

Role of Perfusion, Extent, Depth, Infection and Sensation Scores in Determining the Outcome of Patients with Diabetic Foot Ulcers: A Prospective Cohort Study

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ABSTRACT

Introduction: Diabetes mellitus is a major public health problem in India. A Diabetic Foot Ulcer (DFU) is characterised by a full-thickness wound, skin necrosis, or gangrene below the ankle brought on by peripheral neuropathy or peripheral artery disease in diabetic patients. Numerous classification schemes have been put forth to classify and forecast the clinical outcomes of DFUs. The Perfusion, Extent, Depth, Infection and Sensation Score (PEDIS) classification system was developed to objectively categorise and define DFUs, facilitating communication between healthcare providers.

Aim: To determine the utility of the PEDIS score in predicting the outcomes of patients with DFUs.

Materials and Methods: The present single-centre prospective cohort study was conducted in the Department of General Surgery, Tezpur Medical College and Hospital, Tezpur, Assam, India, from August 1, 2022 to January 30, 2023, involving 60 patients. A PEDIS score was calculated and recorded for each patient. Patients were then classified into low-score (0-7) or high-score (8-12) groups and followed up for six months.

Outcomes were categorised as healed, unhealed, amputated, or deceased. Categorical data were presented as percentages and compared using the Chi-square test. The Receiver Operating Characteristic (ROC) curve was utilised to determine the cut-off value. A p-value <0.05 was considered statistically significant.

Results: The mean±Standard Deviation (SD) age at presentation was 49±14 years with a male preponderance (Male:Female= 2:1). Of all patients, 40 (66.67%) were healed following debridement and dressing, 11 (18.3%) had non healing ulcers, 5 (8.3%) underwent amputation, and 4 (6.67%) expired. Thirty-four (85%) of healed patients had PEDIS scores below eight, and 7 (63.6%) of patients with non healing ulcers had high PEDIS scores. Those undergoing amputation, 4 (80%) had high PEDIS scores and all deceased patients had high PEDIS scores.

Conclusion: Patients with DFUs who had higher PEDIS scores were more likely to develop complications such as non healing ulcers or require amputation. Therefore, the PEDIS score is a valuable system in clinical practice and can be uniformly applied to compare the outcomes of DFUs.

Keywords: Amputation, Brachial index, Dorsalis pedis, Surgical

INTRODUCTION

Diabetes mellitus is a major public health problem in India. Every year, 2-3% of diabetic patients will develop DFUs and 15% will develop DFUs in their lifetime [1-5]. A DFU is characterised by a full-thickness wound, skin necrosis, or gangrene below the ankle, brought on by peripheral neuropathy or peripheral artery disease in diabetic patients [6]. The most commonly affected sites of ulceration are the pressure points such as the plantar aspect of the toes, metatarsal heads and heel. It is a very common, severe and costly complication of diabetes that might lead to amputation, significantly deteriorating the quality of life and increasing mortality [7]. The high prevalence of DFUs in India can be attributed to the following risk factors such as walking barefoot, low literacy rate, arriving late, having no knowledge of the primary healthcare system, and belief in alternative systems of medicine [8]. Therefore, it is imperative to establish a uniform and effective protocol for the early treatment of DFUs. The initial stage in this process is accurately determining the level of risk for ulcer-related complications in individuals with DFUs [9].

Many DFU classification systems such as Wagner, Sinbad, Amit Jain, etc., have been proposed to classify DFUs and predict their clinical outcomes [10-12]. However, these systems have shortcomings. Firstly, most of these classification systems focus only on the local pathology of DFUs without giving proper importance to other parameters affecting ulcer healing. For example, the Wagner system focuses only on ulcer depth, while co-morbidities such as ischaemia and neuropathy are not taken into consideration [13]. Secondly,

these classification systems usually lack standardised definitions of the factors most important for wound healing, such as ischaemia, infection and other systemic variables. The PEDIS classification system was created by the International Working Group of the Diabetic Foot (IWGDF) to objectively define and classify DFUs and aid healthcare providers in communication [6]. Under this system, DFUs are categorised based on five factors thought to be the most important for the formation of DFUs: i) perfusion; ii) extent/ size; iii) depth/tissue loss; iv) infection; and v) sensation. Each subcategory is further defined by stringent standards derived from objective methodologies that are globally relevant [14].

Numerous research studies have demonstrated the predictive value of the PEDIS score in assessing the degree and course of DFUs [6,9]. Higher PEDIS scores are often associated with poorer wound healing and an increased risk of amputation. In clinical practice, the PEDIS score is considered a helpful tool for determining the severity of DFUs, aiding medical professionals in deciding on courses of action and the necessary level of care. However, although the PEDIS score has been widely used, more validation research is still required to ensure its reliability for various patient populations and healthcare environments. The efficacy of the score may vary depending on variables such as co-morbidities and patient demographics. The present study was conducted to investigate the relationship between PEDIS scores and co-morbidities like peripheral neuropathy and peripheral arterial disease. The study also sought to establish the threshold for a "high" PEDIS score. Finally, the present study was aimed to test the validity of the PEDIS score in managing

DFUs in a tertiary care centre in a part of Assam, India, where data and literature on this type of study are sparse.

MATERIALS AND METHODS

The present was a single-centre, prospective cohort study carried out in the Department of General Surgery, Tezpur Medical College and Hospital, Tezpur, Assam, India, from August 1, 2022 to January 30, 2023, involving 60 patients. Institutional Ethics Committee Board (IEC Sl.No: 120/2022/TMC&H) approval was obtained, and informed written consent was obtained from all participants.

Sample size calculation: The sample size was determined by the statistical method:

$$n = z^2 pq / d^2$$

Where, $p = 2.05\%$ (DFU complications overall in population [9]), $q = 100 - p = 97.95\%$,

$d = \text{error} = 5\%$,

$\alpha = \text{level of significance} = 1\%$, hence $z = 2.58$

Minimal sample size, $n = z^2 pq / d^2 = 53.46 = 54$ patients.

Hence, the study included total 60 patients.

Inclusion criteria: All patients with Type 2 Diabetes and DFU attending the Department of General Surgery at Tezpur Medical College and Hospital, Assam, India, were included in the study. If more than two foot ulcers were present, the most recent and largest ulcer identified was selected as the index ulcer [15].

Exclusion criteria: The DFUs related to autoimmune disease, malignancy and acute limb ischaemia were excluded from the study [16].

Study Procedure

A proforma that included demographic details such as age, sex, any co-morbidity, the endpoint of treatment and PEDIS grading was used to collect data.

PEDIS classification: The PEDIS score was calculated after all variables were categorised for a given patient and documented [Table/Fig-1].

Grade	Perfusion	Extent	Depth	Infection	Sensation	Score
1	No PAD	Skin intact	Skin intact	None	No loss	0
2	PAD, No CLI	<1 cm ²	Superficial	Surface	Loss	1
3	CLI	1-3 cm ²	Fascia, muscle, tendon	Abscess, fasciitis, septic arthritis		2
4		>3 cm ²	Bone or joint	SIRS		3

PAD: Peripheral arterial disease; CLI: critical limb ischemia.

[Table/Fig-1]: PEDIS classification system [6].

- A combination of physical examination findings (dorsalis pedis or posterior tibial pulse), and non invasive studies (ankle-brachial index and toe-brachial index) were used to estimate perfusion.
- The extent of the ulcer was estimated in cm² and allocated into three groups:
 - <1 cm²
 - 1-3 cm²
 - >3 cm²
- The depth of the ulcer was determined using a sterile blunt probe.
- Diagnosis of infection was based on the presence of signs and symptoms of infection, the presence of pus and laboratory results of culture and sensitivity.
- Sensation was evaluated with a 10 gram monofilament sensation on 10 sites of the foot (plantar and dorsal surface).

The PEDIS score was recorded for each patient. The PEDIS score ranges from 1 to 12 for each patient.

All patients were followed for six months or until death, whichever is earlier. The outcome was categorised as healed, unhealed, amputated, or death. Screening for diabetic peripheral neuropathy

was done using the Semmes-Weinstein Monofilament Examination (SWME) method [17].

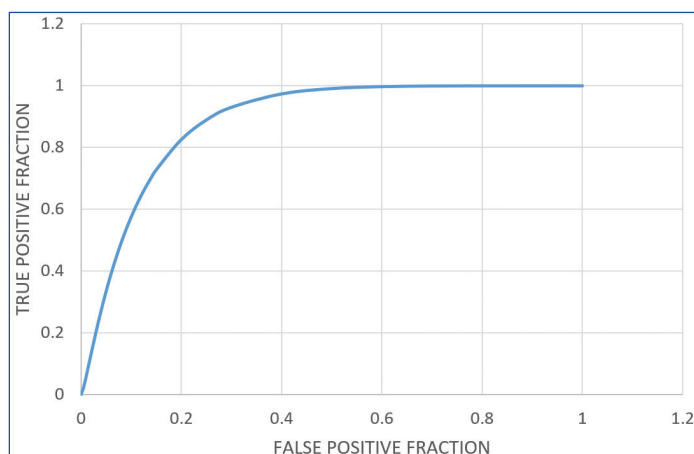
STATISTICAL ANALYSIS

A descriptive analysis was conducted of the obtained data. The Shapiro-Wilk test was used to assess the normal distribution of the data. Normally distributed data were expressed as mean \pm SD, while categorical data were expressed as a percentage and compared using the Chi-square test. Subsequently, the ROC curve was obtained to determine the cut-off value. A significance level of p -value <0.05 was considered statistically significant. Data were entered into Writer, Presentation, Spreadsheets (WPS) Excel, and International Business Machines (IBM) Statistical Package for Social Sciences (SPSS) Statistics for Windows software version 25.0 was used for statistical analysis.

RESULTS

In the present study, males were observed to be more affected by DFU than females, with 40 males affected compared to 20 females (Male:Female=2:1). The mean \pm SD age was 49 \pm 14 years, with the youngest being 26 and the oldest 86.

The ROC curve was plotted [Table/Fig-2], and a PEDIS score of 7.5 was identified as the threshold to predict DFU outcomes, with a sensitivity of 100% and a false-positivity of 18.5%. The PEDIS score of 7.5 was rounded off to 8 for analytical purposes. Patients were then divided into two groups: the low PEDIS score group with scores between 0 to 7 and the high PEDIS score group with scores between 8 to 12.



[Table/Fig-2]: ROC curve.

A total of 39 patients had low PEDIS scores, while 21 had high PEDIS scores [Table/Fig-3]. The relationship between gender and high PEDIS score was found to be not significant (Chi-square value=0.329, p -value=0.565).

Gender	PEDIS score			Significance
	0-7	8-12	Total	
Male	25	15	40	Chi-square=0.329 p-value=0.565
Female	14	6	20	
Total	39	21	60	

[Table/Fig-3]: Classification of patients based on PEDIS scores.

Elevated White Blood Cell (WBC) counts were found in 24 (40%) patients [Table/Fig-4]. The cut-off value for high WBC was considered to be more than 11,000 cells/mm³ [18]. Patients with high PEDIS scores tended to have increased WBC counts.

The cut-off value for high Glycated Haemoglobin (HbA1c) was set at 6.5% [18]. Approximately 41 (68.3%) patients had uncontrolled HbA1c levels [Table/Fig-5]. Patients with high PEDIS scores tended to have elevated HbA1c levels [Table/Fig-3].

Raised WBC	PEDIS score		Total	Significance
	0 to 7	8 to 12		
No	29	7	36	Chi-square=9.572 p-value= 0.0019
Yes	10	14	24	
Total	39	21	60	

[Table/Fig-4]: Elevated WBC counts in DFU.
The p-value in bold font indicates statistically significant value

Raised HbA1C	PEDIS score		Total	Significance
	0 to 7	8 to 12		
No	17	2	19	Chi-square=7.320 p-value= 0.00681
Yes	22	19	41	
Total	39	21	60	

[Table/Fig-5]: Uncontrolled HbA1C and DFU.

Out of all the patients, 25 (41.6%) had peripheral neuropathy, showing a significant association with high PEDIS score (Chi-square value =8.307, p-value=0.0039) [Table/Fig-6]. Peripheral arterial disease was observed in 20 (33.3%) patients, with 11 (55%) of them having a high PEDIS score (Chi-square value=5.274, p-value=0.0216) [Table/Fig-7].

Peripheral neuropathy	PEDIS score		Total	Significance
	0 to 7	8 to 12		
No	28	7	35	Chi-square=8.307 p-value= 0.0039
Yes	11	14	25	
Total	39	21	60	

[Table/Fig-6]: PEDIS score and peripheral neuropathy.

Peripheral arterial disease	PEDIS score group		Total	Significance
	0 to 7	8 to 12		
No	30	10	40	Chi-square=5.274 p-value= 0.0216
Yes	9	11	20	
Total	39	21	60	

[Table/Fig-7]: PEDIS score and peripheral arterial disease.

Of all patients with DFU, 40 (66.67%) were healed following debridement and dressing, with five patients requiring skin grafting. A total of 34 (85%) of these patients had PEDIS scores below 8. One patient with a high PEDIS score underwent skin grafting at a later date. Eleven (18.3%) patients had non healing ulcers, with seven of them having high PEDIS scores, showing statistical significance (Chi-square=4.855, p-value=0.0275). Five (8.3%) patients underwent amputation, with four of them having high PEDIS scores, again showing statistical significance (Chi-square value=4.855, p-value=0.0275). Four (6.67%) patients passed away due to comorbidities, all of whom had high PEDIS scores [Table/Fig-8].

Outcome	PEDIS score group		Total	Significance	
	0 to 7	8 to 12		Chi-square	p-value
Healed	34	6	40	21.098	0.00001
Non healed	4	7	11	4.855	0.0275
Amputation	1	4	5	4.855	0.0275
Death	0	4	4	-	-
Total	39	21	60	-	-

[Table/Fig-8]: PEDIS score and outcome.

DISCUSSION

Numerous scoring systems exist to classify or grade DFUs. These classification systems are designed to guide the treating physician towards a better line of management and prognosis for DFUs. Researchers developing and evaluating new therapies, as well as, clinicians managing patients daily, may find it easier to develop and evaluate a validated DFU classification system [19]. To the

best of the authors knowledge, this is the first time the PEDIS classification system has been validated for clinical outcomes in Assam, India. According to the present study findings, there was a positive association between a high PEDIS score and the likelihood of either a persistent ulcer or death.

The DFU is a heterogeneous entity with various etiological factors [20]. A study by Lavery LA et al., showed a significant relationship between the severity of infection and amputation [21]. Oyibo SO et al., have demonstrated the association between the outcome of DFUs and factors such as blood supply, presence of infection, depth of ulcers and area of ulcers [22]. The PEDIS system includes five categories, with a higher score in each subcategory correlating with poorer outcomes.

In a study by Gandhi C et al., a PEDIS score higher than 7.5 was associated with more adverse outcomes [9]. Authors found that classifying DFUs into low-score (up to 7) and high-score (8 to 12) was a more convenient way to classify DFUs and predict the prognosis.

Studies by Ahmad W et al., and Iraj B et al., have shown that uncontrolled blood glucose levels and high WBC counts adversely affect the outcome of foot ulcers [23,24]. In the present study, these findings were reinforced with uncontrolled Random Blood Sugar (RBS) and HbA1c levels, as well as, raised WBC counts, being associated with high PEDIS scores and worse outcomes.

Peripheral neuropathy leading to the loss of protective sensation plays a crucial role in the pathogenesis of most DFUs [8]. In the current study, patients with sensory peripheral neuropathy had higher PEDIS scores and experienced more adverse outcomes after treatment (p-value=0.0039). Peripheral vascular disease in diabetic patients occurs prematurely and progresses at an accelerated rate, particularly in the lower limbs' more distal vessels [8]. In the present study, peripheral vascular disease was observed in 20 (33.3%) patients, with 11 of them having a high PEDIS score (p-value=0.0216). These findings align with previous studies by Gandhi C et al., which demonstrated a significant association of a high PEDIS score with peripheral neuropathy, with 25 (40.98%) patients found to be associated with peripheral neuropathy (Chi-square value=9.28 and p-value=0.003). Peripheral arteriopathy was seen in 10 (16%) patients, all of whom had high PEDIS scores (Chi-square value=17.22 and p-value=0.001) [9].

Studies by Chuan F et al., and Gandhi C et al., demonstrated that higher PEDIS scores were associated with more complications such as non healing, amputation, or death [6,9]. The present study also revealed a significant association between a high PEDIS score and DFU complications. Sivakumar S et al., showed that even patients with a low PEDIS score but with higher WBC or uncontrolled blood sugar levels could develop DFU complications, similar to those with higher PEDIS scores [18]. Similarly, in the current study, four patients with a PEDIS score under seven progressed to non healing ulcers, and one patient had to undergo amputation. These patients were found to have elevated WBC counts or uncontrolled blood sugar levels.

Monteirosoares M et al., utilised ROC curve analysis to assess the diagnostic accuracy of various systems for DFU development, concluding that this approach was the most effective method to determine a system's discriminatory capacity [25]. In the present study, the diagnostic accuracy of the PEDIS score system in predicting the outcome of DFUs was validated using the Area under the ROC Curve (AUC) value in conjunction with ROC curve analysis. The results of the current study indicate that the PEDIS score system has a high degree of accuracy in predicting the outcomes of DFUs. Furthermore, the present study demonstrates that PEDIS scores can be categorised into two groups: low (0 to 7) and high (8 to 12), with the high group having a significantly higher risk of complications and non healing. Therefore, the authors believed that there is broad applicability of the PEDIS score system in clinical practice.

Limitation(s)

Firstly, the study's data set was obtained from a single hospital, which limited its potential for extrapolation to other hospitals. The impact of co-morbidities such as hypertension, hypercholesterolemia, etc., was not explored in the present study. Additionally, there was no comparison made between the various scoring systems for DFUs in the present study. Therefore, future validation studies should concentrate on larger sample sizes, diverse settings, and longer follow-up periods to address these limitations.

CONCLUSION(S)

In the present study, the majority of ulcers with low scores healed successfully. Patients with DFUs who had a higher PEDIS score were more likely to develop complications such as non healing ulcers or amputation. Therefore, the PEDIS score is a very useful system in clinical practice and can be uniformly applied to compare the outcomes of DFUs.

Authors' contributions: Nirmal Kumar Agarwal has made substantial contributions to the concept and design, and is the main author. Dharendra Nath Choudhury, Biswajit Das and Tapash Kumar Kalita have been involved in the drafting of the manuscript and revised it critically for important intellectual content. All authors have agreed to be accountable for all aspects of the work. Tapash Kumar Kalita is the corresponding author. All authors have read and approved the final manuscript.

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