ORIGINAL ARTICLE

USING PEDAL ACCELERATION TIME TO PREDICT ISCHEMIC WOUND HEALING IN DIABETIC PATIENTS

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Abstract

Aim: *Diabetes Mellitus is one of the main factors for peripheral arterial disease (PAD), while also being associated with medial arterial calcification, thus limiting the use of the ankle-brachial index. Pedal acceleration time (PAT), has emerged as a diagnostic alternative, by measuring the systolic acceleration in the arteries of the foot, with higher PAT values corresponding to a worse prognosis and with the literature suggesting a cut-off of 180 ms as a predictor of wound healing. We aimed to confirm whether we could use PAT to predict wound healing, need for revascularization and amputation in diabetic patients and whether this cut-off was valid in our population.*

Methods: *A retrospective cross-sectional study was carried on diabetic patients referred to our department with PAD and lower limb wounds. Each limb was assessed individually in case of bilateral wounds. Limbs with unmeasurable PAT were excluded. Limbs were assessed on follow-up and classified as: healed wounds (HW), non-healed wounds (NHW), revascularized or amputated. PAT cut-off for wound healing was measured with ROC curve. Significance was defined at $p \leq 0.05$.*

Results: *A total of 88 patients and 100 limbs were included, mostly males (80.68%) with a median age of 75 years. Cut-off for wound healing was validated at 180.5 ms. Among the assessed limbs, 26% HW, 31% NHW, 33% revascularized limbs and 7% amputations. Mean PAT in each group was 159.81 ms (HW), 199.32 ms (NHW), 239.18 ms (revascularized), 279.14 ms (amputated). When comparing the HW and NHW groups, 61.3% of NHW had PAT >180ms versus 19.2% HW, $p<0.001$ (OR=6.65; 95%CI [1.98-22.39]). In the sub-set of NHW we further analysed whether the wound was clinically better or worse: wounds with a positive healing process had a mean PAT of 189.96 ms vs 231.43 ms ($p=0.14$) in wounds with worse evolution.*

Conclusion: *The results of our study validate the cut-off of 180 ms and reinforce using PAT as a predictor for wound healing, even among diabetic patients. In our analysis, only patients with HW had mean PAT ≤180 ms, with higher values of PAT being associated with worse outcomes (need for revascularization/amputation). Furthermore, in NHW patients, those with a PAT closer to 180 ms were associated with more favourable wound healing outcomes.*

Keywords: *Pedal Acceleration Time; Peripheral Arterial Disease; Diabetes Mellitus; Diabetic Foot; Wounds*

INTRODUCTION

Diabetes Mellitus is a well-established risk factor for peripheral arterial disease (PAD), with a prevalence of 20-28% among the diabetic population. This association underscores the systemic impact of diabetes on vascular health, driven by chronic hyperglycemia, inflammation, and endothelial dysfunction. In patients with diabetic foot ulcers, the prevalence of PAD is even more pronounced, reaching up to 50%[1]. These individuals represent a vulnerable subgroup where the coexistence of PAD and diabetic neuropathy significantly increases the risk of late diagnosis and complications such as infection, delayed wound healing, and tissue necrosis. The consequences of these complications are severe, with diabetic foot ulcers being the leading cause of non-traumatic lower limb amputations, accounting for up to 85% of such cases globally[2]. This imposes a profound burden not only on patients' quality of life but also on healthcare systems, contributing to increased hospitalizations, prolonged care, and substantial economic costs.

Taking into consideration the associated risks, early

detection of PAD in diabetic patients is crucial to guiding clinical decisions and improving outcomes. Identifying PAD at an early stage allows for timely interventions that can halt disease progression, reduce the risk of limb-threatening ischemia, and promote wound healing. A critical component of this effort is the accurate assessment of ischemic lesions, which directly influences the prognosis of diabetic foot ulcers[1,2]. However, the diagnostic process is often complicated by medial artery calcification (MAC), also known as Mönckeberg's arteriosclerosis, a condition prevalent among diabetic patients. MAC, differs from atherosclerosis as it is characterized by the formation of calcium deposits within the medial layer of the arterial wall, rather than the intimal and is strongly linked to diabetic neuropathy, significantly impairing the reliability of traditional non-invasive diagnostic tools like the ankle-brachial index (ABI)[1, 3]. By inadequately raising ankle pressures, MAC can lead to false-negative or inconclusive results, underscoring the need for alternative diagnostic approaches[1, 3].

Pedal acceleration time (PAT), assessed using Duplex ultrasound, has emerged as a valuable tool in this context. Unlike ABI, PAT is not influenced by calcification and provides a direct measurement of the systolic acceleration in the arteries of the foot[4]. Higher PAT values indicate delayed blood flow and are associated with worse outcomes, including impaired wound healing and an increased likelihood of complications[4-6]. In recent studies, a PAT threshold of 180 ms has been proposed as a predictor of wound healing, offering a potentially reliable metric for assessing the severity of ischemia and guiding treatment strategies[5-7]. The non-invasive nature of PAT measurement also makes it a practical option for routine clinical use, particularly in patients where other diagnostic tools are less effective.

This study aims to further evaluate the clinical utility of PAT in diabetic patients, focusing on its ability to predict wound healing outcomes, need for revascularization and risk of amputation. Additionally, we aimed to validate whether the proposed cut-off value of 180 ms for wound healing is applicable to our patient population, providing insights into its potential role in improving risk stratification and tailoring individualized treatment approaches.

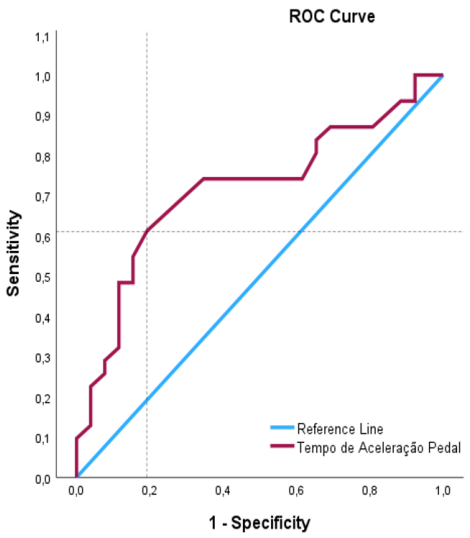

Figure 1 *Receiver operating characteristic (ROC) curve of pedal acceleration time for predicting wound healing in diabetic patients. AUC=0.72, 95%CI [0.58-0.85]; p<0.05.*

METHODS

We performed a retrospective cross-sectional study on diabetic patients referred to the Angiology and Vascular Surgery consult of our department with lower limb wounds and clinical suspicion of PAD. Data was collected throughout 2023, consisting of a non-consecutive, non-randomized, sample of patients.

The demographic characteristics of the population, such as age and sex, were documented alongside relevant cardiovascular risk factors and comorbidities, including smoking habits, dyslipidemia, hypertension, chronic kidney disease, coronary artery disease, and cerebrovascular disease. Each limb was evaluated individually in cases of bilateral wounds, ensuring that data from each affected limb was independently analysed. Limbs with unmeasurable pedal acceleration time were excluded from the study.

PAT was measured during the initial assessment of the patient. Measurements were made in milliseconds (ms) from the onset, to the peak of the systolic slope using the ACUSON NX3™ Elite Duplex ultrasound system (Siemens Healthineers, Erlangen, Germany). A linear array transducer with pulsed-Doppler frequencies ranging from 4 to 12 MHz was employed for these measurements. Whenever feasible, the most distal artery in the foot with adequate Doppler signal was selected for assessment (plantar, dorsalis pedis, arcuate, deep plantar, etc.), taking into account the artery directly responsible for supplying the area where the wound was present.

Wound re-evaluation was performed on follow-up appointments between 3 to 6 months after the initial assessment, during which the condition of each limb was classified into one of the following categories: healed wounds (HW), non-healed wounds (NHW), revascularized limbs or amputated limbs. In cases where wounds were not healed at 3 months but were fully healed by 6 months, the limb was classified as healed according to the final clinical outcome at the latest follow-up.

Demographic characteristics and risk factors were summarized through descriptive statistics. Categorical variables were reported as absolute and relative frequencies, while continuous variables were analysed using measures of central tendency, such as mean and median, alongside measures of dispersion, including standard deviation.

To validate the cut-off value for wound healing with PAT, a Receiver Operating Characteristic (ROC) curve was used with a 95% confidence interval. Association between qualitative variables was analysed using Pearson's Chi-square Test and Fisher's Exact Test. The strength of the association was measured with the Phi Coefficient. Statistical significance was established at $p \leq 0.05$ for all analysis.

All data were anonymized and processed electronically, with each patient identified solely by a clinical record number accessible only to the research team. The data were analysed using IBM SPSS® (version 29; SPSS, IBM Corp., Armonk, NY).

RESULTS

Our analysis included a total of 88 patients, the majority of which were men (80.68%), with a median age of 75 (67-83) years. Most patients had hypertension and dyslipidemia (85.23% and 76.14%, respectively) and only 27.27% were smokers or had prior history of smoking. These and other cardiovascular risk factors are summarized in Table 1.

Among the included patients, 12 (13.63%) presented with bilateral lower limb wounds, leading to the inclusion of 100 limbs for assessment. During follow-up, the limbs were categorized into four outcome groups: healed wounds accounted for 26% of cases, non-healed wounds for 31%, revascularized limbs for 33%, and amputated limbs for 7%. Three patients died during the follow-up period, and their outcomes were excluded from further analysis. Mean pedal acceleration time for each group was 159.81 ms (HW), 199.32 ms (NHW), 239.18 ms (revascularized limbs), 279.14 ms (amputated limbs).

The ROC curve analysis (Figure 1) showed a cut-off value for wound healing at a PAT value of 180.5 ms with an 81% specificity (AUC=0.72, 95%CI [0.58-0.85]; $p<0.05$).

When comparing the healed and non-healed (HW vs NHW) groups, we found that 61.3% of NHW had PAT >180 ms versus 19.2% in the HW group, $p<0.001$ (OR=6.65; 95%CI [1.98-22.39]), with a moderate association between PAT and wound healing (phi= 0.42).

Furthermore, within the subset of non-healed wounds, further analysis was conducted to evaluate differences in clinical progression and wounds were further classified as showing signs of clinical improvement (despite uncomplete healing) or worse clinical evolution. Among the 31 limbs in the NHW group, 61.29% had mean PAT > 180 ms and among those with worse clinical evolution (n=7), 85.71% had mean PAT > 180 ms. In this sub-set of patients, wounds showing signs of clinical improvement had a mean PAT of 189.96 ms, while those with worsening wound evolution exhibited a higher mean PAT of 231.43 ms, p= 0.14 (OR=5.07, 95%CI [0.53-48.86]).

Table 1 **Population demographics and cardiovascular risk factors**

Population Characteristics	
Number of Patients	88
Age (years) (median (Q1-Q3))	75 (67-83)
Gender	
Male	71 (80.68%)
Female	17 (19.32%)
Cardiovascular Risk Factors	
Hypertension	75 (85.23%)
Dyslipidemia	67 (76.14%)
Active Smoker or Smoking History	24 (27.27%)
Coronary Heart Disease	27 (30.68%)
Hemodialysis	18 (20.45%)
Stroke	8 (9.09%)

DISCUSSION

This study highlights the utility of pedal acceleration time as a predictive tool for ischemic wound healing in diabetic patients with peripheral arterial disease, reinforcing that PAT can serve as an indicator of wound healing potential and outcomes (phi= 0.42). The validation of the 180.5 ms cut-off for wound healing in our cohort aligns with the initially defined cut-off of 180 ms for wound healing, first described by the team of investigators responsible for developing this technique5 and supported by other recent publications[7].

In our sample it was clear that the only group achieving a favourable outcome (wound healing) was the one with mean PAT ≤ 180 ms (159.81 ms), with a statistically significant difference between the HW and NHW groups ($p<0.001$); furthermore, patients who required revascularization or amputation were in the groups with the highest registered PAT, 239.18 ms and 279.14 ms, respectively, highlighting the severity of the ischemia in these cases.

In fact, in a classification for PAD using PAT, proposed by Sommerset et al8 the latter two groups were in the most severe category for limb ischemia (category 4, PAT > 225 ms), while HW were in the mild ischemia category (category 2, PAT 121-180 ms) and NHW in the moderate ischemia category (category 3, PAT 181-224 ms)8.

Regarding the sub-analysis conducted on the NHW group, it was also found that non-healed wounds with favourable evolution had lower PAT (189.96 ms) than those with an unfavourable evolution (231.43 ms); despite this finding not reaching significance ($p=0.14$), it still had and odds ratio of 5.07. The former subgroup may represent a particular subset of patients on which careful wound monitoring and management may be beneficial as some might fully heal without requiring further surgical revascularization, due to their proximity to the cut-off value of 180 ms.

There are several limitations to this study that should be considered when interpreting the results. First, the study's retrospective design limits its ability to control for confounding factors that could have influenced the outcomes. The accuracy and completeness of the clinical records may vary, which could impact the reliability of the findings. Additionally, the sample size remains relatively small (n=100). A larger sample size would improve the statistical power of the study and provide more robust conclusions. Follow-up consults did not follow a pre-established protocol due to individual wound needs, furthermore it was only considered the presence of diabetic wounds without further analysing the severity of the wound at presentation and concomitant presence of infection, both of which could impact the healing outcomes. Lastly, the sub-analysis conducted on the NHW group (favourable and unfavourable wound evolution) was based on clinical examination, which may be subject to observer bias or variability in interpretation. Using more objective measures, could have provided more precise outcomes.

In cases where PAT did not accurately predict clinical outcomes (e.g., patients in the HW group with high PAT or NHW with lower PAT), several unmeasured factors may have influenced healing. These include, as previously mentioned,

wound location and extent, presence of infection, adequacy of local wound care in primary settings, and comorbidities such as diabetes and smoking habits. Additionally, limitations in the study design—such as the relatively short follow-up duration (up to 6 months) and inter-observer variability in assessing clinical wound progression—may also have contributed to these discrepancies.

Regarding technical limitations, extensive trophic lesions involving the foot sometimes physically prevented probe positioning or waveform acquisition for PAT measurement. The presence of occluded or small sized arteries at the forefoot may have also limited the detection of Doppler signal to enable PAT measurements near the wound, which could possibly be avoided by using smaller ultrasound probes or dedicated Doppler presets for the foot.

Although this study did not quantify time to complete wound healing, future prospective studies should aim to capture time-to-event data. A more strict, standardized follow-up protocol and healing assessment would allow for a more nuanced understanding of how PAT correlates not only with wound outcomes but also with the speed of wound recovery.

These results and limitations reinforce the importance of implementing a multicentric database registry with a more diverse cohort of patients and a standardized methodology to validate the potential of PAT as a reliable predictive tool in the setting of PAD.

CONCLUSION

This study provides valuable evidence supporting the use of pedal acceleration time as a predictive tool for wound healing outcomes in diabetic patients with peripheral arterial disease. The results validate the 180 ms cut-off for wound healing, highlighting its potential to guide clinical decisions and improve patient management. Although the study's limitations, such as its retrospective design and sample size suggest the need for further research, the findings offer promising insights into how PAT can assist in assessing ischemia severity and predicting the need for revascularization or amputation.

Ultimately, this study emphasizes the potential of PAT as a non-invasive, reliable measure that could be integrated into routine clinical practice, improving the prognosis and treatment of diabetic foot ulcers.

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