

A Comparison of the Association of Different Imaging Methods of Diabetic Foot Complications with Blood Flow Findings

Diyabetik Ayak Komplikasyonlarının Farklı Görüntüleme Yöntemlerinin Kan Akımı Bulguları ile İlişkisinin Karşılaştırılması

Sunay Sibel KARAYOL¹, Mustafa SEVER², Saime SHERMATOVA¹, Abdurrahim DUSAK¹

¹Department of Radiology, Faculty of Medicine, University of Harran, Şanlıurfa, TÜRKİYE

² Department of Emergency, Health Sciences University Izmir Tepecik Health Practices and Research Hospital, Izmir, TÜRKİYE

Abstract

Background: The aim of this study was to determine the relationship of soft tissue and bone lesions with vascular flow according to different imaging methods in patients with diabetic foot.

Materials and Methods: This retrospective, cross-sectional, descriptive study was conducted in the Radiodiagnostic Department of a university hospital.

Results: The most commonly seen finding was cellulitis (n:57, 72.2%) and the least seen was subchondral cyst (n:14, 17.7%). According to the CDUS findings, arterial blood flow was absent in 24.1%, and was monophasic in 27.8%. Vascular blood flow on CDUS was accepted as insufficient in 41 (51.9%) patients. On the CTA images, complete obstruction was determined in 21.5% of patients and >70% narrowing in 20.3%. Vascular blood flow was accepted as insufficient in 46 (58.2%) patients according to the CTA findings. In the interpretation of the CDUS findings, insufficient blood flow was determined in 63% of the patients determined with osteomyelitis, in 61% with cellulitis, in 34% with abscess, in 34% with tenosynovitis, in 29% with joint effusion, and in 17% with subchondral cyst. A statistically significant difference was determined in the blood flow determined with CDUS only in the patients determined with cellulitis (p=0.021).

Conclusions: In the diagnosis of complications developing secondary to diabetes, and in the decision for amputation, both CDUS and CTA imaging methods are of value.

Key Words: Colour Doppler Ultrasonography, Computed Tomography Angiography, Diabetic foot, Magnetic Resonance Imaging

Öz.

Amaç: Bu çalışmanın amacı diyabetik ayak hastalarında farklı görüntüleme yöntemlerine göre yumuşak doku ve kemik lezyonlarının vasküler akım ile ilişkisini belirlemektir.

Materyal ve Metod: Bu retrospektif, kesitsel, tanımlayıcı çalışma bir üniversite hastanesinin Radyodiagnostik bölümünde yapıldı.

Bulgular: En sık görülen bulgu selülit (n:57, %72.2) ve en az görülen bulgu subkondral kist (n:14, %17.7) idi. RDUS bulgularına göre %24,1'inde arteriyel kan akımı yoktu, %27,8'inde monofazik idi. 41 (%51,9) hastada RDUS'ta vasküler kan akımı yetersiz olarak kabul edildi. BTA görüntülerinde hastaların %21.5'inde tam tıkanıklık, %20.3'ünde >%70 daralma saptandı. BTA bulgularına göre 46 (%58,2) hastada vasküler kan akımı yetersiz kabul edildi. RDUS bulgularının yorumlanmasında osteomyelit saptanan hastaların %63'ünde, selülit saptananların %61'inde, apse saptananların %34'ünde, tenosinovit saptananların %34'ünde, eklem efüzyonu saptananların %29'unda ve subkondral kist saptanan hastaların %29'unda yetersiz kan akımı saptandı. Sadece selülit saptanan hastalarda RDUS ile belirlenen kan akımında istatistiksel olarak anlamlı fark saptandı (p=0.021).

Sonuç: Diyabete bağlı gelişen komplikasyonların tanısında ve amputasyon kararında hem RDUS hem de BTA görüntüleme yöntemleri değerlidir.

Anahtar kelimeler: Renkli Doppler Ultrasonografi, Bilgisayarlı Tomografi Anjiyografi, Diyabetik ayak, Magnetik Rezonans Görüntüleme

Corresponding Author/Sorumlu Yazar

Dr. Sunay Sibel KARAYOL
Department of Radiology,
Faculty of Medicine,
University of Harran,
Şanlıurfa, TÜRKİYE

E-mail: ssibelkarayol@gmail.com

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Introduction

Diabetic foot wounds developing as a result of chronic complications of Diabetes Mellitus (DM) are a clinical condition leading to great physical, mental and socio-economic damage, and can result in organ loss (1). The frequency is significantly higher in males (2). It has been reported that every diabetic patient has a lifelong 15% risk of developing a diabetic foot wound, and in 7-20% of these patients, these wounds result in amputation of the extremity (1, 3). In the USA, approximately two-thirds of non-traumatic amputations are associated with diabetic foot wounds (1, 4). Peripheral artery disease is a major risk factor for lower extremity amputation. Although foot ulcers are not the most common reason, they are an accompanying factor in 25% of patients. The presence of a palpable pulse does not exclude peripheral vascular disease (5). Parameswaran et al (6) reported that evaluation with the Ankle Brachial Pressure Index had 63% sensitivity and 97% specificity. Therefore, the contribution of radiology to diabetic foot management cannot be ignored.

In the clinic, the main aim in the treatment of diabetic foot patients is to differentiate infection from changes secondary to neuropathy and to prevent amputations associated with delayed osteomyelitis. Differentiation of these two pathologies is achieved with imaging methods (7), the most widespread of which is direct radiography. According to the American College of Radiology Appropriate Use Criteria list, it has been reported as the most appropriate method in different combinations of findings consisting of soft tissue swelling, neuropathy and ulcer (7,8).

Colour Doppler Ultrasonography (CDUS), which encodes blood flow information as a colour spectrum in a selected area on an ultrasonography image is the basic non-invasive imaging method of the vascular system. Changes occurring at different degrees from the early stages to the late stages of vascular complications in the process of diabetic foot development can be identified (7).

Lower extremity arterial Computed Tomography Angiography (CTA), which can be shown in great detail, can give more quantitative information about vascular structures and is a diagnostic method which has been used more often recently. Magnetic Resonance Imaging (MRI) has higher sensitivity and specificity than other methods, and is an imaging method which can better differentiate changes associated with neuropathy and infection (7).

The aim of this study was to determine the relationship of soft tissue and bone lesions with vascular flow according to different imaging methods in patients with diabetic foot.

Materials and Methods

This retrospective, cross-sectional, descriptive study was conducted in the Radiodiagnostic Department of a university hospital. Approval for the study was granted by the Local Ethics Committee of Harran University (decision no:E.35550, dated: 28.08.2019). The study included adult patients diagnosed with diabetic foot between January

2018 and February

2020, for whom radiological imaging was requested. The patients included in the study were those who were applied with foot MRI, lower extremity arterial CDUS and lower extremity arterial CTA. CDUS examinations were performed by radiologists with at least 2 years of experience. Patients were excluded from the study if any one of these 3 examinations had not been performed at the same time. From the hospital PACS (Picture Archiving and Communication Systems), the MR and CTA images of the patients were re-evaluated by an experienced radiology specialist, blinded to the clinical table. Femoral artery, popliteal artery, tibialis anterior and posterior arteries, peroneal artery, dorsalis pedis artery were evaluated in CDUS and CTA examinations. Patient information was retrieved from the hospital medical records system.

Infection findings (cellulitis, abscess, osteomyelitis, tenosynovitis, joint effusion, subchondral cyst) and arterial vascular blood flow (sufficient/insufficient) were evaluated as 2 main parameters and sub-headings. Diagnostic findings of infection obtained on foot MRI were accepted as the gold standard.

The same patients were separated into 2 groups according to the CTA images, as those with insufficient arterial blood flow (those with no arterial blood flow [full obstruction] and those with arterial narrowing of $\geq 70\%$), and those with sufficient arterial blood flow (those with 50-70% arterial narrowing and those with $< 50\%$ narrowing).

The CDUS results were evaluated from a re-interpretation of the old reports. Patients were separated into 2 groups according to the CDUS results as those with insufficient arterial flow (no flow or monophasic flow) and those with sufficient arterial flow (biphasic or triphasic flow).

To evaluate the relationship between the blood flow evaluation methods and prognosis, comparisons were made by separating the patients into 2 groups as those applied with medical treatment or debridement (Group 1), and those applied with amputation (Group 2). MR examinations were performed using a Magnetom Skyra[®], (Siemens Healthcare Erlangen Germany) device with 3-T magnetic power, and a 16-channel extremity coil. The same parameters were used for all patients in the acquisition of axial fat-suppressed T2A TSE images (NEX: 1, TR:2870ms, TE:45ms, FA:140, Thk:4 mm) and T1A images (NEX: 1, TR: 521ms, TE: 12ms, FA:150 Thk: 4 mm). In the CTA imaging, a 256-slice Dual CT[®] (General Electric Healthcare, Waukesha, WI, USA) was used. CDUS examinations were performed using an ACUSON S3000 (Siemens Healthcare Erlangen Germany) device with a 9L4 linear probe.

On the MRI findings, the presence of abscess was accepted as fluid with characteristics similar to fluid on fluid-sensitive sequences, thick irregular walls with oedema observed in the surrounding and peripheral staining on post-contrast images. Osteomyelitis was accepted as a low signal in bone marrow on T-weighted images, a high signal, loss of cortex,

and an increased signal in the surrounding associated with periosteal reaction on T2-weighted series, and excessive contrast involvement following the administration of contrast material. Cellulitis was accepted as thickening in the skin, evident lines in subcutaneous tissues, and intense staining after contrast material administration. Tenosynovitis was accepted as thickening in the tendon sheath and the presence of fluid, joint effusion as increased fluid in the joint space, and the presence of subchondral cyst as cystic changes in the subchondral area (9, 10).

Statistical Analysis

Data obtained in the study were analyzed statistically using IBM SPSS for Windows Ver. 23.0 software (Statistical Package for Social Sciences, IBM Inc., Illinois-USA®). Conformity of the data to normal distribution was evaluated with the Shapiro-Wilk Normality test. Descriptive statistics were stated as mean \pm standard deviation or median (min-max) values, frequency (n) and percentage (%), in accordance with the distribution. The Chi-square test was used to compare categorical variables in groups, and the Mann Whitney U test was used for continuous variables. A value of $p < 0.05$ was considered statistically significant.

Results

Evaluation was made of a total of 79 patients, comprising 52 (65.8%) females and 27 (34.2%) males with a mean age of 59.9 ± 8.8 years (range, 41-81 years). The most commonly seen finding was cellulitis (n:57, 72.2%) and the least seen was subchondral cyst (n:14, 17.7%) (Table 1). According to the CDUS findings, arterial blood flow was absent in 24.1%, and was monophasic in 27.8%. Vascular blood flow on CDUS was accepted as insufficient in 41 (51.9%) patients. On the CTA images, complete obstruction was determined in 21.5% of patients and $>70\%$ narrowing in 20.3%. Vascular blood flow was accepted as insufficient in 46 (58.2%) patients according to the CTA findings (Table 2). In the CTA examinations, insufficient blood flow was determined in 65% of the patients determined with osteomyelitis, in 48% with abscess, in 76% with cellulitis, in 26% with tenosynovitis, in 35% with joint effusion, and in 22% with subchondral cyst. No statistically significant difference was determined between the clinical findings and the blood flow status when the grouping was made according to the CTA reports. In the interpretation of the CDUS findings, insufficient blood flow was determined in 63% of the patients determined with osteomyelitis, in 61% with cellulitis, in 34% with abscess, in 34% with tenosynovitis, in 29% with joint effusion, and in 17% with subchondral cyst. A statistically significant difference was determined in the blood flow determined with CDUS only in the patients determined with cellulitis ($p=0.021$) (Table 3). In 50% of the patients with $>70\%$ narrowing and 11% of those with full obstruction identified on CTA, the presence of biphasic or triphasic flow was reported with CDUS. Monophasic flow was reported to be observed with CDUS in 35% of patients with full obstruction

identified on CTA (Table 4). In 30% of the patients evaluated with insufficient blood flow on CTA, flow was determined to be sufficient according to the CDUS findings, and in 39% of the patients evaluated with sufficient blood flow on CTA, flow was determined to be insufficient according to the CDUS findings. A statistically significant difference was determined in the comparison of the CTA vascular narrowing rates and the CDUS blood flow findings ($p=0.007$) (Table 4). Recovery was determined in 30 (38%) patients with medical treatment only and in 21 (26.6%) with debridement and medical treatment. Amputation was performed in 35.4% of patients: toe amputation (n:16, 20.3%), foot amputation (n:6, 7.6%) and below-the-knee amputation (n:6, 7.6%). The relationship between prognosis and imaging methods was evaluated. In the patient group determined with insufficient blood flow in both CDUS and CTA imaging methods, significantly more amputations were performed ($p=0.035$, $p=0.000$) (Table 5). (Figure 1a,b,c) (Figure 2a,b,c)

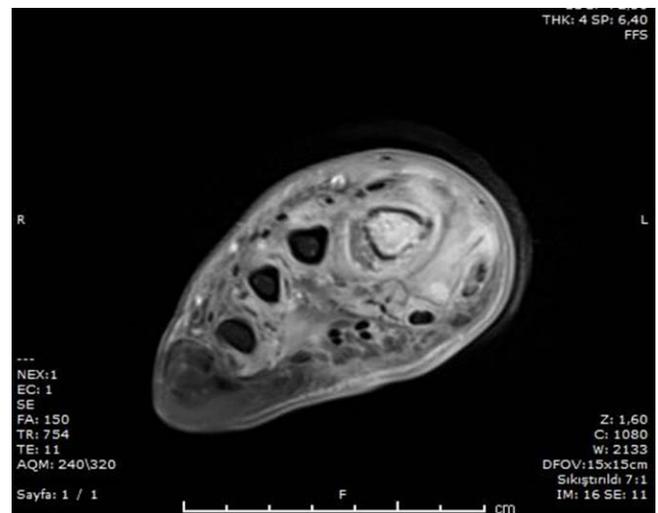


Figure 1a. Axial T2.

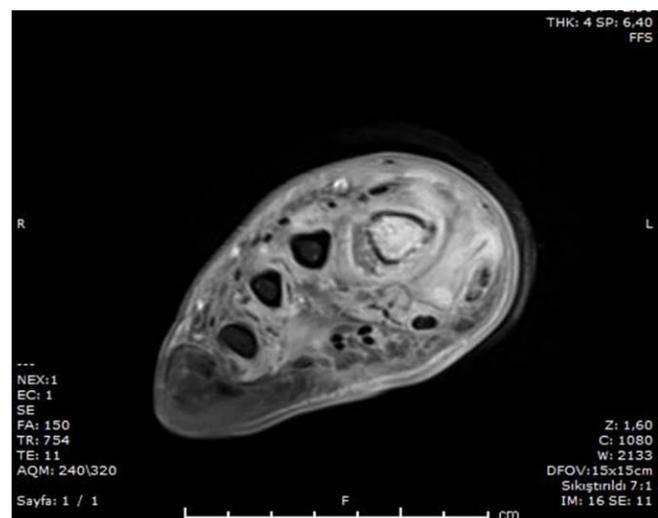


Figure 1b. Axial T1 In weighted MR images, signal changes reflecting the proximal phalanx of the first finger and osteomyelitis in the first metatarsal bone, an abscess formation of approximately 22x19 mm fistulized to the skin at the level of the first metatarsopharyngeal joint, and diffuse signal increases reflecting edema-inflammation in the surrounding soft tissue

planes were observed.

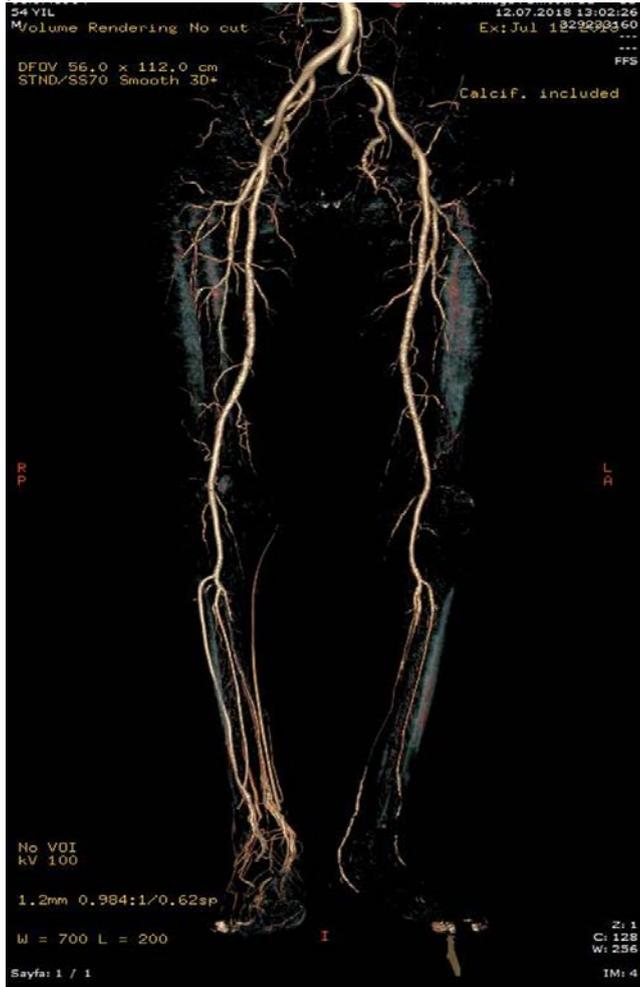


Figure 1c. In MIP CT angiography image; The tibialis anterior posterior and peroneal arteries on the left show less contrast than expected, and the peroneal artery cannot be traced in the lower half (Stenosis?).

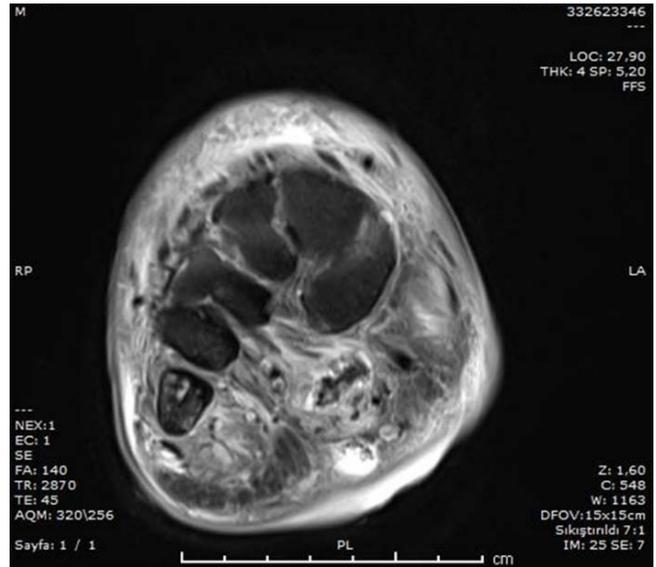


Figure 2b. Axial T1 weighted MR images are compatible with the phalanges of the fifth finger and the fourth and fifth metatarsal bone osteomyelitis and accompanying soft tissue abscess formations.

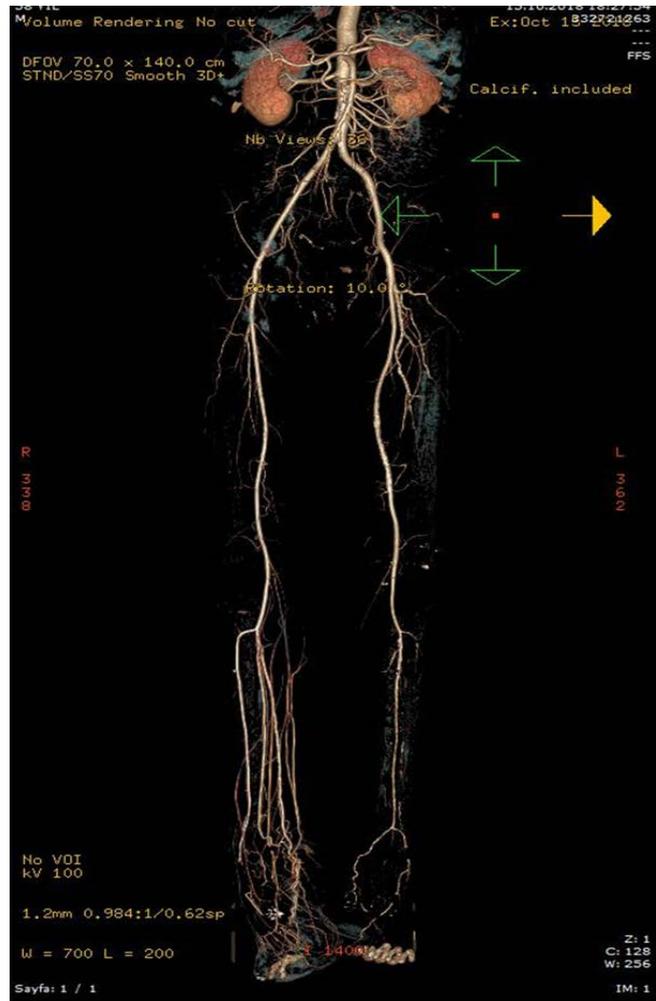


Figure 2c. In MIP CT angiography image; The peroneal artery on the left is very fine calibrated, but cannot be traced in the lower half (occluded?).

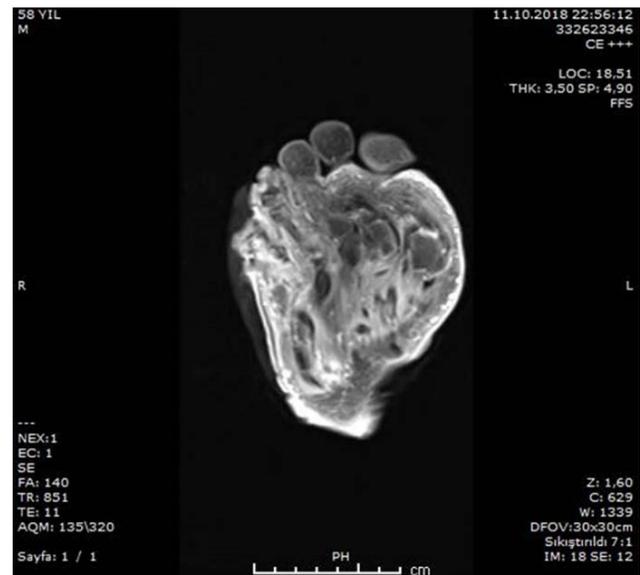


Figure 2a. Axial T2.

Table 1. Clinical characteristics according to the MRI findings.

Clinical Characteristics		n	(%)	Total n (%)
Osteomyelitis	Absent	32	40.5	79 (100)
	Present	47	59.5	
Abscess	Absent	47	59.5	79 (100)
	Present	32	40.5	
Cellulitis	Absent	22	27.8	79 (100)
	Present	57	72.2	
Tenosynovitis	Absent	52	65.8	79 (100)
	Present	27	34.2	
Joint effusion	Absent	52	65.8	79 (100)
	Present	27	34.2	
Subchondral cyst	Absent	65	82.3	79 (100)
	Present	14	17.7	

Table 2. The relationship between blood flow and imaging methods.

Imaging methods		n	(%)	n (%)	
CDUS Flow Findings	Insufficient blood flow	No flow	19	24.1	41 (51.9)
		Monophasic flow	22	27.8	
	Sufficient blood flow	Biphasic or triphasic flow	38	48.1	38 (48.1)
Total				79 (100)	
CTA Flow Findings	Sufficient blood flow	< 50% narrowing	36	45.6	46 (58.2)
		50-70% narrowing	10	12.7	
		>70% narrowing	16	20.3	
		Total narrowing	17	21.5	
Total				79 (100)	

CDU: Colour Doppler Ultrasound; CTA: Computed Tomography Angiography

Table 3. The relationship between CDUS flow findings and the sociodemographic and clinical characteristics.

Sosyodemografik ve klinik özellikler		CDUS blood flow			p value	CTA blood flow			p value
		Insufficient n (%)	Sufficient n (%)	Total n (%)		Insufficient n (%)	Sufficient n (%)	Total n (%)	
Gender	Male	31 (75.6)	21 (55.3)	52 (65.8)	0.057	28 (60.9)	24 (72.7)	52 (65.8)	0.273
	Female	10 (24.4)	17 (44.7)	27 (34.2)		18 (39.1)	9 (27.3)	27 (34.2)	
Osteomyelitis	Absent	15 (36.6)	17 (44.7)	32 (40.5)	0.461	16 (34.8)	16 (48.5)	32 (40.5)	0.221
	Present	26 (63.4)	21 (55.3)	47 (59.5)		30 (65.2)	17 (51.5)	47 (59.5)	
Abscess	Absent	27 (65.9)	20 (52.6)	47 (59.5)	0.232	24 (52.2)	23 (69.7)	47 (59.5)	0.118
	Present	14 (34.1)	18 (47.4)	32 (40.5)		22 (47.8)	10 (30.3)	32 (40.5)	
Cellulitis	Absent	16 (39.0)	6 (15.8)	22 (27.8)	0.021	11 (23.9)	11 (33.3)	22 (27.8)	0.357
	Present	25 (61.0)	32 (84.2)	57 (72.2)		35 (76.1)	22 (66.7)	57 (72.2)	
Tenosynovitis	Absent	27 (65.9)	25 (65.8)	52 (65.8)	0.995	34 (73.9)	18 (54.5)	52 (65.8)	0.073
	Present	14 (34.1)	13 (34.2)	27 (34.2)		12 (26.1)	15 (45.5)	27 (34.2)	
Joint effusion	Absent	29 (70.7)	23 (60.5)	52 (65.8)	0.339	30 (65.2)	22 (66.7)	52 (65.8)	0.893
	Present	12 (29.3)	15 (39.5)	27 (34.2)		16 (34.8)	11 (33.3)	27 (34.2)	
Subchondral cyst	Absent	34 (82.9)	31 (81.6)	65 (82.3)	0.875	36 (78.3)	29 (87.9)	65 (82.3)	0.270
	Present	7 (17.1)	7 (18.4)	14 (17.7)		10 (21.7)	4 (12.1)	14 (17.7)	

Percentage (%) values are the column percentage. CDU: Colour Doppler Ultrasound; CTA: Computed Tomography Angiography

Table 4. Comparisons of the CTA and CDUS narrowing and blood flow findings.

CDUS Flow Findings		CTA Narrowing Rates				Total n = 79 (%)
		Sufficient flow		Insufficient flow		
		< 50% n = 36 (%)	50%-70% n = 10 (%)	> 70% n = 16 (%)	Full obstruction n = 17 (%)	
<i>Insufficient flow</i>	<i>No flow</i>	2 (5.6)	3 (30)	5 (31.3)	9 (52.9)	19 (24.1)
	<i>Monophasic</i>	10 (27.8)	3 (30)	3 (18.8)	6 (35.3)	22 (27.8)
<i>Sufficient flow</i>	<i>Biphasic or triphasic</i>	24 (66.7)	4 (40)	8 (50)	2 (11.8)	38 (48.1)

CDUS Flow Findings	CTA Flow Findings		Total n (%)	p value
	Sufficient n (%)	Insufficient n (%)		
<i>Sufficient</i>	28 (60.9)	10 (30.3)	38 (48.1)	0.007
<i>Insufficient</i>	18 (39.1)	23 (69.7)	41 (51.9)	
Total n (%)	46 (58.2)	33 (41.8)	79 (100)	

Percentage (%) values are the column percentage. CDUS: Colour Doppler Ultrasound; CTA: Computed Tomography Angiography

Table 5. Relationships between prognosis and blood flow according to the imaging methods.

Prognosis	CDUS Flow Findings			p value	CTA Flow Findings			p value
	Insufficient n (%)	Sufficient n (%)	Total n (%)		Insufficient n (%)	Sufficient n (%)	Total n (%)	
Group 1	22 (27.8)	29 (36.7)	51 (64.6)	0.035	13 (16.5)	38 (48.1)	51 (64.6)	0.000
Group 2	19 (24.1)	9 (11.4)	28 (35.4)		20 (25.3)	8 (10.1)	28 (35.4)	
Total n (%)	41 (51.9)	38 (48.1)	79 (100)		33 (41.8)	46 (58.2)	79 (100)	

Percentage (%) values are the column percentage. CDUS: Colour Doppler Ultrasound; CTA: Computed Tomography Angiography

Discussion

The aim of using non-invasive methods in the treatment of diabetic foot is to obtain basic information on which decisions will be based related to advanced tests or treatment. Although catheter angiography is the gold standard in the evaluation of vascular structures, it is an invasive and expensive method. In addition, not only physiological information but also more anatomic information is provided. While CTA provides anatomic evaluation, CDUS also provides functional evaluation. As peripheral artery disease is known to be a functional problem, CTA, which provides a more morphological and limited hemodynamic evaluation, remains insufficient and so a functional examination such as CDUS is required (11). When the relationship of these two modalities with prognosis is examined, it can be seen that amputation rates increase when there is insufficient blood flow.

Of the cases seen to have sufficient blood flow on CTA, 39% were identified as having insufficient blood flow on CDUS, or from another perspective, 30% of the patients with insufficient blood flow on CTA, were identified with sufficient blood flow.

Although this seems to be a negative aspect of the CDUS method, that mono and biphasic flow was determined on CDUS in 8 of 17 patients with a diagnosis of diabetic foot with complete obstruction on CTA seems to be a more realistic diagnosis. In a review by Kilicoğlu (7), it was reported that although rare, very low flows could be determined with CDUS in distal arteries determined with complete obstruction on angiography.

With the exception of cellulitis clearly determined on MRI, no difference was seen between the two imaging methods in respect of the demonstration of any of the 7 clinical criteria. Blood flow was reported to be sufficient more often with CDUS, only when cellulitis was present in the patients with diabetic foot. From the basic known pathophysiology, although this could be due to an increase in vasodilatation and blood circulation associated with neuromediators in inflammatory reactions, it may also be because of an acceleration in systolic flow in this region as the narrowness increases in the vascular lumen (7, 11).

Another important finding of the study was that the blood flow was determined to be insufficient on CDUS in more than 60% of the diabetic foot patients diagnosed with osteomyelitis and cellulitis on MRI (63%, 61%, respectively). Although not to a statistically significant level, higher rates of insufficient flow were determined on CTA, in the presence of these two diagnoses, including other clinical diagnoses (65%, 76%, respectively). In comparison with diagnostic angiography, the sensitivity and specificity of CDUS examination has been reported to be extremely high in the evaluation of blood flow (7, 11).

It has been reported that amputation rates in patients with diabetic foot could be reduced by 50% with a multidisciplinary approach to correct diagnosis and treatment (5). CTA is a non-invasive examination method which is used in the evaluations of lower extremity vascular structures, which can show collateral circulation and variations in addition to normal anatomy, and from which 3-dimensional

images can be formed. Although there are also disadvantages such as exposure to ionising radiation and the need to use contrast material, CTA is widely used in evaluation before surgery to arterial structures or endovascular interventional procedures (13).

MRI is another imaging method with an important place in the management of diabetic foot. It is a method which does not contain ionising radiation, has high soft tissue resolution and provides a definitive diagnosis in many diseases. It has been reported to have 90% sensitivity and 83% specificity in diabetic foot (8, 14). Contrast MRI examination of diabetic foot provides detailed information about abscess, osteomyelitis, tendinitis, tenosynovitis, joint effusion, and neuropathic arthropathy, which cannot be seen on inspection (15). It is also useful in surgical planning and determining localisation (13).

Changes in neuropathic arthropathy start first from bone tissue and result in deformation, while infection emerges with defects such as ulcers and calluses developing primarily in the skin. Anatomic differentiation of changes in the bone structure, the preservation of skin integrity, and the contrast pattern are important in the differential diagnosis (7). The application of dynamic contrast MRI is a reliable, non-invasive imaging method, providing parameters which can be repeated in the differential diagnosis of osteomyelitis from acute neuropathic arthropathy. Thus, clinicians can select subsequent procedures appropriate for osteomyelitis in diabetic foot, and treatments can be planned accordingly (17).

There were some limitations to this study, primarily that the retrospective design could have caused difficulties in accessing some data. There was no interobserver reliability evaluation of the radiologist who re-interpreted the CTA findings, but the mandatory specialist training received was accepted as the gold standard. The CDUS comments were used in their original form because the procedure could not be applied again.

Conclusion

In conclusion, the relationships between CTA flow findings and clinical diagnosis provided similar results when compared with the relationships between the diagnosis and the flow findings of CDUS, which is less expensive and easy to apply. In the diagnosis of complications developing secondary to diabetes, and in the decision for amputation, both CDUS and CTA imaging methods are of value. The clinical and examination findings of the diabetic patient should not be ignored when deciding which of the MRI, CDUS and CTA examinations should be applied.

Ethical Approval: This retrospective, cross-sectional, descriptive study was conducted in the Radiodiagnostic Department of a university hospital. Approval for the study was granted by the Local Ethics Committee of Harran University (decision no:E.35550, dated: 28.08.2019).

Author Contributions:

Concept: SSK, MS.

Literature Review: SSK

Design : SSK, AD

Data acquisition: SSK

Analysis and interpretation: SSK, MS, SS

Writing manuscript: MS, SSK

Critical revision of manuscript: . MS, SSK, SS, AD

Conflict of Interest: None

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