Reply 2:

Thank you for your valuable suggestions. We agreed with your opinion. The stented patients should be considered technically unsuccessful angioplasty. As a result, we modified our text as advised, especially for the part of the definition of technical success and technical success rate.

Changes in the text:

Technical success was achieved in 33 of 37 (89.2%) patients and 40 of 45 (88.9%) lesions, without surgery-related complications. (Page 2, line 31)

Technical success was characterized as a residual stenosis ≤30% on angiography after balloon dilation. In patients with severe residual stenosis (>50%), which were considered as technically unsuccessful angioplasty, bailout stent selection was made at the surgeon's discretion. (Page 6, line 111-114)

For treatment, 43 lesions were treated with balloon dilation, and in 3 lesions, balloon dilatation was followed by stent implantation due to severe residual stenosis (>50%). The technical success rate was 88.9% (40/45). (Page 9, line 169-170)

Comment 3:

Flow limiting dissection requiring stent insertion should be considered a complication given that previous publications suggest stenting renal arteries in children results in a worse outcome (in terms of frequency and number of re-interventions required).

Reply 3:

Thank you for your comment. For treatment, balloon dilatation was followed by stent implantation in 3 lesions. All 3 lesions presented severe residual stenosis (>50%) and no flow-limiting dissection after ballooning was found. We defined flow limiting dissection requiring stent insertion as a complication. We have modified our text.

Changes in the text:

In patients with severe residual stenosis (>50%), which were considered as technically unsuccessful angioplasty, bailout stent selection was made at the surgeon's discretion. (Page 6, line 112-114)

Complications including renal arterial rupture, embolization, dissection or aneurysm were recorded. (Page 8, line 140-141)

Comment 4:

Line 129 - to eliminate influence of natural kidney growth, a ratio of kidney length pre and post procedure has been used. It is unclear how this eliminates the influence of natural growth as this ration would increase with natural growth. Please use ratio of age based centile pre and post intervention (this can be easily calculated for example by using an online Pediatric Kidney Size Percentile Calculator such as at https://radiology-universe.org/calculator/pediatric-kidney-sizes/calculator.php). This would provide a much better reflection of 'catch up growth' post intervention.

Reply 4:

Thank you for your valuable advice. The ratio of age based centile pre and post intervention is essential for assessing changes in kidney length. We have modified our text as advised.

Changes in the text:

To compare with natural physical development of kidneys in healthy children, the kidney length ratio (KLR) of age-based percentile pre and post intervention, which was presented as percentile value, was calculated (28). (Page 7, line 128-133)

The mean kidney length and KLR increased from 8.89 ± 1.55 cm and 29.47 ± 17.28 % before the procedure to 9.79 ± 1.51 cm (t = -5.50, P < 0.001) and 40.13 ± 11.37 % (t = -3.56, P = 0.001) at 18-month (range, 4-104 months) follow-up after initial PTRA. (Page 11, line 208-210)

By restoring renal blood flow, the affected kidneys were significantly enlarged, with improved KLR percentile value. The increased length of the kidney after PTRA predicts the recovery of parenchyma and the long-term preservation of renal function. (Page 14, line 284-285)