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# A Diagnostic Comparison Study between Maximal Systolic Acceleration and Acceleration Time to Detect Peripheral Arterial Disease

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**Background:** Detecting peripheral arterial disease (PAD) can be particularly challenging in patients with diabetes mellitus (DM) or chronic kidney disease (CKD) due to medial arterial calcification (MAC). Current bedside tests, such as the ankle-brachial index, are less accurate in these patient groups. The primary aim of this study is to evaluate the diagnostic accuracy of point-of-care duplex ultrasound parameters maximal systolic acceleration ( $ACC_{max}$ ) and acceleration time (AT) to detect PAD, including a comparison of both metrics.

**Methods:** Patients suspected of having PAD, who underwent point-of-care duplex ultrasound measurements ( $ACC_{max}$  and AT) of the posterior tibial artery (PTA) and/or anterior tibial artery (ATA) at ankle level along with computed tomography angiography were eligible for inclusion. PAD was defined as a stenosis  $>50\%$  on computed tomography angiography. Diagnostic accuracy of AT was evaluated at calculated (Youden index) and prespecified cut-off values (121 ms), using the sensitivity, specificity, positive likelihood ratio, negative likelihood ratios, and area under the curve. The McNemar test compared  $ACC_{max}$  with AT at prespecified and calculated cut-off values. Subgroup analyses of patients prone to MAC (i.e., those with DM and/or CKD) were also performed.

**Results:** This study included 184 patients (267 legs) with a high prevalence of DM (53%) and CKD (36%). The diagnostic accuracy of AT to identify PAD for PTA showed a sensitivity of 84%, specificity of 98%, positive likelihood ratio of 42.00, negative likelihood ratio of 0.16 and area under the curve of 0.96. Regarding the ATA, the results were 81%, 93%, 11.57, 0.20, and 0.92, respectively. Statistical comparisons favored  $ACC_{max}$  over AT in detecting PAD at prespecified and calculated cut-off values for both the PTA and ATA ( $P < 0.001$ ). Additionally, in patients prone to MAC,  $ACC_{max}$  also outperformed AT in detecting PAD ( $P$  values ranging from  $<0.001$  to 0.039). For patients without PAD, no significant differences were observed in the ability to rule out the disease.

**Conclusions:**  $ACC_{max}$  proved to be more accurate than AT in detecting PAD, also in patients prone to MAC. While no significant difference was found between  $ACC_{max}$  and AT in their diagnostic accuracy to exclude PAD,  $ACC_{max}$  should be favored in the diagnostic work-up in patients suspected of PAD due to its superior ability to detect an arterial stenosis.

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## INTRODUCTION

Peripheral arterial disease (PAD) is a progressive condition caused by atherosclerosis, leading to intermittent claudication or critical limb-threatening ischemia (CLTI).<sup>1,2</sup> The estimated worldwide prevalence of PAD currently exceeds 200 million individuals, with numbers expected to rise due to aging and other significant risk factors.<sup>3</sup> The primary diagnostic evaluation of PAD relies on noninvasive bedside tests, such as the ankle-brachial index (ABI), toe-brachial index (TBI), and toe pressure (TP) measurements.<sup>2</sup> However, the diagnostic accuracy of these index tests diminishes in the presence of medial arterial calcification (MAC), predominantly observed in patients with diabetes mellitus (DM) or chronic kidney disease (CKD).<sup>4,5</sup> Previous systematic reviews showed a declining diagnostic performance in these patients, in particular for ruling out PAD.<sup>4,6</sup> Since early diagnosis of PAD is crucial for initiating cardiovascular risk management and avoid potential complications, previous reviews and guidelines have emphasized the need for more accurate noninvasive diagnostic tools.<sup>2,4–6</sup>

In recent years, there has been renewed interest in point-of-care duplex ultrasound (DUS) to analyze systolic waveforms to diagnose PAD, including maximal systolic acceleration ( $ACC_{max}$ ) and acceleration time (AT).<sup>7–11</sup> These point-of-care DUS measurements should not be equated with the conventional DUS, which is time-consuming and dependent on the investigator's proficiency. Point-of-care DUS introduces a new convenient and efficient method for bedside diagnostics. For diagnosing PAD, these measurements ( $ACC_{max}$  and AT) are obtained at the ankle level and reflect arterial perfusion up to that point.<sup>2</sup>

The  $ACC_{max}$  ( $m/s^2$ ) is measured at the maximum slope of the bloodflow velocity curve during the systolic upstroke. Previous in-vitro and in-vivo studies by Brouwers et al. showed a strong correlation between  $ACC_{max}$  measurements and the intra-arterial pressure gradient.<sup>8,12</sup> Additionally,  $ACC_{max}$  outperformed noninvasive tests like ABI and TBI in healthy volunteers.<sup>12</sup> Recent research by Willems et al. demonstrated an excellent diagnostic accuracy of  $ACC_{max}$  to diagnose PAD in a large cohort of patients with computed tomography angiography (CTA) as reference test, achieving a sensitivity and specificity above 90%.<sup>7</sup> Notably, the diagnostic performance of  $ACC_{max}$  did not diminish in patients prone to MAC (i.e., those with DM and/or CKD).

The AT (ms) represents the duration between the start and peak of systole on the blood-flow velocity

curve. A study of Sommerset et al. analyzed the AT at the pedal arteries (pedal AT) and demonstrated that pedal AT is highly correlated to ABI in nondiabetic patients.<sup>9</sup> Moreover, Trihan et al. evaluated pedal AT to TBI in diabetic patients, finding a strong correlation and high diagnostic accuracy to detect CLTI.<sup>11</sup> However, the AT was only compared to other index tests (ABI and TBI) in these studies. Since (pedal) AT has never been compared to a reliable reference standard (such as CTA, magnetic resonance angiography, or digital subtraction angiography), its true diagnostic accuracy remains uncertain.

This study aimed to compare the diagnostic accuracy of  $ACC_{max}$  and AT for detecting PAD, with special emphasis on patients prone to MAC, using CTA as the reference test. Secondary aims included investigating the reliability of AT in patients prone to MAC and analyzing AT's distribution in correlation with the severity of symptoms.

## METHODS

### Study Design

This retrospective study was conducted in a tertiary referral hospital in the Netherlands and received ethical approval (2022–047) from the Research and Science Committee of the Surgery Division on September 7, 2022. The study enrolled patients aged 18 years and older with suspected PAD who underwent point-of-care DUS measurements, specifically  $ACC_{max}$  and AT, of the distal posterior tibial artery (PTA) and/or distal anterior tibial artery (ATA). CTA scans of the abdominal aorta and lower extremities served as the reference test. To ensure assessor blindness, only those patients in whom point-of-care DUS was performed before CTA were included. Exclusion criteria encompassed a time gap exceeding 90 days or any vascular intervention between the point-of-care DUS and CTA. Additionally, patients were excluded if CTA could not reliably differentiate between the presence or absence of a 50% stenosis in cases with extensive crural calcifications. However, patients were not excluded if a >50% stenosis had already been detected proximally in the arterial pathway, thereby confirming the presence of PAD.

PAD was defined as a stenosis >50% on CTA (consistent with previous literature<sup>4,6,7</sup>) anywhere from the distal abdominal aorta down to the distal tibial arteries. All CTAs were assessed by vascular radiologists. The point-of-care DUS measurements were performed by experienced vascular

sonographers with the Acuson S2000 System (Siemens Medical Solutions, Ultrasound Division, Issaquah, WA) equipped with a 9L4 9–4 MHz linear transducer. To reliably assess diagnostic accuracy, Willems et al. defined the arterial pathways for each crural vessel separately.<sup>7</sup> Point-of-care DUS measurements were obtained at the PTA and ATA at the ankle level, allowing for assessment of the arterial pathways. An arterial pathway was defined as all segments proximal to the designated arteries, including the PTA and ATA. Both arterial pathways included the distal abdominal aorta, iliac artery, common femoral artery, superficial femoral artery, and popliteal artery. For the PTA, the tibioperoneal trunk was added. All designated arteries (PTA and ATA) were included in their own arterial pathway as well.

### Maximal Systolic Acceleration

The  $ACC_{max}$  ( $m/s^2$ ) is measured at the maximum slope of the systolic upstroke on the blood-flow velocity curve, which is calculated by manually marking 2 points along the maximum slope (Fig. 1A, B). An extensive overview of  $ACC_{max}$  can be found in the article by Willems et al.<sup>7</sup> In general, a steeper curve corresponds to a higher  $ACC_{max}$  value, indicating a lower risk of proximal stenosis. Previous research identified optimal cut-off values of  $ACC_{max}$  for PTA and ATA at 5.55 and 5.15  $m/s^2$  to diagnose PAD, respectively.<sup>7</sup> Since these values are already known, these prespecified cut-off values were used in the diagnostic comparison analysis between  $ACC_{max}$  and AT.

### Acceleration Time

The AT (ms) represents the time from the start of the systolic upstroke to the peak of systole. AT is derived by marking the onset of the systolic upstroke and the peak systolic velocity point: the interval between these points is then utilized as AT, as shown in Figure 1C, D. In general, a lower AT value indicates a lower risk of proximal stenosis. According to Teso et al., a pedal AT >121 ms suggests mild ischemia and ABI <0.90, indicative of PAD.<sup>10</sup> Notable, the AT value of Teso et al. reflects the pedal arteries instead of PTA or ATA.<sup>10</sup> In addition, the (pedal) AT has not been compared to a reliable reference standard previously, such as CTA. For these reasons, we conducted a primary analysis to evaluate the diagnostic accuracy of AT for detecting PAD using CTA as the reference standard and to determine optimal cut-off values (based on highest Youden index as explained in statistical analysis) for AT at the PTA and ATA. Moreover, the

prespecified value of 121 ms mentioned by Teso et al. was also included in the diagnostic comparison analysis as well.<sup>10</sup>

### Subgroup Definition

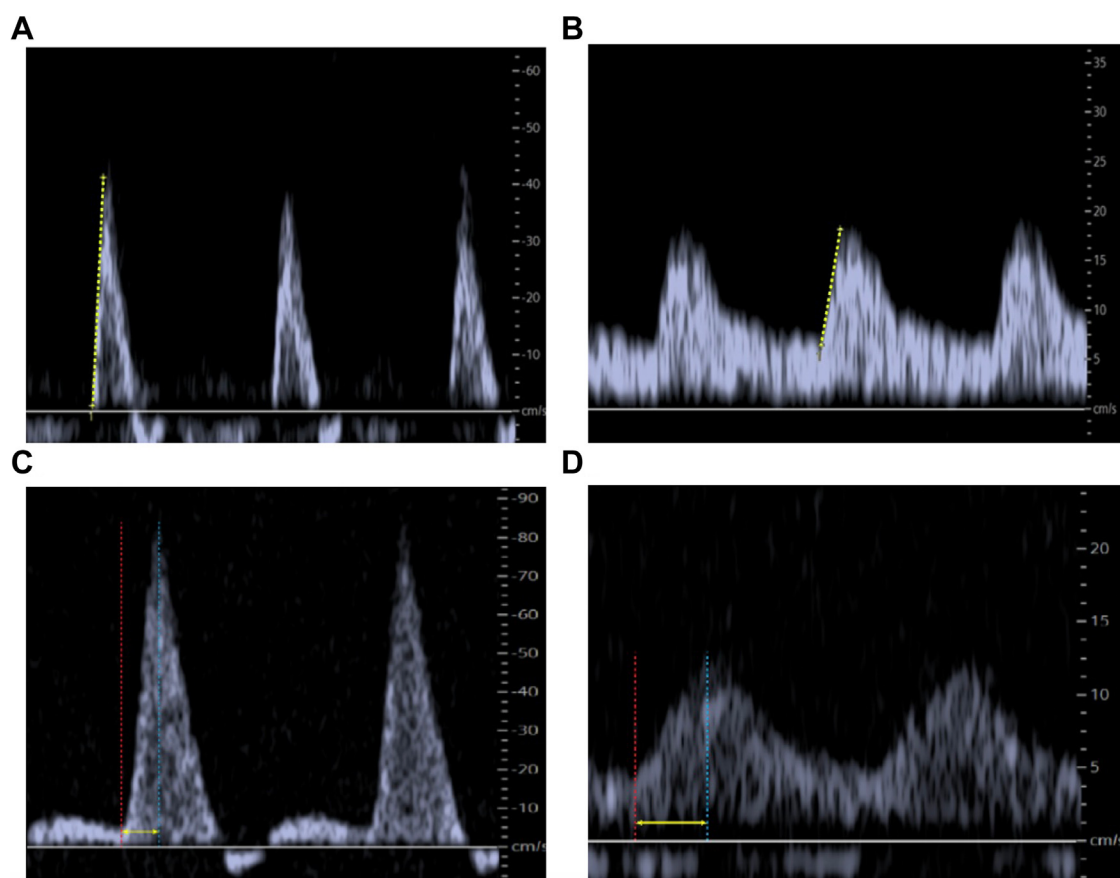
The subgroup of patients prone to MAC was defined as all patients with DM and/or CKD, including those with kidney transplantations. This approach was chosen to address the primary issue of MAC in PAD evaluation, as both DM and CKD patients are highly susceptible to MAC, creating a larger sample size for statistical analysis.

### Statistical Analysis

First, the optimal cut-off value of AT to detect or exclude PAD was determined by using the Youden Index. At this threshold, the sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR) and area under the curve with corresponding 95% confidence interval were calculated. PLR and NLR indicate the impact on the post-test probability of disease. The ratios were categorized as follows: no effect (PLR, 1; NLR, 1), small effect (PLR, 2–5; NLR, 0.2–0.5), moderate effect (PLR, 5–10; NLR 0.1–0.2) and large effect (PLR, >10; NLR, <0.1).<sup>13</sup> Separate analyses were conducted for the PTA and ATA, and subgroup analyses were performed for patients prone to MAC. These statistical analyses were performed for the prespecified cut-off value of AT as well (121 ms).

Furthermore, box plots were used to depict the distribution of AT across patient groups with varying severity of symptoms, showing median values and interquartile ranges (IQRs). These groups include patients without PAD, asymptomatic patients with PAD, patients with intermittent claudication (lower-extremity skeletal muscle pain during exercise), and patients with CLTI (rest pain, gangrene or a lower-limb ulceration for more than 2 weeks). These box plots exclusively display the lowest AT values for PTA and ATA to accurately represent the clinical condition of the patient. Statistical differences among categorical groups were analyzed using the Mann-Whitney *U* test, with significance set at a *P* value below 0.05.

Subsequently, the McNemar test was applied to compare diagnostic accuracy between  $ACC_{max}$  and AT at cut-off values based on the highest Youden index (calculated) and prespecified values of AT with prespecified values of  $ACC_{max}$ .<sup>7,10</sup> McNemar tests were conducted separately for patients with and without PAD on CTA, leading to a diagnostic comparison in detecting and excluding PAD. In addition, subgroup analyses were performed for patients



**Fig. 1.** Point-of-care duplex ultrasound (DUS) examination of ACCmax and AT. **(A)** Normal triphasic waveform showing an ACCmax measurement of 7.6 m/s<sup>2</sup>, measured at the maximal slope of the systolic upstroke (indicated by yellow tangent line). **(B)** Abnormal waveform showing an ACCmax measurement of 1.4 m/s<sup>2</sup>, measured at the maximal slope of the systolic upstroke (indicated by yellow tangent line). **(C)** Normal triphasic

waveform showing an AT measurement of 81 ms, derived from the interval (yellow line) between the start (red tangent line) and peak (blue tangent line) of systole. **(D)** Abnormal waveform showing an AT measurement of 149 ms, derived from the interval (yellow line) between start (red tangent line) and peak (blue tangent line) of systole. Note the difference in scale between the figures.

prone to MAC (i.e., those with DM and/or CKD). A *P* value below 0.05 was considered significant. Corresponding 2x2 tables illustrated the distribution of PAD in the cohort. All analyses were conducted using SPSS for Windows Version 29.0 (IBM, Armonk, NY).

## RESULTS

In total, 201 patients were initially included in this study. Seventeen participants were excluded due to extensive crural calcifications on CTA in which PAD could not reliably be diagnosed, resulting in a final study population of 184 patients (267 legs).

Mean age of patients was 69 years (standard deviation = 10.1, range: 38–91 years), and two-third of the cohort were male (67%). A high prevalence of comorbidities was observed, including cardiovascular disease (50%), DM (53%), and CKD (36%). The subgroup of patients prone to MAC included 105 patients (57%), accounting for a total of 149 legs (56%). The predominant clinical presentations were intermittent claudication (45%) and CLTI (35%). The mean time span between point-of-care DUS and CTA was 18 days (standard deviation = 16.7, range: 0–90 days). An overview of all patient characteristics can be found in [Table I](#).

**Table I.** Demographic characteristics

| Demographic characteristics                                 | No. (%)         |
|-------------------------------------------------------------|-----------------|
| Total patients and limbs                                    | 184–267         |
| Sex                                                         |                 |
| Male                                                        | 124 (67.4)      |
| Female                                                      | 60 (32.6)       |
| Side                                                        |                 |
| Right limb                                                  | 134 (50.2)      |
| Left limb                                                   | 133 (49.8)      |
| Total measurements per location                             |                 |
| PTA                                                         | 216 (80.9)      |
| ATA                                                         | 127 (47.6)      |
| Age, years, mean $\pm$ SD                                   | 68.6 $\pm$ 10.1 |
| Age range, years                                            | 38–91           |
| Comorbidities                                               |                 |
| History of smoking                                          | 155 (84.2)      |
| Hypertension                                                | 146 (79.3)      |
| Hypercholesterolemia                                        | 139 (75.5)      |
| Cardiovascular disease                                      | 92 (50.0)       |
| DM                                                          | 97 (52.7)       |
| On insulin therapy                                          | 60 (32.6)       |
| Kidney transplantation                                      | 8 (4.3)         |
| Kidney function, eGFR                                       |                 |
| Normal function, eGFR $\geq$ 60                             | 117 (63.6)      |
| CKD, eGFR <60                                               | 67 (36.4)       |
| Prone to MAC                                                | 105 (57.1)      |
| Clinical symptoms                                           |                 |
| No PAD                                                      | 31 (11.6)       |
| Asymptomatic with PAD                                       | 23 (8.6)        |
| Claudication                                                | 120 (44.9)      |
| CLTI                                                        | 21 (34.8)       |
| Postintervention in medical history (open and endovascular) | 95 (35.6)       |
| PAD prevalence (stenosis on CTA >50%)                       | 234 (87.6)      |

Prone to MAC, all patients with DM and/or CKD (including kidney transplantations).

SD, standard deviation; eGFR, estimated glomerular filtration rate.

### Diagnostic Accuracy AT

The diagnostic accuracy of AT based on receiver operating characteristics curve analysis, highest Youden index and the prespecified cut-off value is summarized in Table II. For the PTA, the optimal cut-off value of 112.50 ms yielded an area under the curve of 0.96, sensitivity of 84%, specificity of 98%, PLR of 42.00, and NLR of 0.16. Similarly, for the ATA, with a cut-off value of 119.50 ms, the accuracy was 0.92, 81%, 93%, 11.57, and 0.20,

respectively. Notably, similar diagnostic accuracies were seen for patients prone to MAC, as depicted in Table II.

**AT distribution.** Figure 2 displays box plots showing the distribution of AT based on symptom severity. Median values were as follows: 76 ms (IQR, 70–89) for patients without PAD, 111 ms (IQR, 82–160) for asymptomatic patients with PAD, 133 ms (IQR, 112–165) for the intermittent claudication group and 160 ms (IQR, 137–184) for the CLTI group. Significant differences between the groups were observed ( $P < 0.001$ ), except between asymptomatic patients with PAD and intermittent claudication patients ( $P = 0.053$ ).

### Diagnostic Comparison ACC<sub>max</sub> versus AT

A summary of the statistical comparison between ACC<sub>max</sub> and AT for the entire cohort is shown in Figure 3. Across patients with PAD, ACC<sub>max</sub> demonstrated significant superior accuracy ( $P < 0.001$ ) compared to AT at all prespecified and calculated cut-off values in both the PTA and ATA. For instance, when examining the  $2 \times 2$  table of PTA with PAD (Fig. 3A), there were 20 misclassifications of the AT versus 2 misclassifications of the ACC<sub>max</sub> for every 176 patients (when using the prespecified ACC<sub>max</sub> value of 5.55 m/s<sup>2</sup> and calculated AT value of 112.50 ms). An even greater difference was present when using the prespecified value of the AT (121 ms), in which a misclassification of 33 versus 1 in favor of ACC<sub>max</sub> was seen. In general, the same results applied for the ATA (Fig. 3C). However, among patients without PAD, no significant differences between ACC<sub>max</sub> and AT to exclude PAD were observed, as can be found in the corresponding  $2 \times 2$  tables (Fig. 3B, D).

**Prone to MAC.** In the subgroup analyses for patients prone to MAC (i.e., those with DM and/or CKD), ACC<sub>max</sub> also outperformed AT at all cut-off values to detect PAD. For the PTA, using the prespecified ACC<sub>max</sub> value of 5.55 m/s<sup>2</sup> and the calculated AT value of 112.50, there were 20 misclassifications of AT versus 2 misclassifications of ACC<sub>max</sub> for every 92 patients with PAD ( $P = 0.039$ ). Moreover, the disparity was even greater with the prespecified AT value of 121 ms, resulting in 17 misclassifications of AT versus 1 of ACC<sub>max</sub> ( $P < 0.001$ ). For the ATA, similar results were observed: using the prespecified ACC<sub>max</sub> value of 5.55 m/s<sup>2</sup> and calculated AT value of 119.50 ms, there were 8 misclassifications of AT versus 0 of ACC<sub>max</sub> for every 67 patients with PAD ( $P = 0.008$ ). In addition, with the prespecified AT value (121 ms), the result showed 11

Table II. Diagnostic accuracy of AT

| Artery                 | AUC (95% CI)     | Cut-off value AT:<br>calculated and prespecified | Sensitivity (95% CI) | Specificity (95% CI) | PLR   | NLR  |
|------------------------|------------------|--------------------------------------------------|----------------------|----------------------|-------|------|
| PTA                    |                  |                                                  |                      |                      |       |      |
| All patients (N = 216) | 0.96 (0.94–0.99) | 112.50                                           | 0.84 (0.78–0.89)     | 0.98 (0.90–1.00)     | 42.00 | 0.16 |
| Prone to               |                  | 121.00                                           | 0.76 (0.70–0.82)     | 0.98 (0.90–1.00)     | 38.00 | 0.24 |
| MAC (N = 113)          | 0.91 (0.80–1.00) | 112.50                                           | 0.87 (0.79–0.93)     | 0.95 (0.81–1.00)     | 17.40 | 0.14 |
| ATA                    |                  | 121.00                                           | 0.78 (0.69–0.86)     | 0.95 (0.81–1.00)     | 15.60 | 0.23 |
| All patients (N = 127) | 0.92 (0.84–1.00) | 119.50                                           | 0.81 (0.73–0.88)     | 0.93 (0.74–1.00)     | 11.57 | 0.20 |
| Prone to MAC           |                  | 121.00                                           | 0.75 (0.67–0.82)     | 0.93 (0.74–1.00)     | 10.71 | 0.27 |
| (N = 77)               | 0.94 (0.86–1.00) | 119.50                                           | 0.87 (0.77–0.93)     | 0.90 (0.63–0.99)     | 8.70  | 0.14 |
|                        |                  | 121.00                                           | 0.82 (0.72–0.90)     | 0.90 (0.63–0.99)     | 8.20  | 0.20 |

Prone to MAC, all patients with DM and/or CKD (including kidney transplantations).  
AUC, area under the curve; CI, confidence interval.

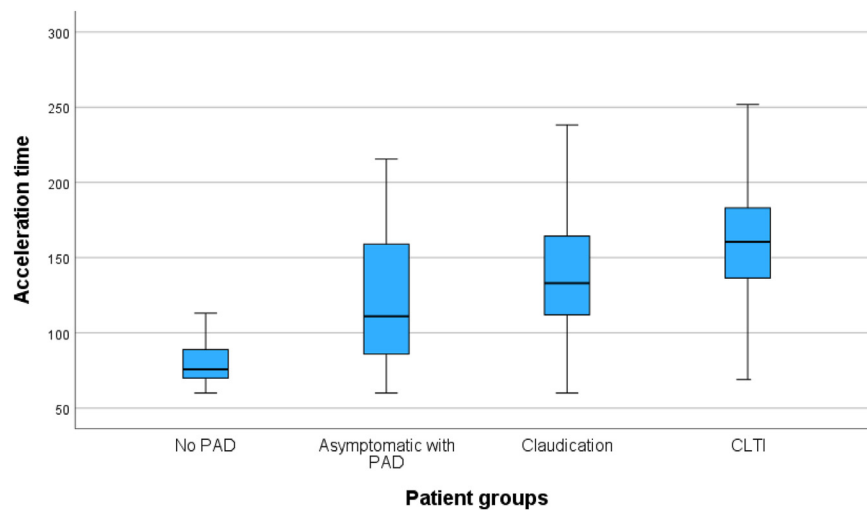
misclassifications of AT versus 0 of ACC<sub>max</sub> ( $P < 0.001$ ). No significant differences were noted between ACC<sub>max</sub> and AT in excluding PAD among patients prone to MAC in both the PTA and ATA for every 21 and 10 patients, respectively ( $P$ -values ranging from 0.500 to 1.000).

DISCUSSION

This diagnostic comparison study showed a superior diagnostic accuracy of ACC<sub>max</sub> compared to AT for diagnosing PAD, indicating a greater potential of ACC<sub>max</sub> as primary point-of-care DUS parameter in daily clinical practice. Although AT showed good diagnostic performance (Table II), the prespecified ACC<sub>max</sub> values corresponded better with PAD than the prespecified or calculated values of AT. For ruling out PAD, no significant differences between ACC<sub>max</sub> and AT were found. This study highlights the clinical value of ACC<sub>max</sub> as a new noninvasive bedside point-of-care DUS measurement as a screening tool for the detection of PAD. Special emphasis is placed on patients prone to MAC, in whom the diagnostic performance of ACC<sub>max</sub> did not diminish and outperformed the AT as well.

The findings of this study showed that ACC<sub>max</sub> holds great promise in the diagnostic work-up of PAD. Statistical superiority ( $P < 0.001$ ) of ACC<sub>max</sub> compared to AT was observed in patients with PAD across all prespecified and calculated cut-off values for AT. As previously explained, when considering the  $2 \times 2$  table of the PTA with PAD in Figure 3A, there is a discrepancy of 20 misclassifications of AT versus 2 misclassifications of ACC<sub>max</sub> for every 176 patients with PAD. Notably, subgroup analyses indicated that ACC<sub>max</sub> was also more accurate than AT in detecting PAD in patients prone to MAC ( $P$  values ranging from  $<0.001$  to 0.039). Moreover, Brouwers et al. reported a lower interobserver variability for ACC<sub>max</sub> compared to AT, with intraclass correlation coefficients of 0.97 and 0.72 respectively. This suggests that AT may be more prone to inaccuracies to assess PAD.<sup>12</sup> These insights could be important in clinical practice, as timely and accurate of PAD is essential to initiate cardiovascular risk management to prevent potential complications.

Furthermore, as depicted in Figure 2, AT measurements moderately correlated with symptom severity. Patients without PAD had a median AT of 76 ms, while those with asymptomatic, intermittent claudication and CLTI symptoms had AT values of 111, 133, and 160 ms, respectively. Significant differences were observed, except between the



**Fig. 2.** Distribution of AT in relation to symptom severity. Box plot illustrating the distribution of the lowest AT in relation to symptoms. The box contains the 25th to 75th percentiles, and the center line denotes the median value

(50th percentile). The upper and lower whiskers mark the 5th and 95th percentiles. Values beyond these bounds are considered outliers.

asymptomatic with PAD and intermittent claudication groups. It should be noted that there is also considerable overlap between all groups, as shown in Figure 2. While our data indicate that higher AT values correlate with increased symptom severity, accurately staging ischemia using AT remains challenging.

Both the diagnostic accuracy of ACC<sub>max</sub> and AT (Table II) revealed better diagnostic performances than currently used bedside tests. This is of great relevance, since the ABI exhibited a low sensitivity of 63.5% in patients prone to MAC.<sup>4</sup> Although TBI measurements are recommended in these cases, their accuracy remains suboptimal, with a sensitivity of 83.0% and a specificity of 66.3%.<sup>2,4</sup> Additionally, absolute TP also showed inconsistent diagnostic reliability results across various thresholds (50, 70, and 98 mm Hg) in patients prone to MAC.<sup>5</sup> Previous findings by Willems et al. already demonstrated an excellent and superior diagnostic performance of the ACC<sub>max</sub> with PLRs of 12.8 and 32.1 for the PTA and ATA and NLRs of 0.11 and 0.06, respectively.<sup>4,7</sup> This study elaborates on and confirms these findings.

In general, point-of-care DUS (ACC<sub>max</sub> and AT) offers practical advantages over current noninvasive bedside tests and conventional DUS. Firstly, point-of-care DUS enhances diagnostic efficiency for diagnosing and ruling out PAD. ACC<sub>max</sub> and AT are obtained at a measurement point (at the level of the

ankle) and reflect macrovascular perfusion up to that point. This is not done with conventional DUS, where all lesions are separately assessed, resulting in a prolonged and observer-dependent examination. Point-of-care DUS measurements can be obtained in 5 mins at the distal PTA and distal ATA, which can lead to significant efficiency improvements. With the projected increase in patients prone to MAC and PAD in the coming years, we can utilize these parameters to ensure daily care with high accuracy and in limited time.

## LIMITATIONS

These findings should be interpreted with caution due to several limitations stemming from the single-center and retrospective design of this study. Since all patients underwent CTA assessment based on suspected PAD, there is a risk of selection and spectrum bias. Additionally, CTA has limitations in evaluating calcified crural arteries, which may lead to misclassifications of PAD. The high prevalence of PAD within the cohort also means that the limited number of participants without PAD may have reduced the power to detect significant differences between ACC<sub>max</sub> and AT in ruling out the condition. To enhance the accuracy and validation of ACC<sub>max</sub> and AT, a prospective study adhering to the QUADAS-2 tool should be conducted.<sup>14</sup> Such a

**A** Posterior tibial artery with PAD (N=176)

|    |        |        |  |
|----|--------|--------|--|
|    |        | ACCmax |  |
|    |        | 5.55   |  |
| AT | 112.50 | 0.625  |  |
|    | 121.00 | 0.250  |  |

|    |         |        |       |
|----|---------|--------|-------|
|    |         | ACCmax |       |
|    |         | <5.55  | ≥5.55 |
| AT | ≥112.50 | 0      | 1     |
|    | <112.50 | 3      | 36    |

|    |         |        |       |
|----|---------|--------|-------|
|    |         | ACCmax |       |
|    |         | <5.55  | ≥5.55 |
| AT | ≥121.00 | 0      | 0     |
|    | <121.00 | 3      | 37    |

**B** Posterior tibial artery without PAD (N=40)

|    |        |        |  |
|----|--------|--------|--|
|    |        | ACCmax |  |
|    |        | 5.55   |  |
| AT | 112.50 | 0.625  |  |
|    | 121.00 | 0.250  |  |

|    |         |        |       |
|----|---------|--------|-------|
|    |         | ACCmax |       |
|    |         | <5.55  | ≥5.55 |
| AT | ≥112.50 | 0      | 1     |
|    | <112.50 | 3      | 36    |

|    |         |        |       |
|----|---------|--------|-------|
|    |         | ACCmax |       |
|    |         | <5.55  | ≥5.55 |
| AT | ≥121.00 | 0      | 0     |
|    | <121.00 | 3      | 37    |

**C** Anterior tibial artery with PAD (N=112)

|    |        |        |  |
|----|--------|--------|--|
|    |        | ACCmax |  |
|    |        | 5.15   |  |
| AT | 119.50 | <0.001 |  |
|    | 121.00 | <0.001 |  |

|    |         |        |       |
|----|---------|--------|-------|
|    |         | ACCmax |       |
|    |         | <5.15  | ≥5.15 |
| AT | ≥119.50 | 90     | 1     |
|    | <119.50 | 20     | 1     |

|    |         |        |       |
|----|---------|--------|-------|
|    |         | ACCmax |       |
|    |         | <5.15  | ≥5.15 |
| AT | ≥121.00 | 83     | 1     |
|    | <121.00 | 27     | 1     |

**D** Anterior tibial artery without PAD (N=15)

|    |        |        |  |
|----|--------|--------|--|
|    |        | ACCmax |  |
|    |        | 5.15   |  |
| AT | 119.50 | 0.500  |  |
|    | 121.00 | 0.500  |  |

|    |         |        |       |
|----|---------|--------|-------|
|    |         | ACCmax |       |
|    |         | <5.15  | ≥5.15 |
| AT | ≥119.50 | 1      | 0     |
|    | <119.50 | 2      | 12    |

|    |         |        |       |
|----|---------|--------|-------|
|    |         | ACCmax |       |
|    |         | <5.15  | ≥5.15 |
| AT | ≥121.00 | 1      | 0     |
|    | <121.00 | 2      | 12    |

**Fig. 3.** Diagnostic comparison of ACCmax and AT with corresponding 2 × 2 tables. This figure presents the results of the McNemar analysis for both the anterior and posterior tibial arteries, comparing ACCmax to AT (calculated and prespecified cut-off values). The top tables display the *P* values of the comparison analyses, while the bottom 2 tables provide an overview of the absolute differences between the prespecified ACCmax and the

calculated or prespecified AT. **(A)** Statistical comparison of ACCmax and AT at the PTA in patients with PAD. **(B)** Statistical comparison of ACCmax and AT at the PTA in patients without PAD. **(C)** Statistical comparison of ACCmax and AT at the ATA in patients with PAD. **(D)** Statistical comparison of ACCmax and AT at the ATA in patients without PAD.

study would allow a more standardized approach to these point-of-care DUS parameters, and enable a thorough assessment of both intraindividual reproducibility and interobserver variability, which are relevant for the broader applicability of these diagnostic tools.

## CONCLUSION

In general, this study supports the additional value of point-of-care DUS parameters ( $ACC_{max}$  and AT) in the diagnostic work-up of PAD. While both  $ACC_{max}$  and AT exhibited good diagnostic performances,  $ACC_{max}$  ( $<5.5 \text{ m/s}^2$ ) proved to be more accurate in detecting PAD, also in patient prone to MAC. Although no significant differences were found between  $ACC_{max}$  and AT in their diagnostic accuracy for excluding PAD,  $ACC_{max}$  should be preferred over AT and current noninvasive bedside tests (such as ABI, TBI, TP) in the diagnostic work-up of patients suspected of PAD.

## CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

**Siem A. Willems:** Writing – original draft, Visualization, Validation, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Obrecht O. van Bennekom:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Abbey Schepers:** Writing – review & editing, Supervision, Methodology. **Jan van Schaik:** Writing – review & editing, Supervision, Methodology. **Joost R. van der Vorst:** Writing – review & editing, Supervision, Methodology. **Jaap F. Hamming:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Jeroen J.W.M. Brouwers:** Writing – original draft, Supervision, Project administration, Methodology, Formal analysis, Conceptualization.

## REFERENCES

1. Nordanstig J, Behrendt CA, Baumgartner I, et al. Editor's choice – European Society for Vascular Surgery (ESVS) 2024 clinical practice guidelines on the management of asymptomatic lower limb peripheral arterial disease and intermittent claudication. *Eur J Vasc Endovasc Surg* 2024;67:9–96.
2. Conte MS, Bradbury AW, Kolh P, et al. Global vascular guidelines on the management of chronic limb-threatening ischemia. *Eur J Vasc Endovasc Surg* 2019;58:S1–109.e33.
3. Song P, Rudan D, Zhu Y, et al. Global, regional, and national prevalence and risk factors for peripheral artery disease in 2015: an updated systematic review and analysis. *Lancet Glob Health* 2019;7:e1020–30.
4. Normahani P, Mustafa C, Shalhoub J, et al. A systematic review and meta-analysis of the diagnostic accuracy of point-of-care tests used to establish the presence of peripheral arterial disease in people with diabetes. *J Vasc Surg* 2021;73:1811–20.
5. Brouwers J, Willems SA, Goncalves LN, et al. Reliability of bedside tests for diagnosing peripheral arterial disease in patients prone to medial arterial calcification: a systematic review. *EClinicalMedicine* 2022;50:101532.
6. Forsythe RO, Apelqvist J, Boyko EJ, et al. Effectiveness of revascularisation of the ulcerated foot in patients with diabetes and peripheral artery disease: a systematic review. *Diabetes Metab Res Rev* 2020;36:e3279.
7. Willems SA, Dolfing SG, van Wissen RC, et al. Diagnostic accuracy of the maximal systolic acceleration to detect peripheral arterial disease. *J Vasc Surg* 2024;79:405–11.
8. Brouwers J, van Doorn LP, van Wissen RC, et al. Using maximal systolic acceleration to diagnose and assess the severity of peripheral artery disease in a flow model study. *J Vasc Surg* 2020;71:242–9.
9. Sommerset J, Karmy-Jones R, Dally M, et al. Plantar acceleration time: a novel technique to evaluate arterial flow to the foot. *Ann Vasc Surg* 2019;60:308–14.
10. Teso D, Sommerset J, Dally M, et al. Pedal acceleration time (PAT): a novel predictor of limb salvage. *Ann Vasc Surg* 2021;75:189–93.
11. Trihan JE, Mahé G, Croquette M, et al. Accuracy of acceleration time of distal arteries to diagnose severe peripheral arterial disease. *Front Cardiovasc Med* 2021;8:744354.
12. Brouwers J, van Doorn LP, Pronk L, et al. Doppler ultrasonography derived maximal systolic acceleration: value determination with artificially induced stenosis. *Vasc Endovascular Surg* 2022;56:472–9.
13. Hayden SR, Brown MD. Likelihood ratio: a powerful tool for incorporating the results of a diagnostic test into clinical decisionmaking. *Ann Emerg Med* 1999;33:575–80.
14. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011;155:529–36.