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ORIGINAL

Actinic Keratosis: Diagnosis and Management

Queratosis actínica: diagnóstico y tratamiento

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ABSTRACT

Actinic Keratoses (AKs) develop at a rate of up to 20 % during ten years thus making them one of the most common Cutaneous Cancer (CC) types and potential developments into Squamous Cell Carcinoma (SCC). The diagnostic procedures of clinical examination and histology fail to identify subclinical Actinic Keratoses so the research requires novel non-invasive imaging alternatives. High-Frequency Ultrasound (HFUS) demonstrates value in AK diagnosis because it provides detailed real-time visualization of multiple skin levels. A comparison of HFUS diagnostic capabilities against standard histological assessment exists in this research. A clinical checkup alongside HFUS imaging and histological testing were conducted on 150 patients who displayed at least one case of AK. Through its precision evaluation with histological results and its minimal detection errors totaling just 3,5 %, HFUS successfully detected AKs in 96,5 % of studied cases. Medical professionals can use HFUS with success as an alternative to standard biopsy practices because it identifies AK early without surgery and provides enhanced diagnostic accuracy in standard clinical settings.

Keywords: High-Frequency Ultrasound (HFUS); Non-Invasive Imaging; Non-Melanoma Skin Cancer (NMSC); Actinic Keratoses (AK).

RESUMEN

Las queratosis actínicas (QA) se desarrollan a una tasa de hasta un 20 % durante diez años, lo que las convierte en uno de los tipos de cáncer cutáneo (CC) más comunes y en una posible evolución hacia el carcinoma de células escamosas (CCE). Los procedimientos diagnósticos de examen clínico e histología no permiten identificar las queratosis actínicas subclínicas, por lo que la investigación requiere nuevas alternativas de imagenología no invasivas. La ecografía de alta frecuencia (EHF) demuestra su utilidad en el diagnóstico de QA, ya que proporciona una visualización detallada en tiempo real de múltiples niveles de la piel. En esta investigación se compara la capacidad diagnóstica de la EHF con la evaluación histológica estándar. Se realizó un chequeo clínico, junto con imágenes de EHF y pruebas histológicas, en 150 pacientes que presentaban al menos un caso de QA. Gracias a su evaluación precisa con resultados histológicos y a sus errores de detección mínimos de tan solo el 3,5 %, la EHF detectó con éxito las QA en el 96,5 % de los casos estudiados. Los profesionales médicos pueden utilizar la ecografía de alta frecuencia (HFUS) con éxito como alternativa a las biopsias convencionales, ya que permite la identificación temprana de la queratosis actínica

sin cirugía y proporciona una mayor precisión diagnóstica en entornos clínicos convencionales.

Palabras clave: Ecografía de Alta Frecuencia (HFUS); Imagenología no Invasiva; Cáncer de Piel no Melanoma (CPNM); Queratosis Actínica (QA).

INTRODUCTION

Adults are commonly affected by photoinduced chronic cutaneous lesions known as Actinic Keratoses (AK), or solar keratoses. One of the clinical indicators of skin photoaging, it appears on parts of the skin that have been exposed to the sun on a regular basis.[1] Actinic lentigines (sunspots) or wrinkles prior to the development of AK are the most common characteristics of this photoaging. According to histology, AK are abnormal regions of keratinocyte differentiation and proliferation. Ithas a propensity to develop into invasive Squamous-Cell Carcinomas (SCC) of the skin.[2] Itis also thought to be a sign of skin cancer risk. SCC incidence rates are shown in figure 1.

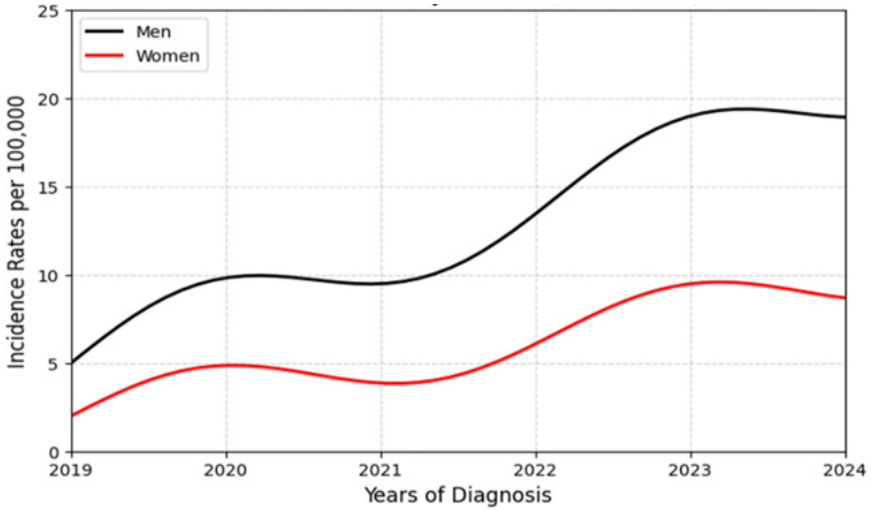

Figure 1. Squamous cell cancer occurrence rates

In individuals aged 40 and 70, the prevalence of actinic keratoses is high, at 15,4 % and 34 % for males and 5,9 % and 18,2 % for women.[3] In older populations with light skin types, the prevalence couldrange from 40 to 60 percent in the southern hemisphere. Due to cumulative sun exposure over a person's lifetime, its frequency sharply increases with age, especially in predisposed populations with pale skin phototypes. Although the prevalence of AK in France is unknown, it is thought to affect 5 % of people who see a dermatologist.[4] The possibility of AK transformation to SCC and population aging could make managing AK a public health concern in the future. Figure 2 represents the effectiveness in AK (a) 5-FU's 0,5 % and (b) 5-FU's 0,5 % + CS.[5]

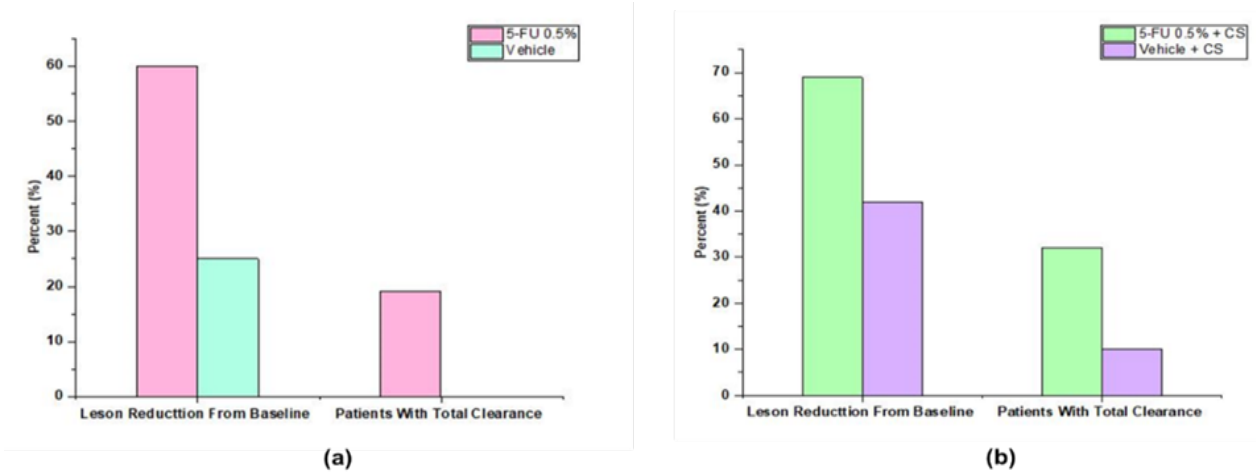

Figure 2. Effectiveness in AK (a) 5-FU's 0,5 % and (b) 5 FU's 0,5 % + CS

The majority of national and European AK management guidelines are derived from reviews of clinical studies with extremely stringent inclusion requirements.[6] It couldbe challenging for the dermatologist to incorporate these options into their daily therapeutic strategy, which involves a much wider range of patients with frequently other illnesses and treatments as well as frequently poor treatment adherence, even though these guidelines and systematic reviews give the reader an assessment of the evidence level of the various therapeutic options.[7] The researches on field-directed therapy for AK, comparing the effectiveness were explored.[8] The morphological characteristics of Basal Cell Carcinomas (BCCs) Ultra-High-Frequency Ultrasound Scan (UHFUS) were examined and BCC.[9] The integrating clinical and pathological frequency, Denmark investigated the risk factors for skin cancer in a cohort of solid organ transplant recipients (SOTR).[10] The tirbanibulin is more cost-effective than other regularly prescribed drugs; developed a health economic model to present to the Scottish Medicines Consortium was discovered by this research [11] the largest to date in the field and also attempted to identify biological traits that can be used to objectively distinguish distinct AK signals.[12] Patients with cSCC, BCC, AK, and Field Cancerization (FC) have been evaluated using topical photosensitizers and adjusted light delivery regimens, as well as the outcomes have been analyzed.[13] Sun exposure causing atopic keratoses AK Convolutional Neural Network (AKCNN) was built, with the convolutional component optimally translated from a pre-trained Visual Geometry Group (VGG16), and digital images with cross-polarization of the affected Skin Surfaces (SS) were acquired. This allows for the separation of AK from normal skin with the possible proximity of benign growths.[14] OW (Ocularist Workshop) and non-OW are compared for the incidence cutaneous.[15] An S.aureus in skin cancer development with the therapeutic potential of S.aureus-competing bacteria for restoring microbial eubiosis in the skin was examined.[16] The increased protoporphyrin IX (PpIX) photosensizerlevels and cell death ensue when combining aminolevulinate-based PDT (Photodynamic Therapy) with differentiation inducing medications.[17] The daylight photodynamic therapy (dPDT) often known as daylight photodynamic therapy for short, can be utilized to activate the protoporphyrin IX to treat Aks.[18] SCC which make up the majority of skin malignancies, are thought to originate from AKs, and this is one of the reasons why therapy is recommended.[19] The available research on the clinical categorizations and treatment of AK, provide recommendations on how to direct patient diagnosis, treatment, and monitoring.[20] Several treatment recommendations for AK have been released in recent years. Cryotherapy regarded as a routine first-line treatment for single lesions among damaging techniques. The effectiveness and safety of the therapy method was discussed.[21] The potential of clinical and dermoscopy signs of early invasion to reliably identify early SCC from AK explored.[22] The consensus guidelines for reporting, naming, and diagnostic standards for AK and cSCCprovided.[23] The clinical efficacy of three treatment regimens in managements of suspect AK with biopsies analyzed histopathological and Immunohistochemical for matrix metalloproteinase expression were evaluated by this work.[24,25] The distribution of BCC, SCC, and AK among frequent body areas and whether or whether it changes with age and sex in patients receiving teledermoscopy at the clinic.[26] Following the guidelines registered protocol in the Prospero database. The tool Quality in Prognosis Studies (QUIPS) was employed to assess the possibility of bias.[27] The presently accessible home-based and doctor-managed therapies and focuses on the therapeutic approaches to AK.[28] To improve the patient care, highlighted the most recent AK diagnostic and therapeutic approaches.[29] SCC is thought to originate from AKs.[30] Invasive SCC can arise due to the transformation of neoplastic intraepidermal keratinocytes across histological grades I, II, and III. Grade I lesions have the potential to infiltrate deeper tissues, progressing into fully invasive tumors. The number of AK lesions is considered a more accurate predictor of SCC occurrence than the histological grade of an individual lesion.

METHOD

Data collection

Assessing the demographic traits, risk factors, and therapeutic results of individuals with AK was the goal of this research. Seventy AK patients who had been diagnosed and were receiving therapy were among the 150 participants. The demographic distribution, skin type classification, amount of sun exposure, smoking status, and history of AK among research participants are shown in this table 1.

Table 1. Research Participants' Clinical and Demographic Characteristics

Variables	Categories	No. of participants (n=150) (%)
Age group (years)	30-40	30 (20 %)
	41-50	35 (23,3 %)
	51-60	45 (30 %)
	Above 60	40 (26,7 %)
Gender	Male	90 (60 %)
	Female	60 (40 %)

Skin type (Fitzpatrick Scale)	Type I (Very Fair)	20 (13,3 %)
	Type II (Fair)	40 (26,7 %)
	Type III (Medium)	50 (33,3 %)
	Type IV (Olive)	40 (26,7 %)
Sun Exposure (Hours/Day)	Below 2 hours	30 (20 %)
	2-4 hours	60 (40 %)
	>4 hours	60 (40 %)
Smoking status	Smoker	50 (33,3 %)
	Non-Smoker	100 (66,7 %)
History of AK	Yes	70 (46,7 %)
	No	80 (53,3 %)
Treatment Modality Used	Cryotherapy	60 (40 %)
	Topical Therapy	40 (26,7 %)
	Photodynamic Therapy	30 (20 %)
	Surgical Excision	20 (13,3 %)

Cryotherapy, topical therapy, photodynamic therapy, and surgical excision are among the therapeutic options described for AK patients. The information sheds light on treatment choices, disease prevalence, and risk factors. Examining these variables aids in determining how patient traits and treatment results are related.

Clinical Analysis

A physical examination enabled researchers to select one patch from each patient according to clinical diagnosis preferences for low-grade AK in early stages. Doctors documented skin lesion photos from 150 AK patients within a sterilized controlled environment using a digital camera. Additional tests by sophisticated equipment were performed to evaluate lesions that exhibited possible AK traits. The chosen approach produced precise medical diagnosis together with therapy planning in alignment with the research goal to examine superior AK diagnosis methods and treatments.

Ultrasound-Based High-Frequency Ultrasound (HFUS) Imaging for the Vivo Evaluation of Actinic Keratosis

General practitioners should utilize High-Frequency Ultrasound (HFUS) imaging because it provides non-invasive skin evaluations for diagnosing dermatological conditions including AK. HFUS enables detailed live imaging of skin structures that used to analyses AK-related structural variations in skin tissue. The research included imaging only one clinically suspected AK lesion per patient when determining early diagnosis and evaluation. Importing lesions into the HFUS machine for scanning presented frequencies varying from 20 to 50 MHz then generated multiple cross-sectional images for examining essential characteristics like vascular patterns along with echogenicity and epidermal thickness. The method enables diagnostics of specific AK features that include both dermal echogenicity changes that result from inflammation or fibrosis and hyperechoic bands which represent hyperkeratosis as well as epidermal hypertrophy. HFUS allows medical practitioners to identify AK through the evaluation of distinctive characteristics that differentiate it from other skin problems both benign and malignant.

RESULTS AND DISCUSSION

The goal of this research assesses how HFUS identifies the severity level of AKs and its relationship to standard laboratory results. HFUS enables clinicians to conduct non-invasive assessments which detect skin structural modifications for both treatment design and early healthcare measures. The analysis revealed epidermal thickening (≥0,8 mm) in 82,7 % of cases with Grade I AK having the biggest prevalence (table 2). The tool demonstrated its diagnostic worth for severe dysplasia through its ability to detect vascularity in every case of Grade III AKs. The echogenicity of dermis proved to diminish in 93,9 % of Grade III cases as a sign of advanced clinical disease progression. The obtained results confirm that HFUS functions as a valuable diagnostic imaging approach for AK evaluation and classification.

Table 2. Association Between Actinic Keratosis Histopathologic Grades and HFUS Outcomes

HFUS features	Grade I AK (n=72)	Grade II AK (n=45)	Grade III AK (n=33)
Epidermal Thickening (≥0,8 mm)	62 (86,1 %)	35 (77,8 %)	27 (81,8 %)
Hypoechoic Band in Dermis	55 (76,4 %)	37 (82,2 %)	30 (90,9 %)

Increased Vascularity (Doppler)	45 (62,5 %)	34 (75,6 %)	33 (100,0 %)
Irregular Hyperechoic Foci	18 (25,0 %)	22 (48,9 %)	27 (81,8 %)
Dermal Echogenicity Reduction	50 (69,4 %)	38 (84,4 %)	31 (93,9 %)

The main HFUS parameters used to assess the severity of actinic keratosis are shown in table 3. All indicators showed significant differences ($p < 0,001$), suggesting that structural alterations progressed as AK grade increased. Greater epidermal thickening, deeper dermal hypoechoic bands, increased vascularity, and decreased echogenicity were all observed in higher-grade AKs, confirming HFUS as a valid method for determining severity.

Table 3. Quantitative Evaluation of Actinic Keratosis Severity Using HFUS

HFUS parameter	Grade I AK (n=72)	Grade II AK (n=45)	Grade III AK (n=33)	p-value
Mean Epidermal Thickness (mm)	0,85 ± 0,12	1,05 ± 0,18	1,26 ± 0,22	<0,001**
Mean Dermal Hypoechoic Band Depth (mm)	0,52 ± 0,09	0,68 ± 0,14	0,85 ± 0,17	<0,001**
Mean Vascularity Index (%)	27,8 ± 6,3	38,5 ± 7,2	52,6 ± 8,5	<0,001**
Mean Echogenicity Reduction (%)	43,2 ± 5,8	57,9 ± 6,4	72,3 ± 7,1	<0,001**

The distribution of AK severity by skin type, sun exposure, and treatment method is shown in this table 4. Sun exposure and AK severity were found to be significantly correlated ($p < 0,05$), with 60,6 % of Grade III cases reporting more than four hours of sun exposure per day. While topical therapy was less common in higher-grade AKs, cryotherapy was the most popular treatment across all AK grades. These results inform treatment choices and highlight the part sun exposure plays in the development of AK.

Table 4. Actinic Keratosis Grade Distribution by Treatment and Demographic Factors

Variables	Grade I AK (n=72)	Grade II AK (n=45)	GradeIIIAK (n=33)	Total (n=150)
Skin type (Fitzpatrick Scale)				
Type I (Very Fair)	10 (13,9 %)	6 (13,3 %)	4 (12,1 %)	20 (13,3 %)
Type II (Fair)	18 (25,0 %)	13 (28,9 %)	9 (27,3 %)	40 (26,7 %)
Type III (Medium)	26 (36,1 %)	14 (31,1 %)	10 (30,3 %)	50 (33,3 %)
Type IV (Olive)	18 (25,0 %)	12 (26,7 %)	10 (30,3 %)	40 (26,7 %)
Sun Exposure (Hours/Day)				
Below 2 hours	18 (25,0 %)	7 (15,6 %)	5 (15,2 %)	30 (20,0 %)
2-4 hours	33 (45,8 %)	19 (42,2 %)	8 (24,2 %)	60 (40,0 %)
>4 hours	21 (29,2 %)	19 (42,2 %)	20 (60,6 %)	60 (40,0 %)
Treatment Modality Used				
Cryotherapy	28 (38,9 %)	18 (40,0 %)	14 (42,4 %)	60 (40,0 %)
Topical Therapy	24 (33,3 %)	11 (24,4 %)	5 (15,2 %)	40 (26,7 %)
Photodynamic Therapy	12 (16,7 %)	8 (17,8 %)	10 (30,3 %)	30 (20,0 %)
Surgical Excision	8 (11,1 %)	8 (17,8 %)	4 (12,1 %)	20 (13,3 %)

According to the field cancerization theory, subclinical preneoplastic alterations in the surrounding skin are frequently present in conjunction with actinic keratosis (AK). According to recent research, there could be continuous areas of genetically clonal preneoplastic keratinocytes. Nevertheless, due to the limits of traditional diagnostic methods, it is not feasible to collect biopsy samples from every affected and nearby skin area. Non-invasive imaging methods that improve AK detection and visualization beyond clinical evaluation are therefore becoming more and more necessary. High-frequency ultrasound (HFUS), which offers high-resolution imaging and real-time structural evaluation, was employed in this research as a non-invasive technique to evaluate AK lesions. Although repeated biopsies are frequently impractical due to lesion location, histopathology is still the gold standard for diagnosing AK. Consequently, combining HFUS with histological evaluation can increase the precision of the diagnosis. Findings from HFUS showed a strong correlation with various histologic grades of AK, confirming its use in disease classification. Key markers of AK severity were epidermal thickening, vascularity alterations, and a decrease in dermal echogenicity, indicating that HFUS is a viable early detection and classification method. The dependability of HFUS was demonstrated by the results, which showed that

it correctly identified 97,7 % of AK lesions with only 2,3 % misclassified as noncancerous. Its shortcomings in identifying deeply invasive lesions, especially in hyperkeratosis instances, indicate that more improvements in imaging resolution are necessary. In contrast to RCM, which has trouble assessing thick hyperkeratotic layers, HFUS offers deep penetration that is unaffected by the stratum corneum's refractive index. Furthermore, there were inconsistent patterns in inflammatory infiltration and exocytosis, suggesting that these could not be the main criterion for AK assessment based on HFUS. Although the main goal of this investigation was not to differentiate between invasive Squamous Cell Carcinoma (SCC) and AK, HFUS could be able to do so. These results highlight how HFUS and histopathology can improve AK diagnosis and treatment by offering a more effective, non-invasive substitute for recurrent biopsies. Table 5 details the main risk factors for CC.

Table 5. Risk factors of SCC

Risk factors	Environmental Exposure (EE)	Pre-Existing Skin Lesions (PSL)	Skin types	Record
Melanoma	UV light	Atypical Moles Dysplastic nevus Congenital Syndrome Melanocytic Nevi	Light Hair (LH) Fair Skin (FS) Freckling (F)	Family or personal history of melanoma Immuno suppression Elderly Male (MIMEM)
SCC	Polycyclic UV light Arsenic Exposure (AE) Hydrocarbons Coal Tar (HCT)	Basal Cell Nevus Syndrome (BCNS) Actinickeratosis Bowenoidpapulosis Epidermodysplasiaverruciformis	Freckling (F) Fair Skin (FS) Light Hair (LH)	Psoriasis treatment smoking HPB Prior SCC lesions Male Lymphoma Albinism Genodermatoses Xeroderma pigmentsum

CONCLUSIONS

By comparing imaging results with histological grades, this research sought to assess that well HFUS diagnoses and categorizes AK. With only 2,3 % misclassification, HFUS showed 97,7 % accuracy in detecting AK lesions, demonstrating its dependability as a non-invasive diagnostic method. Significant correlations were found between the severity of AK and key variables such increased vascularity, decreased dermal echogenicity, and epidermal thickness. HFUS offered real-time, high-resolution imaging in contrast to traditional histology, which made it an effective tool for disease stratification and early identification. According to these results, HFUS is a good substitute for repeated biopsies, which enhances clinical judgment and diagnostic effectiveness in the treatment of AK. The limitation of this research is that extensive hyperkeratosis lesions cannot be completely resolved by HFUS, which could result in misclassification. Future studies should concentrate on combining multimodal imaging methods with AI-driven image processing to improve AK progression tracking and diagnosis precision.

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