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Interobserver and inter-modality concordance of quiescent interval slice selective magnetic resonance angiography and CT angiography in assessment of critical lower limb ischemia

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Abstract

Background We evaluated the noncontrast MRA as an alternate method to CT angiography in assessment of patients with lower limb ischemia, 30 patients were included in a prospective cohort study; they underwent quiescent interval slice selective magnetic resonance angiography (QISS-MRA) and computed tomographic angiography (CTA). The assessment of images was evaluated by two independent consultants. The overall subjective image quality, interobserver and intermodality concordance were calculated.

Results The median acquisition time in QISS-MRA was 20 min (range 18–30 min), The overall subjective image quality was rated similarly with QISS-MRA (3.13 [95% CI 2.84–3.42]) and CTA (3.23 [95% CI 2.94–3.52]; $p = 0.08$) with interobserver concordance for lesion ratings in QISS-MRA reached ($\kappa = 0.987$ (SD 0.006)), while for CTA it was ($\kappa = 0.99$ (SD 0.006)), while the intermodality concordance between QISS-MRA and CTA in lesion ratings were calculated on a per segment basis and was ($\kappa = 0.944$ (SD 0.013)) for reader 1 and ($\kappa = 0.947$ (SD 0.013)) for reader 2, with sensitivity 100% and specificity 97.6%

Conclusions QISS-MRA is a reliable modality for assessment of patients with critical limb ischemia.

Keywords Ischemia, Angiography, Non-contrast, CT, MR, PAD, CLI

Background

Critical limb ischemia (CLI) is the most severe pattern of peripheral arterial disease (PAD) affecting from 12 to 14% of general population [1]. CLI is defined when there is ischemic rest pain, ulceration or gangrene due to arterial variable degree of occlusion, it is a major health problem as it is may be complicated by cardiovascular disease and death, also it may be associated with high risk of major amputation, mortality rate of about 20% within six months after diagnosis and 50% at five years has been reported [1, 2]. Early diagnosis of CLI is essential as it may be complicated by ulceration, gangrene infection and increased risk of lower limb amputation (10–40%) of patients at six months especially nondiagnosed and untreated cases, so it is a challenging disease that needs a specific attention in the diagnosis, decision

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of revascularization, risk reduction and close follow-up to save the limb from major amputation [1].

Color coded Doppler imaging is a noninvasive technique used as first step in patients with claudication pain, it can be used with ankle brachial index (ABI) [3]. Computerized tomographic angiography (CTA) remained the most important tools in delineation of the arterial pathologies before revascularization procedure, but its major limitation is in the patients suffering from renal insufficiency, as it needs contrast administration which could be harmful [4]. Magnetic resonance imaging (MRI) has had extensive clinical value in the assessment of the peripheral vascular system in patients with lower extremity arterial disease, however, the MRI contrast media administration (gadolinium) is hazardous in patients with chronic kidney disease and low glomerular filtration rate due to increase the incidence of nephrogenic systemic fibrosis in these patients, also the consequences of prolonged deposition of gadolinium in the brain, so the demands for non-contrast enhanced magnetic resonance angiography (NCE-MRA) approaches has been increased [5, 6].

Non-contrast MRA includes inflow dependent techniques like time of flight (TOF), however, and it has some disadvantages such as, longer time for scan, it can only evaluate one single station at a time [7]. Cardiac pulse and flow related techniques include three-dimension fast spin echo (3D –FSE), its disadvantages include long scan time, poor image quality regarding pelvic vessels and small caliber arteries especially of foot and calf [8]. On the other hand, there are flow sensitive dephasing techniques, its disadvantages are flow dependent artifacts and venous contamination which make it non applicable in patients with peripheral vessels [9]. Flow dependent technique include phase contrast MRA, however its disadvantages include prolonged scan time, high sensitivity to signal loss caused by turbulent flow and tortuous vessels so it is not suitable for assessment of peripheral arterial disease [9].

Newer non-contrast MRA techniques have been developed recently due to recent improvements in machines hardware and pulse sequences that provide high spatial resolution, allowing the evaluation of distal (infragenicular and pedal) vessels in patients with critical limb ischemia [3]. Furthermore, many of these sequences are non-time consuming, allowing rapid evaluation of the entire lower limb vessels [3, 10, 11].

Quiescent interval slice selective (QISS-MRA) is an inflow-based technique with reasonable scan time that allows coverage of entire lower extremity vessels, also it is helpful in low-flow conditions in patients with stenosis it is the most suitable technique for assessment of PAD [12]. QISS is a cardiac (i.e., electrocardiogram [EKG])-gated technique initially described by Edelman and his colleagues for the evaluation of the lower extremities [2]. This technique uses a single-shot 2D balanced steady-state free precession (bSSFP) readout, it overcomes many of the limitations of time of flight (TOF) imaging by reducing scan time and arterial saturation effects and leveraging the pulsatile nature of blood flow to better visualize lower extremity arteries [2, 13].

QISS-MRA is a bright blood sequential 2D NCE-MRA technique compared to other NCE-MRA technologies, QISS has an easy "push-button" workflow, eliminating the need for extensive patient-to-patient parameter modification, techniques, In QISS-MRA, a presaturation pulse is used inferior to the slice to suppress the signal from venous blood it has high image quality and high resolution as compared to other NCE-MRA [14, 15].

The aim of the study was to evaluate the diagnostic feasibility and interobserver validity of QISS-MRA in diagnosis of CLI and comparing this technique to the CTA as a gold standard.

Patients and methods

Study population

In this prospective cohort study, we included all patients with chronic limb ischemia Rutherford class1 (minor claudication), class 2 (moderate claudication), class 3 (severe claudication), and critical limb ischemia Rutherford class 4 (rest pain), class 5 (minor tissue loss), and class 6 (major tissue loss) presented to our hospital from May to November 2021. After obtaining an institutional review board (IRB) approval, we excluded the patients with GFR less than 30 ml /min and those with general contraindication to MRI like claustrophobia or patients with pacemaker. All patients underwent QISS MRA and CTA.

QISS-MRA technique

The QISS-MRA was done on 1.5 Tesla MRI scanner (Siemens Medical Systems, Erlangen, Germany), the patient is placed supine, feet first, it is EKG gated and the EKG electrodes were placed on the chest, synchronization of the quiescent interval with the systolic phase of rapid blood flow ensures adequate inflow into the imaging slice.

We used peripheral vascular coil, after that we performed a scout image of the pelviabdomen and lower limbs, after localization QISS MRA was done in the transverse plane with the following parameters time of repetition (TR) 642 time of echo (TE) 2.01ms, field of view (FOV) 400mm x 260mm, matrix 400×261 and slice thickness 3mm. The sequence was performed in nine segments to cover the distance from lower abdomen to the distal calf, we could increase or decrease the scout depends on the patient region of interest then these segments were composed to create only one series and after, at the abdominal region we used breath holding to avoid motion artifact, finally maximum intensity projection (MIP) was done automatically or manually, the acquisition time was about 15–20 min.

CTA technique

All the participating patients went for CT angiography; all patients were scanned on a 128-MDCT scanner (Ingenuity, Philips Healthcare). CTA was done from the upper abdomen to the lower end of the feet in the craniocaudal direction. The parameters for each scan were 0.5-s rotation time, 1.25-mm detector-row width, 0.516 helical pitch (beam pitch), 41.2-mm/s table movement, and 50-cm scanning FOV. The scanning time ranged from 25 to 30 s. The iodinated contrast material was injected through a 20-gauge catheter into the antecubital vein using an automated injector. The contrast material (85 mL) was injected at rate of 3 mL/s and was followed by administration of 20 mL of a saline solution at rate of 3 mL/s. In all patients, acquisition of the dynamic monitoring scans began 18 s after the start of the contrast material injection.

Image analysis

The quality of MRA images was evaluated blindly by two consultants who were experienced in MR image interpretations for 12 and 15 years and overall subjective image quality was calculated according to Likert 5-point scale from 0 to 4 as follows.

- 0 for a nondiagnostic image.
- 1 for poor image quality (the observer not confident due to severe image artifacts, significant venous contamination, and/or poor vascular signals).
- 2 for fair image quality (the observer marginally confident due to minor artifacts, mild-to-moderate venous contamination, and/or moderately homogenous vascular signal).
- 3 for good image quality (the observer confident).
- 4 for excellent image quality (no or minimal venous contamination and/or artifacts and homogenous vascular signals, thereby enabling the observer to be highly confident).

Intermodality concordance between the MRA and CTA, and interobserver concordance for each modality were calculated.

In each patient, we examined 19 segments (Aorta, two common iliac arteries, two external iliac arteries, two common femoral arteries, two superficial femoral arteries, two profunda femoris arteries, two Popliteal arteries, two anterior tibial arteries, two posterior tibial arteries, two Peroneal arteries), each segment was evaluated for patency; stenosis (mild = less than 50%, moderate = from 50 to 74%, severe = from 75 to 99%) or total occlusion. In patient with previous conduits as femoropopliteal or femoro-distal bypass we add three segments for examination: proximal (inflow), middle (conduit), and distal (outflow). The interpretations of the images were done blindly by two consultants and interobserver concordance was collected and calculated using exact count per interval.

Statistical analysis

Descriptive demographic data were presented using by mean and standard deviation for parametric data and by median and range for nonparametric data, sensitivity and specificity were estimated for this technique as compared to gold standard (CTA) using ROC curve, binomial variables were tested by chi square, a statistical threshold of ($p < 0.05$) was used as the criterion for statistical significance.

Diagnostic image quality for QISS-MRA and CT angiography were compared by Likert scores. Interobserver concordance between QISS-MRA and CT was tested using Kappa test. Kappa > 0.8 was considered as excellent concordance. 0.6–0.8 was considered good. 0.4–0.59 was considered fair. Kappa < 0.4 was considered as poor agreement. P-values less than 0.05 were considered statistically significant.

Results

This study was conducted on 33 patients with PAD and critical limb ischemia, excluding three patients with a GFR below 30 ml/min. The final sample included 30 patients with a mean age of 63 ± 9 years, including 26 males and four females. Among them, 20 patients were diabetic, 21 were hypertensive, and 14 had hyperlipidemia. According to Rutherford's scale, four patients had severe claudication (Class 3), 15 patients experienced rest pain (Class 4), ten patients had critical limb ischemia with minor tissue loss (Class 5), and one patient had major tissue loss (Class 6). One patient had a history of femoropopliteal bypass surgery, but none had stents placed in their affected legs (Table 1). All patients underwent QISS-MRA and CTA imaging, with CTA serving as the gold standard.

The median acquisition time in QISS-MRA was 20 min (range 18–30 min), while the median acquisition time for CTA was 6 min (range 4–12 min) ($Z = -4.87$ $p < 0.0001$), but when we added the time taken for creatinine analysis and cannula insertion the median acquisition time was 28 min (22–50 min) ($Z = -3.93$ $p < 0.0001$).

Table 1 Patient demographics (30 patients)

Mean age ± Std dev	63 ± 9
Gender	
Males	26
Females	4
Comorbidities	
DM	20 (67%)
HTN	21 (70%)
Hyperlipidemia	14 (47%)
BMI	29.2
History of stent	0
History of bypass surgery	1 (3.3%)
Rutherford grading	
3 severe claudication	4 (13.3%)
4 rest pain	15 (50%)
5 minor tissue loss	10 (33.3%)
6 major tissue loss	1 (3.3%)

A total of 573 vascular segments were imaged by QISS-MRA and CTA (Figs. 1, 2). The overall subjective image quality was rated similarly with QISS-MRA (3.13 [95% CI 2.84–3.42]) and CTA (3.23 [95% CI 2.94–3.52]; $p = 0.08$).

Interobserver concordance for lesion ratings in QISS-MRA reached (κ = 0.987 (SD 0.006)), while for CTA it was (κ = 0.99 (SD 0.006) (Table 2), while the intermodality concordance between QISS-MRA and CTA in lesion ratings were calculated on a per segment basis and was (κ = 0.944 (SD 0.013)) for reader 1 and (κ = 0.947 (SD 0.013)) for reader 2 (Table 3).

On calculation of the sensitivity and specificity of the QISS MRA as regard to CTA we found the sensitivity equals 100%, while the specificity equals 97.6% and the area under curve 0.998 (CI 0.997–1.0) for reader 1 and 0.999(CI 0.997–1.0) for reader 2(p value < 0.001) (Fig. 3, Table 4).

One of our patients had a graft which was occluded, and the small segment occlusion can be detected with high resolution on QISS MRA.

Discussion

In our study, we found that QISS-MRA is a promising reliable alternative modality to CTA and postcontrast MRA in patients with critical limb ischemia suffering from impaired renal function to avoid nephrogenic systemic fibrosis. This prospective study in patients with PAD detected the diagnostic accuracy of non-contrast QISS-MRA versus contrast-enhanced CTA for the detection of lower extremity vascular stenosis. For each-segment analysis, QISS-MRA showed high sensitivity and specificity in diagnosis of arterial stenosis.

As regard significant stenosis (50–100%), we found that no significant difference in sensitivity or specificity between QISS-MRA and CTA, as MRA shows sensitivity that reaches 100% and specificity 97%, this is in concordance with a study conducted by Akos Varga et al. who stated that the accuracy of detection > 50% stenosis was similar to that of CTA [4].

Akos Varga and his colleagues reported the high sensitivity (84.9%) and specificity (97.2%) of QISS MRA compared to DSA in PAD, and importantly showed similar

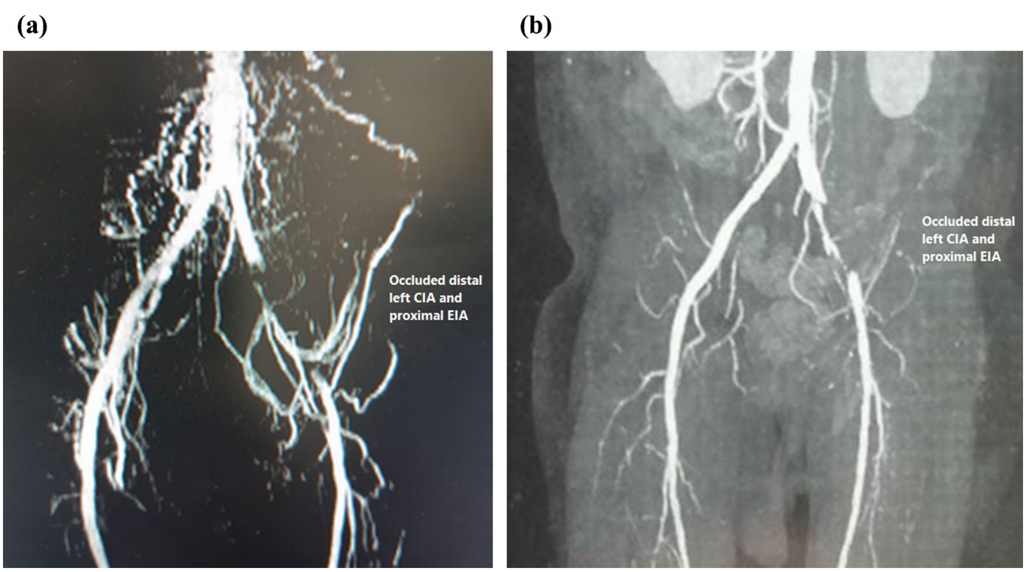

Fig. 1 Case radiographs of magnetic resonance angiography (**A**) and computed tomography angiography (**B**) showed occlusion at distal left common iliac (CIA) and proximal left external iliac arteries (EIA)

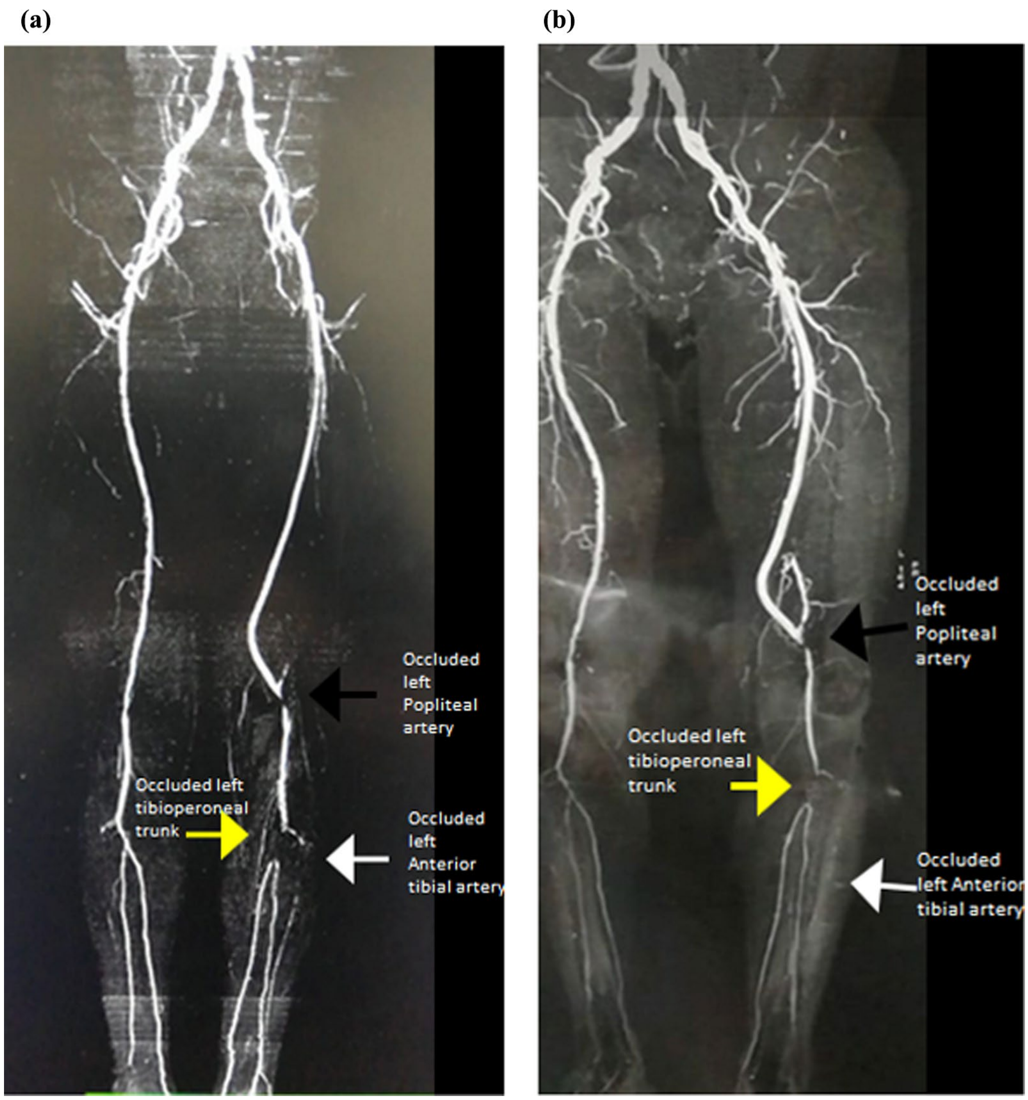

Fig. 2 Case radiographs of magnetic resonance angiography (**A**) and computed tomography angiography (**B**) showed a patient with synthetic graft occluded at left popliteal artery (black arrow), occluded left tibioperoneal trunk (yellow arrow), occluded left anterior tibial artery (ATA) (white arrow)

Table 2 Interobserver agreement for MRA and CTA in lesion rating

MRA							**CTA**						
		Reader 1							**Reader 1**				
		0	**1**	**2**	**3**	**4**			**0**	**1**	**2**	**3**	**4**
Reader 2	0	367	0	0	0	0	Reader 2	0	376	0	0	0	0
	1	0	31	2	0	0		1	0	28	3	0	0
	2	0	0	17	2	0		2	0	0	13	0	0
	3	0	0	0	34	0		3	0	0	0	33	0
	4	0	0	0	0	120		4	0	0	0	0	120
Kappa	0.987 ± 0.006						Kappa	0.990 ± 0.006					

0 = patent arterial segment, 1 = stenosis less than 50%, 2 = stenosis from 50 to 74%, 3 = stenosis from 75 to 99%, 4 = total occluded segment

Table 3 Intermodality agreement between MRA and CTA in lesion rating

Reader 1							**Reader 2**						
		MRA							**MRA**				
		0	**1**	**2**	**3**	**4**			**0**	**1**	**2**	**3**	**4**
CTA	0	367	8	1	0	0	CTA	0	367	9	0	0	0
	1	0	23	5	0	0		1	0	24	6	1	0
	2	0	0	13	3	0		2	0	0	13	0	0
	3	0	0	0	33	0		3	0	0	0	33	0
	4	0	0	0	0	120		4	0	0	0	0	120
Kappa	0.944 ± 0.013						Kappa	0.947 ± 0.013					

0 = patent arterial segment, 1 = stenosis less than 50%, 2 = stenosis from 50 to 74%, 3 = stenosis from 75 to 99%, 4 = total occluded segment

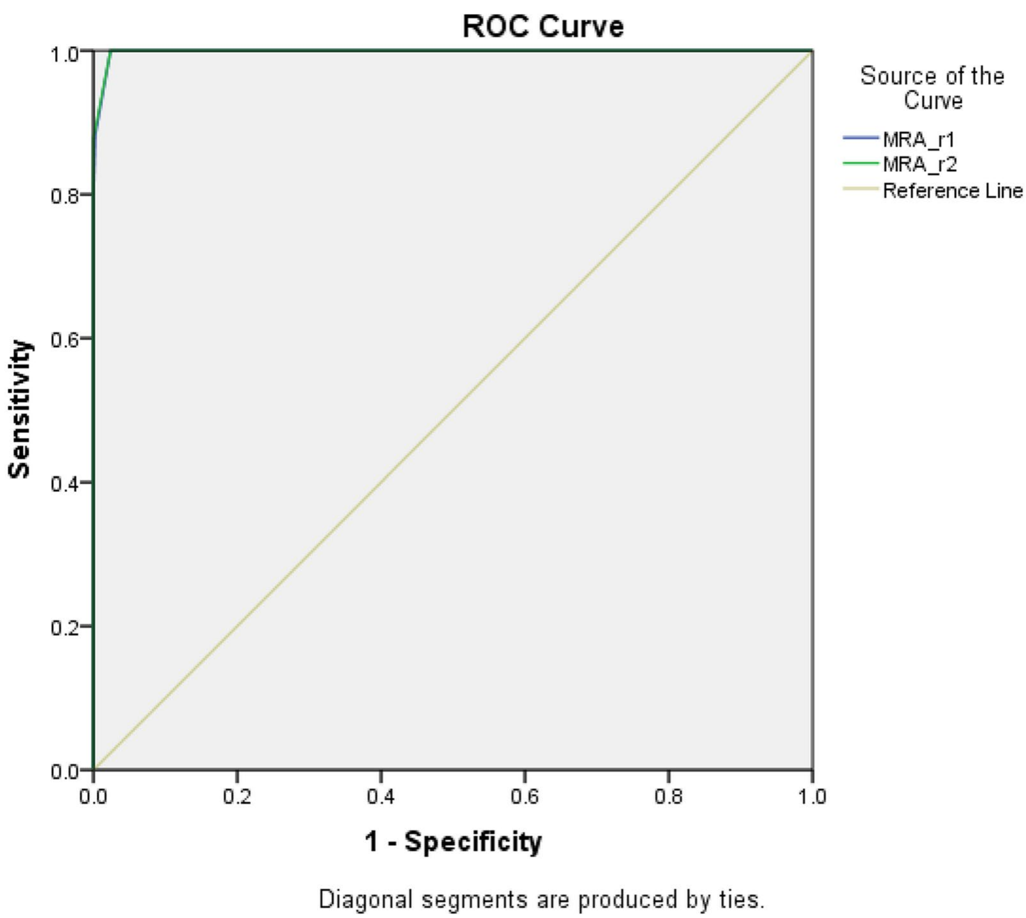

Fig. 3 ROC curve showing sensitivity and specificity of quiescent-interval single-shot magnetic resonance angiography (QISS- MRA) compared to computed tomography angiography (CTA)

accuracy to CTA with better evaluation of heavily calcified arterial segments [4], In another study, a technique called proton density–weighted in-phase stack-of-stars quiescent interval slice selective magnetic resonance imaging (PDIP-SOS/ QISS-MRI) was tested for its accuracy in estimating stenosis and yielded superior compared to CTA and QISS-MRA, although the image quality of MRA remained inferior to CTA [16].

Hodnett et al. conducted a study on 25 diabetic patients with symptomatic PAD, they reported high sensitivity (87.4%) and high specificity (92.1%) of OISS-MRA in comparison with contrast-enhanced MRA and high

Table 4 Area under the curve for sensitivity and specificity of MRA

Test result variable(s)	Area	Std. error[a]	Asymptotic Sig.[b]	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
MRA_reader1	0.998	0.001	0.000	0.997	10.000
MRA_reader2	0.999	0.001	0.000	0.997	10.000

[a] Under the nonparametric assumption

[b] Null hypothesis: true area = 0.5

The test result variable(s): MRA_reader1, MRA_reader2 has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased

sensitivity (96.2%) and specificity (96.1%) in comparison to DSA [17]. Hodnett et al. conducted another study on 53 patients with known or suspected PAD also reported high sensitivity (85.0–89.7%) and specificity (94.6–96.8%) of QISS MRA compared to contrast-enhanced MRA, high sensitivity (91.0%) and specificity (96.6%) compared to DSA [18].

Klasen et al.'s study of 27 patients, reported sensitivity (98.6%) and specificity (96%) of QISS MRA in comparison to contrast-enhanced MRA [19], also Ward et al.'s study of 20 patients referred for PAD, reported sensitivity (90.8%) and specificity (94.5%) of QISS MRA in comparison to contrast-enhanced MRA [20]. Furthermore, Altaha et al.'s study of 19 patients with chronic lower limb ischemia comparing QISS MRA against DSA showed sensitivities of 92% and 81% for two readers and specificities of 95% and 97% [12]. However, in study done by Gang Wu stated that the overall image quality obtained by QISS MRA was lower than that in CTA [14], this may be due to difference in scan protocol.

There is an excellent interobserver concordance between two radiologists in both CTA and QISS MRA. Interobserver concordance for lesion ratings in QISS-MRA reached ($\kappa = 0.987$ (SD 0.006)), while for CTA it was ($\kappa = 0.99$ (SD 0.006), while the intermodality concordance between QISS-MRA and CTA in lesion ratings were calculated on a per segment basis and was ($\kappa = 0.944$ (SD 0.013)) for reader 1 and ($\kappa = 0.947$ (SD 0.013)) for reader 2. These findings differ from those of Akos Varga and his colleagues, who observed artifacts in CTA images due to calcifications in the examined arteries [4]. However, they found a strong similarity between MRA and DSA, which highlighted the superiority of MRA over CTA in the presence of arterial calcifications. In our study, we did not encounter this issue, as none of the examined arteries exhibited calcifications.

Motion artifacts are one of the most challenging obstacles of QISS-MRA in patients with chronic limb ischemia. The scan time of QISS-MRA is more prolonged than CTA, the patients were asked not to move their legs during the exam. Due to 2D nature of data sampling (1 slice per heart beat), only slices acquired during the motion would be affected and in abdominal area we used breath hold technique which decrease the motion artifact, therefore the diagnostic images was in general maintained with good quality, and this was similar to observations in a study by Altaha and his colleagues [12], also in study by Li Ming Wei and his colleagues [21].

In case of nonsatisfactory image quality because of motion artefact, QISS-MRA can provide the advantage of repeating acquisitions of arterial segments, in this study motion artefact was evident in two patients and the acquisition was repeated at the affected segments with better image quality.

Although the time scan is shorter in CTA but when we add the time of creatinine test and cannula placement, the whole time is equal to that of MRA. We used slice thickness 3mm which is adequate with high image resolution, if smaller slice thickness is used the scan time will be increased and it is difficult for the patient to be in supine position for a long time without motion.

One of the obstacles in CTA is overestimation of stenosis in patients with heavily calcified plaques, however in these patients QISS MRA can overcome this problem and shows excellent resolution and this goes with all previous studies. The diagnostic accuracy is higher in QISS in vessels with calcific wall which is very common in patients with chronic limb ischemia [4].

The limitation in this study was the small sample size underwent diagnostic DSA for comparison as patients were only referred to DSA for treatment of their lesions.

Conclusion

QISS MRA is a reliable modality for assessment of patients with critical limb ischemia, it has high sensitivity and specificity as CTA specially at 50–100% stenosis and can be used as alternative to CTA to avoid risk of ionizing radiation and in patient with chronic renal insufficiency, QISS-MRA can overcome the CTA overestimation of stenosis in patients with heavily calcified plaques.

Abbreviations

3D-FSE	Three-dimension fast spin echo
ABI	Ankle brachial index
ATA	Anterior tibial artery

BMI	Body mass index
bSSFP	Balanced steady-state free precession
CI	Confidence interval
CIA	External iliac artery
CLI	Critical limb ischemia
CT	Computed tomography
CTA	Computed tomographic angiography
DM	Diabetes mellitus
DSA	Digital subtraction angiography
EIA	Common iliac artery
EKG	Electrocardiogram
FOV	Field of view
GFR	Glomerular filtration rate
HTN	Hypertension
IRB	Institutional review board
MRA	Magnetic resonance angiography
NCE-MRA	Non-contrast enhanced magnetic resonance angiography
PAD	Peripheral arterial disease
PDIP-SOS/ QISS-MRI	Proton density–weighted in-phase stack-of-stars quiescent interval slice selective magnetic resonance imaging
QISS-MRA	Quiescent interval slice selective magnetic resonance angiography
SD	Standard deviation
TE	Time of echo
TOF	Time of flight
TR	Time of repetition

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Declarations

Ethics approval and consent to participate
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Consent for publication
All participants have signed a consent for publication.

Competing interests
The authors declare that they have no conflicts of interest.

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