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ORIGINAL ARTICLE

Intravascular ultrasound versus digital subtraction angiography: direct comparison of intraluminal diameter measurements in pediatric and adolescent imaging

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Abstract

Background Intravascular ultrasound (IVUS) allows intraluminal imaging of blood vessels rather than the one-dimensional luminal outline depicted by digital subtraction angiography (DSA). Despite extensive literature in multiple adult vascular diseases, IVUS has not been directly compared to DSA in pediatric and adolescent vascular pathologies.

Objective The purpose of this manuscript is to compare absolute luminal diameter measurements obtained via IVUS and DSA during a variety of pediatric endovascular procedures.

Materials and methods We conducted a retrospective review of all pediatric and adolescent endovascular procedures from October 2014 to March 2016 in which IVUS and DSA were used. We compared the vessel diameter measurements and analyzed them using SAS software with a paired *t*-test.

Results There were 102 total measurements (DSA = 56; IVUS = 56; 22 procedures; 20 patients). On average, IVUS measured 0.6 ± 2.1 mm larger than DSA (95% confidence interval [CI] −0.01 to 1.12; $P = 0.06$; $r = 0.90$). When venous compression syndrome (May–Thurner, Nutcracker, superior vena cava syndrome) measurements were excluded, IVUS measured 0.7 ± 1.6 mm larger than DSA (95% CI 0.14 to 1.18; $P = 0.01$; $r = 0.93$). When venous compression syndrome measurements were evaluated separately, IVUS measured 0.3 ± 3.0 mm larger than DSA (95% CI −1.16 to 1.82; $P = 0.65$; $r = 0.45$).

Conclusion Overall, IVUS measurements were slightly larger than DSA measurements in all data subsets. Absolute vessel diameter measurements obtained with IVUS in the pediatric and adolescent population are statistically significantly larger than those obtained using DSA when excluding venous compression syndromes. In venous compression syndromes, IVUS might provide a more accurate representation of vessel compression and diameter than DSA.

Keywords Children · Digital subtraction angiography · Intravascular ultrasound · Measurement · Venous compression syndromes

Introduction

Intravascular ultrasound (IVUS) allows luminal and transmural imaging of blood vessels rather than the outline of the vessel lumen depicted by traditional digitally subtracted angiography (DSA) [1]. Certain features of IVUS are potentially appealing for pediatric interventional radiologists. Specifically, IVUS allows pediatric interventional radiologists to measure two-dimensional intraluminal vessel diameter and lesion length and evaluate stent apposition following deployment without the use of ionizing radiation. Additional potential safety benefits include reduction in volume of intravascular contrast agents and fewer digitally subtracted fluoroscopic angiograms.

Despite its promise, IVUS has not been directly compared to DSA, the gold standard in pediatric and adolescent vascular imaging. Separate evaluation of IVUS in children and teens is particularly important because pediatric vascular diseases are different from those more commonly encountered in adults. More specifically, atherosclerosis — for which IVUS has been

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used most extensively to evaluate and treat adults — is exceedingly uncommon in children. In the pediatric and adolescent population, rather, IVUS has the potential to aid in treatment of vascular compression syndromes, post-transplant anastomotic stenoses, and a variety of other pediatric vascular diseases.

The purpose of this study was to compare absolute luminal diameter measurements obtained via IVUS and DSA during a variety of pediatric/adolescent endovascular procedures and discuss potential implications for balloon, stent and coil sizing. This analysis is warranted because the type of image used for measurements obtained with IVUS (2-D intravascular image) is different from a single-plane image obtained with DSA.

Materials and methods

Our institutional review board approved this retrospective review of all procedures with IVUS and DSA, using data from both the imaging archive and electronic medical record, from October 2014 (when IVUS was first used) through March 2016 at a single tertiary care pediatric hospital. All patients consented for IVUS. We assessed vascular diseases and imaged vessels (Table 1). Both pre- and post-intervention (if performed) measurements were obtained, via both modalities, in the areas of interest (Table 2). Additionally, if a stenosis was detected, measurements of the normal vessel diameter were obtained via both modalities. DSA vessel diameter measurements were obtained by intra-procedural measurement on a dedicated angiography workstation (Interventional Tools 8.3.1; Philips Healthcare, Amsterdam, The Netherlands) in the interventional radiology suite using Philips auto-calibration, or post-procedurally on a picture archiving and communication system via manual calibration with imaged endovascular catheters or sheaths. The fluoroscopy unit was calibrated daily as part of routine quality control. DSA measurements obtained during the procedure were considered final. All post-procedural DSA measurements (obtained via manual calibration) were reviewed by two interventional radiologists (C.M.H., with 4 years, and A.E.G., with 2 years of experience) for accuracy and were obtained in the same region of the vessel as the accompanying IVUS measurements. A third radiologist resolved any discrepancies. Vessel diameter measurements were obtained via IVUS during the procedure by cross-sectional luminal measurement or circumferential tracing of the vessel lumen. The IVUS system does not require routine calibration. The largest measured diameter for each modality was used for comparison (Fig. 1). A single attending pediatric interventional radiologist performed all procedures included in this analysis (C.M.H., 4 years of experience).

Statistical analysis

Measurements from both modalities yielded percentage and absolute differences that were statistically analyzed using SAS software (version 9.3 for Windows; SAS Institute, Cary, NC). We conducted a paired *t*-test to compare the IVUS and DSA measurements. We analyzed data on three measurement cohorts: all IVUS and DSA vessel measurements ($n=102$), IVUS and DSA vessel measurements with venous compression syndrome data removed ($n=84$), and IVUS and DSA vessel measurements of venous compression syndromes alone ($n=18$).

Procedural technique

Digital subtraction angiography of the vessel of interest was performed first, at either two or three frames per second. If a stenosis was observed, intra-procedural measurements of the normal and narrowed segments were obtained. Otherwise a single measurement of the normal vessel was obtained. IVUS was then performed by pulling the IVUS catheter back through the vessel of

Table 1 Disease processes and vessels imaged with both intravascular ultrasound (IVUS) and digital subtraction angiography (DSA)

Disease process	Number evaluated	Vessels imaged with IVUS	Number of vessels imaged
Liver transplant (8)			
Portal vein stenosis	5	Portal vein	5
Hepatic artery stenosis	2	Hepatic artery	2
Hepatic vein stenosis	1	Hepatic vein	1
Renal artery stenosis	5	Main renal artery	6
		2nd/3rd-order renal artery	3
May–Thurner syndrome	4	Common iliac vein	4
Nutcracker syndrome	3	Left renal vein	3
SVC syndrome	1	Superior vena cava	1
Subclavian-to-brachial artery bypass graft stenosis	1	Subclavian artery	1
		Brachial artery	1

SVC superior vena cava

Table 2 All diameter measurements from 20 patients evaluated with IVUS and DSA

Pathology	Measurement	IVUS (mm)	DSA (mm)	Absolute difference (mm)	Measurement characteristics[a]
RAS	1	4.9	3.4	1.5	normal artery
	2	2.6	1.3	1.3	stenosis-pre
	3	2.7	2.6	0.1	stenosis-post
RAS	1	3.5	2.7	0.8	normal artery
RAS	1	4	3.8	0.2	normal artery
	2	3.7	3.2	0.5	normal artery
RAS	1	5.9	3.7	2.2	normal artery
	2	1.7	1.3	0.4	stenosis-pre
	3	3	2.1	0.9	stenosis-post
RAS	1	3.9	2.8	1.1	normal artery
	2	2	0.8	1.2	stenosis-pre
MTS	1	9.1	7.3	1.8	stenosis-pre
	2	15.3	14.9	0.4	stenosis-post
MTS	1	12.7	12.5	0.2	normal vein
	2	10.6	9.7	0.9	stenosis-pre
	3	12.6	11.8	0.8	stenosis-post
MTS	1	9.5	12.4	−2.9	normal vein
MTS	1	14.9	20	−5.1	normal vein
	2	10.7	13.1	−2.4	stenosis-pre
	3	11.2	11.5	−0.3	proximal stent
	4	13	13.8	−0.8	distal stent
HAS	1	7.2	5.7	1.5	normal artery
	2	6.5	5.4	1.1	normal artery
HAS	1	3.7	3.3	0.4	normal artery
	2	2.1	1.7	0.4	stenosis-pre
	3	3.8	2.4	1.4	stenosis-post
NS	1	8	12.4	−4.4	normal vein
	2	13.6	10.2	3.4	stenosis-pre
NS	1	11.7	9.6	2.1	normal vein
	2	12.5	5.3	7.2	stenosis-pre
NS	1	12.4	10.5	1.9	normal vein
	2	14.3	16.4	−2.1	stenosis-pre
	3	12.4	9.8	2.6	peripheral stent
	4	15	12.4	2.6	stenosis-post
HVS	1	9.1	9.7	−0.6	normal vein
SVCS	1	12.2	7.4	4.8	normal vein
	2	9	4.4	4.6	stenosis-pre
PVS	1	12.6	12.6	0	normal vein
	2	11.9	11.2	0.7	normal vein
PVS	1	14.6	18.6	−4	normal vein
	2	3.5	5	−1.5	stenosis-pre
	3	12.3	13.4	−1.1	stenosis-post
	4	13.6	14.1	−0.5	normal vein post
PVS	1	10.6	10	0.6	normal vein
	2	2	3.3	−1.3	stenosis-pre
	3	8.6	11.1	−2.5	stenosis-post

Table 2 (continued)

Pathology	Measurement	IVUS (mm)	DSA (mm)	Absolute difference (mm)	Measurement characteristics[a]
PVS	1	12.9	10.6	2.3	normal vein
	2	4.7	4.3	0.4	stenosis-pre
	3	8.5	7.2	1.3	stenosis-post
PVS	1	10	9	1	normal vein
	2	5.8	6	−0.2	stenosis-pre
	3	9.4	8.8	0.6	normal vein post
	4	9.9	8.5	1.4	stenosis-post
Subclavian artery graft	1	6.1	4.1	2	Normal artery (graft)
	2	3.3	2	1.3	stenosis-pre
	3	4.3	3.6	0.7	stenosis-post

DSA digital subtraction angiography, *HAS* hepatic artery stenosis, *HVS* hepatic vein stenosis, *IVUS* intravenous ultrasound, *MTS* May–Thurner syndrome, *NS* Nutcracker syndrome, *PVS* portal vein stenosis, *RAS* renal artery stenosis, *SVCS* superior vena cava syndrome

[a] The last column clarifies the characteristic of the measured vessel (normal artery/vein or stenosis) and whether the measurement was performed at the area of greatest luminal narrowing before (stenosis-pre) or after (stenosis-post) an intervention

interest over a wire [2]. The size of the IVUS catheter (Volcano; Philips Healthcare, Amsterdam, The Netherlands) was determined by the type and size of the vessel imaged and the disease process. The 0.014” 3.5-French monorail catheter (imaging radius = 20 mm) was used in arterial evaluation (minimum sheath = 4 F). The 0.018” 3.5-F monorail catheter (imaging radius = 24 mm) was used in portal vein and hepatic vein evaluation (minimum sheath = 6 F). The 0.035” 8.2-F over-the-wire catheter (imaging radius = 60 mm) was used in the inferior vena cava, common iliac and renal vein evaluation (minimum sheath = 9 F). The sheath size required for the planned procedure was not impacted by the use of IVUS.

Following intervention (if performed), IVUS was performed first via the same pull-back technique over the wire [2]. Following IVUS evaluation, DSA (2–3 frames per second) was performed through a sheath with the wire still in place or through a diagnostic catheter.

Results

There were 112 total measurements (DSA = 56; IVUS = 56) obtained during 22 procedures on 20 patients (median age 14.5 years; range 3–18 years).

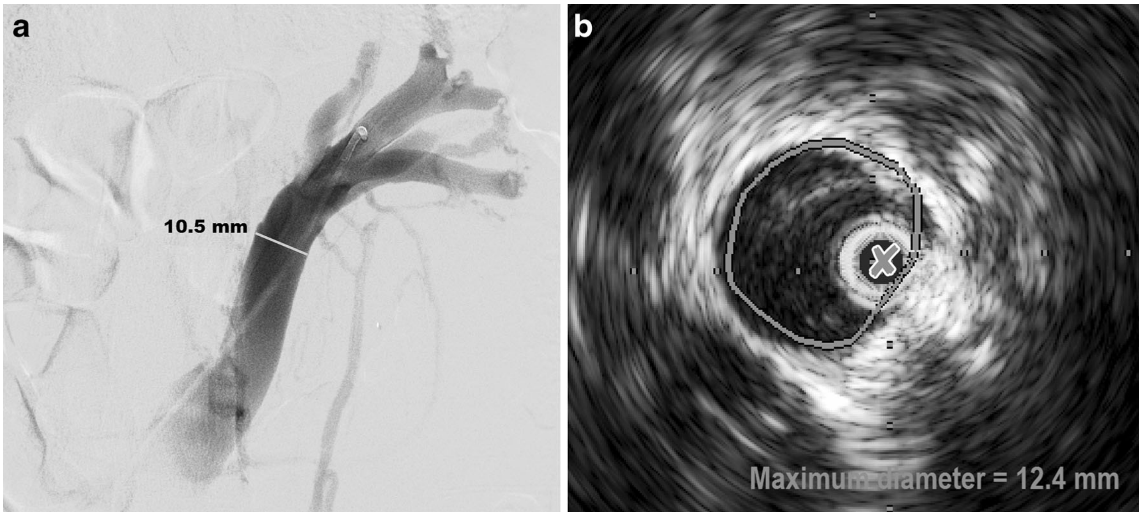

Fig. 1 Measurement techniques. **a**, **b** Digital subtraction angiography (DSA; **a**) and intravenous US (IVUS; **b**) images demonstrate measurement techniques in the left renal vein in a 18-year-old man with a single retroaortic left renal vein resulting in Nutcracker syndrome. Note the collateral draining vessels on initial angiogram and lack of contrast agent draining into the inferior vena cava. The measurement on DSA (10.5 mm) correlates with a maximum diameter of 12.4 mm on IVUS. Note the IVUS transducer (*X*)

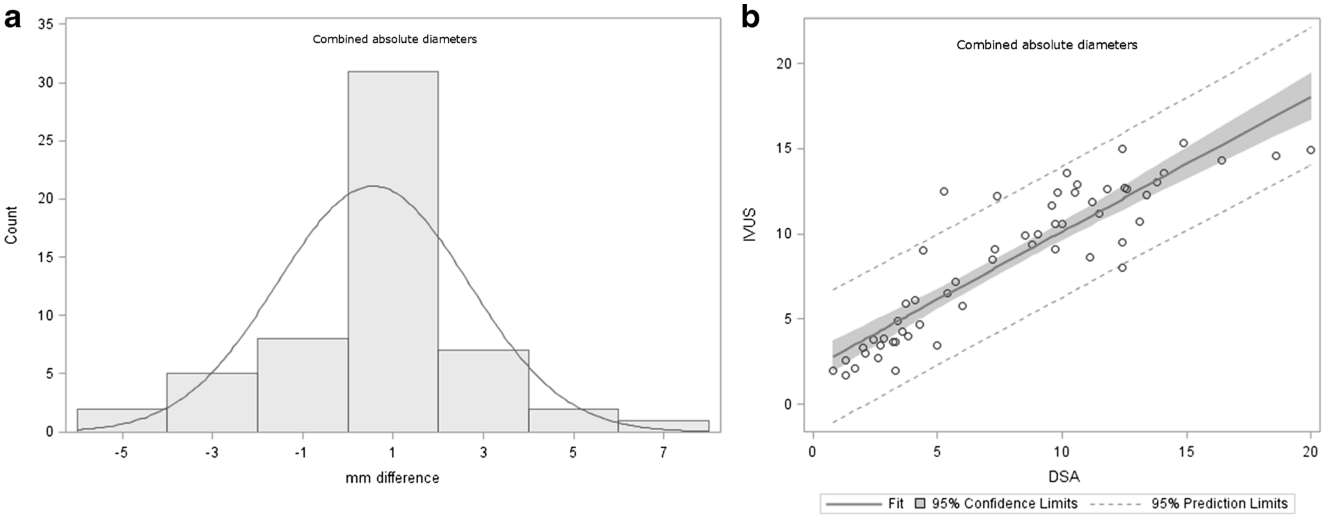

Fig. 2 Absolute diameter measurements. **a** All intravenous US (IVUS) and digital subtraction angiography (DSA) absolute diameter measurements are plotted as distribution of difference. **b** All IVUS and DSA measurements are modeled with a fit plot ($r = 0.90$)

On average, IVUS measured the vessel diameter 0.6 ± 2.1 mm larger than DSA (95% CI −0.01 to 1.12; $P = 0.06$; $r = 0.90$; Fig. 2).

Repeat analysis was performed on a subset of 84 measurements obtained from all vascular pathologies not including venous compression syndromes. This subset analysis demonstrated a mean difference of IVUS measuring 0.7 ± 1.6 mm larger than DSA (95% CI 0.14 to 1.18; $P = 0.01$; $r = 0.93$; Fig. 3).

Analysis of an additional subset of measurements obtained during evaluation and treatment of venous compression syndromes (May–Thurner, Nutcracker, and superior vena cava syndrome) demonstrated an average difference of 0.3 ± 3.0 mm, where IVUS still measured larger than DSA (95% CI −1.16 to 1.82; $P = 0.65$; $r = 0.45$; Fig. 4).

Discussion

This retrospective analysis compares vessel diameter measurements obtained with IVUS as compared to DSA (gold standard) in pediatric and adolescent vascular diseases. For all measurements, IVUS measured vessel diameters 0.6 ± 2.1 mm larger than DSA (95% CI −0.01 to 1.12; $P = 0.06$;

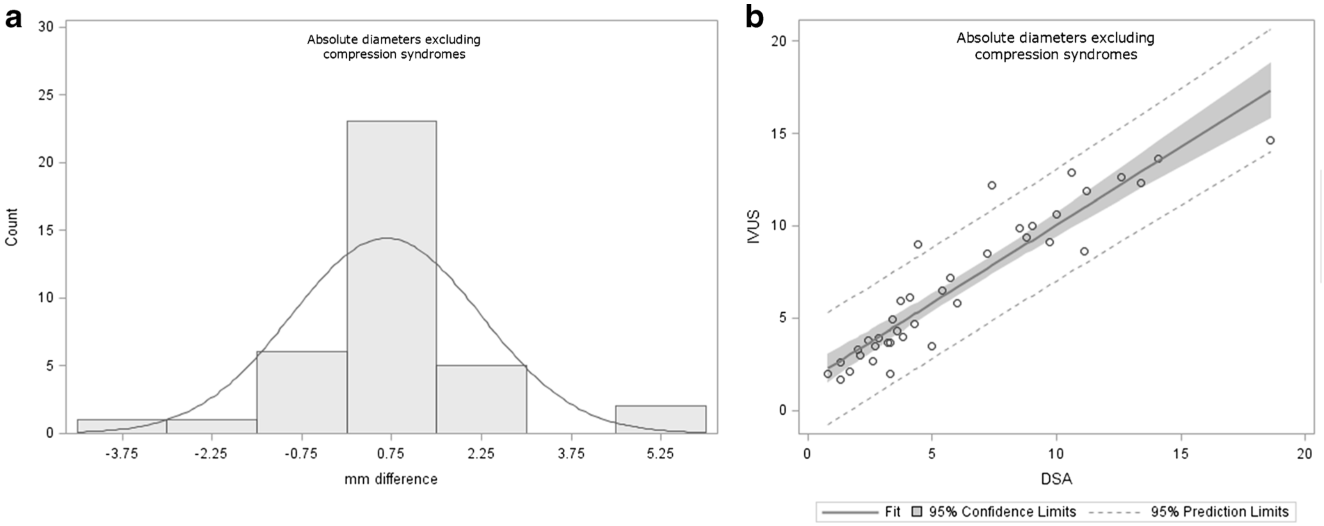

Fig. 3 Diameter measurements excluding venous compression syndromes. **a** Intravenous US (IVUS) and digital subtraction angiography (DSA) absolute vessel diameters excluding measurements from venous compression syndromes are plotted as distribution of difference. **b** IVUS and DSA measurements excluding measurements from venous compression syndromes are modeled with a fit plot ($r = 0.93$)

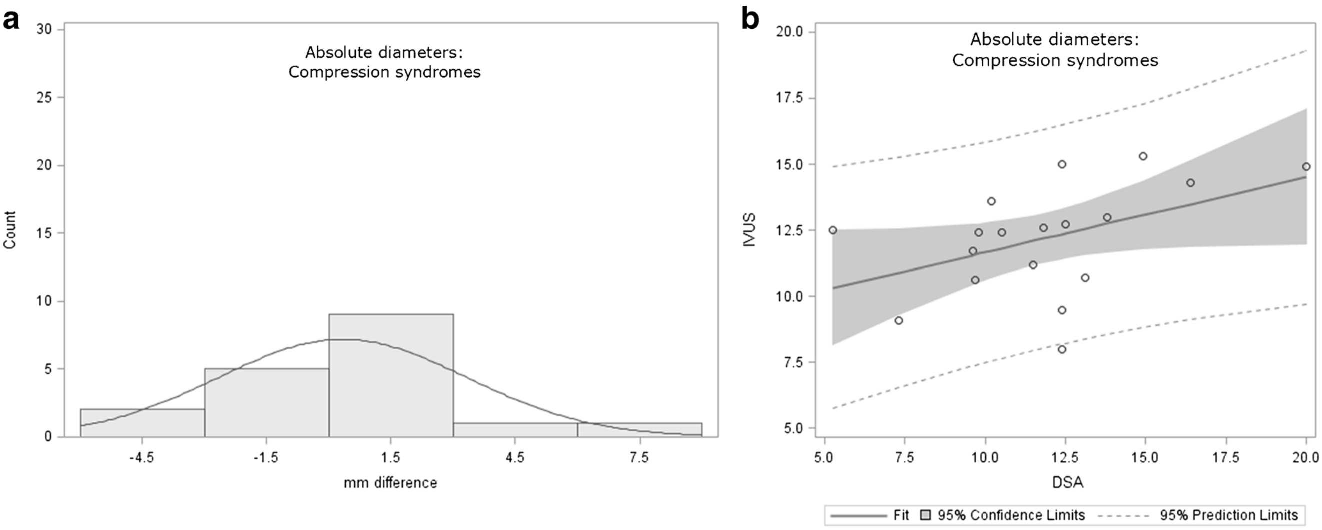

Fig. 4 Diameter measurements of venous compression syndromes. **a** Intravenous US (IVUS) and digital subtraction angiography (DSA) absolute vessel diameters of the venous compression syndromes (May–Thurner syndrome, Nutcracker syndrome and superior vena cava syndrome) are plotted as distribution of difference. **b** IVUS and DSA measurements of the venous compression syndromes are modeled with a fit plot ($r = 0.45$)

$r = 0.9$). When venous compression etiologies were removed from the analysis, the vessel diameter measurements obtained via IVUS were 0.7 ± 1.6 mm larger than DSA (95% CI 0.14 to 1.18; $P = 0.01$; $r = 0.93$], which was statistically significant. This is the first study directly comparing absolute intraluminal vessel measurements obtained from these modalities in a pediatric and adolescent population.

The statistically significant difference, albeit small (0.7 ± 1.6 mm), between IVUS and DSA is seen in the data subset not including venous compression syndromes. This can be explained by the wide variability in venous compression measurements by DSA, which are represented as outliers in our data set (both the minimum and maximum differences in diameter measurements were obtained in venous compression cases, and as such significantly alter our data analysis). The improved P-value of 0.01 and strong linear correlation (0.93) from the subset where venous compression cases were removed exemplify this fact. The clinical significance of this difference (0.7 mm) is likely negligible, although unknown.

The slightly larger measurements obtained via IVUS likely resulted from incorporation of the vessel wall — which is not visible on traditional DSA — in the measured diameter. This difference might also be accounted for by the 2-D images of DSA, and thus more accurate measurements might be obtained using maximal diameter shown by IVUS. Additionally, in certain instances when imaging very small vessels (such as second- and third-order renal arteries), the catheter was occlusive to the vessel, which might have artificially increased the diameter of the vessel by slight luminal expansion from the IVUS catheter.

Prior peer-reviewed literature addressing the accuracy of IVUS has primarily focused on the use of the device for imaging and intervening in carotid arteries, aortic dissections, aortic grafts and limited venous interventions [1, 3]. One study sought to quantify the discrepancy between IVUS and DSA in adult venous interventions and found that DSA underestimated the percentage of stenosis by 30% [4]. Interestingly, these authors stated that venous compression was not always apparent on DSA because of the planar compression [4]. The authors compared percentage stenosis measured by each modality rather than absolute diameter measurements [4]. Because these measurements are often used to guide selection of appropriate-size balloons, stents and coils, we used absolute size measurements (rather than percentage stenosis measurements) in our analysis.

Measurements obtained for venous compression syndromes, such as May–Thurner syndrome and Nutcracker syndrome, had the poorest correlation between IVUS and DSA and warrant separate discussion. For these diseases, the average difference between measurements obtained via DSA and IVUS was 0.3 ± 3.0 mm (95% CI −1.16 to 1.82; $P = 0.65$; $r = 0.45$). The literature has described the difficulties in accurately assessing planar compression of veins with 2-D imaging, such as DSA [5]. Neglén and Raju [4] described a decrease in the venous luminal diameter and circular area after dilation or stenting because the vessel reverts to a more circular shape. Others have suggested that IVUS is the most sensitive and dynamic imaging modality available when treating May–Thurner syndrome and other vascular compression syndromes [5–9]. IVUS also has the benefit of demonstrating the intraluminal webs and spurs, and the exact point where the over-riding vessel causes maximal compression (Fig. 5). Our experience confirms these benefits because external compression in both May–Thurner and Nutcracker syndromes was readily apparent using IVUS but was much more conspicuous with DSA. A recently published article suggests that cone beam CT is an adequate substitution for IVUS to evaluate stent apposition [10]. However because of the increased radiation dose from cone beam CT, IVUS might be preferred in the pediatric population.

Furthermore the venous compression syndrome subset analysis demonstrated a wider standard deviation and poorer correlation of data points when comparing IVUS and DSA diameter measurements. This finding, in combination with work from prior investigators, further suggests that IVUS is superior to DSA when evaluating and treating venous compression syndromes.

Last, IVUS offers additional potential safety benefits for pediatric patients: less intravascular contrast agent and decreased radiation exposure. As operators become accustomed to the very small diameter measurement differences between the two modalities, as indicated by the data presented in this manuscript, pre- and post-intervention DSA might be eliminated. In our current practice, initial DSA is still performed to evaluate for areas of disease. However following stent deployment and angioplasty (when performed), IVUS alone is used to evaluate response to angioplasty or stent apposition (Fig. 5). This subsequently reduces radiation exposure to the operator and the child and also decreases intravascular contrast dose. The radiation and contrast dose reduction is entirely dependent on the size of the imaged vessel and the patient size and vessel location.

There are a number of limitations to this study, including a small patient population at a single institution and its retrospective nature. Additionally the vascular conditions evaluated in the study are relatively rare, which makes it difficult to study a larger cohort of a single disease and also makes it challenging to predict the number of children in whom IVUS would be used in pediatric interventional radiology practice. In this study the two most common conditions imaged with both IVUS and DSA were post-liver-transplant sequelae (8) and renal artery stenosis (5). However the use of IVUS is likely to be substantially influenced by geographic and practice-specific variables. Last, a single attending physician performed all procedures and was not blinded during intra-procedural vessel diameter measurement. For example, the operator obtained DSA measurements before performing IVUS, so the previously obtained measurements might have biased the operator measuring the vessel diameter via IVUS. However it should be emphasized that DSA was performed first prior to interventions, and IVUS was performed first following interventions.

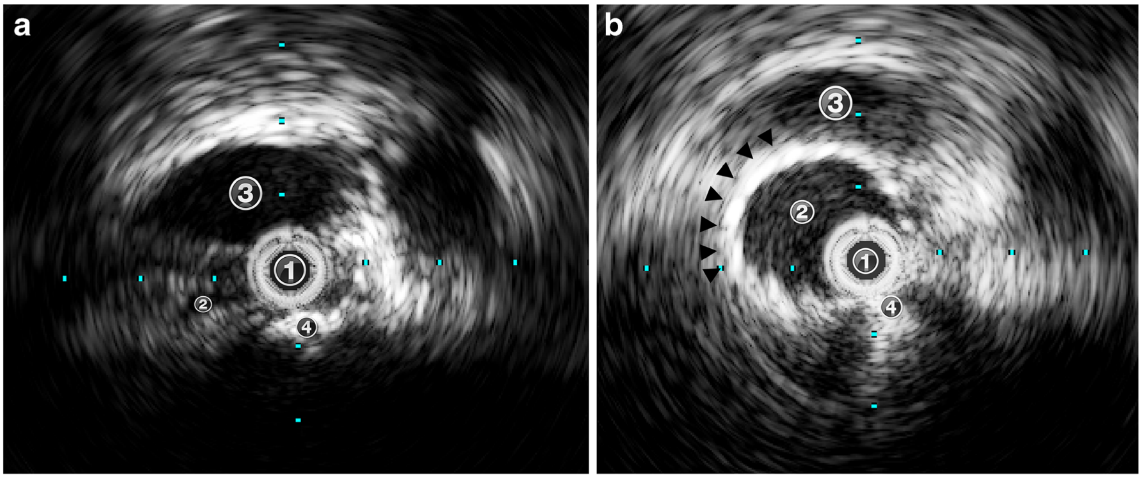

Fig. 5 IVUS post-procedure in a 16-year-old girl. **a** IVUS image with the transducer (*1*) within the compressed left common iliac vein (*2*) between the overlying right common iliac artery (*3*) and underlying lumbar vertebral body (*4*). **b** IVUS (*1*) demonstrates improved compression of the left common iliac vein (*2*) following stent (*arrowheads*) deployment with good stent apposition. The overlying right common iliac artery (*3*) and underlying lumbar vertebral body (4) are again seen. *IVUS* intravenous ultrasound

Conclusion

Absolute vessel diameter measurements obtained with IVUS in the pediatric population are statistically significantly larger (0.7 ± 1.6 mm [95% CI 0.14 to 1.18; $P = 0.01$; $r = 0.93$]) than those obtained via DSA when excluding venous compression syndrome data. The implications of these findings related to sizing of balloons, stents and coils are unknown. In the setting of vascular compression syndromes, the data suggest that IVUS provides a more accurate representation of vessel compression and diameter than DSA. Last, as users become more accustomed to IVUS, there is potential for radiation reduction and decreased volume of intravascular contrast agent.

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Compliance with ethical standards

Conflicts of interest None

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