Dermatology Practical & Conceptual

Dermoscopy as a Predictor of Photodynamic Therapy Outcomes in Actinic Keratoses and Bowen's Disease: Prospective Study in Solid Organ Transplant Patients

Laura Bernal Masferrer[1], Tamara Gracia Cazaña[1], Marcial Álvarez-Salafranca[1], Isabel Bernad Alonso[1], Sara España Fernández de Valderrama[2], Mariana Claudia Matei[1], Javier Paul Ramos[3], Yolanda Gilaberte[1]

1 Department of Dermatology, Miguel Servet University Hospital, 2IIS Aragón, Zaragoza, Spain
2 Department of Orthopedic and Trauma Surgery, Miguel Servet University Hospital, Zaragoza, Spain
3 Department of Nephrology, Miguel Servet University Hospital, Zaragoza, Spain

Key words: actinic keratoses, bowen's disease, photodynamic therapy, dermatoscopy, transplant recipients

Citation: Bernal Masferrer L, Gracia Cazaña T, Álvarez-Salafranca M, et al. Dermoscopy as a Predictor of Photodynamic Therapy Outcomes in Actinic Keratoses and Bowen's Disease: Prospective Study in Solid Organ Transplant Patients. *Dermatol Pract Concept*. 2025;15(4):5645. DOI: https://doi.org/10.5826/dpc.1504a5645

Accepted: June 17, 2025; **Published:** October 2025

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

Corresponding Author: Laura Bernal Masferrer, Paseo Fernando el Católico 48, principal derecha, Zaragoza, España. ORCID ID: 0000-0002-8328-6678). E-mail: laurabermas@gmail.com

ABSTRACT

Introduction: Solid organ transplant recipients (SOTRs) have a significantly higher risk of developing cutaneous squamous cell carcinoma. Identifying predictive markers for response to non-surgical treatments such as photodynamic therapy (PDT) may help optimize management strategies.

Objectives: To evaluate the association between dermatoscopic features in actinic keratoses (AK) and Bowen's disease (BD) and response to PDT in SOTRs.

Methods: A prospective observational study was conducted, including 35 SOTRs with clinically and histologically confirmed AK or BD treated with methyl aminolevulinate-PDT. Thirteen dermatoscopic features were analyzed to assess their correlation with treatment response.

Results: Response rates were 62.5% for AK and 89.47% for BD. Among the dermatoscopic features evaluated, white structureless areas in AK and rosettes in BD were significantly associated with resistance to PDT.

Conclusions: Dermoscopy may serve as a valuable tool to predict PDT response in SOTRs with AK and BD, potentially improving patient selection and treatment outcomes.

Introduction

Actinic keratoses (AK) and in situ squamous cell carcinoma (SCC) are considered precursor lesions of invasive cutaneous squamous cell carcinoma (cSCC). Their development is influenced by cumulative exposure to ultraviolet (UV) radiation, advanced age, immunosuppression, and other factors [1-3]. Given their high incidence linked to an ageing population and prolonged sun exposure, early treatment is essential to prevent progression to invasive cSCC [4].

Solid organ transplant recipients (SOTRs) represent a particularly complex group, with a 65-fold increased risk of developing cSCC [1]. This heightened risk is intrinsically linked to immunosuppression and the use of specific treatments for transplant maintenance such as calcineurin inhibitors. Therefore, early diagnosis and effective treatment are especially crucial for this population [2].

Photodynamic therapy (PDT) has emerged as a valid, effective, and repeatable treatment for AK and Bowen's disease (BD) or in situ cSCC. Compared to cryotherapy, PDT offers the added advantage of treating the cancerization field [2,3]. However, PDT's indirect immunomodulatory action may be less effective in transplant patients, potentially reducing its efficacy and explaining the lower success rates observed compared to immunocompetent patients [2].

In this context, diagnostic tools like dermoscopy not only aid in the early and accurate recognition of lesions but may also provide valuable insights into the effectiveness of treatments such as PDT, particularly in patients with unique clinical characteristics like transplant recipients.

Dermoscopy is a non-invasive technique that has become an essential tool for clinicians in identifying these lesions. Dermoscopic patterns associated with AK and BD have been shown to increase diagnostic sensitivity, and their disappearance has been correlated with lesion resolution [4,5]. However, only one study has investigated the possible relationship between dermoscopic signs of AK and response to PDT [6], while another focused on basal cell carcinoma (BCC) [7]. To our knowledge, no study has explored these correlations in BD or in SOTRs.

The aim of this study was to identify dermoscopic signs associated with the response to conventional PDT in BD and daylight PDT in AK in SOTRs.

Materials and Methods

A prospective observational clinical practice study was conducted. The study population consisted of SOTRs referred from the Nephrology and Cardiology Transplant Clinics to the specialized transplant skin cancer unit at Miguel Servet University Hospital between January 2022 and December 2023. Patients had to meet the following inclusion criteria: aged 18 years or older; solid organ transplant recipient; diagnosed with at least five Grade I or II Olsen AKs within a field of cancerizations or histologically confirmed in situ SCC; eligible for treatment with MAL-PDT and having provided informed consent to participate (Annex II); no hypersensitivity to any component of Metvix®; no photodermatosis diagnosis.

Exclusion criteria were: allergic to any treatment component; refused treatment with PDT; did not provide consent to participate in the study; unable to complete treatment or follow-up; had undergone treatment for non-melanoma skin cancer (NMSC) within the previous three months.

A baseline biopsy was performed for all patients to confirm clinical diagnoses, accompanied by clinical and dermoscopic photography (DermLite Handyscope 2020). The study was approved by the Ethics Committee of the Autonomous Community of Aragon (CEICA) EPA22/0007.

Treatment Protocols

For BD patients, two sessions of conventional PDT were conducted. Lesions were first curetted, followed by application of 16% methyl aminolevulinate (MAL, Metvix®, Galderma). After three hours of occlusive incubation, the area was illuminated using a red diode device (Aktilite CL 128, Galderma Nordic AB, Sweden) at 37 J/cm² for eight minutes from a distance of 10 cm. The second session was conducted 7–14 days later [8]. For AK patients, one session of daylight PDT was conducted. Lesions were curetted, followed by MAL 16% application. Patients were then exposed to sunlight for two hours, after which the photosensitizer residue was removed [9].

Outcome Measures

Three months post-treatment, lesion biopsies were repeated to confirm histological clearance or persistence. Dermoscopic evaluations were conducted by a blinded observer (M.A.S) using pre-treatment dermoscopic photographs. The evaluated dermoscopic signs included superficial scales, thick white-yellow scales, white circles, white structureless areas, erythema, rosettes, red pseudonetwork or perifollicular vessels, strawberry pattern, glomerular vessels, hairpin vessels, irregular linear vessels, erosions, and ulcerations [4].

Treatment response was assessed clinically and histologically three months post-treatment. Follow-up visits were conducted over the subsequent 12 months, with persistent lesions excised.

Statistical Analysis

Qualitative variables are presented as absolute numbers and percentages. Chi-squared tests (Chi^2) were used for group comparisons, with statistical significance defined as $P<0.05$. Statistical analyses were performed using SPSS® software (version 25.1).

Results

A total of 35 patients were included in the study: 16 with at least five Grade I or II Olsen AKs and 19 with BD, all with histopathological confirmation. Complete response rates were 62.5% for AK and 89.47% for BD.

Among the dermoscopic features analyzed, only the absence of rosettes in BD and the absence of white structureless areas in AK were significantly associated with response to PDT. No other dermoscopic structure showed a statistically significant correlation with treatment response. The statistical analysis of all dermoscopic structures is summarized in Tables 1 and 2.

Discussion

Photodynamic therapy (PDT) is considered the most effective treatment for actinic keratoses (AK) in solid organ transplant recipients (SOTRs) [10]. Our study achieved similar results in terms of clinical and histological effectiveness.

Table 1. Statistical Analysis of Dermoscopic Structures in Bowen's Disease and Response to Photodynamic Therapy.

Variable	Response	No response	p-value
Superficial scales			
Yes	7 (41.2%)	1 (50%)	1.00
No	10(58.8%)	1 (50%)	0.81
White-yellow scales			
Yes	10 (58.8%)	1 (50%)	1.00
No	7 (42.1%)	1 (50%)	0.81
White circles			1.00
Yes	1 (5.3%)	0 (0%)	0.72
No	16 (94.1%)	2 (100%)	
White structureless areas			0.38
Yes	3(17.6%)	1 (50%)	0.28
No	14 (82.4%)	1 (50%)	
Erythema		2 (100%)	1.00
Yes	16 (94.1%)	0 (0)	0.72
No	1 (5.3%)		
Rosettes			
Yes	0 (0%)	1 (50%)	0.10
No	17 (100%)	1 (50%)	**0.003**
Red pseudonetwork			
Yes	5 (31.6%)	1 (50%)	1.00
No	12 (70.6%)	1 (50%)	0.55
"Strawberry pattern"			
Yes	4 (23.5%)	1 (50%)	0.46
No	13 (76.5%)	1 (50%)	0.42
Glomerular vessels			
Yes	8 (47.1%)	1 (50%)	1.00
No	9 (52.9%)	1 (50%)	0.93
Hairpin vessels			1.00
Yes	2 (11.8%)	0 (0)	0.60
No	15 (88.2%)	2 (100%)	
Linear irregular vessels			
Yes	1 (5.3%)	0 (0)	1.00
No	16 (94.1%)	2 (100%)	0.72
Erosions			
Yes	1 (5.3%)	0 (0)	1.00
No	16 (94.1%)	2 (100%)	0.72
Ulceration			-
Yes	0 (0)	0 (0)	
No	17 (100%)	2 (100%)	

Table 2. Statistical Analysis of Dermoscopic Structures in Actinic Keratoses and Response to Photodynamic Therapy.

Variable	Response	No response	p-value
Superficial scales			
Yes	6 (60%)	2(33.3%)	0.60
No	4 (40%)	4(66.7%)	0.30
White-yellow scales			
Yes	3 (30%)	3 (50%)	0.60
No	7 (70%)	3 (50%)	0.42
White circles			-
Yes	0 (0%)	0 (0%)	
No	10 (100%)	6 (100%)	
White structureless areas			
Yes	0(0%)	2(33.3%)	0.12
No	10 (100%)	4(66.7%)	**0.05**
Erythema			
Yes	9 (90%)	6 (100%)	1.00
No	1 (10%)	0 (0)	0.42
Rosettes			
Yes	2 (20%)	0 (0%)	0.50
No	8 (80%)	6 (100%)	0.24
Red pseudonetwork			
Yes	6 (60%)	2(33.3%)	0.60
No	4 (40%)	4(66.7%)	0.30
"Strawberry pattern"			
Yes	3 (30%)	1(16.7%)	1.00
No	7 (70%)	5(83.3%)	0.55
Glomerular vessels			
Yes	1 (10%)	0 (0%)	1.00
No	9 (90%)	6 (100%)	0.42
Hairpin vessels			-
Yes	0 (0%)	0 (0)	
No	10 (100%)	6 (100%)	
Linear irregular vessels			-
Yes	0 (0%)	0 (0)	
No	10 (100%)	6 (100%)	
Erosions			-
Yes	0 (0%)	0 (0)	
No	10 (100%)	6 (100%)	
Ulceration			-
Yes	0 (0)	0 (0)	
No	10 (100%)	6 (100%)	

Dragieva et al. conducted a prospective study involving 17 SOTRs with 129 AK lesions. The patients received two consecutive treatments (one with methyl aminolevulinate [MAL] and the other with placebo), resulting in complete resolution in 13 patients and partial response in three others [11]. The clinical response of some patients is summarized in Figure 1.

For Bowen's disease (BD), Antonetti et al. conducted a systematic review, reporting clinical response rates of 88–100% with MAL-PDT in immunocompetent patients. They hypothesized that efficacy could be maintained in immunosuppressed individuals, which aligns with our findings, though current evidence remains limited [12].

Our study analyzed dermoscopic signs in AK and BD lesions in SOTRs and their association with PDT response. Rosettes correspond histopathologically to hyperkeratosis within follicular openings interspersed with a normal peripheral stratum corneum [13]. Meanwhile, white structureless areas represent hyperkeratosis and parakeratosis overlying dysplastic epidermis [4]. Both features are indicators of lesion keratinization and hyperkeratosis, potentially

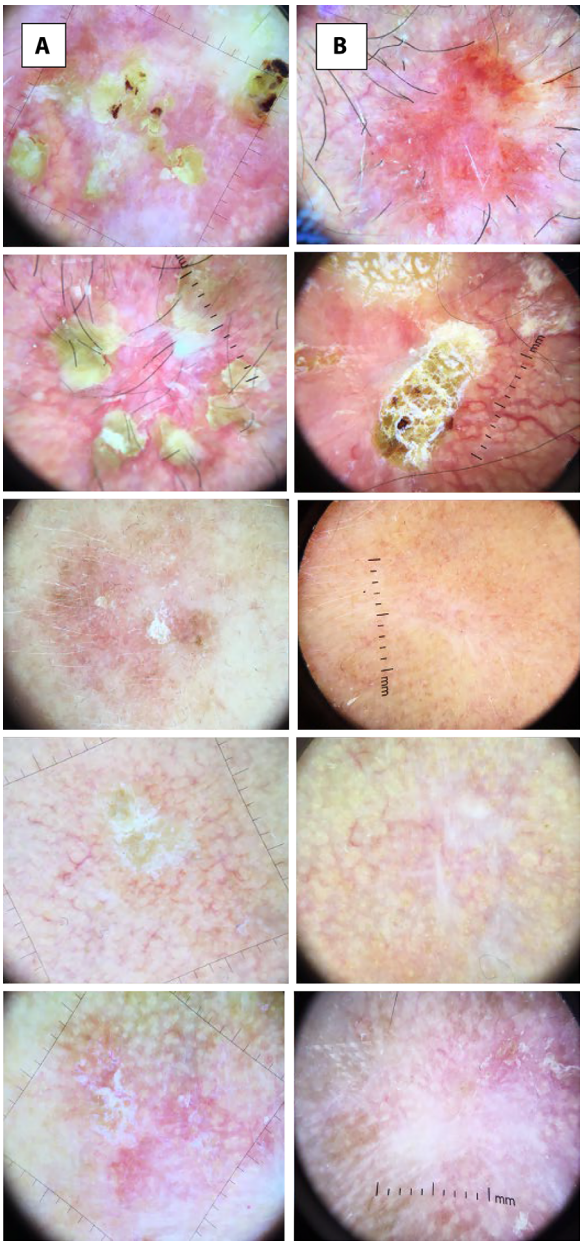

Figure 1. Photographs of the lesions before the treatment with MAL-PDT (A) and after three months of the treatment (B). In the first two pictures we can see the white structureless areas associated with the lack of response to PDT.

hindering photosensitizer penetration and reducing treatment effectiveness.

Zalaudek et al. proposed that white structureless areas could also signal lesion progression to invasive SCC, with vertical growth increasing lesion thickness and complicating dermal penetration. Lesion thickness is a key predictor of resistance to PDT [14].

In a study by Lee et al. [5], the most frequent dermoscopic findings in AK lesions were superficial scales (79.4%) and red pseudonetwork pattern (73.5%). Following treatment with PDT, imiquimod, or cryotherapy, most dermoscopic structures disappeared in tandem with histological clearance. However, superficial scales persisted in 20.6% of cases and red pseudonetwork pattern in 14.7%, even when histological atypia was absent. Similarly, Mun et al. concluded that the disappearance of vascular patterns in BD lesions correlated with treatment success, while their persistence indicated histological disease presence [15].

Wang et al. identified red pseudonetwork pattern as positive predictors of PDT response in AK, whereas microerosions and white structureless areas were negatively associated. However, their findings are not fully comparable to ours due to methodological differences, including the use of cryotherapy or CO2 laser as neoadjuvant treatments, higher photosensitizer concentrations (20% aminolevulinic acid vs. 16% MAL in our study), and fluences exceeding three times the standard (100–120 J/cm² vs. 37 J/cm²). Nevertheless, both studies identified white structureless areas as predictors of treatment resistance [6].

This study has some limitations, including a relatively small sample size from a single center, which may affect generalizability. Moreover, dermoscopic evaluation was performed by a single observer, which may introduce observer bias or limit the reproducibility of the findings. Despite these limitations, the prospective design and histological confirmation strengthen the reliability of the findings.

Conclusions

To summarize, photodynamic therapy (PDT) is an effective treatment for actinic keratoses (AK) and Bowen's disease (BD) in solid organ transplant recipients (SOTRs), with response rates of 62.5% and 89.47%, respectively. Among the dermoscopic features evaluated, the presence of rosettes in BD and white structureless areas in AK were negatively correlated with treatment response. These findings suggest that dermoscopy may serve as a useful tool for predicting PDT outcomes in this specific patient population.

Further research with larger cohorts is needed to confirm these results and to better understand the factors influencing treatment response and the utility of dermoscopy in this clinical context.

References

1. Berg D, Otley CC. Skin cancer in organ transplant recipients: epidemiology, pathogenesis, and management. *J Am Acad Dermatol.* 2002; 47(1): 1–20. DOI:10.1067/mjd.2002.125579. PMID: 12077575
2. Basset-Seguin N, Baumann Conzett K, Gerritsen MJP, et al. Photodynamic therapy for actinic keratosis in organ transplant patients. *J Eur Acad Dermatol Venereol.* 2013; 27: 57–66. DOI: 10.1111/j.1468-3083.2011.04356.x PMID: 22151793
3. Morelló Vicente A, Oteiza Rius I, Aguado Gil L. Actinic keratosis in solid organ transplant recipients: a medical literature review. *Actas Dermosifiliogr.* 2024; 115(4): 368–373. DOI: 10.1016/j.ad.2023.10.021. PMID: 37925069

4. Álvarez-Salafranca M, Zaballos P. Dermoscopy of squamous cell carcinoma: from actinic keratosis to invasive forms. *Actas Dermosifiliogr.* 2024; 115: 270–273. DOI: 10.1016/j.ad.2024.03.037. PMID: 39102978
5. Lee JH, Won CY, Kim GM, Kim SY. Dermoscopic features of actinic keratosis and follow up with dermoscopy: a pilot study. *J Dermatol.* 2014; 41(6): 487–493. DOI: 10.1111/1346-8138.12282. PMID: 25032251
6. Wang T, Han Q, Hu W, Ren H. Efficacy evaluation and dermoscopy predictors of photodynamic therapy with different pretreatments in the treatment of actinic keratosis. *J Dermatolog Treat*. 2022; 33(6): 2853–2857. DOI: 10.1080/09546634.2022.2089325. PMID: 35694912
7. Navarro-Bielsa A, Cerro-Muñoz P, Almenara-Blasco M, Gracia-Cazaña T, Gilaberte Y. Dermoscopic structures predictive of response to photodynamic therapy in basal cell carcinoma. *Acta Derm Venereol.* 2023; 103: adv00892. DOI: 10.2340/actadv.v103.4838. PMID: 36939536
8. Gilaberte Y, Serra-Guillén C, de las Heras ME, et al. Photodynamic therapy in dermatology. *Actas Dermosifiliogr*. 2006; 97(2): 83–102. DOI: 10.1016/s0001-7310(06)73359-2.PMID: 16595110
9. Gilaberte Y, Aguilar M, Almagro M, et al. Spanish-Portuguese consensus statement on use of daylight-mediated photodynamic therapy with methyl aminolevulinate in the treatment of actinic keratosis. *Actas Dermosifiliogr.* 2015; 106(8): 623–631. DOI: 10.1016/j.ad.2015.06.001. PMID: 26115793
10. Bernal Masferrer L, Gracia Cazaña T, Bernad Alonso I, et al. Topical immunotherapy for actinic keratosis and field cancerization. *Cancers (Basel)*. 2024; 16(6): 1133. DOI: 10.3390/cancers16061133. PMID: 38539468
11. Dragieva G, Prinz BM, Hafner J, et al. A randomised controlled clinical trial of topical photodynamic therapy with methyl aminolaevulinate in the treatment of actinic keratoses in transplant recipients. *Br J Dermatol.* 2004; 151(1): 196–200. DOI: 10.1111/j.1365-2133.2004.06054.x. PMID: 15270891
12. Antonetti P, Pellegrini C, Caponio C, et al. Photodynamic therapy for the treatment of Bowen's disease: a review on efficacy, non-invasive treatment monitoring, tolerability, and cosmetic outcome. *Biomedicines*. 2024; 12(4): 795. DOI: 10.3390/biomedicines12040795. PMID: 38672152
13. Yélamos O, Braun RP, Liopyris K, et al. Dermoscopy and dermatopathology correlates of cutaneous neoplasms. *J Am Acad Dermatol*. 2019; 80(2): 341–363. DOI: 10.1016/j.jaad.2018.07.073. PMID: 30321581
14. Zalaudek I, Giacomel J, Schmid K, et al. Dermoscopy of facial actinic keratosis, intraepidermal carcinoma, and invasive squamous cell carcinoma: a progression model. *J Am Acad Dermatol.* 2012; 66(4): 589–597. DOI: 10.1016/j.jaad.2011.02.011. PMID: 21839538
15. Mun JH, Park JM, Song M, et al. The use of dermatoscopy to monitor therapeutic response of Bowen disease: a dermoscopic pathological study. *Br J Dermatol*. 2012; 167: 1382–1385. DOI: 10.1111/j.1365-2133.2012.11124.x. PMID: 22759263