Predictive values of foot plantar pressure assessment in patients with midfoot deformity secondary to Charcot neuroarthropathy.

Structured Abstract

Aims: The principal aim of this study was to identify a cut-off point along the spectrum of peak plantar midfoot pressure that has an optimum combination of sensitivity and specificity to screen for neuropathic ulceration in patients with Charcot neuroarthropathy (CN).

Methods: A 1-year outcome study was performed in twenty-five patients with diabetes, affected with chronic CN midfoot deformity. Peak plantar pressure (PPP) and pressure/time Integral (PTI) in the midfoot region were registered. For selecting the optimal diagnostic cut-off points on the scale of pressure measurement, ROC curves were used.

Results: Twelve (48%) patients developed a plantar midfoot ulcer. Baseline PPP (24.04 □ 6.33 Vs. 12.85 □ 3.29 N/cm^2) and PTI (11.89 □ 4.60 Vs. 5.42 □ 2.26 N/cm^2/s) were significantly higher in the ulcerated group ($p<.001$ and $p<.001$, respectively). Using ROC analyses, optimal cut-off point for PPP was 16.45 N/cm^2, yielding a sensitivity of 92% and a specificity of 85%; and for PTI, optimal cut-off point was 7.2 N/cm^2/s, yielding a sensitivity of 92% and a specificity of 77%.

Conclusions: Patients with CN midfoot deformity with cut-off values for PPP of 16.45 N/cm^2 and PTI of 7.2 N/cm^2/s showed an elevated risk of neuropathic ulceration in the plantar area of the midfoot.

Keywords: diabetic foot, re-ulceration, plantar pressure, prevention, Charcot foot.

1. Introduction

Charcot neuro-osteoarthropathy (CN) has become one of the most challenging complications related to patients with diabetes [1]. Diabetic polyneuropathy (DPN), previous trauma in the foot, increased stress forces, and inflammation disorders [2-3] are the most reliable precipitating factors described in the literature for CN occurrence. CN has been linked to higher rates of morbidity and quality of life reduction [4, 5].

Charcot midfoot deformity is a long-standing consequence of CN that occurs in the 60% of patients with CN diagnosis; it is characterized by Lisfranc affection secondary to cuneiform-metatarsal luxation, producing bony prominences in the plantar aspect of the foot, in the medial or lateral surface [6-9].

Previous studies in the United Kingdom (UK), during a 20-month follow-up period, found that most patients with acute CN developed lesions in the midfoot and hindfoot [10]. International guidelines [11, 12] classify DFU located in the midfoot as a predisposing factor of amputation and death.

The International Working Group on the Diabetic Foot (IWGDF) states that high plantar pressures are a significant independent risk factor for foot ulceration and should therefore be avoided to prevent DFU and further complications [13]. Previous studies have focused on screening patients at high risk of neuropathic ulceration and found that values above 200 kpa of pressure predict an ulceration event in the forefoot [13]. Despite these results, patients with CN and midfoot deformity form a small group of patients, and the role of elevated plantar pressure is inconsistent, showing that peak plantar pressure (PPP) was higher in the affected and contralateral foot compared to patients with diabetes and control subjects. Nevertheless, this PPP was higher in the forefoot than in the midfoot, and thus the authors could not link the elevated PPP to midfoot ulceration [14]. Other studies have focused on the prediction of barefoot plantar pressure in patients with a history of DPN and ulceration, showing that CN midfoot deformity was a factor independently associated with PPP to predict midfoot ulceration [15]. For several years, researchers have attempted to identify if there exists a critical cut-off point to predict DFU in the forefoot, but they found that there is no optimal cut-off point for clearly screening patients for risk of DFU [16, 17].

To date, none of the studies revised in populations of persons with diabetes have included the prediction of pressures in the midfoot region in patients with CN for DFU occurrence, with the majority focusing on plantar pressure in the forefoot region.

To the best of our knowledge, no previous studies have analyzed a cut-off point to screen patients at risk of midfoot ulceration in patients with a diagnosis of CN and midfoot deformity. Midfoot re-ulceration is indicative of CN severity, and depending on it, the aggressiveness of the treatment will vary. Therefore, this study primarily aimed to identify a cut-off point along the spectrum of peak plantar midfoot pressure that has an optimum combination of sensitivity and specificity to screen for neuropathic ulceration in patients with CN and midfoot deformity.

2. Methods

2.1 Subjects

Twenty-five patients who were at high risk for foot ulceration and suffered from CN midfoot deformity foot participated in this 1-year prospective study in a specialized

diabetic foot unit between December 2018 and January 2020 to assess the risk of ulceration.

The inclusion criteria were confirmed type 1 or type 2 diabetes, age > 18 years, affected with chronic CN stage 3 according to Eichenholtz classification [18] affecting the midfoot location, and loss of protective foot sensation because of peripheral neuropathy.

Exclusion criteria were ulcers during the examination, transmetatarsal or major amputation in the contralateral limb (below or above the knee), history of rheumatoid disease, other causes of neuropathy, critical limb ischemia as defined according to the IWGDF guidance [19], and the need for walking aids. Patients with reconstructive or offloading surgery in the midfoot were also excluded.

After institutional review, board approval was obtained, and the medical records and clinicopathologic conditions of patients were recorded.

2.2 Clinical evaluation

At baseline, clinical characteristics were assessed after informed consent was signed by the patient on day 0. Midfoot CN deformity was defined as a bony midfoot prominence of the foot [20]; the apex of the deformity is located at the midtarsal joint and was identified radiographically by signs of previous bone fracture or luxation according to Eichenholtz classification [18]. CN midfoot deformity pattern was stratified into a medial column pattern (located in the midtarsal joint with a dorsal talar-first metatarsal subluxation), and a lateral column pattern (located in the midtarsal joint with a dorsal calcaneocuboid subluxation) [20].

Body mass index (BMI) was calculated as weight (kg) divided by height (m^2). Clinicopathologic data, including diabetes type, mean duration of diabetes, mean duration of CN diagnosis, hypertension, smoking history, and HbA1c (%) values in the previous 3 months were collected. The patients' renal, cardiac, and retinopathy status and previous minor amputation were recorded in the CRF from the patient's clinical history.

According to the IWGDF guidelines, critical limb ischemia is defined as the absence of both distal pulses and a brachial ankle index of ≤ 0.39, systolic ankle pressure < 50 mmHg, and toe pressure < 30 mmHg [19].

2.3 Plantar Pressure Measurement

A dynamic pressure measurement system (Footscan® system, RSscan International, 3583 Olen, Belgium) was used to record the PPP (N/cm^2) and pressure time integral (PTI) ($N/cm^2/s$) in dynamic barefoot condition at baseline. The hardware included a 2-m plate

with four sensors/cm^2 and a 3D-Box interface that was synchronized with a motion capture system. All data were recorded at a measurement frequency of 500 Hz and were processed using Scientific Footscan® software (RSscan International, 3583 Olen, Belgium). The clinician removed the calluses in the plantar surface of the foot prior to dynamic pressure system capture, and then, patients were instructed to walk barefoot for 3 min before measuring the plantar pressure with the aim of accommodating the patient to the normal gait and speed. After this, four registers were taken to calculate the mean of both measurements (PPP and PTI) with a two-step approach to the platform [21]. The software divides every foot into ten sectors: the hallux, toes, first to fifth metatarsal head, midfoot, medial heel, and lateral heel. Midfoot pressures include medial, lateral and at the apex of the deformity. Additionally, entire foot pressures were defined as summary of all the sectors previously described. The investigator who analyzed and extracted data from PPP and PTI parameters was blinded to the clinical and radiological data from every patient; both investigators are experienced podiatrist with more than 5 years of experience in the treatment of diabetic foot complications.

2.4 Follow-up

All patients were followed-up for 1 year or until they suffered from an ulcer ulceration event in the midfoot region. Patients came monthly to the outpatient clinic, according to the international guidelines [13]. In every visit, the principal investigator performed debridement of high-risk points, such as minor lesions, defined as nonulcerative lesions of the skin on the plantar aspect of the foot and included abundant callus, hemorrhage, or a blister [22]. Also, all the patients wore an extra-depth custom made shoe with a fully customized insole in order to decrease peak pressures in the plantar aspect of the foot.

2.5 Outcome measures

The main outcome measure was to select the optimal cut-off point on the scale of pressure measurement that has an optimum combination of sensitivity and specificity to screen for neuropathic ulceration in the midfoot of patients with CN.

Midfoot ulcer ulceration was defined according to the IWGDF guidelines as a break of the skin of the foot that involves, as a minimum, the epidermis and part of the dermis [23]. The investigator who assessed DFU ulceration was blinded to the plantar pressure measurement to avoid bias in plantar pressure interpretation.

The secondary outcome measure was to evaluate clinicopathological characteristics and their relationships with midfoot ulceration in the midfoot of patients with CN.

2.6 Statistical analyses

Quantitative variables were presented as the mean and standard deviation (SD), while qualitative variables were presented as the percentage and frequencies. To explore differences in clinical features between patients with and without midfoot ulcer occurrence, the Chi-square test for categorical variables and the Student T-test for quantitative variables were performed. For selecting the optimal diagnostic cut-off points on the scale of pressure measurement (PPP and PTI), ROC curves were used. This is a graphical method of representing sensitivity and specificity for a given test. In addition, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR) and negative likelihood ratio (NLR) were calculated for PPP and PTI.

P-values <0.05 were considered statistically significant, with confidence intervals of 95%. All statistical analyses were performed using SPSS statistics version 25.0 for Mac OS (SPSS, Chicago, IL, USA).

3. Results

Three patients dropped out of the study because of their refusal to wear extra-depth custom made shoe and/or fully customized insole and were thus removed from the analyses. Patients presented no ulcers at the time of inclusion in the study. Finally, 25 patients were included in the analysis. Patients were followed up prospectively for a 1year period or until they developed an ulceration event in the midfoot.

Baseline data on demographic characteristics and diabetes complications are shown in Table 1.

Table 1. Patients' baseline characteristics (N=25).

Table 1 Legend: DM, diabetes mellitus; SD, standard deviation; Kg, kilograms; cm^2, squared centimeters.

Regarding plantar pressure assessment, we did not find any difference between PPP and PTI in the entire foot of patients with CN and midfoot deformity; despite this, patients who suffered from an ulceration event had higher PPP and PTI in the midfoot region compared to those without an ulceration event (Table 2).

Table 2. Differences between plantar pressure patterns for midfoot ulceration. Table 2 Legend: SD, standard deviation; N, newton; cm^2, squared centimeters; s, seconds.
*P < 0.05 indicates statistical significance.

During the follow-up period, 12 (48%) patients suffered from an ulceration event in a median duration time of 4.5 [Interquartile Range (25th – 75th); 3 – 8.75] weeks.

We did not detect any statistical differences regarding demographic characteristics and diabetes complications between patients who suffered an ulceration event and patients who did not (Table 3).

Regarding foot characteristics, statistical differences were documented between patients who suffered and ulcer event and patients who did not, such as minor lesions presence. Patients who presented at baseline with a lateral column pattern were more prone to develop an ulceration event on the midfoot in comparison with the medial column pattern; despite this, with the numbers available this difference did not reach statistical significance (Table 3).

Table 3. Differences between the risk factors for midfoot ulceration.

Table 3 Legend: DM, diabetes mellitus; SD, standard deviation; Kg, kilograms; cm^2, squared centimeters; □, degrees. *P < 0.05 indicates statistical significance.

3.1 Main outcome

Using ROC analyses, we obtained a midfoot PPP optimal cut-off point, determined by a balance of sensitivity and specificity, of 16.45 N/cm^2, yielding a sensitivity of 92% and a specificity of 85%, area under the curve 0.95 (p<.001 (95% CI 0.88–1).

Also, for midfoot PTI, we found that the optimal cut-off point, determined by a balance of sensitivity and specify, was 7.2 $N/cm^2/s$, yielding a sensitivity of 92%, a specificity of 77%, and an area under the curve of 0.92, p<.001 (95% CI 0.82–1). Table 4 shows the pooled accuracy and reliability obtained for PPP and PTI in the midfoot region.

Table 4. Performance characteristics of peak plantar pressure and pressure time integral in the midfoot region.

Table 4 Legend: PPV, positive predictive value; NPV, negative predictive value; PLR, positive likelihood ratio; NLR, negative likelihood ratio

Additionally, ROC curves were performed for the entire foot PPP and PTI achieving worse results to screen for ulceration patients; for the entire foot PPP, we found an area under the curve of 0.48, p=.913 (95% CI 0.24–0.76); for the entire foot PTI, we found an area under the curve of 0.59, p=.45 (95% CI 0.36–083) (Figure 1).

Figure 1. ROC curves for PPP and PIT in CN midfoot deformity subjects. Figure 1 legend. a. ROC curves for pressure patterns in the midfoot region; b. ROC curves for pressure patterns in the entire foot. Abbreviations: PPP, Peak plantar pressure (N/cm^2); PTI, Pressure Time Integral ($N/cm^2/s$).

4. Discussion

The primary objective of the present longitudinal 1-year outcome study was to identify a cut-off point along the spectrum of PPP and PTI, that have an optimum combination of sensitivity and specificity, to screen for ulceration in patients with CN and midfoot deformity. We found that patients with CN midfoot deformity who developed ulceration in the midfoot have increased midfoot PPP and PTI values compared with non-ulceration patients with CN midfoot deformity. Pressure patterns in the entire foot were not useful to screen patients with CN midfoot deformity due to the lack of any statistical association in our results. The data from this research support the screening of patients at high risk of ulcer with diabetes by using a dynamic plantar pressure system in the at-risk region, more than to analyze general foot pressures, due to the optimum levels of sensitivity and specificity to predict DFU on the midfoot of patients with CN midfoot deformity.

Previous studies have analyzed the role of dynamic plantar pressure measurement to identify patients at risk of neuropathic ulceration among those with previous DFU records [16, 17]; these authors found that PPP was not a good diagnostic tool to assesses the risk of ulcer occurrence in the feet of patients with diabetes due to the low sensitivity and specificity as a diagnostic tool. Unfortunately, these authors analyzed foot pressures of the entire foot, and they did not stratify by anatomical regions; it would have been interesting to stratify the foot in different sectors in order to know the specific risk of suffering a DFU, due to the difference in foot biomechanics in different sites of the foot. Additionally, these authors did not analyze PTI, which takes into account loading time, and could be more indicative of DFU risk than PPP in patients at risk of diabetes complications during walking [24].

Additionally, Barn et al. [15] evaluated 171 diabetes patients and a recently healed neuropathic ulceration; only 22 of those patients were patients with CN midfoot deformity and 11 with previous DFU in the midfoot. These authors found that patients with CN midfoot deformity had higher pressures in the midfoot in comparison with the forefoot and the heel; in a multivariate regression analysis, CN midfoot deformity was identified as an independent factor associated with elevated PPP. These authors evaluated mean PPP in the midfoot, but they did not aim to perform any cut-off point to clearly screen patients at risk of foot ulceration. A cut-off reference point of 16.45 N/cm^2 could be useful to identify those patients with a high probability of developing midfoot ulceration.

We found that 75% of patients reulcerated in the lateral column and only 25% in the medial column pattern, we hypothesize that if we will increase the sample size, we might find that it will reach statistical significance. It has been demonstrated that lateral column ulcers are much more difficult to treat, so the clinical relevance of this finding remain very important [25].

Clinicians should consider these patients as a non-plantigrade foot and instable for their high risk for foot ulceration; in spite of the use of preventive therapies (orthosis and extra-depth footwear) and implement reconstructive foot surgeries [26], and further studies should focus on preventive therapies in patients with midfoot CN.

Although the present study becomes to date the highest sample of patients with CN midfoot deformity assessed for PPP in the midfoot, the authors did not analyze cutoff points to diagnose DFU in the midfoot of patients with CN.

To our knowledge, this is the first study to investigate cut-off values to screen for neuropathic ulceration in patients with CN midfoot deformity. Also, the present study has the highest reported sample of patients with CN and midfoot deformity followed-up for 1 year and screened with a plantar pressure system.

However, our results should also be interpreted with caution because of some limitations; first, the study did not analyze shear pressures, which might increase the understanding of plantar foot mechanics and their role in the development of DFU [27].

Also, in-shoe plantar pressure was not analyzed, and it could provide further information, as some authors suggest analyzing the effect of used footwear conditions in plantar pressure variations [28].

5. Conclusions

Patients with CN midfoot deformity presented with specific midfoot cut-off values for PPP of 16.45 N/cm^2 and PTI of 7.2 N/cm^2/s and showed an elevated risk of neuropathic ulceration in the plantar area of the midfoot. To implement dynamic barefoot plantar pressure measurement in the specific region at risk of ulceration in the clinical practice could help clinicians to implement preventive and operative therapies to decrease diabetic foot complications.

Acknowledgments

The authors gratefully acknowledge the support of the staff and patients of the Diabetic Foot Unit of the Complutense University of Madrid.

Declaration of Interest None.

Funding

The authors received no funding from an external source.

Authors' Contribution Statement

MLM, RJMB, EGM, JLLM designed the study. MLM, RJMB, EGM, YGA, FJAA, JLLM conducted the study. MLM, RJMB, EGM, YGA, FJAA, JLLM were involved in sample processing and analysis. MLM performed the statistical analyses. MLM drafted the manuscript and RJMB, EGM, YGA, FJAA and JLLM critically reviewed the manuscript for important intellectual content and approved the final version to be published. MLM and JLLM are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Figures

Figure 1. ROC curves for PPP and PIT in CN midfoot deformity subjects.

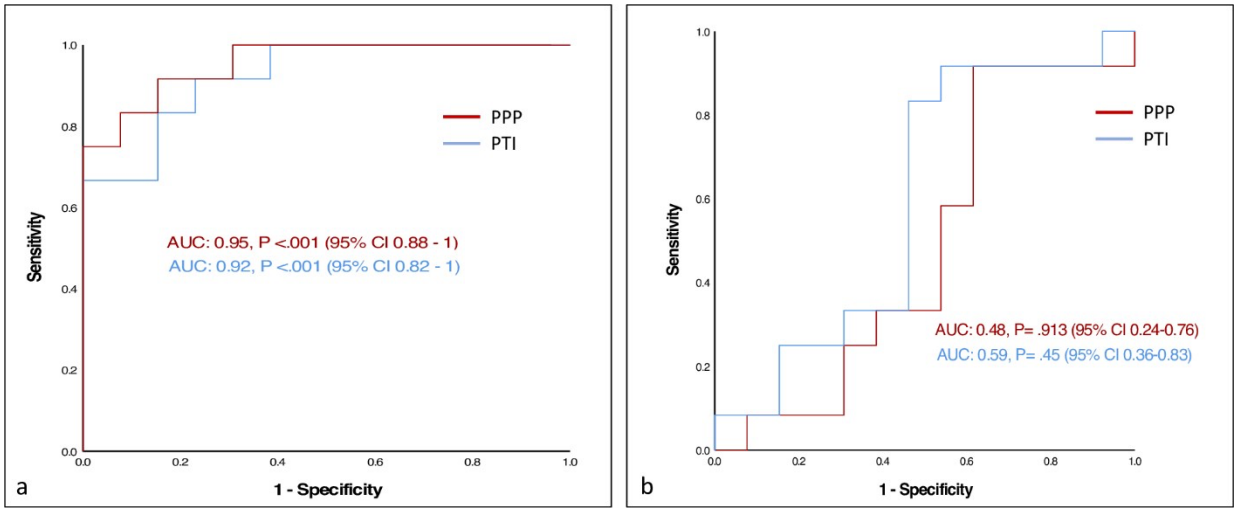

Figure 1 Legend. a. ROC curves for pressure patterns in the midfoot region; b. ROC curves for pressure patterns in the entire foot.

Abbreviations: PPP, Peak plantar pressure (N/cm^2); PTI, Pressure Time Integral ($N/cm^2/s$).

Tables

Table 1. Patients' baseline characteristics (N=25).

Baseline Characteristics	Patients (N=25)
Male, n (%)	23 (92%)
Female n, (%)	2 (8%)
Retinopathy, n (%)	20 (80%)
Nephropathy, n (%)	15 (60%)
Hypertension, n (%)	20 (80%)
Hypercholesterolemia, n (%)	23 (92%)
Previous Ulceration, n (%)	17 (68%)
Ankle Brachial Pressure Index, mean ± SD	1.24 ± 0.29
Toe Brachial Pressure Index, mean ± SD	0.89 ± 0.31
Mean age ± SD (years)	64.32 ± 9.73
Body mass index (kg/cm^2), mean ± SD	29.41 ± 5.80
Glycated hemoglobin mmol/mol (%), mean ± SD	7.47 ± 1.39
Diabetes mellitus (years), mean ± SD	17.24 ± 9.19
Duration of Charcot foot prior to inclusión (years), mean ±SD	7.4 ± 4.89

Legend: DM, diabetes mellitus; SD, standard deviation; Kg, kilograms; cm^2, squared centimeters.

Table 2. Differences between plantar pressure patterns for midfoot ulceration.

Plantar pressure measurements	All Patients (N=25)	Ulceration Patients (n=12)	Non ulceration Patients (n=13)	P-value
Barefoot mean peak plantar pressure in the entire foot (N/cm^2), mean ± SD	71.69 ± 27.72	71.29 ± 24.28	72.07 ± 1.57	.946
Barefoot mean pressure time integral pressure in the entire foot (N/cm^2/s), mean ± SD	20.20 ± 6.69	21.30 ± 5.55	19.18 ± 7.69	.441
Barefoot mean peak plantar pressure in the midfoot (N/cm^2), mean ± SD	17.87 ± 18.56	23.21 ± 7.33	12.95 ± .15	**< .001***
Barefoot mean Pressure Integral Time in the midfoot (N/cm^2/s), mean ± SD	8.32 ± 5.10	11.39 ± 5.29	5.48 ± 2.85	**.002***

Legend: SD, standard deviation; N, newton; cm^2, squared centimeters; s, seconds. *P < 0.05 indicates statistical significance.

Table 3. Differences between the risk factors for midfoot ulceration.

Baseline Characteristics	All Patients (N=25)	Ulceration Patients	Non ulceration Patients	P-value
Male, n (%)	23 (92%)	11 (91.7%)	12 (92.3%)	.955
Female n, (%)	2 (8%)	1 (8.3%)	1 (7.7%)	
Retinopathy, n (%)	20 (80%)	8 (66.7%)	9 (69.2%)	.175
Nephropathy, n (%)	15 (60%)	8 (66.7%)	7 (53.8%)	.533
Hypertension, n (%)	20 (80%)	9 (75%)	11 (84.6%)	.567
Hypercholesterolemia, n (%)	23 (92%)	11 (91.7%)	12 (92.3%)	.571
Previous Ulceration, n (%)	17 (68%)	8 (66.7%)	9 (69.2)	.613
Ankle Brachial Pressure Index, mean ± SD	1.24 ± 0.29	1.30 ± 0.36	1.18 ± 0.22	.347
Toe Brachial Pressure Index, mean ± SD	0.89 ± 0.31	0.95 ± 0.32	0.83 ± 0.29	.368
Mean age ± SD (years)	64.32 ± 9.73	67.67 ± 9.39	61.23 ± 9.33	.099
Body mass index (kg/cm^2), mean ± SD	29.41 ± 5.80	29.47 ± 6.42	29.35 ± 5.43	.955
Glycated hemoglobin (%), mean ± SD	7.5 ± 1.4	7.6 ± 1.5	7.4 ± 0.3	.720
Diabetes mellitus (years), mean ± SD	17.24 ± 9.19	18.5 ± 10.42	16.08 ± 8.15	.522
Duration of Charcto foot prior to inclusion (years), mean ± SD	7.4 ± 4.89	8.66 ± 5.51	6.23 ± 4.12	.221
Previous minor Amputation, n (%)	17 (68%)	9 (75%)	8 (61.5%)	.492
Lateral column pattern, n (%)	15 (60%)	9 (75%)	6 (46.2%)	.141
Medial column pattern, n (%)	10 (40%)	3 (25%)	7 (53.8%)	.226
Minor lesion, n (%)	15 (60%)	12 (100%)	3 (23.1%)	**< .001***

Legend: DM, diabetes mellitus; SD, standard deviation; Kg, kilograms; cm^2, squared centimeters; □, degrees. *P < 0.05 indicates statistical significance.

Table 4. Performance characteristics of peak plantar pressure and pressure time integral in the midfoot region.

Pooled	Peak Plantar Pressure	Pressure Time Integral
Sensitivity	0.92 (0.87 – 0.96)	0.92 (0.84 – 0.94)
Specificity	0.85 (0.79 – 0.88)	0.77 (0.71 – 0.81)
PPV	0.91 (0.88 – 0.94)	0.91 (0.86 – 0.94)
NPV	0.85 (0.82 – 0.88)	0.78 (0.73 – 0.84)
PLR	6.13 (5.75 – 6.45)	4.0 (3.7 – 4.5)
NLR	0.09 (0.082 – 0.11)	0.10 (0.092 – 0.11)

Legend: PPV, positive predictive value; NPV, negative predictive value; PLR, positive likelihood ratio; NLR, negative likelihood ratio