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Prognostic Performance of the Maximal Systolic Acceleration at the Hallux in Healing of Foot Ulcers: A Retrospective Cohort Study

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Background: The accurate prediction of foot ulcer healing remains a major challenge in clinical practice. To date, no reliable bedside tests are available. The primary aim of this study was to determine the prognostic performance of the maximal systolic acceleration (ACC_{max}) to predict ulcer healing. Secondary objectives comprised the investigation of the prognostic accuracy in patients prone to medial arterial calcification and to assess the potential risk of amputation.
Methods: A single-center retrospective cohort study was conducted. Patients aged ≥18 years who presented with a new-onset ulcer (i.e. Fontaine IV and neuropathic ulcers) on the foot and underwent an ACC_{max} measurement at the hallux were included. Ulcer healing was defined as an intact skin with epithelialization after 3 or 12 months of follow-up. Prognostic performance was calculated by using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), and negative likelihood ratio (NLR).
Results: In total, 136 patients with 143 wounds were included. Almost half of the patients were diagnosed with diabetes mellitus (47%), and wound infection was present in 42% of cases. After 3 months of follow-up, an NPV of 97.9%, PLR of 3.25, and NLR of 0.19 were found when applying an ACC_{max} threshold of 0.5 m/s^2. When looking at 12 months, these numbers were 85.6%, 2.72, and 0.50, respectively. Subgroup analysis for patients with diabetes mellitus and chronic kidney disease showed comparable results. The risk of amputation increased significantly when a measurement below 1.0 m/s^2 was present (odd ratio 5.3, $P = 0.010$).
Conclusions: ACC_{max} measurements at the hallux can have additional prognostic value in patients with foot ulcers. An ACC_{max} below 1.0 m/s^2 is associated with nonhealing of an ulcer and a higher risk of amputation, while higher ACC_{max} values are associated with limb salvage. Therefore, ACC_{max} could be used for grading ischemia in a wound classification system.

INTRODUCTION

Chronic limb-threatening ischemia (CLTI) represents the end stage of peripheral artery disease (PAD) and is characterized by rest pain, gangrene, or lower-limb ulceration for more than 2 weeks.[1] This clinical syndrome is associated with an impaired quality of life and a higher rate of amputation and mortality.[2,3] After major amputation, approximately 57% of patients have died within 5 years.[4] In these patients, accurately staging the severity of limb threat is of great importance to guide diagnostic and treatment strategies. Currently, the Wounds, Ischemia and foot

Authors' disclosure of conflicts of interests: None.

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Ann Vasc Surg 2024; 108: 385–392
https://doi.org/10.1016/j.avsg.2024.06.016

Manuscript received: April 14, 2024; manuscript accepted: June 10, 2024; published online: 25 July 2024

Infection (WIfI) classification system is used as a predictor for important clinical outcomes, such as amputation risk and the potential benefit of revascularization.[5] This system categorizes 3 major factors, of which ischemia is established by using the ankle-brachial index (ABI), systolic blood pressure (SBP), absolute toe pressure (TP), or transcutaneous oxygen pressure ($TcPO_2$). Depending on the aforementioned value of the test, ischemia is classified in 4 grades to cover the perfusion spectrum.[5]

Although these tests could indicate arterial perfusion of the wound, applied thresholds should be used with caution due to confounding factors.[2] The CLTI guideline advises to correlate the results with Doppler arterial waveforms, since medial arterial calcification (MAC) can lead to a falsely elevated ABI and SBP.[2] This applies to patients with diabetes mellitus (DM) and chronic kidney disease (CKD) in particular, who account for most CLTI cases.[6] In these patients, TP and $TcPO_2$ measurements are advised.[7] However, according to previous systematic reviews, TP and $TcPO_2$ also showed unreliable results in predicting (diabetic) ulcer healing.[8,9] The recent prospective TEsting for Arterial disease in Diabetes (TrEAD) study by Elghazaly et al. also showed a poor prognostic performance of TP and $TcPO_2$ indicating that both seem to be inadequate for proving or ruling out healing.[10] Other bedside tests, such as the ABI and SBP, proved to be insufficient as well. Hence, it remains difficult to predict whether a wound will heal or not. Therefore, refinement in the evaluation of arterial perfusion is still needed to improve the management of patients with CLTI.

The maximal systolic acceleration (ACC_{max}) is a relatively new noninvasive point of care test measured by duplex ultrasonography (DUS). Previous studies on the diagnostic performance showed promising results in PAD.[11] These measurements were performed at the tibialis anterior artery and tibialis posterior artery at the ankle level and reflect arterial perfusion proximal to the measurement point. However, most of the ulcers in CLTI are located at the foot. Therefore, the primary aim of this study was to determine the prognostic performance of the ACC_{max} measured at the hallux (as local perfusion parameter) to predict ulcer healing. Secondary objectives comprised the investigation of the prognostic reliability in patients prone to MAC and to assess the potential risk of amputation.

METHODS

Study Design

This is a single-center retrospective cohort study conducted at a tertiary academic hospital located in the Netherlands. The Research and Science Committee of the surgery division (2022-047) granted ethical approval on September 7th, 2022.

Patients aged $\geq$18 years who presented with a new-onset nontraumatic ulcer of any type (i.e., Fontaine IV, neuropathic and neuroischemic ulcers) on the foot and underwent an ACC_{max} measurement of the foot were included. In case 2 ulcers were present during first referral, both were included for analysis. If early revascularization was performed, ulcers were only included if a new ACC_{max} measurement after revascularization was known. Patients with simultaneous prednisone or chemotherapy use were excluded, as these factors are known to influence wound healing. In case primary amputation was performed due to severe tissue loss or advanced infection, patients were excluded as well. A follow-up period of at least 3 months was applied.

Data were extracted by using CTcue® and involved patient information from the first of January 2006 until the first of January 2022. Patient characteristics such as age at presentation, sex, affected leg, history of smoking, DM (including insulin dependency), kidney function, hypertension, hypercholesterolemia, and cardiac disease were obtained from electronic patient files. CKD was defined as an estimated glomerular filtration rate (eGFR) $<$60 mL/min/1.73 m^2. Also wound characteristics were collected, which included wound size (depth and diameter), involvement of tissue loss, presence of gangrene, and the suspicion of infection. Two researchers (SAW and JDP) extracted the data and created the database.

Primary Endpoint and Clinical Outcome

The primary endpoint of this study was the prognostic performance for predicting ulcer healing at 3−12 months of follow-up. Ulcer healing was defined as an intact skin with epithelialization. An amputation or the need for revascularization (after at least 4 weeks) during the follow-up period was regarded as a non-healed ulcer. Prognostic performance was determined by calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio

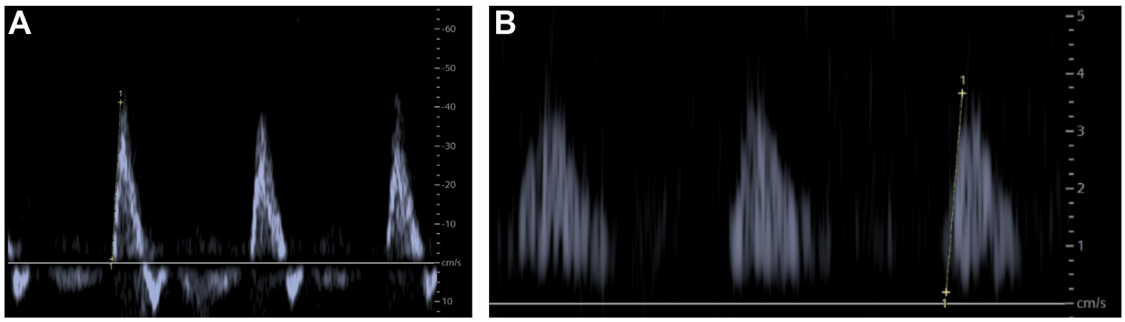

Fig. 1. Doppler ultrasonography. **(A)** Normal triphasic waveform showing an ACCmax measurement of 7.6 m/s^2, calculated at the maximal slope in the systolic phase of an arterial flow (tangent line indicated by 1). **(B)** Abnormal monophasic waveform at the hallux showing an ACC_{max} measurement of 0.5 m/s^2, calculated at the maximal slope in the systolic phase of an arterial flow (tangent line indicated by 1). Note the differences in scales between the figures.

(PLR), and negative likelihood ratio (NLR). PPV and NPV were used to reflect the probability of ulcer healing within this patient group. The PLR and NLR represent the effect on post-test probability of disease. In our study, the PLR indicates the ratio between the proportion of patients showing wound healing and presenting with a positive test (i.e., high ACC_{max} value) result compared to the proportion of patients not showing wound healing and presenting with a positive test result.[10] The NLR represents the ratio between the proportion of patients showing wound healing and presenting with a negative test result (i.e., low ACC_{max} value) compared to the proportion of patients not showing wound healing and presenting with a negative test result. Thus, in our study, the PLR reflected the chance of wound healing, whereas the NLR indicated the chance that the wound would not heal during follow-up. These 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).[12]

Maximal Systolic Acceleration

The ACC_{max} is a velocimetric DUS-derived parameter, which is measured in the systolic phase of an arterial flow (expressed in m/s^2). A tangent line can be made manually by connecting 2 points exactly following the maximal slope of an upstroke (Fig. 1). Notably, in this study, we examined the ACC_{max} in the digital artery of the hallux instead of measurements at the ankle level (as in previous studies). One measurement of a digital artery takes about 1−5 minutes, and no additional software is needed. A detailed description of the background of the ACC_{max} can be found in previous articles by *Brouwers* et al. and *Willems* et al.[11,13]

Statistical Analysis

Descriptive statistics were calculated for patient characteristics using means for continuous variables and proportions for categorical variables. A 2 × 2 contingency table was constructed to display sensitivity, specificity, PPV, NPV, PLR, and NLR with 95% confidence intervals (CI). PLR and NLR were calculated by using sensitivity and specificity, expressed as PLR: Sensitivity/(1 − Specificity) and NLR: (1 − Sensitivity)/Specificity. Receiver operating characteristic (ROC)-curve analysis and Youden's index were used to identify the optimal cutoff value of ACC_{max} to predict wound healing. All these analyses were performed at different points in time during the follow-up period (3 and 12 months). To investigate differences in prognostic performance between subgroups, the same calculations were performed for patients with DM and CKD separately.

In order to evaluate the relationship between various predictor variables and wound healing/amputation risk, a logistic regression analysis was performed. Odds ratios (ORs) were calculated to estimate the magnitude of effect, whereas *P*-values were obtained to assess significance. Univariable analysis was used to evaluate the effect of each parameter separately. A multiple logistic regression model was performed to correct for variables with significant *P*-values in the univariable analysis and known confounding variables such as wound infection and Wagner score. To prevent multicollinearity, the presence of gangrene and Wagner

Table I. Patient and ulcer characteristics

Variable	*N* (%)
Total patients	136 (100)
Mean age, years (SD)	70.1 (12.3)
Age range, years	28–93
Sex	
Male	92 (68)
Female	44 (32)
Diabetes mellitus	64 (47)
Insulin dependency	48 (75)
Comorbidities	
Chronic kidney disease (eGFR <60 mL/min/1.73 m^2)	30 (22)
Cardiac disease	75 (55)
Hypertension	95 (70)
Hypercholesterolaemia	77 (57)
History of smoking	47 (35)
Total ulciers	143 (100)
Side	
Right limb	81 (57)
Left limb	62 (43)
Mean size of ulcer in mm	24.8
Mean depth of ulcer in mm	14.5
Infection	
Not present	67 (47)
Mild	37 (26)
Moderate	21 (15)
Severe	2 (1)
Missing	16 (11)
Wagner classification	
1	80 (56)
2	17 (12)
3	13 (9)
4	25 (18)
5	0 (0)
Missing	8 (6)
Revascularization	
3 months	35 (24)
6 months	49 (34)
12 months	52 (36)
Ulcer healing	
3 months	14 (10)
6 months	24 (17)
12 months	36 (25)
Amputations	
3 months	38 (27)
6 months	48 (34)
12 months	52 (36)

SD, standard deviation.

score were not used together in the multiple logistic regression model. Furthermore, limb salvage prediction was performed by comparing ACC_{max} measurements (toes and the dorsal pedal artery) of patients with major amputation to patients with a healed or nonhealed ulcer. *P*-values of below 0.05 were regarded as significant. All statistical analyses were performed using SPSS version 29.0 for Windows (IBM Corp., Armonk, NY).

RESULTS

In total, 136 patients with 143 wounds were included. Almost all measurements were performed on the same day as presentation, with a maximum of 4 weeks in difference. The mean age of patients was 70.1 years, and most were male (68%). Almost half of the patients were diagnosed with DM (47%), whereas 75% of these diabetic patients were insulin-dependent. CKD was seen in 22% of patients. Of all ulcers, the mean size and depth were 25 and 15 mm, respectively. Wound infection was present in 42% of cases. Thirty-six ulcers (25%) healed after 12 months of follow-up. In total, 36% of ulcers was amputated. Approximately one-third of patients had the need for revascularization during the follow-up period. All patient and wound characteristics can be found in Table I. A flow chart of patient selection is summarized in Figure 2.

Prognostic Performance

Table II shows the prognostic performance of the ACC_{max} (0.5 and 1.0 m/s^2) to predict ulcer healing after 3 and 12 months of follow-up. ROC-curve analysis and Youden's Index revealed an optimal cutoff value of 0.5 m/s^2. After 3 months of follow-up, an NPV of 97.9%, PLR of 3.25, and NLR of 0.19 were seen. When looking at 12 months, these numbers were 85.6%, 2.72, and 0.50, respectively. In general, the prognostic performance of the ACC_{max} to predict ulcer healing increased when using a threshold of 1.0 m/s^2, reflected by higher specificity and PLRs at different time points during follow-up. Subgroup analysis for patients with DM showed an NPV of 89.3%, PLR of 4.00, and NLR of 0.36 after 12 months of follow-up when applying a cutoff value of 0.5 m/s^2. For patients with CKD, an NPV of 90.5%, PLR of 2.78, and NLR of 0.44 were observed. Overall, a high predictive value to predict nonhealing (NPV >80%) within this patient group was seen.

Ulcer Healing Analysis

Logistic regression analysis was used to evaluate the relationship between various predictor variables and wound healing (Table III). For univariable analysis, only ACC_{max} showed significance in predicting healing (OR 5.44, 95% CI 2.42–12.21) and non-

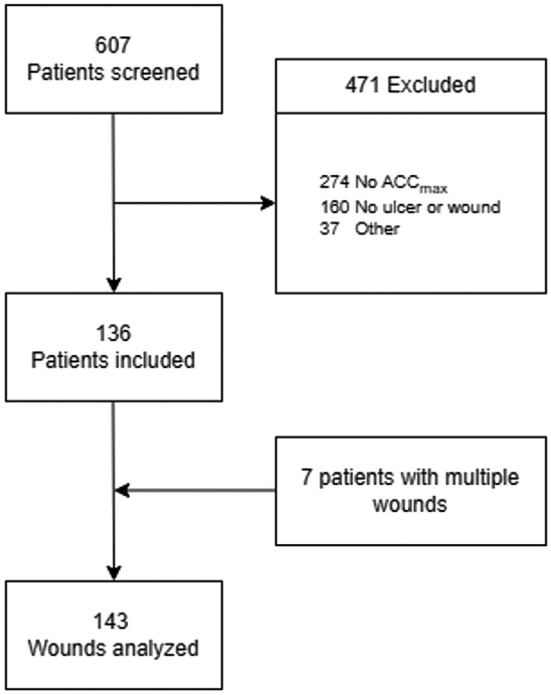

Fig. 2. Flow chart of patient selection.

healing (OR 0.18, 95% CI 0.08−0.41) of ulcers (both *P*-values <0.001). In addition, insulin dependency and Wagner score had a trend toward significance (*P*-values of 0.057 and 0.051, respectively). Therefore, these variables were included in a multivariable analysis. ACC_{max} remained significant for predicting ulcer healing when corrected for insulin dependency, wound infection, and Wagner score. This resulted in an OR of 7.77 (95% CI 1.96−30.81) and *P*-value of 0.004 for achieving wound healing.

Amputation Risk

To determine the relation between ACC_{max} measurements and the risk for minor or major amputation, a logistic regression analysis was applied. An OR of 5.3 (95% CI 1.48−19.28) for amputation was found in case a measurement below 1.0 m/s^2 was present ($P = 0.010$).

Limb Salvage

For 12 months of follow-up, mean ACC_{max} measurements at the hallux differed significantly ($P = 0.001$) between patients with a major amputation (mean $ACC_{max} = 0.28$ m/s^2) and patients with a (non)-healed ulcer of the foot (mean $ACC_{max} = 1.44$ m/s^2). The same applied to measurements at the dorsal pedal artery, in which a mean of 0.41 m/s^2 was seen in the major amputation group in comparison with a mean of 2.89 m/s^2 in the (non)-healed group ($P = 0.003$).

DISCUSSION

To date, no reliable bedside tests are available to predict whether a foot ulcer will heal or not. A recent systematic review by Chuter et al.[9] advocated that further research is required to more accurately identify patients at risk of non-healing or amputation. Our results indicate that the ACC_{max} could be a new promising tool for decision-making in patients with CLTI. If an ACC_{max} below 1.0 m/s^2 is measured in the hallux, the risks for minor and major amputation significantly rise (OR 5.3). Conversely, a high ACC_{max} in the hallux and dorsal pedal artery is correlated with limb salvage.

A low ACC_{max} value makes ulcer healing unlikely, as measurements below 0.5 m/s^2 were associated with very low healing rates (NLR 0.19, NPV 97.9% within 3 months). No difference in prognostic performance was seen for patients with DM or CKD. This result could facilitate the decision to opt for early revascularization in clinical practice. Although these results are promising, an insufficient PPV and PLR were seen for the prediction of ulcer healing. When increasing this threshold to 1.0 m/s^2, a trend toward improved prediction of ulcer healing was seen. This is in line with the physiology of the ACC_{max}, as a higher measurement indicates better hemodynamic perfusion. In clinical practice, this would mean that the test is able to exclude ulcer healing but is not able to predict healing of an ulcer.

Overall, prognostication of ulcer healing remains a major challenge. A recent international guideline by the intersocietal working group on the diabetic foot states that currently used bedside tests, such as the ABI and TP, have a weak prognostic performance on wound healing.[9] An ABI > 0.9 showed a very poor prognosis for healing (PLRs around 1−2). In addition, a TP above 45 mm Hg was not indicative for ulcer healing (PLR between 1.43 and 2.87), whereas measurements below 30 mm Hg could not convincingly prove non-healing (NLR between 0.28 and 0.88). A recent prospective study (TrEAD) by Elghazaly et al.[10] even showed inferior results to predict ulcer healing after 12 months of follow-up. In their study, very poor prognostic performances regarding the ABI, ankle pressure, TP, and $TcPO_2$ at different thresholds were seen. For example, a TP of 40 mm Hg resulted in a PLR of 0.80 and NLR of 1.08. Another new modality of interest is the pedal acceleration time (PAT). This parameter, just as the ACC_{max}, is based on waveform analysis of

Table II. Prognostic performance of maximal systolic acceleration for ulcer healing.

Cutoff value ACC_{max}	Time point during follow-up	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	PLR % (95% CI)	NLR % (95% CI)
<0.5 m/s^2	3 months	85.7 (57.2−98.2)	73.6 (65.2−81.0)	26.1 (19.8−33.6)	97.9 (92.9−99.4)	3.25 (2.27−4.66)	0.19 (0.05−0.70)
	12 months	61.1 (43.5−76.9)	77.6 (68.5−85.1)	47.8 (37.2−58.7)	85.6 (79.5−90.0)	2.72 (1.76−4.22)	0.50 (0.33−0.76)
<1.0 m/s^2	3 months	57.1 (28.9−82.3)	85.3 (78.0−90.9)	29.6 (18.5−43.8)	94.8 (90.9−97.1)	3.88 (2.10−7.18)	0.50 (0.27−0.92)
	12 months	44.4 (27.9−61.9)	89.7 (82.4−94.8)	59.3 (42.7−73.9)	82.8 (78.1−86.6)	4.32 (2.22−8.43)	0.62 (0.46−0.84)
Diabetes mellitus							
<0.5 m/s^2	3 months	66.7 (22.3−95.7)	72.6 (59.8−83.2)	19.1 (105−32.1)	95.7 (87.8−98.6)	2.43 (1.21−4.88)	0.46 (0.15−1.44)
	12 months	70.6 (44.0−89.7)	82.4 (69.1−91.6)	57.1 (40.6−72.2)	89.3 (79.9−94.7)	4.00 (2.05−7.80)	0.36 (0.17−0.75)
<1.0 m/s^2	3 months	33.3 (4.3−77.7)	82.3 (70.5−90.8)	15.4 (4.9−38.9)	92.7 (87.7−95.8)	1.88 (0.54−6.57)	0.81 (0.45−1.44)
	12 months	47.1 (23.0−72.2)	90.2 (78.6−96.7)	61.5 (37.7−80.9)	83.6 (76.4−89.0)	4.80 (1.81−12.70)	0.59 (0.37−0.93)
Chronic kidney disease							
<0.5 m/s^2	3 months	100.0 (29.2−100.0)	75.00 (55.1−89.3)	30.0 (18.4−44.9)	100.0 (83.9−100.0)	4.00 (2.11−7.60)	0
	12 months	66.7 (22.3−95.7)	76.0 (54.9−90.6)	40.0 (21.4−62.1)	90.5 (75.0−96.8)	2.78 (1.13−6.82)	0.44 (0.14−1.39)
<1.0 m/s^2	3 months	66.7 (9.4−99.1)	89.3 (71.8−97.7)	40.0 (14.9−71.7)	96.2 (83.4−99.2)	6.22 (1.64−23.66)	0.37 (0.07−1.86)
	12 months	50.0 (11.8−88.2)	92.0 (74.0−99.0)	60.0 (24.1−87.6)	88.5 (77.4−94.5)	6.25 (1.32−29.49)	0.54 (0.24−1.22)

the systolic upstroke and is measured with DUS. PAT reflects the duration from the onset of the systolic upstroke until the peak of systole (in the plantar arch). The study group of Sommerset et al.[14] and Teso et al.[15] showed that PAT is correlated with ABI and improvement after revascularization. Trihan et al.[16] recently published that acceleration time could be used to diagnose a low TP. However, none of these studies presented prognostic data (such as the PLR and NLR) for ulcer healing, which prevents us from comparing its performance to currently used bedside tests. Moreover, as previously mentioned, it is well-known that the ABI and TP are not sufficient for the prediction of (non)-healing, posing questions about its value.

When comparing our results to those of previously mentioned articles, slightly better prognostic accuracies of the ACC_{max} were found. In particular, prediction of non-healing could be addressed with more certainty. This could be of additional value in clinical practice. However, as described before, the complex multifactorial etiology of ulcers indicates that only assessing macrovascular perfusion of the wound seems inadequate for predicting healing or non-healing. Another important item to address in this setting is microvascular perfusion. Most tests that are previously mentioned focus on the macrovascular level. However, new techniques have been introduced in this research field. Among others, near-infrared fluorescence imaging with indocyanine green seems promising for the evaluation of tissue perfusion.[17] Recent studies have shown that there is additional value for predicting the clinical outcome of these ulcers, also after revascularization.[18] Other experimental microvascular imaging techniques, including laser Doppler flowmetry and hyperspectral imaging, are emerging as well.[19,20] Although these techniques are still at an early stage, it seems logical to combine macrovascular perfusion and tissue perfusion assessment to better predict ulcer healing in the future. Because DM is associated with microvascular complications, these new tests could be particularly useful in this patient group.

Currently, the WIfI classification system is applied in clinical practice and uses the ABI, SBP, absolute TP, or $TcPO_2$ to determine ischemia.[5] The purpose of this classification is to provide accurate and early risk stratification for patients with CLTI. Previously, ACC_{max} proved to have a better diagnostic performance for PAD than current bedside tests, and this study shows that the ACC_{max} could have added value in a wound classification study as well.[11] This is supported by the amputation risk

Table III. Logistic regression analysis − interaction variable and wound healing.

	Univariable analysis		Multivariable analysis	
Parameter	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age <70 years	0.78 (0.37−1.67)	*0.527*		
Sex	0.90 (0.41−1.98)	*0.787*		
Diabetes	0.98 (0.46−2.10)	*0.963*		
Insulin dependency	0.33 (0.11−1.04)	*0.057*	0.44 (0.11−1.81)	*0.257*
Hypertension	0.60 (0.29−1.26)	*0.177*		
Hypercholesterolemia	0.93 (0.45−1.90)	*0.840*		
Cardiac history	0.67 (0.33−1.36)	*0.266*		
CKD	0.62 (0.22−1.78)	*0.376*		
Gangrene	0.48 (0.22−1.05)	*0.068*		
Wound infection	0.58 (0.27−1.29)	*0.184*	0.57 (0.14−2.36)	*0.436*
Wagner score	0.39 (0.15−1.00)	*0.051*	0.34 (0.05−2.20)	*0.257*
ACC_{max} < 0.5	0.18 (0.08−0.41)	***<0.001***	0.13 (0.03−0.51)	***0.004***
ACC_{max} > 0.5	5.44 (2.42−12.21)	***<0.001***	7.77 (1.96−30.81)	***0.004***

Bold values indicate statistical significance.
Italic values signify statistical non-significance.

Table IV. Maximal systolic acceleration classification for assessing severity of ischemia at the level of ankle

	No ischemia Class I	Mild ischemia Class II	Moderate ischemia Class III	Severe ischemia Class IV
ACC_{max}	>5.5 m/s^2	3.0−5.5 m/s^2	1.0−3.0 m/s^2	<1.0 m/s^2

and limb salvage analyses. Therefore, a suggestion for assessment of the severity of ischemia with ACC_{max} measurements is presented in Table IV. Because prognostic accuracies for patients with DM and CKD were not different, these types of patients can also be evaluated with this modality. Therefore, we feel that ACC_{max} measurements could be applied in all patients presenting with a suspicion of PAD or new-onset ulcer. As this diagnostic tool does not need any other equipment than an ultrasound machine, no impact on financial resources will be made. Of course, these results should be interpreted with caution as a prospective study is needed to truly verify the added clinical value of the ACC_{max} in ulcer healing.

Limitations

This study has several limitations. First of all, due to its retrospective design, selection bias could have occurred. Second, although all patients received the most optimal wound care, differences in treatment strategies between clinical caregivers could have led to possible confounding. At last, a relatively low incidence of ulcer healing was seen. While these numbers are known from previous research as well, this might have limited the analysis of the prognostic performance.

CONCLUSION

Accurate prediction of foot ulcer healing remains a major challenge in patients with CLTI. The ACC_{max} at the hallux could be beneficial in clinical practice, since values below 0.5 m/s^2 are associated with non-healing of an ulcer and a higher risk of amputation. Conversely, higher ACC_{max} values are correlated with limb salvage (mean ACC_{max} of 1.44 m/s^2). No difference in prognostic performance was seen for patients prone to MAC.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Siem A. Willems: Writing − original draft, Visualization, Validation, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jochem D. Pruim:** Writing − original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Joost R. van der Vorst:** Writing − review & editing, Methodology, Investigation. **Jan van Schaik:** Writing − review & editing, Methodology, Investigation. **Abbey Schepers:** 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.

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