Multi-slice computed tomographic angiography for stenosis detection in forearm hemodialysis arteriovenous fistulas

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Abstract: ***Purpose:*** **A method of diagnosing the extent and severity of arteriovenous fistula (AVF) stenoses is multi-slice computed tomographic angiography (MS-CTA). The aim of this prospective study was to assess the accuracy of MS-CTA for the detection and grading of stenoses in AVF in comparison to digital subtraction angiography (DSA), which was used as the gold standard of reference.**
Methods: **Fifteen hemodialysis (HD) patients with dysfunctioning forearm AVF were included. These AVFs were evaluated by both DSA and MS-CTA and were read in a prospective, blinded manner by two radiologists experienced in vascular imaging.**
Results: **ROC analysis revealed areas under the curve of 0.90 ± 0.07 for observer I and 0.87 ± 0.08 for observer II at a stenosis cut-off level of ≥50% diameter reduction. The combined results for MS-CTA showed sensitivity, specificity and positive and negative predictive values of 82%, 98%, 82% and 98% for stenoses ≥50% and 71%, 99%, 77% and 98% for stenoses ≥75%. Inter-observer agreement for the detection of stenoses ≥50% diameter reduction was 0.70 and 1.0, for MS-CTA and DSA, respectively.**
Conclusion: **MS-CTA can provide good visualization of forearm HD access AVF and has moderate sensitivity, but high specificity for the detection of flow-limiting stenoses. (J Vasc Access 2008; 9: 278-84)**

Key words: *Hemodialysis access, Arteriovenous fistula, Multi-slice computed tomographic angiography, Digital subtraction angiography, Stenosis detection*

INTRODUCTION

Patients with end-stage renal disease depend on a well-functioning arteriovenous fistula (AVF) for hemodialysis (HD) treatment. However, the most important complication of AVFs is thrombotic occlusion due to intimal hyperplastic stenoses, eliminating blood flow (1). Access monitoring, by flow measurement, with the purpose of early detection and pre-emptive intervention of these stenoses has proved to be beneficial to diminish thrombosis and improve patency rates (2). In current clinical practice, vascular access stenosis detection and grading are usually performed using duplex ultrasonography and digital subtraction angiography (DSA). Analysis of the DSA images can be difficult due to vessel overlap, in particular at the level of the anastomoses, where multiple vessels may cross. An alternative method of diagnosing the extent and severity of AVF stenoses is multi-slice computed tomographic angiography (MS-CTA). MS-CTA offers the ability to acquire three-dimensional (3D) data sets, which may potentially solve the problem of vessel overlap and increase the diagnostic accuracy. To date, the experience with MS-CTA for the imaging of stenoses and the diagnosis of access malfunction has been limited (3-6).
The aim of this prospective study was to assess the accuracy of MS-CTA for the detection and grading of stenoses in AVF in comparison to DSA, which was used as the gold standard of reference.

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PATIENTS AND METHODS

Patients

In this study, 15 consecutive hemodialysis (HD) patients (12 males, 3 females; mean age 55 yrs; range 26-75 yrs) with failing AVF were included. All patients had a forearm AVF (seven radial-cephalic and eight prosthetic forearm loop grafts). The mean dialysis vintage was 7.2 ± 2.3 months (range 4-14 months). In all radial-cephalic AVFs sufficient blood flow (≥250 mL / min) within 6 weeks after fistula creation was obtained; and therefore, they were considered as matured. Patients were only included when their forearm AVF was considered at risk for thrombosis. An AVF was considered at risk for thrombosis if absolute AVF at any time was <600 mL / min or if a patient exhibited a flow decline of >25% between two consecutive measurements in combination with an absolute flow of <1000 mL / min measured using an ultrasound dilution technique (Transonic® Systems Inc, Ithaca, NY) (2). In addition, study inclusion required DSA imaging within 3 weeks of MS-CTA.

All patients signed informed consent before they were enrolled in the study. The Medical Ethics Committee of the participating hospital approved this study, and all patients signed informed consent.

MS-CTA

MS-CTA was performed with a General Electric (Milwaukee, Wisc, USA) 4 slice CT scanner. An unenhanced scan with 2.5 mm collimation was obtained from axilla to wrist to cover the arteriovenous anastomosis, the inflow artery and the outflow vein. A 20 gauge intravenous catheter was inserted into a peripheral vein of the contralateral arm. By power injector, 100 ml preloaded non-ionic contrast (Ultravist 300, Schering, Berlin, Germany) was infused with a speed of 3 mL / sec. Bolus tracking (SmartPrep, GE Healthcare) was applied by selecting an engorged vessel proximal to the AVF with a threshold level of 120 H (6).

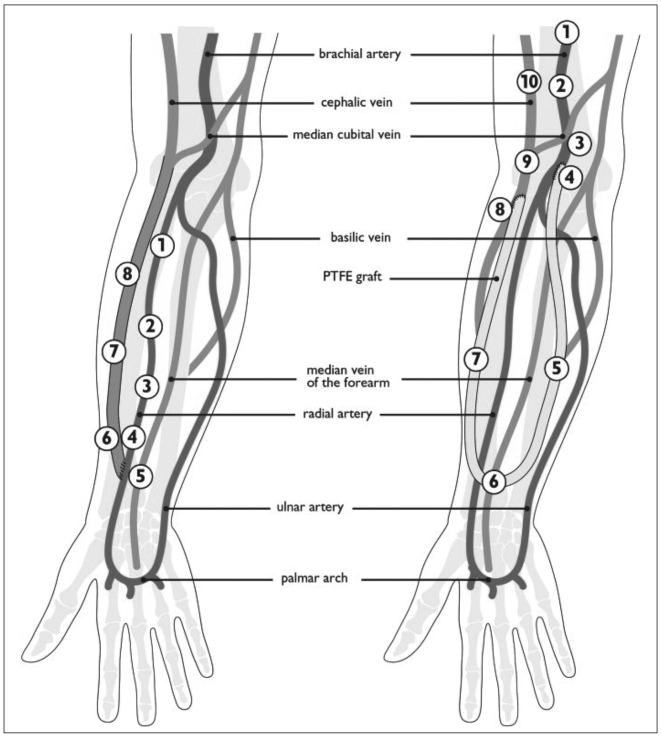
DSA

Experienced interventional radiologists performed all DSA examinations. Selective arteriograms were obtained by puncturing the AVF in a retrograde fashion with a 19-gauge needle. Images of the feeding artery, arterial anastomosis (in the case of prosthetic AVF), the AVF, venous anastomosis and efferent vein(s) were obtained by retrograde filling of the AVF with contrast material due to flow interruption, according to Staple (7). The amount of contrast medium used varied between 60 and 80 mL Iohexol (Visipaque; Nycomed-amersham, Oslo, Norway) and was administered in a variable number of runs. Contrast medium was administered with a power injector (Medrad, Indianola, PA). The number of contrast injections and view angles varied per patient and depended on the complexity of the vascular anatomy. If a stenosis ≥50% luminal diameter reduction was found on DSA imaging, subsequently, percutaneous transluminal angioplasty was performed. If no significant stenosis was found at DSA, CTA images were made available and compared with DSA images. Any significant lesions found on CTA and initially not visualized at DSA were then, if possible, depicted with DSA and, subsequently treated.

Image analysis

For image analysis purposes, all MS-CTA data sets were transferred to an off-line workstation (GE, Milwaukee, Wisc, USA), with dedicated post processing software. Review was done on the dynamic series, which exhibited the best selective AVF enhancement. The reviewers used real-time 3D volume rendering (SSD) and maximum intensity projection (MIP) and had the availability over source images when necessary. Stenosis measurements were carried out using an electronic caliper with an accuracy of 0.1 mm. DSA images were filmed and analyzed on the hard copies with a loupe and caliper.

MS-CTA and DSA images were read in random order, in a prospective, blinded manner by two radiologists experienced in vascular imaging. Between the two reads of the same patient, a period of at least 2 weeks elapsed. Both radiologists were not involved in either the DSA or MS-CTA procedures and were unaware of each other’s results and of results obtained with any other imaging modality (eg, duplex ultrasonography). Upper extremity vessels and AVF were subdivided into segments for analysis, which are shown in Figure 1 (8). In every segment, all visible vessel diameter reductions were measured. Stenoses were measured by dividing the luminal diameter that exhibited the highest grade of stenosis by the luminal diameter of the closest adjacent normal part of the vessel and classified on a 5-point scale (1 = 0-20%, 2 = 21-49%, 3 = 50-74%, 4 = 75-99%, 5 = occlusion). Diameter reductions ≥50% were considered hemodynamically significant (2). For analysis purposes, only the most severe stenosis per vessel segment was taken into account. In addition to the number and grading of stenoses, the MS-CTA and DSA images were also judged with respect to image quality on a 3-point scale (0 = non diagnostic, 1 = mediocre diagnostic, 2 = excellent diagnostic).



1 afferent artery > 10cm proximal from anastomosis
2 afferent artery 5-10 cm proximal from anastomosis
3 afferent artery 2-5 cm proximal from anastomosis
4 afferent artery < 2cm proximal from anastomosis
5 anastomosis
6 efferent vein < 2cm proximal from anastomosis
7 efferent vein 2-5cm proximal from anastomosis
8 efferent vein > 5cm proximal from anastomosis

1 afferent artery > 5cm proximal from arterial anastomosis
2 afferent artery 2-5cm proximal from arterial anastomosis
3 afferent artery < 2cm proximal from arterial anastomosis
4 arterial anastomosis
5 arterial part of the PTFE loop graft
6 middle part of the PTFE loop graft
7 venous part of the PTFE loop graft
8 venous anastomosis
9 efferent vein < 2cm proximal from venous anastomosis
10 efferent vein < 5cm proximal from venous anastomosis

Fig. 1 - ***Schematic overview of both AVF types with the different segmental subdivisions. On the left, the radiocephalic AVF is shown (divided into 8 segments), and on the right, the polytetraflourethylene (PTFE) loop graft AVF is shown (divided into 10 segments) (8).***

Fig. 2a - ***Semicoronal image obtained with MS-CTA of a radial-cephalic AVF, displayed a grade 4 stenosis in the efferent vein (arrow head).***
2b - ***Antero-posterior image obtained with DSA of the same radial-cephalic AVF displayed almost the mirror image of MS-CTA. Also the stenosis in the efferent vein (arrow head) is scored as a grade 4 stenosis.***

Statistical analysis

Upper extremity vessels and AVF were subdivided into segments for analysis (8). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each observer using DSA as the gold standard. The diagnostic properties of MS-CTA were evaluated using ROC analysis, in which the sensitivity of MS-CTA was plotted against the complement of specificity for different grades of stenosis. To assess the overall accuracy of MS-CTA compared to the standard of reference, areas under the curve were calculated for both observers (9). With the Wilcoxon signed ranks test (SPSS, version 10.1; SPSS Inc, Chicago, IL), any differences between MS-CTA and DSA in image quality were analyzed on patient level. To determine interobserver agreement with regard to stenosis detection between the two radiologists, the linear weighted kappa statistic was calculated for both DSA and MS-CTA (10). Values $p<0.05$ were considered significant.

RESULTS

Imaging procedures

All 15 patients (seven radial-cephalic and eight prosthetic forearm loop AVFs) underwent DSA and MS-CTA successfully. Figure 2 shows a typical example of both modalities.

Stenosis detection

One hundred and thirty-six vessel segments were available for analysis with MS-CTA in 15 patients. All segments were considered diagnostic by both observers. Observer I found 99% of the segments of excellent diagnostic quality and observer II 88%. With the use of DSA, observer I considered 134 vessel segments diagnostic (87% of which were excellent) and observer II found all segments diagnostic (99% of which were excellent). ROC analysis of both obser-

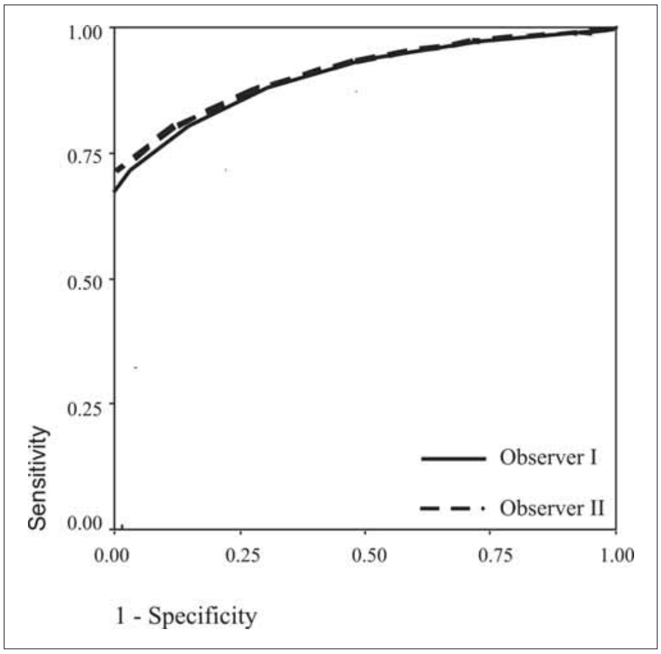


Fig. 3 - ***ROC graph showing sensitivity and specificity of ≥75% stenosis detection through MS-CTA with DSA as gold standard.***

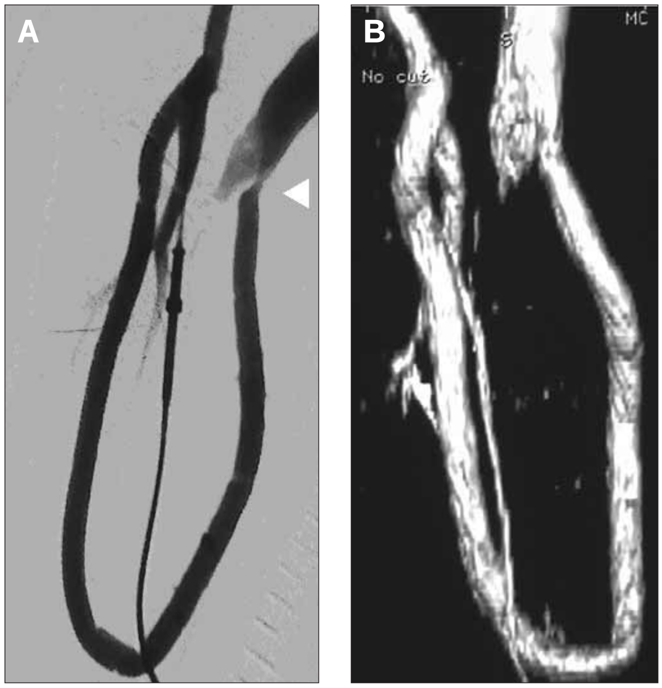


Fig. 4a - ***Antero-posterior image obtained with DSA of a prosthetic PTFE AVF showed a grade 4 stenosis in the efferent vein (arrow head).***
4b - ***Semicoronal image obtained with MS-CTA of the same prosthetic PTFE AVF. However, this stenosis is not visible on MS-CTA, and as such, the MS-CTA is false negative.***

vers' interpretations yielded areas under the curve of 0.90 ± 0.07 for observer I and 0.87 ± 0.08 for observer II at a stenosis cut-off level of ≥50% diameter reduction. At a threshold of ≥75% stenosis detection the area under the curve was 0.85 ± 0.10 and 0.86 ± 0.10, respectively (Fig. 3).
On patient level, Table I shows the sensitivity and specificity for identifying ≥50% and ≥75% stenosis for both observers. Furthermore, positive and negative predictive values are reported. The combined results of both observers showed a sensitivity, specificity and positive and negative predictive values of 82%, 98%, 82% and 98% for stenoses ≥50% and 71%, 99%, 77% and 98% for stenoses ≥75%. Table II lists the numbers of true positive, true negative, false positive, and false negative vessel segments for both observers. On patient level, the overall discriminatory power for the detection of stenoses was somewhat better when ≥50% stenosis was used as a positive test result instead of ≥75%. Both observers detected an equal amount of stenoses on MS-CTA and DSA images. At the ≥50% threshold, observer I detected 12 stenoses on MS-CTA and 11 on DSA. Observer II identified 10 stenoses on MS-CTA and 11 on DSA. At the ≥75% cut-off threshold these numbers were 7 and 7 stenoses and 6 and 7 stenoses on MS-CTA and DSA, respectively.

Image quality

According to the judgement of observers I and II, both imaging modalities offered images of diagnostic image quality. Observer I found 12/15 (80%) images on DSA of excellent and 3/15 (20%) of mediocre diagnostic quality. Observer II graded DSA image quality excellent in 14/15 (93%) patients and

TABLE I - SENSITIVITY, SPECIFICITY, POSITIVE PREDICTIVE VALUE (PPV), AND NEGATIVE PREDICTIVE VALUE (NPV) OF MS-CTA COMPARED TO DSA FOR THE DETECTION OF STENOSES ≥50% AND ≥75% IN ARTERIOVENOUS FISTULAS FOR HEMODIALYSIS AS DETECTED BY TWO INDEPENDENT OBSERVERS

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Observer I				
≥50%	82	98	75	98
≥75%	71	98	71	98
Observer II				
≥50%	82	99	90	98
≥75%	71	99	83	98

Fig. 5a - ***Semicoronal image obtained with MS-CTA of a prosthetic PTFE graft displayed a grade 4 stenosis in the efferent vein (arrow head).***
5b - ***Antero-posterior image obtained with DSA of the same prosthetic PTFE graft also displayed the stenosis in the efferent vein (arrow head). However, the stenosis is scored as a grade 3 stenosis, so the MS-CTA overestimated the stenosis.***

mediocre in 1/15 (7%). For the diagnostic quality of the MS-CTA images, observers I and II concluded excellent in 93% and 73% and mediocre in 7% and 27%, respectively. The mean segment scores on patient level were: for observer I, MS-CTA, 1.99 ± 0.12; DSA, 1.87 ± 0.34 (p<0.001) and for observer II, MS-CTA, 1.88 ± 0.33; DSA, 1.99 ± 0.12 (p<0.001). The overall mean segment score on patient level for both observers I and II were: MS-CTA, 1.93 ± 0.26; DSA, 1.93 ± 0.26 (p=0.85).

Agreement between MS-CTA and DSA for the detection of stenosis

The linear weighted kappa value regarding the detection of hemodynamically significant stenoses, ie ≥50%, was 0.75 and 0.86 for observers I and II, respectively, indicating good agreement of stenosis detection on MS-CTA and DSA.

Inter-observer agreement

For the detection of hemodynamically significant stenoses, ie ≥50%, the linear weighted kappa value was 0.70 and 1.0, for MS-CTA and DSA, respectively. This indicates excellent inter-observer agreement on DSA and fairly good agreement on MS-CTA.

DISCUSSION

With this study we have shown that spiral MS-CTA is a reliable and reproducible method for the detection of stenoses in HD AVF. No complications were noted during or after the examination. MS-CTA images of all AVF were considered by both observers to be of diagnostic quality. Unfortunately, in one patient, with a prosthetic loop AVF, DSA detected a stenosis that was not depicted with MS-CTA. This stenosis was located in the efferent vein (Fig. 4). Because failure to detect a significant stenosis may lead to access thrombosis, the sensitivity of a diagnostic test should be as high as possible. On the other hand, in a few patients MS-CTA overestimated the grade of stenosis (Fig. 5).

TABLE II - STENOSIS DETECTION OF MS-CTA COMPARED TO DSA FOR BOTH OBSERVERS

		Observer I DSA							Observer II DSA				
Stenosis grade		1	2	3	4	5	Stenosis grade		1	2	3	4	5
	1	**120**	0	0	1	0		1	**120**	0	0	1	0
	2	0	**2**	1	0	0		2	0	**4**	1	0	0
MS-CTA	3	0	2	**2**	1	0	MS-CTA	3	0	1	**2**	1	0
	4	0	1	1	**5**	0		4	0	0	1	**5**	0
	5	0	0	0	0	**0**		5	0	0	0	0	**0**

Grade 1 = 0-20% stenosis, grade 2 = 21-49% stenosis, grade 3 = 50-74% stenosis, grade 4 = 75-99% stenosis, grade 5 = occlusion

The greatest limitation of this study lies in the small number of patients. However, comparisons were made on a segment-to-segment basis, providing 136 segments to be analyzed and increasing the overall data sample. Other limitations may be the maximum span of 3 weeks between MS-CTA and DSA imaging. It must be considered that new stenoses could develop during this interval and may have accounted for differences between MS-CTA and DSA in the detection of stenoses. In addition, the CT-technique used in this study may be considered as less accurate as compared to newer scanners. Instead of scanning at 2.5 mm collimation on a 4 detector scanner, most centers currently have scanners that can obtain collimated images at 0.5 to 1.25 mm; and therefore, the resolution is much better. Finally, the inclusion criteria for participating in the study were extensive, and probably with more strict inclusion criteria, the accuracy and clinical utility of MS-CTA could be improved.

Lin et al concluded in their study that MS-CTA nicely correlates to angiography for the evaluation of AVF (3). Cavagna et al concluded that MS-CTA ensures panoramic and high-resolution angiographic-like depiction of vessels, providing excellent pre- and post-operative evaluation of patients with AVF malfunction (4). In a study by Ko et al (6), 43 patients underwent multi-detector CT angiography, and only 14 also underwent DSA within 3-5 days after multi-detector angiography. They found no significant difference in the detection and grading of stenoses at various segments. Therefore, they concluded that multi-detector CT angiography is clinically feasible for evaluating the complete vascular tree of failing AVFs and in showing uncommon complications, including brachial aneurysm and central vein lesions. Nevertheless, the current MS-CTA technique also has limitations. Large coverage of the region of interest may hinder the resolution of the vasculature imaging. Therefore, we have focused on the region of interest at the AVF and adjacent arterial inflow and venous outflow vessels during scanning to obtain better image quality. With this technique, stenoses outside the imaging field in the central arterial and venous vessels may be missed. Another limitation of MS-CTA is the impossibility of performing corrective intervention immediately, should a hemodynamically significant stenosis be detected. However, Duijm et al achieved in all but one of the patients a DSA of the complete arterial inflow, followed by endovascular intervention of significant inflow stenoses, using a retrograde venous access puncture technique (11).

MS-CTA may have several advantages compared to conventional DSA imaging: (a) through an intravenous contrast medium injection, the scans can be obtained in the arterial phase, reducing time and discomfort of the arterial puncture in conventional angiography and shortening the examination time; (b) the data can be reconstructed to create angiographic projections through any plane and in 3D reconstructions. These reconstructions can help to estimate the degree of stenoses. In comparison to conventional DSA, MS-CTA examinations can offer information regarding not only the vessel lumen but also the vessel wall (12). MS-CTA examination is time-saving. In our experience, MS-CTA scans were performed in 8-10 min or less. Post-scan image processing required only about 4-5 min with current computer capacity. However, at least 40-45 min were needed from access puncture to hemostasis in DSA. In addition, the literature reports less skin radiation dose of MS-CTA in comparison to DSA during abdominal aorta image studies (0.00224 vs. 0.071 Gy) (13) and this may be another advantage of spiral MS-CTA. DSA may also exhibit complications like contrast extravasation, bleeding at the puncture site, and acute thrombosis of the vessel, all which can be avoided by MS-CTA.

Still there are several other imaging modalities available to detect the extent and severity of AVF stenoses. Color Doppler ultrasonography (CDUS) is a readily available, inexpensive, and a non-invasive method, and has no radiation exposure. However, the quality of the images depends on the skill of the operator (14-16). Other drawbacks of CDUS are the inaccurate detection of central venous obstructions, overestimation of stenoses at the arterial anastomoses, and the absence of an angiographic map, which may be desired for surgery or percutaneous therapy (17).

Another option to detect the extent and severity of AVF stenoses is MRA, which is not accompanied by radiation exposure and offers the ability to acquire 3D data sets. Varying results have been published concerning the ability of MRA to depict and detect flow-limiting stenoses in AVF using time-of-flight (TOF) (4, 18-21), phase contrast (PC), and contrast enhanced (CE) MRA (8, 18, 22-24) techniques. In these studies, the use of TOF- and PC-MRA resulted in stenosis overestimation because of flow voids caused by post-stenotic intravoxel phase dispersion (4, 18-21). With CE-MRA, better results have been obtained (8, 18, 22-24). However, the presence of vascular metallic stents, especially those made of stainless steel, may be a limitation of MRA, as it is well known that these objects can hamper post-interventional MRA (25). In addition, about 10% of patients exhibit claustrophobia, which makes MRA investigation impossible.

In conclusion, MS-CTA is a minimally invasive procedure that can significantly influence patient care by avoiding potential complications. Moreover, MS-CTA can provide excellent visualization of forearm HD access AVF and has a moderate sensitivity, but high specificity for the detection of significant stenoses.

Conflict of interest: none.

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