European Review for Medical and Pharmacological Sciences 2016; 20: 3078-3086

Comparison of imaging value for diabetic lower extremity arterial disease between FBI and CE-MRA

C.-Y. YI, D.-X. ZHOU, H.-H. LI, Y. WANG, K. CHEN, J. CHEN, B.-C. HUANG, X.-L. XU

Department of Medical Imaging, Shanghai Gongli Hospital, Pudong new area, Shanghai, China

Chunyan Yi and Xiaolan Xu have the co-first authorship

Abstract. – OBJECTIVE: This study adopted self-control study method to assess the efficacy of fresh blood imaging (FBI) and contrast-enhanced MR angiography (CE-MRA) for patients with diabetic lower extremity arterial disease (DLEAD) (Fontaine stage I to IV), and to evaluate the imaging of lower extremity peripheral arterial disease (PAD) in different stages of diabetes mellitus (DM).

PATIENTS AND METHODS: 1. This study recruited 44 diabetic patients with suspected lower extremity PAD to take both FBI and CE-MRA. 2. Two experienced cardiovascular radiologists assessed the image quality, the detection of lower extremity arterial branches, and tissue contamination (veins, arteries, and soft tissues) of FBI and CE-MRA, as well as the presence and severity of stenotic lesions. 3. Statistical differences of the quality of FBI and CE-MRA were determined using paired t-test. 4. Correlation analysis was adopted for determining the direction and strength of the relationship between the changes of the indexes of FBI and the different Fontaine stages.

RESULTS: 1. The quality evaluation results of the image of lower extremity arteries from the 44 diabetic patients indicated no statistically significant difference between FBI and CE-MRA in the patients with Fontaine stage I-III ($p > 0.05$). However, a statistically significant difference was observed in the patients with Fontaine stage IV ($p < 0.05$), and the quality of FBI was slightly worse. 2. Arterial branches that observed from FBI and CE-MRA were 885 and 904, respectively. There was no statistically significant difference for the arterial branches between FBI and CE-MRA in the patients with Fontaine stage I-III ($p > 0.05$). However, a statistically significant difference was observed in the patients with Fontaine stage IV ($p < 0.05$), and CE-MRA indicated more artery branches than FBI. 3. There was a statistically significant difference for the evaluation of venous contamination between FBI and CE-MRA ($p < 0.05$), and there was less venous contamination using FBI. 4. The study results indicated that with Fontaine stages going on the FBI's image quality and arterial branches reduced gradually, and the degree of tissue interference and arteriostenosis was rising gradually.

CONCLUSIONS: The results of this study indicated that using FBI in lower extremity PAD of diabetics had good quality and high diagnostic accurancy, and the tissue contamination (veins and soft tissues of calf) was effectively avoided. Especially in Fontaine stage I-III, FBI can be used as an alternative technique of CE-MRA, and it also can be used in diabetic patients with renal impairment in Fontaine IV.

Key Words:

Non-contrast-enhanced magnetic resonance angiography (NCE-MRA), Contrast-enhanced magnetic resonance angiography (CE-MRA), Fresh blood imaging (FBI), Diabetes mellitus (DM), Peripheral vascular disease (PAD).

Introduction

Diabetes mellitus (DM) is a well-known risk factor that causes progressive arteries atherosclerosis, and can double the risk of getting lower extremity peripheral arterial disease (PAD)[1]. According to a research study from Yang et al[2], the incidence of DM in adults over 20-years-old in China was 9.7%, and about 20% of the patients with lower extremity PDA had DM. Hiatt et al[3] suggested that the risk of getting lower extremity PDA increased gradually with the development of severity and the prolongation of the course of DM. The prevalence rate of lower extremity amputation in patients with DM was 7-15 times higher than non-diabetics[4]. There is no apparent clinical manifestation of lower extremity PAD, and about 60% of lower extremity gangrene and amputation in diabetic patients were caused by lacking of early detection, early diagnosis and

Corresponding Author: Bingcang Huang, MD; e-mail: hbc9209@163.com

timely treatment. Therefore, an early and accurate diagnosis with an individualized treatment plan for diabetic patients with lower extremity PAD can increase the therapeutic efficacy and reduce the complications of lower extremity PAD[5].

In recent years, imaging methods for lower extremity PAD diagnosis have experienced huge changes. Contrast-enhanced MR angiography (CE-MRA) has been identified as a very essential and cost-effective method for noninvasive imaging modalities of lower extremity arteries. Many researchers believed that the effectiveness of using CE-MRA for lower extremity PDA in diabetic patients can be equivalent to digital subtraction angiography (DSA)[6]. Michael et al[7] also suggested that DSA should be performed in patients who need percutaneous transluminal angioplasty (PTA) after the evaluation of CE-MRA. With increase reports on nephrogenic systemic fibrosis (NSF), it is identified that using gadolinium-based contrast agents (GBCA) in patients with severe renal dysfunction can cause NSF. The reasons of causing fibrosis and NSF may be the retention of gadolinium-containing contrast agents in the human body, and the release and deposition of gadolinium ion (Gd^{3+}). Hence, glomerular filtration rate (GFR) <30 ml/min is regarded as a contraindication of CE-MRA examination[8].

Non CE-MRA (NCE-MRA) with the characteristics of non-invasive and no renal impairment caused by contrast agents has been widely recognized by researchers[9]. As early as 2003, Miyazaki et al[10] suggested that fresh blood imaging (FBI) was an appropriate technique to use for lower extremity arterial examination with a good signal-to-noise ratio (SNR), and FBI didn't rely on blood inflow effect. In 1980, Wedeen et al[11] firstly used this technology to perform vascular anatomy imaging research on 0.6 T MR. After years of applied research, the practical value of FBI in whole-body magnetic resonance angiography (WB-MRA) has been proved. Furthermore, FBI can also be used to perform the imaging of veins, lumbar arteries, and lower extremity arteries[12]. Research studies[13,14] indicated that FBI has relatively high sensitivity and specificity for the diagnosis of lower extremity PAD. However, there was no literature focus on the practical value of using FBI for the diagnosis of lower extremity PAD in diabetic patients with different Fontaine stages[15].

This investigation adopted a self-control study method to assess the efficacy between FBI and CE-MRA for the diagnosis of lower extremity PAD in 4 groups of diabetic patients with different Fontaine stages. This paper discussed the relationship between the changes of the indexes of FBI and the different Fontaine stages, and whether FBI could be replaced by CE-MRA by analyzing the practical value of FBI in patients with different Fontaine stages. Thus, the results of this work provide sufficient evidence for the individualized application of FBI in clinical practice, and to guide optimal clinical treatment for diabetic patients with lower extremity PAD.

Patients and Methods

This study recruited 44 diabetic patients with suspected lower extremity PAD from December 1th 2013 to December 31th 2014. The 44 patients participated in the study voluntarily and written informed consent was obtained for each participant. The demographic characteristics of the participants were 27 female and 17 male patients with an age range between 51 to 80 years old, mean age 61.7±1.9 years old, and 2-25 years diabetes history. The diagnosis of DM was confirmed according to American Diabetes Association (ADA) 2013 criteria of diabetes mellitus[16], and the majority of the participants had unsatisfactory blood glucose control.

Patients were divided into four groups according to the Fontaine et al classification (Fontaine stage I-V)[15]. Group 1 (Fontaine stage I): asymptomatic. Group 2 (Fontaine stage II): local ischemia, two sub-stages can be further divided: stage IIa (intermittent claudication after more than 200 meters of pain-free walking), stage IIb (intermittent claudication after less than 200 meters of pain-free walking). Group 3 (Fontaine stage III): severe ischemic rest pain appeared. Group 4 (Fontaine stage IV): gangrene or ischemic ulcers, patients developed limb ulcers or gangrene, can also be combined with infections

Exclusion criteria included: 1. Severe renal function impairment (GRF <30 ml/min), 2. Patients with contraindications to MRI (including patients with a pacemaker, defibrillator or wires in body, metallic foreign body in the eye, deep brain stimulator, Swan-Ganz catheter, bullets or gunshot pellets, cerebral aneurysm clips, cochlear implant, magnetic dental implants, as well as claustrophobic), 3. Patients with the history of lower extremity arterial surgery.

Examination Facility and Scanning Methods

Imaging was performed on the Toshiba Excelart Vantage 1.5T MRI machine (Toshiba, Otawa-

Table I. Scanning parameters of CE-MRA and FBI.

Parameters	CE-MRA	FBI
Time of repetition, TR	5.9 ms	2949 ms
Time of echo, TE	2.7 ms	80 ms
Field of view, FOV	42 cm2	44 cm2
Imaging flip angle	20°	90°
PE-matrix	192 x 320	256 x 256
Slice thick	4 mm	3.5 mm

ra, Tochigi, Japan). Eight-channels speed phased array coil, 32 units phased chest/lumbar and ECG gating were used. Patients were in supine position and feet in first. Sponge-cushion was placed in patients' ankles, in order to keep calf in accordance with ankles. Knees and ankles were fixed with strips, in order to reduce motion artifacts.

FBI scan: Based on 3D electrocardiogram-gated (ECG-gated) fast spin echo (FES) sequence, the bright-blood images of arteries and veins during diastolic period, and the black blood images of arteries and veins during the systolic period were collected. Images of lower artery were collected after subtraction.

CE-MRA scan: The CE-MRA scan sequence was set as five-period consecutive dynamic scan. Venous injections were performed using intravenous contrast agents with injection rate to 2.5 ml/s, and delay time was set as 10 sections. Dotarem Gadoterate Meglumine contrast agent was used with a total dose of 0.1 mmol/kg. Scanning parameters of FBI and CE-MRA can be referred to Table I.

Image Processing and Analysis Methods of FBI and CE-MRA

After scanning, maximal intensity projection (MIP) was used to collect the original images of FBI and CE-MRA. The parameters of original imaging and MIP imaging were observed and collected by 2 experienced cardiovascular radiologists at the same time. According to Transatlantic Inter-Society Consensus II (TASC II)[17], crural arteries were divided into 11 segments. Likert four-point rating scale was used to evaluate the image quality (0 point=very bad, quit treatment; 1 point=bad, unconfident treatment; 2 points=-moderate, fuzzy diagnosis; 3 points=good, treatment; 4 points=very good, confident treatment). Tissue contamination (veins, arterial pulse and soft tissues) was rated with three-point rubric (0 point=none or little; 1 point=slight to moderate; 2 points=significant, interference diagnosis)[18].

Statistical Analysis

SPSS Statistics Version 19.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analysis. A t-test was used to analyze the FBI and CE-MRA as a diagnostic reference standard. p <0.05 was considered as a statistical difference, while p <0.01 was considered as a significantly statistical difference.

Results

Clinical Features of Lower Extremity PAD in Diabetic patients

The clinical features of the 44 diabetic patients with lower extremity PAD can be referred to Table II. Among the 44 patients, 16 patients, 11 patients, 12 patients and 5 patients can be classified as Fontaine stage I, II, III and IV period, respectively. The demographic characteristics of the participants were 27 female and 17 male patients with 2-25 years diabetes history, and all the participants had unsatisfactory blood glucose control. The clinical symptoms and severity of lower extremity PAD in diabetic patients increased along with the increase of age of onset, the length of disease, fasting blood glucose (FBG), two-hour postprandial blood glucose (2h PBG) and glycosylated hemoglobin (GHb).

Comparison Analysis of Imaging Parameters between FBI and CE-MRA

Comparison of Image Quality between FBI and CE-MRA

Comparison analysis of imaging quality between FBI and CE-MRA suggested that there was no statistical difference in overall image quality (t =-1.77, p >0.05). There was no statistically significant difference between FBI and CE-MRA in the patients with Fontaine stage I-III (t =-1.00, p >0.05). However, statistically significant difference was observed in

Table II. Clinical features of lower extremity PAD in the 44 diabetic patients.

	Diabetic patients (n=44)			
Clinical Features (mean/range)	**Fontaine stage I (n=16)**	**Fontaine stage II (n=11)**	**Fontaine stage III (n=12)**	**Fontaine stage 4 (n=5)**
Gender (male/female)	4/12	5/6	5/7	3/2
Age (years)	62.9/51-80	62.2/51-72	68.2/58-80	67.8/57-76
The length of disease (years)	3.9/2-10	12.2/5-20	12.5/4-18	20/17-25
FBG (mmol/L)	8.8/6.2-15.6	12.7/6.51-25.32	11.5/6.82-21.33	18.0/8.78-22.37
2h PBG (mmol/L)	12.4/7.5-20.4	16.1/8.7-27.9	16.5/8.9-28.9	22.0/10.3-28.9
GHb (%)	7.6/6.1-12.4	10.8/6.1-18.8	10.7/6.2-17.4	13.2/6.5-17.8

FGB: fasting blood glucose, 2h PBG: two-hour postprandial blood glucose, GHb: glycosylated hemoglobin.

the patients with Fontaine stage IV (t =-3.67, p <0.05), and the quality of FBI was slightly worse (Table III).

The Detection of Lower Extremity Arterial Branches from FBI and CE-MRA

In the 44 diabetic patients with lower extremity PAD, FBI and CE-MRA indicated 885 and 904 segments, respectively, and there was no statistical difference (t =-1.61, p >0.05). In the patients with Fontaine stage I, FBI and CE-MRA indicated 332 and 324 segments, respectively (t =1.83, p >0.05). In the patients with Fontaine stage II, FBI and CE-MRA indicated 224 and 226 segments, respectively (t =-1.00, p >0.05). In the patients with Fontaine stage II, FBI and CE-MRA indicated 245 and 250 segments, respectively (t =-1.45, p >0.05). Thus, there was no statistical difference between FBI and CE-MRA in the patients with Fontaine stage I-III. However, in the patients with Fontaine stage IV, FBI and CE-MRA indicated 84 and 104 segments, respectively (t =-3.51, p <0.05). There was a statistical difference between FBI and CE-MRA in the patients with Fontaine stage IV. Therefore, there was no difference between FBI and CE-MRA in patients with Fontaine stage I-III, while FBI is worse than CE-MRA in patients with Fontaine stage IV.

Rating results of tissue contamination (veins, arterial pulse and soft tissues) of FBI and CE-MRA

Rating results of tissue contamination of FBI included 38 patients with 0 point, and 6 patients with 1 point (the contamination of arterial pulse). Rating results of tissue contamination of CE-MRA included 1 patient with 0 point, 30 patients with 1 point, 13 patients with 2 points, and the contamination was mainly occurred in veins and soft tissues. According to the rating results above, the tissue contamination of FBI was significantly less than CE-MRA (t =-14.782, p <0.01), and the contamination of arterial pulse did not impact on the diagnosis. Thus, using FBI can effectively avoid the tissue contamination from imaging examination (Table IV).

Comparison Analysis of Imaging Parameters Using FBI (Fontaine Stage I-IV)

With the increase of the severity in different Fontaine stages, the imaging quality and the de-

Table III. Comparison of Image Quality between FBI and CE-MRA (n=44, $\bar{x} \pm s$).

	n	FBI, (mean ± SD)	CE-MRA, (mean ± SD)	t-statistics	*p*-value
Overall	44	2.45 ± 1.20	2.52 ± 1.20	-1.77	0.08
Fontaine stage I	16	2.88 ± 0.99	2.94 ± 0.97	-1.00	0.33
Fontaine stage II	11	2.73 ± 0.96	2.82 ± 1.03	-1.00	0.34
Fontaine stage III	12	1.92 ± 1.19	2.00 ± 1.15	-1.00	0.34
Fontaine stage IV	5	1.80 ± 1.47	3.60 ± 0.49	-3.67	0.02*

FBI: fresh blood imaging, CE-MRA: contrast-enhanced MR angiography *p<0.05.

Table IV. The detection of lower extremity arterial branches from FBI and CE-MRA (n=44, $\bar{x}$±s).

	n	FBI, (mean ± SD)	CE-MRA, (mean ± SD)	*t*-statistics	*p*-value
Overall	44	20.11±2.22	20.55±1.92	-1.61	0.12
Fontaine stage I	16	20.75±1.98	20.25±1.95	1.83	0.09
Fontaine stage II	11	20.36±2.35	20.55±2.06	-1.00	0.34
Fontaine stage III	12	20.42±1.38	20.83±1.4	-1.45	0.18
Fontaine stage IV	5	16.85±1.17	20.80±1.40	-3.51	0.03*

FBI: fresh blood imaging, CE-MRA: contrast-enhanced MR angiography. *p<0.05

tected number of lower extremity arterial branches decreased, while the tissue contamination gradually increased (Figure 1).

Discussion

The Principles of FBI

FBI is an unenhanced magnetic resonance angiography technique that uses pulsatile blood flow to generate vascular contrast. In 2000, Miyazaki et al[19] developed and refined a technique using 3D single-shot FSE (SSFSE) and defined the technique as FBI. At early time, FBI based on spin echo was too slow for practical application. There were some problems, for example, these delays were based solely on heart rates as the heart rates varied by individuals and signal was lost easily, and it took a long time to complete scan[20]. Hence, 3D FBI methods usually involve a multi-phase ECG-gated 2D SSFSE acquisition that acquires increasing delays throughout all phases of the cardiac cycle. These images are evaluated to obtain the highest vascular contrast, in order to determine the appropriate trigger delays for systolic and diastolic phase. Finally, the images of systolic and diastolic phase will be subtracted with the retaining of arterial images.

The Advantages of FBI

FBI had the following advantages[21]: 1. The application of 3D half-Fourier FSE effectively reduced motion artifacts by reducing the single-shot time. The single half-Fourier FSE time with 256×256 matrix was below 1, because the decrease of echo interval. 2. The enhancement of overlapped T2 signals was conducive to bri-

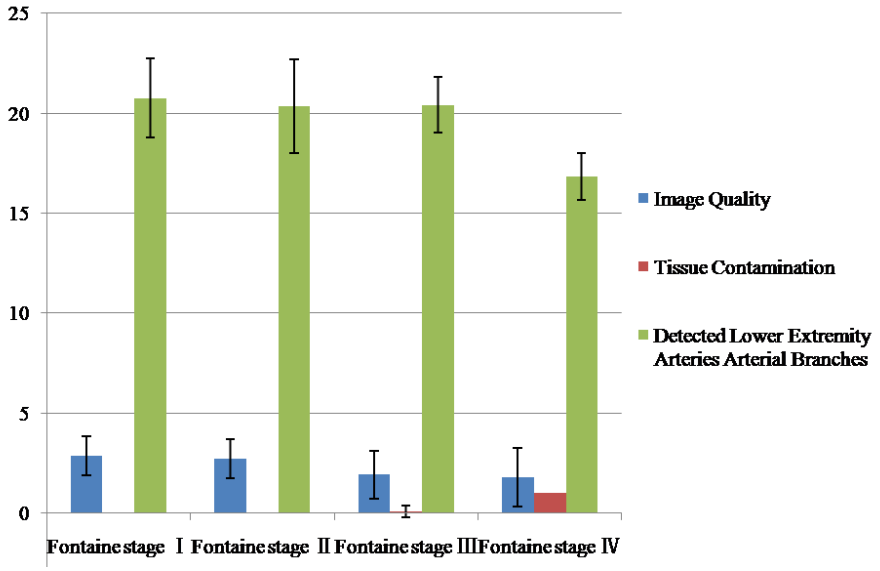

Figure 1. Comparison analysis of imaging parameters using FBI.

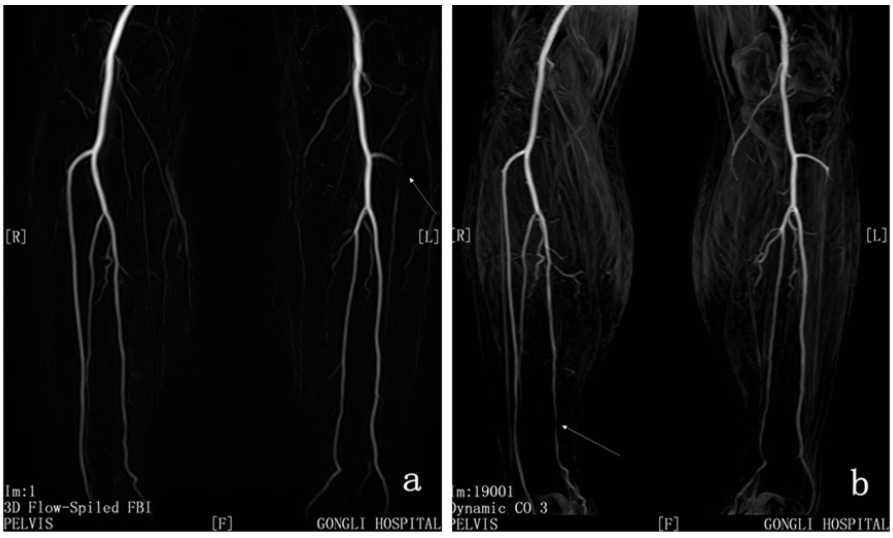

Figure 2. A 74-year-old female patient with 5 years history of diabetes, Fontaine stage I. ***A,*** FBI showed unclear image of left anterior tibial artery *(white arrow).* ***B,*** Right anterior tibial artery was not showed in CE-MRA *(white arrow).*

ght blood flows, when phase encoding direction was placed in vascular. 3. The benefits of using FBI were non-radiative and no requirement of contrast agents. In recent years, many scholars stated that FBI had high sensitivity and specificity in the diagnosis of lower extremity PAD. The study results from Lim et al[13] found that FBI was an optimal treatment method with sensitivity of 92.2% and specificity of 92.4% in the diagnosis of lower extremity PAD. A study from Thierfelder et al[14] compared the imaging results of 21 patients with an advanced peripheral arterial occlusive disease between the methods of CE-MRA and NCE-MRA. The study results indicated that and NCE-MRA had significant value in clinical practice with a sensitivity of 97% and specificity of 96.7%.

The study results of this paper indicated no statistical difference in image quality between FBI and CE-MRA in diabetic patients with Fontaine stage I-III (Table III, Figure 2). The image quality of FBI is worse than CE-MRA in diabetic patients with Fontaine stage IV, and the observers lacked confidence in diagnosing 40% of the patients in Fontaine stage IV. The possible reasons of low image quality were as follow: 1. FBI was not sensible to subtle move. Patients with lower extremity PAD in Fontaine stage IV had severe rest pain and developed an involuntary twitch, which caused low image quality. 2. Low image quality of FBI had a relationship with vascular contractile function, and the patients in Fontaine stage IV had impaired vascular smooth muscle contraction. 3. The observers lacked experience in analyzing the images of FBI in the patients with Fontaine stage IV. Personalized examination indexes should be established based on individual patient condition, to improve the image quality[22]. 4. Patients in Fontaine stage IV had various degrees of arteriostenosis, which caused slow flow velocity in arteries. Thus, images lost after subtraction (Figure 3).

There was a statistical difference in detecting lower extremity arterial branches in the diabetic patients with Fontaine stage IV between FBI and CE-MRA (Table V). About 19% of absence were distal vascular branches (20 branches), which was ascribed to the slow blood flow of calf (Figure 4). The main contamination of CE-MRA included veins and soft tissues. Diabetes lower extremity PAD arteriovenous malformation or feet contamination caused a shadow in CE-MRA examination[23]. The main contamination of FBI was arterial pulse, which did not impact on the diagnosis (Figures 5, 6).

Conclusions

ECG-based FBI technique is very useful in the evaluation of diabetic patients with lower extremity PAD. Compared to CE-MRA, FBI has higher image quality in detecting lower extremity arterial branches, no apparent contamination in veins and soft tissues. Hence,

Table V. Rating results of tissue contamination of FBI and CE-MRA (n=44, $\bar{x}$ ±s).

	No.	FBI, (mean ± SD)	CE-MRA, (mean ± SD)	t-statistics	*p*-value
Overall	44	0.14±0.35	1.27±0.5	-14.782	0**
Fontaine stage I	16	0±0	1.06±0.44	-9.604	0**
Fontaine stage II	11	0±0	2.27±0.47	-9.037	0**
Fontaine stage III	12	0.08±0.29	1.33±0.49	-6.966	0**
Fontaine stage IV	5	1.00±0	1.80±0.45	-4	0.016*

FBI: fresh blood imaging, CE-MRA: contrast-enhanced MR angiography. *p<0.05, **p<0.01.

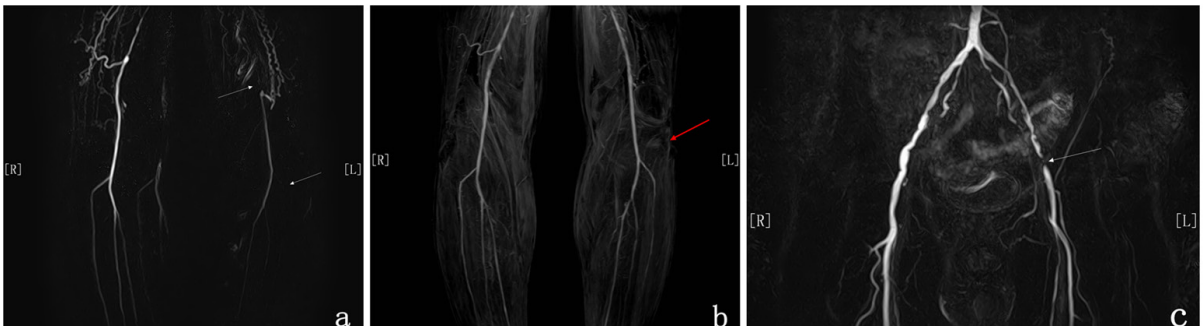

Figure 3. A 75-year-old male patient with 18 years history of diabetes, Fontaine stage IV. ***a,*** Low image quality of 5 lower extremity arterial branches (1 point) in FBI, no shadows of left anterior tibial artery *(white arrow)*. ***b,*** Severe contamination in CE-MRA (*red arrow*), arteriostenosis of bilateral iliac arteries, especially in the left *(white arrow)*.

FBI can replace CE-MRA as the method to examine patients in Fontaine stage I-III. It can also be used in diabetic patients with renal insufficiency in stage Fontaine IV, and the results of FBI examination should be considered with cardiac and renal functions as well as lower extremity arterial functions (Iliac artery and femoral artery). FBI can detect lower

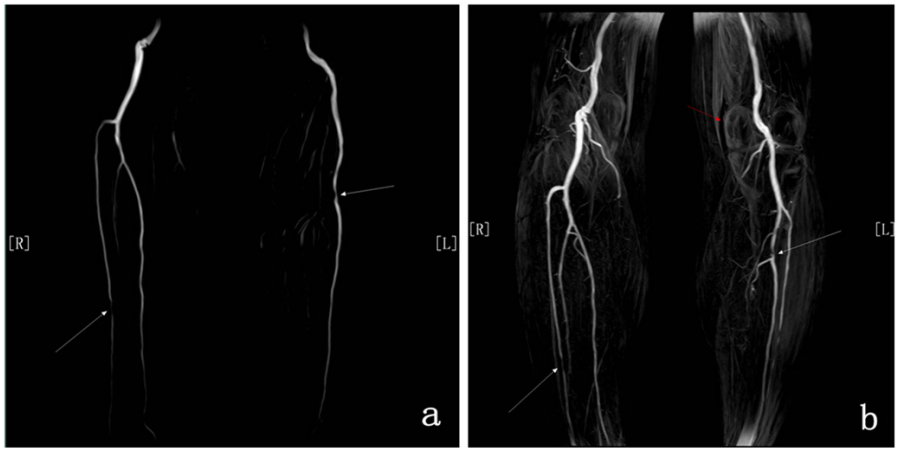

Figure 4. A 68-year-old female patient with 20 years history of diabetes, Fontaine stage IV. ***a,*** The images of right anterior tibial artery and partial left peroneal artery lost after subtraction in FBI (*white arrow*). Nine branches in right anterior tibial artery and 5 branches in left peroneal artery were detected. ***b,*** The sites of lost signals were the same between FBI and CE-MRA. Eleven branches in right anterior tibial artery and 8 branches in left peroneal artery were detected.

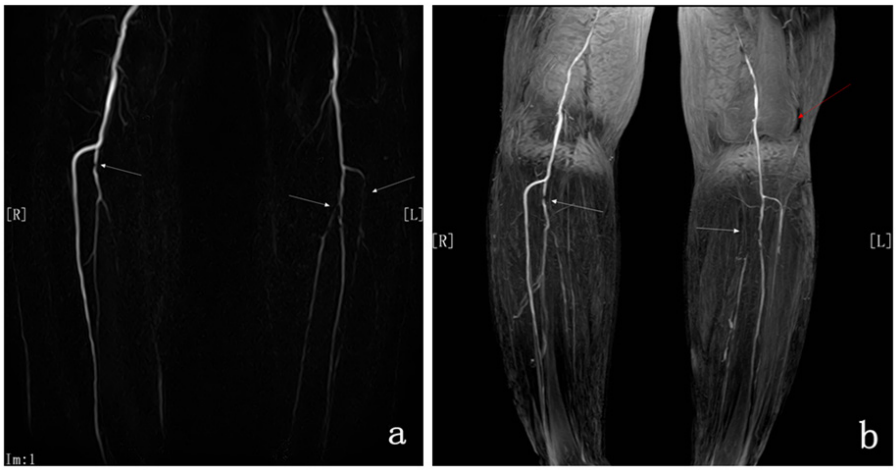

Figure 5. A 76-year-old female patient with 25 years history of diabetes, Fontaine stage IV. ***a,*** The images of right anterior tibial artery and left peroneal artery lost after subtraction in FBI (white arrow), no apparent tissue contamination. ***b,*** The sites of arteriostenosis of CE-MRA is the same as Figure 5a *(white arrow)* with apparent soft tissue shadow *(red arrow).*

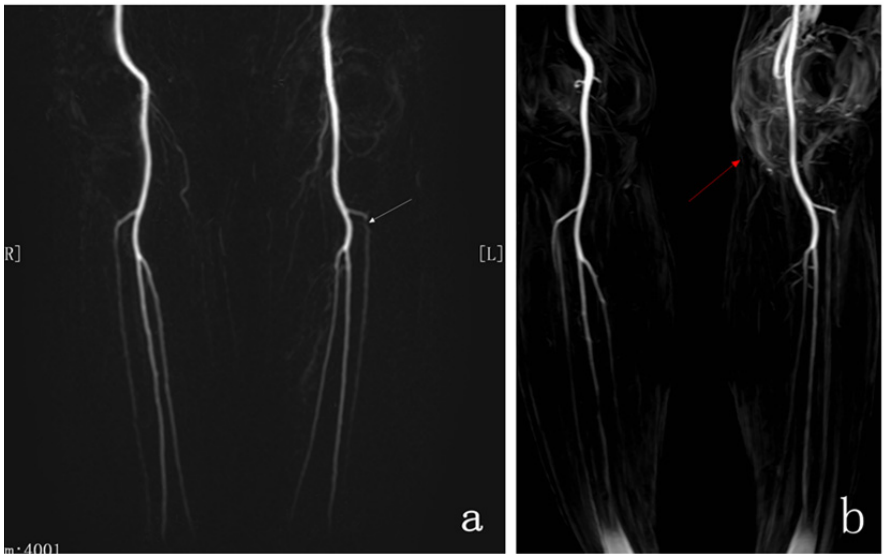

Figure 6. A 68-year-old female patient with 8 years history of diabetes, Fontaine stage II. ***a,*** The images of left anterior tibial artery lost after subtraction *(white arrow).* ***b,*** No abnormal was detected in CE-MRA. Severe contamination in knee joint soft tissues was detected due to gonarthromeningitis *(red arrow).*

extremity PAD in an early stage, and can be considered as a reference result for healthcare professionals in decision making with personalized treatment plans.

Grants

1. Innovation Funds for Development of Science and Technology in new PuDong area, Grant No.: PKJ2014-Y20.

2. Academic Leaders of the Health System of New Pudong Area, Grant No.: PWRd2011-05.

3. Shanghai Municipal Health and Family Planning Foundation, Grant No: 201440458.

Conflicts of interest

The authors declare no conflicts of interest.

References

1) Criqui MH, Denenberg JO, Langer RD, Fronek A. The epidemiology of peripheral arterial disease: importance of identifying the population at risk. Vasc Med 1997; 2: 221-226.

2) Yang W, Lu J, Weng J, Jia W, Ji L, Xiao J, Shan Z, Liu J, Tian H, Ji Q, Zhu D, Ge J, Lin L, Chen L, Guo X, Zhao Z, Li Q, Zhou Z, Shan G, He J, China. Na-

tional Diabetes and Metabolic Disorders Study Group. Prevalence of diabetes among men and women in China. N Engl J Med 2010; 362: 1090-1101.

3) Hiatt WR, Hoag S, Hamman RF. Effect of diagnostic criteria on the prevalence of peripheral arterial disease: the San Luis Valley Diabetes Study. Circulation 1995; 91: 1472-1479.

4) Most RS, Sinnock P. The epidemiology of lower extremity amputations in diabetic individuals. Diabetes Care 1983; 6: 87-91.

5) Dominguez A 3rd, Bahadorani J, Reeves R, Mahmud E, Patel M. Endovascular therapy for critical limb ischemia. Expert Rev Cardiovasc Ther 2015; 2: 1-16.

6) Steffens JC, Schäfer FK, Oberscheid B, Link J, Jahnke T, Heller M, Brossmann J. Bolus-chasing contrast-enhanced 3D MRA of the lower extremity. Comparison with intraarterial DSA. Acta Radiol 2003; 44: 185-192.

7) Hartung MP, Grist TM, François CJ. Magnetic resonance angiography: current status and future directions. J Cardiovasc Magn Reson 2011; 13: 19.

8) Shellock FG, Spinazzi A. MRI safety update 2008: part 1–MRI contrast agents and nephrogenic systemic fibrosis. AJR Am J Roentgenol 2008; 191: 1129-1139.

9) Edelman RR, Sheehan JJ, Dunkle E, Schindler N, Carr J, Koktzoglou I. Quiescent-interval single-shot unenhanced magnetic resonance angiography of peripheral vascular disease: technical considerations and clinical feasibility. Magn Reson Med 2010; 63: 951-958.

10) Miyazaki M, Takai H, Sutiura S, Wada H, Kuwahara R, Urata J. Peripheral MR angiography: separation of arteries from veins with flow spoiled gradient pulses in electro cardiography-triggered three dimensional half fourier fast spin-echo imaging. Radiology 2003; 227: 890-896.

11) Wedeen VJ, Meuli RA, Edelman RR, Geller SC, Frank LR, Brady TJ, Rosen BR. Projective imaging of pulsatile flow with magnetic resonance. Science 1985; 230: 946-948.

12) Hodnett PA, Ward EV, Davarpanah AH, Scanlon TG, Collins JD, Glielmi CB, Bi X, Koktzoglou I, Gupta N, Carr JC, Edelman RR. Peripheral arterial disease in a symptomatic diabetic population: prospective comparison ofrapid unenhanced MR angiography (MRA) with contrast-enhanced MRA. AJR Am J Roentgenol 2011; 197: 1466-1473.

13) Lim RP, Hecht EM, Xu J, Babb JS, Oesingmann N, Wong S, Muhs BE, Gagne P, Lee VS. 3D non gadolinium-enhanced ECG-gated MRA of the distal lower extremities: preliminary clinical experience. J Magn Reson Imaging 2008; 28: 181-189.

14) Thierfelder KM, Meimarakis G, Nikolaou K, Sommer WH, Schmitt P, Kazmierczak PM, Reiser MF, Theisen D. Non contrast-enhanced MR angiography at 3 Tesla in patients with advanced peripheral arterial occlusive disease. PLoS One 2014; 9: e91078.

15) Fontaine R, Kim M, Kieny R. Surgical treatment of peripheral circulation disorders. Helv Chir Acta 1954; 21: 499-533.

16) American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2013; 36(Suppl 1): S67-S74.

17) Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG; TASC II Working Group. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). J Vasc Surg 2007; 45 Suppl S: S5-67.

18) Hodnett PA, Ward EV, Davarpanah AH, Scanlon TG, Collins JD, Glielmi CB, Bi X, Koktzoglou I, Gupta N, Carr JC, Edelman RR. Peripheral arterial disease in a symptomatic diabetic population: prospective comparison of rapid unenhanced MR angiography (MRA) with contrast enhanced MRA. AJR Am J Roentgenol 2011; 197: 1466-1473.

19) Miyazaki M, Sugiura S, Tateishi F, Wada H, Kassai Y, Abe H. Non-contrast-enhanced MR angiography using 3D ECG-synchronized half-Fourier fast spin echo. J Magn Reson Imaging 2000; 12: 776-783.

20) Gutzeit A, Sutter R, Froehlich JM, Roos JM, Sautter T, Schoch E, Giger B, Wyss M, Graf N, Weyman C, Jenelten R, Binkert CA, Hergan K. ECG-triggered non-contrast-enhanced MR angiography (TRANCE) versus digital subtraction angiography (DSA) in patients with peripheral arterial occlusive disease of the lower extremities. Eur Radiol 2011; 21: 1979-1987.

21) Kassamali RH, Hoey ET, Ganeshan A, Littlehales T. A comparative analysis of noncontrast flow-spoiled versus contrast-enhanced magnetic resonance angiography for evaluation of peripheral arterial disease. Diagn Interv Radiol 2013; 19: 119-125.

22) Hoey ET, Ganeshan A, Puni R, Henderson J, Crowe PM. Fresh blood imaging of the peripheral vasculature: an emerging unenhanced MR technique. AJR Am J Roentgenol 2010; 195: 1444-1448.

23) Ho CF, Wu MH, Wu HM, Chang CY, Chen MC, Chou TY. Comparison of auto moving table contrast-enhanced 3-D MRA and iodinated contrast-enhanced DSA for evaluating the lower extremity arteries. J Chin Med Assoc 2004; 67: 511-520.