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Research Article

Diagnostic Performance of Dermoscopy and Clinical Visual Diagnosis for Plantar Warts

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Background: Plantar warts caused by the human papilloma virus (HPV) are one of the most frequent pathologies in podiatry. Diagnosis is usually limited to the clinical presentation of the lesion. Biopsy and polymerase chain reaction (PCR) are expensive and can be difficult to access. However, the dermatoscope is a noninvasive tool that covers the gap between microscopic and macroscopic diagnosis.
Objective: This study compares the effectiveness of diagnosis of plantar warts using a dermatoscope versus visual clinical signs.
Methods: The study evaluated 25 patients with suspected HPV plantar warts by visual or dermatoscopic signs. Upon clinical suspicion of HPV, a sample was taken for PCR analysis. A dermatoscopic image of the plantar wart was collected, and the characteristic clinical signs were evaluated, including the discontinuity of dermatoglyphs, hemorrhagic dots, reddish linear vessels, verruciform surface and frog-spawn appearance.
Results: All 25 patients showed positive results in molecular testing. Dermatoscopic findings compatible with HPV were obtained for 100% (25/25) of patients, while clinical signs were observed in 84% (21/25). The most common finding was the alteration of dermatoglyphs, which was present in all patients at the dermoscopic level. The sensitivity of the dermatoscope was 100% and identical to that of PCR.
Conclusion: The dermatoscope appears to be a useful, noninvasive and rapid tool for clinical use in the diagnosis of plantar warts.

Keywords: cutaneous warts; dermatoscopy; diagnosis; HPV; human papillomavirus; plantar warts

1. Introduction

Plantar warts are benign tumours that are caused by infection of the epidermal cells by human papilloma virus (HPV) [1]. Plantar warts have an annual incidence of 14% [2], and 2% of the population seeks medical attention for the condition due to pain, limitations in daily activity and sport, aesthetic reasons and prevention of infection in other parts of the body [1, 3]. Diagnosis is primarily clinical, and frequent clinical signs include hyperkeratosis due to proliferation of mutated foot cells, thrombosed capillaries, hemorrhagic dots upon delamination of hyperkeratosis and loss of normal dermatoglyphs. Pain on lateromedial compression of the plantar wart is also common [3, 4]. However, these lesions can be misdiagnosed as hyperkeratosis, molluscum contagiosum, warty carcinoma, angiokeratoma and other lesions [2].

In 2022, Aldana et al. [5] surveyed 415 podiatrists in Spain and assessed how many of them performed complementary tests for to confirm the diagnosis plantar warts. They found that

85.5% of the respondents did not consider complementary tests necessary. When comparing various pathologies, 76.6% of respondents made false-positive diagnoses of plantar warts, and in the absence of complementary tests, treatment would generally be painful for the patient.

Diagnosis of plantar warts can be made by polymerase chain reaction (PCR) analysis of hyperkeratosis scales or biopsy, which is considered the gold standard [4, 6]. However, this type of testing has several drawbacks, including invasiveness, additional costs and lack of means of sample processing. In this context, dermoscopy could be a noninvasive and rapid alternative for diagnosis [7, 8]. Previous authors have described the dermoscopic signs of plantar warts, but none have assessed the diagnostic performance of dermatoscopy [7–11]. The main objective of this study was to compare the clinical and dermoscopic findings of suspected plantar warts. The secondary objectives were to determine the risk factors presented by patients with suspected plantar warts, the warts' characteristics, the prevalence of different clinical or dermatoscopic signs of warts caused by HPV and the genotypes.

2. Materials and Methods

2.1. Patients and Sample. This study was conducted in accordance with the Declaration of Helsinki and national legislation on patient research [9]. The protocol was approved by the ethics committee of the Hospital Clínico San Carlos (23/473-E). All patients gave informed consent before the start of the study. A descriptive cross-sectional study was performed with patients suspected of having plantar warts, who were consecutively recruited following the STARD criteria used in diagnostic accuracy studies [12]. The patients were evaluated in a clinic specialising in the management of plantar warts from July 2023 to July 2024.

The inclusion criteria for the study were patients older than 5 years with clinical or dermatoscopic signs of plantar warts. This age was determined based on the clinical protocol, in which all patients with clinical or dermatoscopic signs undergo PCR testing of scalpel scrapings of the hyperkeratosis to confirm the diagnosis and genotype of HPV. Patients were excluded if there was bleeding upon delamination of the most superficial hyperkeratosis, which would have prevented the correct assessment of the lesions with a dermatoscope.

2.2. Dermatoscopic Findings, Clinical Signs and Confirmation. When a plantar wart was suspected, the most superficial hyperkeratosis was removed for evaluation of the clinical signs and assessment with a dermatoscope. The assessment of the plantar wart, dermoscopic diagnosis and specimen collection were always performed by the same clinician, who is experienced in the management of plantar warts. The clinical signs evaluated were the same as those evaluated with the Illuco IDS-100 dermatoscope (Gyeonggi-do, Republic of Korea) at standard x10 magnification and polarised light: discontinuity of dermatoglyphs, hemorrhagic dots, reddish linear vessels, verruciform surface and frog shrimp appearance (Figure 1). Plantar warts caused by HPV were considered to be present when observed dermatoscopically or visually.

The presence of pain upon mediolateral compression was also assessed but was not recorded as a positive sign of plantar warts caused by HPV. After dermoscopic imaging, a sample was taken in an Eppendorf tube by deep scraping of the hyperkeratosis for PCR analysis to confirm the presence of a plantar wart. The more superficial hyperkeratosis was discarded. PCR and HPV genotyping were performed using the methods reported by García-Oreja et al. [4].

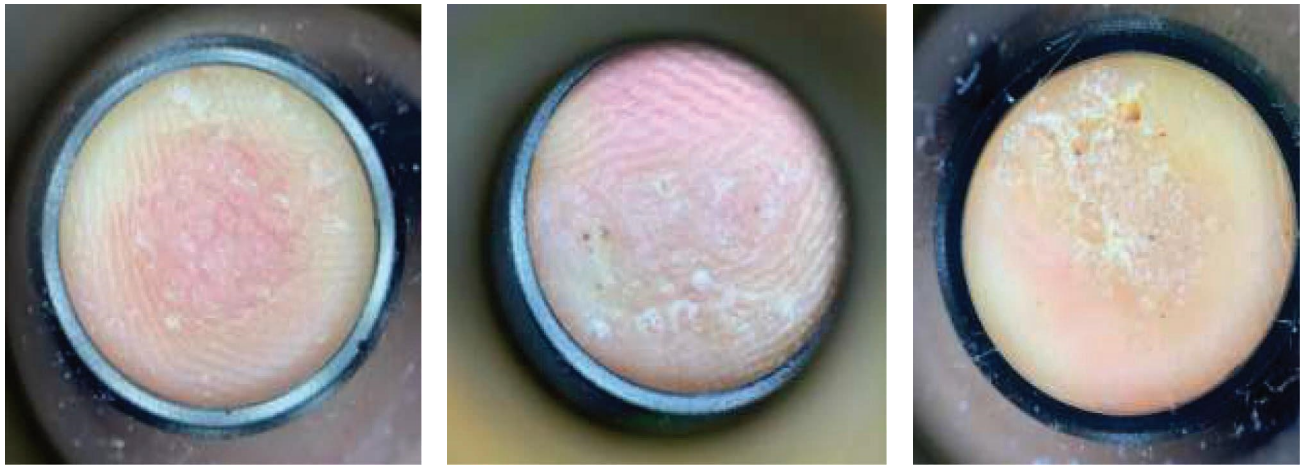
Samples were processed within 24 h of collection. Genomic DNA was extracted from the scales of deep hyperkeratosis layers using the NZY Tissue gDNA Isolation kit (NZYTech), according to the manufacturer's instructions, after 5 h of sample prelysis at 56°C [4].

DNA concentration was quantified after extraction at 260 nm using a Nanodrop 2000 spectrophotometer. The purity was determined by absorbance ratio 260 nm/280 nm [4].

HPV DNA amplification (100 ng of DNA) was performed using a multiplex PCR reaction or by nested PCR (Mastercycler Nexus GSX1) using the NZYTaq II 2x Green Master Mix (NZYTech). Multiplex PCR was performed for detecting and typing HPVs that are related to verrucae vulgaris (HPV1, 2, 27 and 57) using the specific primers and conditions that were proposed by Lei et al. [13] The nested PCR was performed using the primers and conditions that were previously described by Forslund et al. [14] for DNA samples that were not amplified in the multiplex PCR followed by sequencing for HPV typing. Positive and negative controls were included in every amplification cycle. Amplification of the β-globin gene using primers PC04 and GH20 was used as internal control to assess the integrity of human DNA. A 286-bp amplification was considered positive and adequate to the sample quantity for HPV detection. All samples, including HPV negative samples, resulted positive for β-globin test [4].

In any case, DNA was extracted again, and the amplification was repeated for HPV negative samples and samples with a nontypeable HPV. The PCR products were purified using a NZYGelpure PCR purification kit (NZYTech) and sequenced with the Sanger method with a BigDye terminator v3.1cycle sequencing kit (Applied Biosystems) using the nested PCR primers and an ABI 3730 XL genetic analyser (Applied Biosystems). Sequences were analysed using Sequencing Analysis software v.5.1 (Applied Biosystems), and the HPV sequence alignment was determined through comparison with known sequences in the GenBank database using BLASTn software (https://blast.ncbi.nlm.nih.gov/) [4].

2.3. Statistical Analysis. Statistical analyses were performed using SPSS for Windows Version 25.0 (SPSS Inc.). The results are presented using tables and graphs, and quantitative variables are presented as means. The Shapiro–Wilk test was performed to determine the sample distribution, and $p > 0.05$ was obtained, so parametric tests were used.



(a) (b) (c)

Figure 1: Images made with Illuco IDS-100 dermatoscopy with standard ×10 magnification and polarized light. (a) Image of plantar wart showing a frogspawn pattern, loss of dermatoglyphs and hemorrhagic dots under dermatoscopy. (b) Image of plantar wart showing dermatoscopic alteration of dermatoglyphs and hemorrhagic dots. (c) Dermatoscopy image of plantar wart showing verruciform surface, alteration of dermatoglyphs and hemorrhagic dots.

Qualitative variables were represented as frequencies and percentages, and the chi-squared test was used to compare them. Epidat v3.1 (Galicia, Spain) was used to determine the sensitivity and specificity of dermoscopy and visual clinical signs with respect to PCR. A sample size calculation was performed online with the GRANMO calculator Version 7.12 (Institut Municipal d'Investigació Mèdica, Barcelona, Spain). The result was 46 samples with a statistical power of 0.80 and alpha of 0.05.

3. Results

A total of 25 patients were examined in this study. Their mean age was 46.72 ± 23.58 years, 36% (9/25) of the patients were men and 64% (16/25) were women. The mean body mass index was 25.05 ± 4.17. The risk factors for plantar warts are shown in Table 1, and their characteristics are shown in Table 2. The most common sign was loss of dermatoglyphs in both visual findings ($n = 21$) and dermatoscopic findings ($n = 25$), which was found in all lesions with dermatoscopy. The frequency of the other clinical signs is shown in Table 3.

Statistically significant differences were observed with the use of the dermatoscope and visually found clinical signs in hemorrhagic dots ($p < 0.01$), verruciform surface ($p < 0.001$) and frog spawning pattern ($p < 0.001$). Furthermore, 80% ($n = 20$) had pain upon mediolateral compression. The results of genotyping obtained from the samples collected for PCR are shown in Table 4. Mixed HPV genotyping was obtained in six cases with the following biotypes: 2-57, 1-2, 1-27, 2-57, 1-27 and 2-27. A cross table between diagnoses of plantar warts through PCR versus clinical signs and dermatoscopy was obtained, and the result showed a sensitivity of 100% for the dermatoscope versus PCR, while clinical signs had only 84% sensitivity (Table 5).

4. Discussion

In this study, we observed that the prevalence of all clinical signs of plantar warts was higher when using the dermatoscope versus visual diagnosis. Aldana et al. [5] found that podiatrists used complementary tests infrequently, and only 12.7% of clinicians considered a complementary test necessary before treating lesions. Clinicians who used additional testing had a preference for excisional biopsy, which was three times more common than molecular testing. Both tests involve additional cost and are invasive, and not all podiatrists have the means to perform them.

All 25 of the patients with suspected plantar warts had positive PCR and dermoscopic results, while only 21 patients showed visual clinical signs, indicating that the dermatoscope had a higher diagnosis rates than visual diagnosis. Patil et al. [7] did a dermoscopic comparison of plantar warts before removal of superficial hyperkeratosis and after, and the results showed that there was an increase in the prevalence of all dermoscopic signs with removal. Based on this, our study analysed plantar warts after removal of the more superficial hyperkeratosis, which would provide a more accurate diagnosis.

Alteration of the dermatoglyph pattern was observed in all plantar warts evaluated through the dermatoscope. All other findings were present to a lesser extent, as reported previously [7, 8]. Many clinicians consider mediolateral compression of the plantar wart to be pathognomonic, but as we observed in the present study, 20% ($n = 5$) of patients have no pain when performing this manoeuvre [3, 4]. Other studies have used dermatoscopes for clinical follow-up and for clinical discharge after interventions in cases with no clinical signs [9–11, 15].

In regard to risk factors, most of our samples were women, as described in previous studies. Furthermore, 28% had a history of plantar warts, which was the most important

Table 1: Variables of risk characteristics presented by individuals' plantar warts.

Variable	Frequency	Percentage (%)
Water sports	5	20
Use of occlusive footwear	8	32
Plantar hyperhidrosis	9	36
History of plantar wart	7	28

Table 2: Characteristics of patients' plantar warts.

Evolution of the plantar wart	Frequency	Percentage (%)
< 6 months	12	48
Between 6 months and 1 year	4	16
More than 1 year	9	36
Plantar wart area	**Frequency**	**Percentage (%)**
Plantar area of forefoot	20	80
Periungual or distal area of the toes	4	16
Heel	1	4
Type of plantar wart	**Frequency**	**Percentage (%)**
Endophytic	18	72
Exophytic	3	12
Mosaic	4	16

Table 3: Visual and dermatoscopic findings of patients' plantar warts.

	Clinical sign diagnosis	Dermatoscopic signs
Loss of dermatoglyphs	21 (84%)	25 (100%)
Hemorrhagic dots	9 (36%)	15 (60%)
Reddish linear vessels	0 (0%)	5 (20%)
Verruciform surface	5 (20%)	7 (28%)
Frog spawning pattern appearance	2 (8%)	3 (12%)

Table 4: Biotypes found in PCR genotyping of patients.

HPV biotypes	Frequency	Percentage (%)
HPV biotype 1	6	24
HPV biotype 2	4	16
HPV biotype 14	1	4
HPV biotype 27	4	16
HPV biotype 57	4	16
Mixed HPV	6	24

Table 5: Positive and negative diagnosis of PCR versus dermatoscopy and clinical signs.

		PCR diagnosis	
		Positive	Negative
Dermatoscopic diagnosis	Positive	25	0
	Negative	0	0
Clinical sign diagnosis	Positive	21	0
	Negative	4	0
Dermatoscope sensitivity	100%	Clinical sign sensitivity	84%

Note: Sensitivity of the dermatoscope and visual clinical signs with respect to PCR.

risk factor. Excessive sweating was also reported by 36%, which promotes the formation of breaks in the foot [2]. The most prevalent HPV genotypes were biotypes 1 and 2, as described in previous studies [6].

The main strength of the present study was that to our knowledge, it is the first to compare the use of a dermatoscope with clinical signs. In addition, it is the only study that has compared both techniques with molecular testing.

However, one of its limitations is that it was not possible to determine the negative predictive value and specificity with dermoscopy versus CRP because all patients were positive according to the molecular tests. Only patients with clinical or dermatoscopic signs of suspected plantar warts were included, so there was a selection bias that prevented calculation of the negative predictive value and specificity. In future studies, the method used by Garcia-Oreja et al. [4] with a swab on patients with healthy skin and the dermatoscope could be applied to determine the diagnosis accuracy of the dermatoscope.

Another limitation is that the same clinician performed all the dermatoscopic studies, which could have resulted in bias in regard to the interobserver reliability. Therefore, a future study could be conducted to determine the interobserver reliability. Finally, the calculated sample size was not reached, so this study could be considered as a pilot study, and future studies could example larger samples to reach the calculated result.

In conclusion, the dermatoscope appears to be a useful, noninvasive and simple tool that increases detection rates of plantar warts caused by HPV with a sensitivity of 100% compared with PCR.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Statement

The protocol was approved by the medical ethics committee of the Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC) (protocol number 23/473-E).

Consent

All patients voluntarily signed consent statement for the use of their image and publication of their case details.

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Diego León-Herce: conceptualisation; methodology; validation; investigation; data curation; and writing–original draft. Sara García-Oreja: conceptualisation; methodology; software; validation; formal analysis; investigation; and writing–original draft. David Navarro-Pérez: conceptualisation; methodology; software; investigation; writing–original draft; and visualisation. Aroa Tardáguila-García: data curation and writing–review and editing. José Luis Lázaro-Martínez: visualisation; writing–review and editing; and supervision. Francisco Javier Álvaro-Afonso: validation; resources; writing–review and editing; supervision; funding acquisition; and project administration.

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References

[1] S. García-Oreja, F. J. Álvaro-Afonso, Y. García-Álvarez, E. García-Morales, I. Sanz-Corbalán, and J. L. Lázaro Martínez, "Topical Treatment for Plantar Warts: A Systematic Review," *Dermatologic Therapy* 34, no. 1 (2021): e14621, https://doi.org/10.1111/dth.14621.

[2] D. J. Witchey, N. B. Witchey, M. M. Roth-Kauffman, and M. K. Kauffman, "Plantar Warts: Epidemiology, Pathophysiology, and Clinical Management," *Journal of the American Osteopathic Association* 118, no. 2 (2018): 92–105, https://doi.org/10.7556/jaoa.2018.024.

[3] T. C. Vlahovic and M. T. Khan, "The Human Papillomavirus and its Role in Plantar Warts: A Comprehensive Review of Diagnosis and Management," *Clinics in Podiatric Medicine and Surgery* 33, no. 3 (2016): 337–353, https://doi.org/10.1016/j.cpm.2016.02.003.

[4] S. García-Oreja, F. J. Álvaro-Afonso, D. Sevillano-Fernández, A. Tardáguila-García, M. López-Moral, and J. L. Lázaro-Martínez, "A Non-invasive Method for Diagnosing Plantar Warts Caused by Human Papillomavirus (HPV)," *Journal of Medical Virology* 94, no. 6 (2022): 2897–2901, https://doi.org/10.1002/jmv.27514.

[5] A. Aldana-Caballero, R. Mayordomo, and F. Marcos-Tejedor, "Assessment of Visual Diagnosis by Podiatrists for HPV and Onychomycosis: The Need for Complementary Tests," *Journal of Fungi* 8, no. 2 (2022): 135, https://doi.org/10.3390/jof8020135.

[6] S. García-Oreja, F. J. Álvaro-Afonso, D. Sevillano-Fernández, E. A. García-Morales, M. López-Moral, and J. L. Lázaro-Martínez, "Does HPV Biotype Influence the Characteristics and Evolution of Plantar Warts?" *Journal of Evidence-Based Medicine* 17, no. 1 (2024): 10–12, https://doi.org/10.1111/jebm.12584.

[7] S. Patil, M. Borkar, S. Pande, K. Meshram, and M. Oke, "Dermoscopic Findings in Clinically Diagnosed Cases of Plantar Warts, Corns, and Calluses: A Cross-Sectional Study," *Cureus* 15, no. 4 (2023): e38093, https://doi.org/10.7759/cureus.38093.

[8] M. Al Rudaisat and H. Cheng, "Dermoscopy Features of Cutaneous Warts," *International Journal of General Medicine* 14 (2021): 9903–9912, https://doi.org/10.2147/IJGM.S335276.

[9] World Medical Association, "World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects," *JAMA* 310, no. 20 (2013): 2191–2194, https://doi.org/10.1001/jama.2013.281053.

[10] G. Fathy, M. A. Sharara, and A. H. Khafagy, "Intralesional Vitamin D3 versus Candida Antigen Immunotherapy in the Treatment of Multiple Recalcitrant Plantar Warts: A Comparative Case–Control Study," *Dermatologic Therapy* 32, no. 5 (2019): e12997, https://doi.org/10.1111/dth.12997.

[11] M. T. Barkat, R. T. A. Abdel-Aziz, and M. S. Mohamed, "Evaluation of Intralesional Injection of Bleomycin in the Treatment of Plantar Warts: Clinical and Dermoscopic Evaluation," *International Journal of Dermatology* 57, no. 12 (2018): 1533–1537, https://doi.org/10.1111/ijd.14092.

[12] J. F. Cohen, D. A. Korevaar, D. G. Altman, et al., "STARD 2015 Guidelines for Reporting Diagnostic Accuracy Studies: Explanation and Elaboration," https://doi.org/10.1136/bmjopen-2016.

[13] Y. J. Lei, C. Gao, R. An, et al., "Development of a Multiplex PCR Method for Detecting and Typing Human Papillomaviruses in Verrucae Vulgaris," *Journal of Virological Methods* 147, no. 1 (2008): 72–77, https://doi.org/10.1016/j.jviromet.2007.08.005.

[14] O. Forslund, H. Ly, and G. Higgins, "Improved Detection of Cutaneous Human Papillomavirus DNA by Single Tube Nested "Hanging Droplet" PCR," *Journal of Virological Methods* 110, no. 2 (2003): 129–136, https://doi.org/10.1016/S0166-0934(03)00109-5.

[15] W. Albalat, E. Attwa, and H. M. Ebrahim, "Intralesional Cryotherapy versus Cryotherapy Spray for the Treatment of Recalcitrant Plantar Warts: a Prospective, Randomized Study," *Journal of Dermatological Treatment* 33, no. 2 (2022): 857–863, https://doi.org/10.1080/09546634.2020.1782821.