

## Comparing the Efficacy of CT Angiography and Doppler Ultrasound in Diagnosing Peripheral Arterial Disease in Diabetic Saudi Arabian Patients: A Retrospective Study

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### Abstract

Peripheral arterial disease (PAD) is a major complication of diabetes that increases the risk of lower extremity amputation and cardiovascular mortality. Prompt diagnosis of PAD is critical for initiating appropriate management and preventing adverse outcomes. CT angiography (CTA) and Doppler ultrasound (DUS) are two non-invasive imaging modalities commonly used to evaluate PAD, but their comparative effectiveness in diabetic patients remains unclear.

This retrospective study aimed to compare the diagnostic performance of CTA and DUS for detecting PAD in diabetic Saudi Arabian patients, using digital subtraction angiography (DSA) as the reference standard. We reviewed the medical records and imaging studies of 325 diabetic patients (mean age  $59.7 \pm 10.4$  years, 61% male) who underwent CTA, DUS, and DSA for suspected PAD at a tertiary care center in Riyadh between 2015-2020.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of CTA and DUS were calculated for diagnosing  $\geq 50\%$  stenosis, with subgroup analyses based on lesion location (aortoiliac, femoropopliteal, infrapopliteal). CTA demonstrated higher overall sensitivity (93% vs. 81%,  $p < 0.001$ ), specificity (96% vs. 92%,  $p < 0.05$ ), PPV (93% vs. 87%,  $p < 0.05$ ), NPV (96% vs. 89%,  $p < 0.01$ ), and accuracy (95% vs. 88%,  $p < 0.001$ ) compared to DUS. The diagnostic superiority of CTA was most pronounced for detecting infrapopliteal disease.

In conclusion, this large retrospective study found that CTA had greater diagnostic efficacy than DUS for evaluating PAD in diabetic Saudi patients, particularly in assessing distal arterial segments. Incorporating CTA in the diagnostic algorithm for high-risk patients may improve the detection and treatment of PAD, thereby reducing limb loss and mortality in this population. However, the choice of imaging modality should be individualized based on patient factors, resource availability, and clinical expertise.

**Keywords:** *peripheral arterial disease, diabetes mellitus, CT angiography, Doppler ultrasound, diagnostic accuracy, Saudi Arabia*

## Introduction

Peripheral arterial disease (PAD) is a manifestation of systemic atherosclerosis characterized by stenosis or occlusion of the arteries supplying the lower extremities (Criqui & Aboyans, 2015). The global burden of PAD has increased significantly in recent decades, with an estimated prevalence of 237 million cases in 2015 (Song et al., 2019). Diabetes is a major risk factor for PAD, conferring a 2- to 4-fold increased risk compared to non-diabetic individuals (Nativel et al., 2018). Moreover, PAD in diabetic patients tends to have a more aggressive course, with a predilection for distal vessel involvement and a higher risk of critical limb ischemia (Vrsalovic & Vucur, 2016).

The diagnosis of PAD is crucial given its association with significant morbidity, functional impairment, and cardiovascular mortality (Conte et al., 2019). Patients with PAD have a 3- to 5-fold increased risk of death from cardiovascular causes compared to those without PAD (Criqui & Aboyans, 2015). Furthermore, diabetic patients with PAD have a strikingly elevated risk of lower extremity amputation, with rates exceeding 20% at 5 years in some studies (Spreen et al., 2016). Timely detection and treatment of PAD can improve symptoms, functional status, and cardiovascular outcomes (Gerhard-Herman et al., 2017).

Despite its substantial health impact, PAD remains underdiagnosed and undertreated in clinical practice (Hirsch et al., 2007). Current guidelines recommend PAD screening in high-risk patients, including all adults with diabetes over 50 years of age (Aboyans et al., 2018; American Diabetes Association, 2021). While the ankle-brachial index (ABI) is the initial diagnostic test, imaging is often required to confirm and localize PAD (Armstrong et al., 2020). Digital subtraction angiography (DSA) is considered the gold standard but its invasive nature and potential complications limit its routine use (Misra et al., 2021).

Non-invasive imaging techniques like computed tomography angiography (CTA) and Doppler ultrasound (DUS) are increasingly utilized to diagnose PAD (Pollak & Kramer, 2017). CTA provides high-resolution, three-dimensional images of the arterial tree with excellent accuracy but involves radiation exposure and iodinated contrast (Simpson et al., 2021). In contrast, DUS is a relatively inexpensive, radiation-free modality that assesses both vascular anatomy and hemodynamics but has lower spatial resolution and can be technically challenging in heavily calcified arteries (Chaudhari & Rogan, 2022).

Although CTA and DUS are widely used, their comparative effectiveness for detecting PAD in diabetic patients remains incompletely defined. Previous studies have shown conflicting results, with some reporting superior accuracy of CTA and others demonstrating similar performance between the modalities (Hingorani et al., 2008; Ji et al., 2019; Kayhan et al., 2012). Most of these studies were conducted in Western populations, highlighting the need for research in other geographic regions with a high prevalence of diabetes, such as the Middle East.

Saudi Arabia has one of the highest rates of diabetes globally, with an estimated 4.3 million cases in 2021 projected to reach 7.4 million by 2045 (IDF Diabetes Atlas, 2021). This immense diabetes burden likely translates to an increased risk of PAD in the Saudi population. However, limited data exist on the epidemiology and diagnosis of PAD among diabetic individuals in Saudi Arabia. A retrospective study at a single center in Riyadh found a PAD prevalence of 23.1% based on ABI screening, but did not compare imaging modalities (Al-Sheikh et al., 2018).

Given the paucity of research in this area, we aimed to compare the diagnostic performance of CTA and DUS for detecting PAD in diabetic Saudi patients using DSA as the reference standard. Understanding the strengths and limitations of each technique may help optimize the evaluation and management of PAD in this high-risk

population, potentially reducing the incidence of adverse limb events and cardiovascular complications. The results could also guide resource allocation and clinical decision-making in Saudi Arabia and other countries facing a growing epidemic of diabetes and its macrovascular sequelae.

## Literature Review

### Epidemiology and Clinical Significance of PAD

Peripheral arterial disease (PAD) is a highly prevalent condition that affects over 230 million individuals worldwide (Roth et al., 2020). The burden of PAD increases sharply with age, ranging from 5% in those 40-49 years to 20% in those over 80 years (Criqui & Aboyans, 2015). Diabetes is a potent risk factor for PAD, with a prevalence of 20-30% among diabetic patients compared to 10-15% in the general population (Nativel et al., 2018). The combination of diabetes and PAD portends a dismal prognosis, with 5-year mortality rates surpassing 50% (Narula et al., 2018).

PAD is associated with considerable morbidity, functional impairment, and reduced quality of life. Patients with PAD have a 2- to 6-fold increased risk of myocardial infarction, stroke, and cardiovascular death compared to those without PAD (Criqui & Aboyans, 2015). Moreover, PAD can progress to chronic limb-threatening ischemia (CLTI), manifesting as ischemic rest pain, non-healing ulcers, or gangrene (Conte et al., 2019). The risk of major amputation exceeds 20% at 1 year and 50% at 5 years in patients with CLTI, with even higher rates among those with diabetes (Pérez-Panero et al., 2019).

Prompt diagnosis and treatment of PAD is paramount to improve outcomes. Management strategies include cardiovascular risk factor modification, antiplatelet therapy, statins, smoking cessation, exercise therapy, and revascularization in selected cases (Aboyans et al., 2018; Conte et al., 2019). However, PAD remains underrecognized and undertreated, with less than half of affected patients receiving guideline-recommended therapies in some studies (Morley et al., 2018). Improved screening and diagnostic modalities are needed to identify PAD early in its course and prevent devastating complications.

### Diagnostic Imaging Modalities for PAD

A variety of imaging techniques are used to diagnose PAD, each with inherent advantages and disadvantages. Catheter-based digital subtraction angiography (DSA) is the conventional reference standard, offering detailed visualization of the arterial lumen to guide treatment decisions (Ali et al., 2022). However, DSA is invasive, resource-intensive, and carries risks such as bleeding, vascular injury, and contrast nephropathy (Verikokos et al., 2014). Consequently, non-invasive imaging modalities have emerged as attractive alternatives for the initial evaluation of PAD.

Computed tomography angiography (CTA) is a contrast-enhanced cross-sectional technique that provides high-resolution, three-dimensional images of the entire lower extremity vasculature. Numerous studies have validated the excellent accuracy of CTA for detecting significant PAD, with pooled sensitivities of 95-99% and specificities of 91-97% compared to DSA (Healy et al., 2013; Met et al., 2009). CTA reliably delineates the location, severity, and extent of atherosclerotic lesions, aiding in procedural planning and follow-up (Menke & Larsen, 2010). However, the radiation exposure and potential for contrast-induced nephropathy limit the repeatability of CTA in certain patient populations.

Doppler ultrasound (DUS) is a non-invasive, radiation-free modality that combines B-mode imaging of the vessel wall with color and spectral Doppler assessment of blood flow. DUS can diagnose PAD based on the presence of arterial stenosis, abnormal flow velocities, and dampened waveforms (Sibley et al., 2017). Reported sensitivities and specificities of DUS range from 80-98% and 89-99%, respectively, for detecting >50% stenosis, with better performance for proximal disease (Chaudhari & Rogan, 2022; Collins et al., 2007). DUS

is also valuable for serial surveillance and monitoring response to treatment given its wide availability and lack of ionizing radiation.

### Comparative Studies of CTA and DUS

Multiple studies have compared the diagnostic accuracy of CTA and DUS for PAD, yielding mixed findings. A meta-analysis by Jens et al. (2013) evaluated 12 studies using CTA and DUS to detect >50% stenosis, with DSA as the reference standard. CTA demonstrated higher pooled sensitivity (97% vs. 88%) and specificity (94% vs. 92%) compared to DUS, particularly for infrapopliteal disease. The authors concluded that CTA was more accurate than DUS for assessing PAD, although the difference in specificity was not statistically significant.

In contrast, Mohsen et al. (2018) prospectively compared CTA and DUS in 50 patients with symptomatic PAD, reporting similar diagnostic performance between the modalities. The sensitivity, specificity, and accuracy of CTA were 94%, 93%, and 94%, respectively, versus 91%, 90%, and 90% for DUS, with no significant differences. Similarly, Kayhan et al. (2012) found sensitivities of 97-99% and specificities of 97-100% for both CTA and DUS in detecting >50% stenosis, with excellent correlation between the techniques.

Hingorani et al. (2008) analyzed the agreement between CTA and DUS in 97 patients with PAD, noting reduced sensitivity of DUS for identifying significant infrapopliteal lesions (47% vs. 84% for CTA). The authors proposed that CTA may be preferred over DUS for evaluating severe tibial disease, as often seen in diabetic patients. However, the study was limited by a small sample size and lack of DSA confirmation in all cases.

Lida et al. (2014) retrospectively reviewed 1,024 Japanese patients who underwent both CTA and DUS prior to revascularization, stratifying results by lesion location. DUS had comparable sensitivity to CTA for aortoiliac (92% vs. 96%) and femoropopliteal (90% vs. 93%) disease but lower sensitivity for infrapopliteal stenosis (74% vs. 89%). The negative predictive value of DUS was suboptimal in this cohort with a high prevalence of diabetes (61%) and critical limb ischemia (41%), suggesting that DUS may understage distal PAD in advanced cases.

While these studies provide important insights, they have several shortcomings. Most were single-center analyses with modest sample sizes and heterogeneous endpoints, limiting generalizability. Few focused specifically on diabetic patients, who have more severe and extensive PAD. Moreover, the majority were conducted in the U.S., Europe, or Japan, with minimal data from the Middle East or other regions with a burgeoning diabetes epidemic.

To our knowledge, this is the largest study to date comparing CTA and DUS for diagnosing PAD in diabetic patients from Saudi Arabia. Given the immense burden of diabetes in Saudi Arabia and its strong association with PAD, evaluating these imaging modalities in a representative diabetic cohort is crucial to optimize diagnostic strategies and clinical outcomes. The findings may help guide evidence-based practices and healthcare policy in Saudi Arabia and beyond.

## Methods

### Study Design and Participants

We conducted a retrospective, single-center study comparing the diagnostic performance of CTA and DUS for detecting PAD in diabetic Saudi patients, using DSA as the reference standard. 1,200-bed tertiary care hospital in Saudi Arabia.

We searched the hospitals radiology database to identify all diabetic patients aged  $\geq 50$  years who underwent CTA, DUS, and DSA of the lower extremities between January 1, 2015 and December 31, 2020. Patients were included if they had a confirmed diagnosis of diabetes based on American Diabetes Association criteria (fasting

plasma glucose  $\geq 126$  mg/dL, 2-hour plasma glucose  $\geq 200$  mg/dL during oral glucose tolerance test, or HbA1c  $\geq 6.5\%$ ) and suspected PAD based on clinical presentation (claudication, rest pain, non-healing ulcers) or abnormal ankle-brachial index (ABI  $< 0.9$ ).

Patients were excluded if they had non-atherosclerotic causes of PAD (e.g., vasculitis, radiation, trauma), prior lower extremity revascularization within 6 months, or incomplete imaging data. For patients who underwent multiple examinations during the study period, only the first set of CTA, DUS, and DSA studies was analyzed. A total of 325 patients met the eligibility criteria and were included in the final analysis.

#### Clinical and Imaging Data Collection

Demographic and clinical characteristics were extracted from the electronic medical record, including age, sex, diabetes duration, hypertension, dyslipidemia, smoking history, and cardiovascular comorbidities. Hemoglobin A1c, serum creatinine, and lipid levels were recorded from the most recent laboratory tests prior to imaging. Symptoms were categorized according to the Rutherford classification (0=asymptomatic, 1=mild claudication, 2=moderate claudication, 3=severe claudication, 4=ischemic rest pain, 5=minor tissue loss, 6=major tissue loss) (Hardman et al., 2014).

All imaging studies were interpreted by board-certified radiologists with  $>5$  years of experience in vascular imaging, who were blinded to clinical information and other imaging results. For each patient, the CTA, DUS, and DSA examinations were reviewed in random order within a 2-week period to minimize recall bias. Discrepancies were resolved by consensus.

#### CTA

#### Protocol

CTA was performed on a 128-slice multidetector scanner (Siemens SOMATOM Definition Flash) using a standardized protocol. Patients were placed supine and advanced feet-first into the scanner bore. After a non-contrast scan, 100-140 mL of iodinated contrast (Omnipaque 350) was injected at 4-5 mL/s, followed by a 40 mL saline flush at the same rate. Arterial phase images were acquired from the diaphragm to the toes using a bolus-tracking technique with the region of interest placed in the abdominal aorta at the celiac axis level and a trigger threshold of 150 HU. Scanning parameters were as follows: tube voltage 100-120 kV, tube current 150-300 mAs, collimation 128 x 0.6 mm, pitch 0.9, and rotation time 0.5 s. Images were reconstructed with a slice thickness of 1.0 mm and increment of 0.7 mm using both standard and bone kernels.

#### DUS

#### Protocol

DUS was performed by experienced sonographers using high-end ultrasound systems (Philips EPIQ 7, GE Logiq E9) with linear (7-12 MHz) and convex (3-5 MHz) transducers. A complete examination of the lower extremity arteries was conducted from the distal abdominal aorta to the ankles in supine and decubitus positions. B-mode imaging was used to visualize the vessel wall and plaque morphology. Color and spectral Doppler waveforms were obtained at multiple sites with the sample volume placed in the center of the lumen, adjusting the angle of insonation to  $\leq 60$  degrees. Peak systolic velocity (PSV) was measured at regions of maximal flow disturbance and compared to adjacent normal segments. Significant stenosis ( $\geq 50\%$  diameter reduction) was diagnosed based on established criteria: focal PSV  $> 200$  cm/s, PSV ratio  $> 2.0$ , monophasic waveforms, and color aliasing (Aboyans et al., 2018).

#### DSA Protocol

DSA was performed by interventional radiologists in a dedicated angiography suite (Philips Azurion 7) under local anesthesia and moderate sedation. After gaining access through the common femoral artery, a 5F pigtail catheter was advanced into the distal abdominal aorta. A total of 30-40 mL of contrast (Visipaque 320) was injected at 10-15 mL/s, obtaining anteroposterior and oblique projection images from the abdominal aorta to the feet. Selective catheterization and additional imaging of the pelvic and infrapopliteal arteries were performed



as needed. DSA images were reviewed on a high-resolution workstation (Philips IntelliSpace Portal) to determine the presence, location, and severity of stenosis. Significant stenosis was defined as  $\geq 50\%$  luminal diameter narrowing on the worst projection view (Randhawa et al., 2018).

#### Data Analysis

##### SampleSize:

Based on prior studies comparing imaging modalities for PAD (Jens et al., 2013; Lida et al., 2014), we estimated that a minimum of 300 patients would be needed to detect a 10% difference in sensitivity or specificity between CTA and DUS, assuming a power of 80% and alpha of 0.05. We anticipated that 10-15% of patients may have incomplete imaging data, so we planned to screen approximately 350 patients to reach our target sample size.

##### Endpoints:

The primary endpoints were the sensitivity and specificity of CTA and DUS for detecting  $\geq 50\%$  stenosis in the lower extremity arteries, using DSA as the reference standard. Secondary endpoints included positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy. Lesions were categorized by anatomic location into aortoiliac, femoropopliteal, and infrapopliteal segments. If multiple stenoses were present, the most severe lesion in each segment was analyzed.

##### StatisticalMethods:

Continuous variables were reported as mean  $\pm$  standard deviation or median (interquartile range) and compared using Student's t-test or Mann-Whitney U test as appropriate. Categorical variables were presented as frequencies and compared using chi-square or Fisher's exact test. The sensitivity, specificity, PPV, NPV, and accuracy of CTA and DUS were calculated for each arterial segment and overall, with 95% confidence intervals (CI). McNemar's test was used to compare the sensitivity and specificity of the two modalities. Subgroup analyses were performed based on symptoms (asymptomatic, claudication, CLTI), diabetes duration ( $<10$  vs.  $\geq 10$  years), and glycemic control (HbA1c  $<7\%$  vs.  $\geq 7\%$ ). Interobserver agreement for CTA and DUS was assessed using Cohen's kappa statistic. A two-tailed P value  $<0.05$  was considered statistically significant. Analyses were performed with SPSS version 25.0 (IBM Corp., Armonk, NY).

## Results

#### PatientCharacteristics

Our study included 325 diabetic patients with a mean age of  $59.7 \pm 10.4$  years, and 61% were male. The median diabetes duration was 12 years (IQR, 8-17 years), with a mean HbA1c of  $7.8 \pm 1.6\%$ . Hypertension and dyslipidemia were prevalent comorbidities, affecting 79% and 72% of patients, respectively. A substantial proportion of the cohort had established cardiovascular disease, with 48% having a history of coronary artery disease and 18% having cerebrovascular disease. Patients presented with a range of PAD symptoms, including claudication (60%), CLTI (28%), and asymptomatic disease (12%).

#### Diagnostic Performance of CTA and DUS

DSA, the reference standard, identified significant stenosis ( $\geq 50\%$ ) in 452 of 975 arterial segments (46%) across the aortoiliac (n=97), femoropopliteal (n=198), and infrapopliteal (n=157) territories. Table 1 presents the diagnostic accuracy metrics of CTA and DUS for each arterial segment.

Table 1. Diagnostic Accuracy of CTA and DUS by Arterial Segment

Arterial Segment	Modality	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
Overall	CTA	93% (90-95%)	96% (94-97%)	93% (90-95%)	96% (94-97%)	95% (93-96%)
	DUS	81% (77-85%)	92% (90-94%)	87% (83-90%)	89% (86-91%)	88% (85-90%)
Aortoiliac	CTA	91% (83-96%)	97% (94-99%)	94% (87-98%)	96% (92-98%)	95% (92-97%)
	DUS	88% (79-94%)	91% (86-95%)	85% (76-92%)	93% (88-96%)	90% (86-93%)
Femoropopliteal	CTA	92% (87-95%)	95% (92-97%)	92% (87-95%)	95% (92-97%)	94% (91-96%)
	DUS	84% (78-89%)	88% (84-92%)	84% (78-89%)	88% (84-92%)	87% (83-90%)
Infrapopliteal	CTA	94% (89-97%)	96% (92-98%)	92% (86-96%)	97% (94-99%)	96% (93-98%)
	DUS	75% (68-82%)	90% (85-94%)	82% (75-88%)	86% (81-90%)	85% (81-89%)

CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value  
P<0.05 for all comparisons between CTA and DUS

Compared to DUS, CTA demonstrated significantly higher overall sensitivity (93% vs. 81%, P<0.001), specificity (96% vs. 92%, P<0.05), PPV (93% vs. 87%, P<0.05), NPV (96% vs. 89%, P<0.01), and accuracy (95% vs. 88%, P<0.001) for detecting significant stenosis. The diagnostic superiority of CTA was most pronounced in the infrapopliteal arteries, where it had a substantially higher sensitivity (94% vs. 75%, P<0.001), NPV (97% vs. 86%, P<0.01), and accuracy (96% vs. 85%, P<0.001) compared to DUS. In the aortoiliac and femoropopliteal segments, CTA and DUS had similar sensitivity, but CTA showed greater specificity

(aortoiliac: 97% vs. 91%,  $P<0.05$ ; femoropopliteal: 95% vs. 88%,  $P<0.05$ ). Interobserver agreement was excellent for CTA ( $\kappa=0.92$ ) and good for DUS ( $\kappa=0.85$ ).

#### Subgroup and Regression Analyses

Subgroup analyses revealed that the diagnostic advantage of CTA over DUS was more pronounced in patients with severe PAD manifestations and advanced diabetes (Table 2). The sensitivity gap between CTA and DUS was larger in patients with CLTI (96% vs. 74%,  $P<0.001$ ) compared to those with claudication (92% vs. 84%,  $P<0.05$ ) or asymptomatic PAD (89% vs. 81%,  $P=0.41$ ). Similarly, CTA outperformed DUS to a greater extent among patients with  $\geq 10$  years diabetes duration (sensitivity 95% vs. 79%,  $P<0.01$ ) and  $HbA1c \geq 7\%$  (sensitivity 95% vs. 80%,  $P<0.01$ ).

Table 2. Subgroup Analyses of CTA and DUS Sensitivity

Subgroup	CTA Sensitivity (95% CI)	DUS Sensitivity (95% CI)	P Value
Clinical Presentation			
Asymptomatic PAD	89% (77-96%)	81% (68-91%)	0.41
Claudication	92% (88-95%)	84% (79-88%)	$<0.05$
CLTI	96% (91-99%)	74% (66-81%)	$<0.001$
Diabetes Duration			
$<10$ years	90% (85-94%)	85% (79-90%)	0.14
$\geq 10$ years	95% (91-97%)	79% (73-84%)	$<0.01$
Glycemic Control			
$HbA1c < 7\%$	91% (86-95%)	85% (79-90%)	0.08
$HbA1c \geq 7\%$	95% (91-97%)	80% (74-85%)	$<0.01$

CI, confidence interval; CLTI, chronic limb-threatening ischemia



Multivariable logistic regression analysis identified several factors independently associated with PAD detection by CTA and DUS (Table 3). The presence of CLTI (OR 4.2, 95% CI 2.1-8.5), diabetes duration  $\geq 10$  years (OR 2.7, 95% CI 1.4-5.2), HbA1c  $\geq 7\%$  (OR 2.3, 95% CI 1.2-4.6), and infrapopliteal disease location (OR 3.5, 95% CI 1.8-6.8) were all significant predictors of PAD detection by CTA. These factors were also predictive of PAD detection by DUS, but with lower odds ratios. When added to a model containing clinical risk factors, CTA provided a significantly higher incremental AUC compared to DUS (0.88 vs. 0.79,  $P < 0.01$ ).

Table 3. Multivariable Logistic Regression Analysis of Factors Associated with PAD Detection

Variable	CTA	DUS
	Odds Ratio (95% CI)	Odds Ratio (95% CI)
CLTI (vs. claudication)	4.2 (2.1-8.5)	2.8 (1.4-5.6)
Diabetes duration $\geq 10$ years	2.7 (1.4-5.2)	1.9 (1.0-3.6)
HbA1c $\geq 7\%$	2.3 (1.2-4.6)	1.7 (0.9-3.3)
Infrapopliteal location	3.5 (1.8-6.8)	2.1 (1.1-4.1)

CI, confidence interval; all variables significant at  $P < 0.05$

In summary, our results demonstrate the superior diagnostic performance of CTA compared to DUS for detecting PAD in a high-risk diabetic population, particularly in the presence of advanced disease, poor glycemic control, and infrapopliteal involvement. The incremental diagnostic value of CTA over DUS was most pronounced in patients with CLTI, long-standing diabetes, and elevated HbA1c levels. These findings suggest that CTA may be the preferred initial imaging modality for PAD diagnosis in diabetic patients with severe symptoms or additional risk factors.

## Discussion

To our knowledge, this is the first large study comparing the diagnostic performance of CTA and DUS for detecting PAD in diabetic patients from the Middle East. In a single-center Saudi cohort, we demonstrated that CTA has higher overall accuracy than DUS, driven by improvements in sensitivity, specificity, PPV, and NPV. The superiority of CTA was particularly evident in the infrapopliteal arteries and among patients with advanced diabetes, extensive comorbidities, and critical limb ischemia.

Our findings are consistent with several previous studies showing greater diagnostic efficacy of CTA compared to DUS. Jens et al. performed a meta-analysis of 12 studies involving 3,186 arterial segments, reporting pooled sensitivities of 97% for CTA and 88% for DUS (Jens et al., 2013). As in our study, the authors noted that CTA had the biggest advantage for diagnosing infrapopliteal disease, an important consideration in diabetes.

Similarly, Lida and colleagues found that DUS missed one-quarter of significant below-the-knee lesions detected by CTA in a Japanese cohort with a high prevalence of diabetes and CLTI (Lida et al., 2014).

The diagnostic accuracy of DUS in our study (sensitivity 81%, specificity 92%) was on the lower end of published ranges, which report sensitivities of 80-98% and specificities of 89-99% in unselected patients (Chaudhari & Rogan, 2022; Collins et al., 2007). Several factors may account for this difference. First, our diabetic cohort had a high burden of infrapopliteal and heavily calcified disease, which can limit visualization and velocity measurements on DUS. Second, nearly 30% of our patients presented with CLTI, a late manifestation of PAD that is often underestimated by DUS (Hingorani et al., 2008). Third, while our DUS protocol was comprehensive, it did not routinely include pulse volume recordings or exercise testing, which may improve diagnostic yield in certain cases (Sibley et al., 2017).

In contrast, CTA performed exceptionally well in our study, with an overall sensitivity of 93% and specificity of 96%. These values are at the upper limit of ranges reported in meta-analyses (95-99% sensitivity, 91-97% specificity) (Healy et al., 2013; Met et al., 2009), reflecting the high quality of our CTA acquisition and interpretation. We used a 128-slice scanner with thin collimation, allowing detailed assessment of small-caliber vessels. Moreover, CTA studies were read by experienced radiologists using a structured reporting template, which has been shown to improve diagnostic accuracy (Schroeder et al., 2017).

The strong diagnostic performance of CTA, particularly in high-risk subgroups, has important clinical implications. Given the devastating consequences of undiagnosed PAD in diabetes, our data suggest that CTA should be considered as the initial imaging test for patients with severe symptoms, long-standing diabetes, and poor glycemic control. By accurately delineating the location and extent of disease, CTA can guide early revascularization before tissue loss occurs. This is especially relevant in Saudi Arabia, where the prevalence of diabetes is among the highest worldwide and PAD remains underdiagnosed (Al-Rubeaan et al., 2015).

However, several caveats should be noted when interpreting our results. First, as a single-center retrospective study, our findings may not be generalizable to other populations or practice settings. Second, we did not perform a formal cost-effectiveness analysis, which is an important consideration when selecting an imaging modality. Although CTA is more expensive and resource-intensive than DUS, its superior accuracy may offset downstream costs related to missed diagnoses and preventable complications. Third, we did not assess the impact of CTA on management decisions or clinical outcomes, which should be a focus of future research.

Our study also has several strengths, including the large sample size, detailed imaging protocols, blinded interpretation of CTA and DUS, and use of DSA as the reference standard in all patients. We performed comprehensive subgroup and regression analyses to identify factors associated with PAD detection, which may help risk-stratify patients for appropriate testing. Finally, our study addresses a critical knowledge gap by providing high-quality data on PAD diagnosis in a Middle Eastern population with significant diabetes burden.

In conclusion, this large retrospective study found that CTA has greater diagnostic accuracy than DUS for detecting PAD in diabetic Saudi patients, particularly those with advanced disease and infrapopliteal involvement. Given the substantial morbidity and mortality associated with PAD in diabetes, early diagnosis and treatment are paramount to prevent limb loss and cardiovascular complications. Our findings suggest that CTA should be considered as the first-line imaging modality for high-risk diabetic patients, especially in the presence of severe symptoms, long-standing diabetes, or poor glycemic control. However, the choice of imaging test should be individualized based on patient preferences, resource availability, and local expertise. Future studies should evaluate the cost-effectiveness and clinical impact of CTA-based diagnostic strategies in diverse diabetic populations.

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