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Very High Frequency Ultrasonographic Features of Trichofolliculoma: An Observational Study

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Background: Trichofolliculoma (TF) is a rare condition, and its imaging features have been inadequately studied, leading to frequent misdiagnoses in clinical practice.

Objective: The aim of our study was to investigate the very high frequency (VHF) ultrasound characteristics of TF, identify features that could assist in the differential diagnosis of TF versus other benign and malignant lesions.

Methods: We collected clinical data from 24 patients with histologically confirmed TF between February 2019 and June 2024. We retrospectively analyzed the VHF ultrasound image characteristics of the lesions, including their location, skin layers involved, size, shape, margin, boundary, internal echo characteristics, and blood flow patterns.

Results: The VHF ultrasound image features of the 24 TF cases showed that the lesions were located in the epidermis, dermis, and subcutaneous tissue in 8 cases, in the dermis and subcutaneous tissue in 2 cases, and in the deep dermis and subcutaneous tissue in 14 cases. The maximum diameter was approximately 23.3×8.7 mm. The lesions were mostly regular in shape (75%), with predominantly inhomogeneous low echo (95.8%). Most lesions contained cystic echoes (70.8%), some had short linear strong echoes within (66.6%), and partial posterior echo enhancement was observed in some lesions (41.6%). Half (50%) of the lesions showed peripheral blood flow signals. The consistency analysis of the VHF ultrasound image features showed Kappa values greater than 0.7, indicating good agreement.

Conclusion: The VHF ultrasound images of TF exhibit characteristic features. Specifically, the identification of the lesion's location, the involved skin layers, internal echo features, and blood flow patterns offers novel insights that enhance diagnostic accuracy and possesses significant auxiliary value in clinical diagnosis and treatment. This study contributes unique findings to the existing literature, further elucidating the VHF ultrasound characteristics of TF and underscoring its potential in improving clinical practice.

Keywords: very high frequency ultrasonic, diagnosis, trichofolliculoma

Introduction

Trichofolliculoma (TF), a rare, benign, and well-differentiated hair follicle hamartoma.[1] This condition is more prevalent among individuals aged 18 to 49 years, with males exhibiting an 84% higher incidence rate compared to females.[2] TF demonstrates intermediate differentiation between a hair follicular nevus, characterized by simple hyperplasia of the hair follicle, and a trichoepithelioma, which typically lacks mature hair follicles.[3] TF commonly occurs on the face but can also be found on the scalp or neck, and rarely, it may present on the external auditory meatus, intranasal area, genital area, lip, and vulva. Clinically, TF is distinguished by the presence of a central dilated pore with visible white immature hair bundles. Despite the clinical significance of TF, its imaging features have been inadequately studied, leading to frequent misdiagnoses.

Dermoscopic examination of TF has been scantily described, with only one prior report in the literature documenting a dermoscopic "firework" pattern in a 4-month-old lesion, consisting of a central brown zone with radial brown projections.[4] Misdiagnosis of TF as basal cell carcinoma or molluscum contagiosum is possible, especially when the

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hair has been plucked. Other differential diagnoses encompass keratoacanthoma, milium, trichoepithelioma, syringoma, dermal nevus, and sebaceous hyperplasia.[5]

Histopathologically, TF is characterized by one or more central keratinous cysts with radiating vellus hair follicles and can be subdivided into three stages:[6] early, fully developed, and late. In early stages, there are few secondary vellus hair follicles originating from a primary follicle. In mature lesions, vellus hair follicles increase in number, while later stages show a thickened primary follicle and fewer secondary follicles. Treatment of TF typically involves simple excision, and recurrence is rare. However, perineural invasion of the cheek has been reported. Although perineural invasion does not suggest malignancy, long-term follow-up may be necessary when perineural invasion is observed on pathological findings.

Very High Frequency (VHF) ultrasound,[7] a high-frequency ultrasound technique with extremely high resolution, is capable of clearly displaying the fine structures of superficial tissues such as skin and eyeballs, even reaching or exceeding the limit of human naked eye resolution.[8] VHF ultrasound can distinctly reveal the detailed structures of various skin layers and skin appendages, which is significant for the diagnosis of skin diseases.[9,10] Previous studies, such as the dermatoscopic and ultrasonographic comparison of melanocytic nevi, have demonstrated the utility of high-frequency ultrasound in skin lesion analysis.[11] Considering the potential for similar insights in TF, we planned this study to investigate the VHF ultrasound characteristics of this rare skin appendage tumor. This study retrospectively analyzed the VHF ultrasound sonographic features of 24 cases of TF confirmed by histopathology and combined this analysis with the literature to explore the diagnostic value of VHF ultrasound for TF.

Methods and Materials

Study Population

The data of 24 TF patients (11 male, 13 female; age range, 11–64 years; mean age, 37 years) admitted to Hangzhou Third People's Hospital from June 2019 to June 2024 were collected. All of the patients were pathologically confirmed to be TF. Table 1 presents the basic characteristics of the patients.

Image Instruments

All patients were examined with Esaote MyLab™ One (Italy) Color Doppler Ultrasound Diagnostic Apparatus (equipped with 22 MHz high frequency ultrasonic probe). The location of the lesion, skin layer involved, size, shape, margin, boundary, internal echo, blood supply, etc. were recorded. The characteristics of TF detected by VHF ultrasound were summarized. The image analysis process was completed by two senior doctors with more than 5 years of experience in dermatology ultrasound diagnosis. Correlation between the ultrasonographic features and histopathological findings was performed by comparing the ultrasonic images with the histopathology reports of each patient. The histopathological characteristics, including the presence of central keratinous cysts and radiating vellus hair follicles, were matched with the corresponding ultrasonic features such as cystic structures and short linear hyperechoic elements.

Ethics Committee

This study complies with the Declaration of Helsinki and was approved by the local ethics committee (approval number: 2024KA113). Prior to the study, participants were fully informed of the study's purpose and procedure. They were told that participation in the survey was voluntary and that their refusal or dropping out of the study would not affect their treatment in the hospital. It is important to note that for participants under the age of 18, informed consent was duly obtained from their parent or legal guardian.

Results

General Conditions

The study encompassed 24 patients aged between 11 and 64, with a balanced gender distribution of 11 females and 13 males. Trichofolliculomas were observed in multiple locations, specifically the nose (n=4), scalp (n=3), face (n=7), forehead (n=3), ear (n=2, with one case occurring on the earlobe), buttocks (n=1), and back (n=1). Notably, the head and

Table 1 Basic Characteristics of the Study Population, Including Age, Gender, Location, and Involved Skin Layers

Case	Age/ Gender	Site	Thickness (mm)	Involved Layers	Boundary	Shape	Internal Echo Characteristics	Blood Flow Features (Grade)	Remarks
#1	39/F	Nose	4.5 x 2.5	Dermis, Subcutaneous	Clear	Irregular	Inhomogeneous, hypoechoic	3	Posterior echo enhancement
#2	59/F	Forehead	8.5 x 3.7	Epidermis, Dermis, and Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	2 (Periphery-dominated)	Posterior echo enhancement; short linear hyperechoic structures visible internally
#3	52/M	Scalp	9.2 x 5.2	Deep Dermis, Subcutaneous	Unclear	Irregular	Homogeneous, hypoechoic	0	Posterior echo enhancement
#4	64/M	Nose	12.4 x 5.6	Deep Dermis, Subcutaneous	Clear	Irregular	Inhomogeneous, hypoechoic	2 (Periphery-dominated)	Posterior echo enhancement; short linear hyperechoic structures visible internally
#5	31/M	Face	5.6 x 4.3	Deep Dermis, Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	0	Posterior echo enhancement
#6	54/F	Face	5.8 x 4.9	Epidermis, Dermis, and Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	2 (Periphery-dominated)	Short linear hyperechoic structures visible internally
#7	26/F	Face	7.3 x 5.2	Epidermis, Dermis, and Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	2 (Periphery-dominated)	Short linear hyperechoic structures visible internally
#8	52/F	Face	7.2 x 3.1	Deep Dermis, Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	2 (Periphery-dominated)	Short linear hyperechoic structures visible internally
#9	16/M	Buttock	12.0 x 8.0	Deep Dermis, Subcutaneous	Clear	Irregular	Inhomogeneous, hypoechoic	0	–
#10	42/M	Face	8.1 x 4.5	Dermis, Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	2 (Periphery-dominated)	Short linear hyperechoic structures visible internally
#11	37/F	Scalp	18.1 x 7.8	Deep Dermis, Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	0	–
#12	44/F	Forehead	6.4 x 2.8	Deep Dermis, Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	0	Short linear hyperechoic structures visible internally
#13	44/F	Behind the ear	12.7 x 3.5	Deep Dermis, Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	1 (Periphery-dominated)	Posterior echo enhancement; short linear hyperechoic structures visible internally
#14	28/M	Forehead	11.4 x 5.1	Deep Dermis, Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	2 (Periphery-dominated)	Posterior echo enhancement; short linear hyperechoic structures visible internally
#15	32/F	Nose	12.7 x 7.9	Epidermis, Dermis, and Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	3	Short linear hyperechoic structures visible internally
#16	24/F	Face	10.8 x 4.7	Deep Dermis, Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	1 (Periphery-dominated)	Posterior echo enhancement; short linear hyperechoic structures visible internally
#17	43/F	Ear	2.7 x 2.4	Epidermis, Dermis	Clear	Regular	Inhomogeneous, hypoechoic	0	–

(*Continued*)

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Table 1 (Continued).

Case	Age/ Gender	Site	Thickness (mm)	Involved Layers	Boundary	Shape	Internal Echo Characteristics	Blood Flow Features (Grade)	Remarks
#18	44/M	Scalp	13.0 x 6.4	Deep Dermis, Subcutaneous	Clear	Irregular	Inhomogeneous, hypoechoic	0	Short linear hyperechoic structures visible internally
#19	24/M	Face	8.1 x 3.4	Deep Dermis, Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	1 (Periphery-dominated)	Posterior echo enhancement; short linear hyperechoic structures visible internally
#20	19/M	Face	6.5 x 4.4	Deep Dermis, Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	0	Posterior echo enhancement; short linear hyperechoic structures visible internally
#21	11/F	Face	–	Epidermis, Dermis	Unclear	Regular	Inhomogeneous, hypoechoic	0	–
#22	21/F	Back	4.2 x 2.3	Epidermis, Dermis	Clear	Regular	Inhomogeneous, hypoechoic	1 (Periphery-dominated)	Short linear hyperechoic structures visible internally
#23	44/M	Scalp	23.3 x 8.7	Deep Dermis, Subcutaneous	Clear	Regular	Inhomogeneous, hypoechoic	0	–
#24	42/M	Nose	5.6	Epidermis, Dermis, and Subcutaneous	Clear	Irregular	Inhomogeneous, hypoechoic	2 (Periphery-dominated)	Short linear hyperechoic structures visible internally

Notes: Basic Characteristics of the Study Population, Including Age, Gender, Location, and Involved Skin Layers. For entry at sequence number 15, "accompanied by squamous cell carcinoma" indicates a concomitant symptom of malignancy, suggesting a potential association or simultaneous presence of squamous cell carcinoma at the lesion site.

face were the primary sites of occurrence, while other locations exhibited minimal incidence. The involvement of skin layers in the study population varied, with specific counts and percentages as follows: 3 cases (12.5%) involved the epidermis and dermis, 5 cases (20.8%) involved the epidermis, dermis, and subcutaneous tissue, 2 cases (8.3%) involved the dermis and subcutaneous tissue, and 14 cases (58.3%) involved the deep dermis and subcutaneous tissue. These data provide a comprehensive overview of the distribution of skin layer involvement. The size of the TF ranged from 2.7×2.4 mm to 23.3×8.7 mm, with most lesions being several millimeters to a centimeter in length. The boundaries of the lesions were clear in 22 cases and unclear in 2 cases. The shape of the lesions was irregular in 6 instances and regular in 18 instances, indicating variability in their morphological presentation. Table 1 presents the basic characteristics of the patients, with the latter part of the table showcasing these details.

VHF Ultrasound Characteristics of Trichofolliculomas

Ultrasound examination of the 24 TF cases revealed the following characteristics. Specifically, all lesions exhibited uneven low echo patterns (n=24), with cystic structures visible in the ultrasound images of 16 cases and short linear strong echoes present internally in 20 cases. Posterior acoustic enhancement was observed in 13 cases (over half of the total). In terms of blood flow characteristics, peripheral blood flow was the most common feature observed on ultrasound (n=11), while four cases showed a combination of peripheral and central blood flow, and no specific blood flow was noted in 9 cases. Additionally, one case was associated with squamous cell carcinoma.

In the ultrasound images, we can observe the characteristic changes exhibited by the TF. Figure 1 displays the ultrasonic image of the lesion, characterized by inhomogeneous low echogenicity with discernible cystic structures, short linear hyperechoic elements, and posterior acoustic enhancement of the nodule. Figure 2 presents a comparison between TF lesions with irregular morphologies and those with regular morphologies. Lastly, Figure 3 illustrates the diversity of blood flow signals within TF lesions, encompassing a range of presentations from grade 0 to grade 3 blood flow.

Discussion

TF, a rare benign hamartoma, exhibits diverse clinical presentations and can mimic more aggressive skin cancers, leading to potential misdiagnoses.[12] This study aimed to elucidate TF's VHF ultrasound characteristics, to enhance its differential diagnosis from other benign and malignant skin lesions. Our retrospective analysis of 24 histopathologically confirmed TF cases revealed consistent VHF ultrasound features that could facilitate clinical recognition and improve diagnostic accuracy.

The VHF ultrasound images of TF lesions consistently demonstrated inhomogeneous low echogenicity, with discernible cystic structures and short linear hyperechoic elements within the nodules.[13] These findings align with the histopathological characteristics of TF, which include central keratinous cysts surrounded by radiating vellus hair

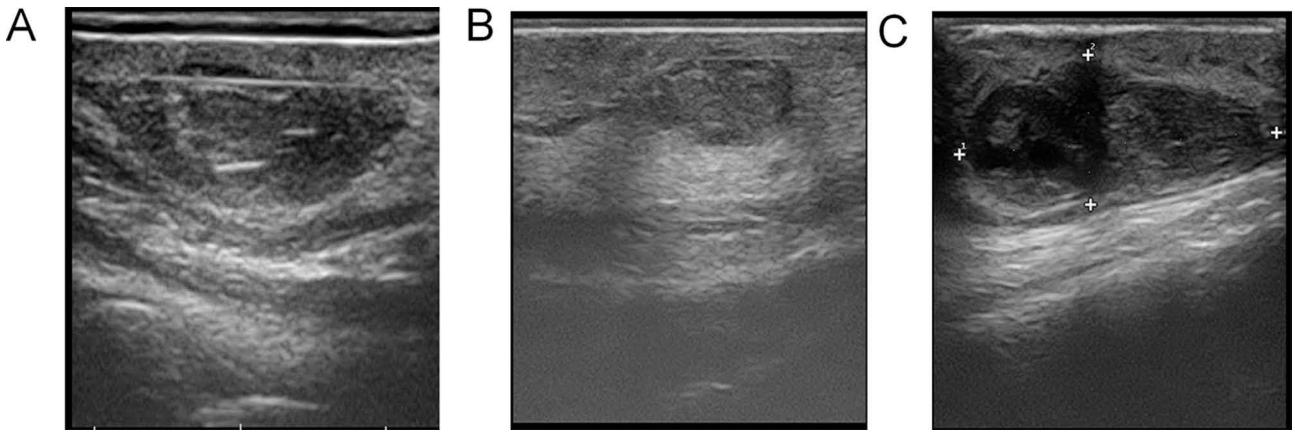

Figure 1 Ultrasonic Features of Trichofolliculoma: Inhomogeneous Low Echogenicity, Cystic Structures, and Posterior Acoustic Enhancement. (**A**) Short linear hyperechoic elements observed within the lesion. (**B**) Inhomogeneous low echogenicity with discernible cystic structures present. (**C**) Posterior acoustic enhancement of the nodule noted.

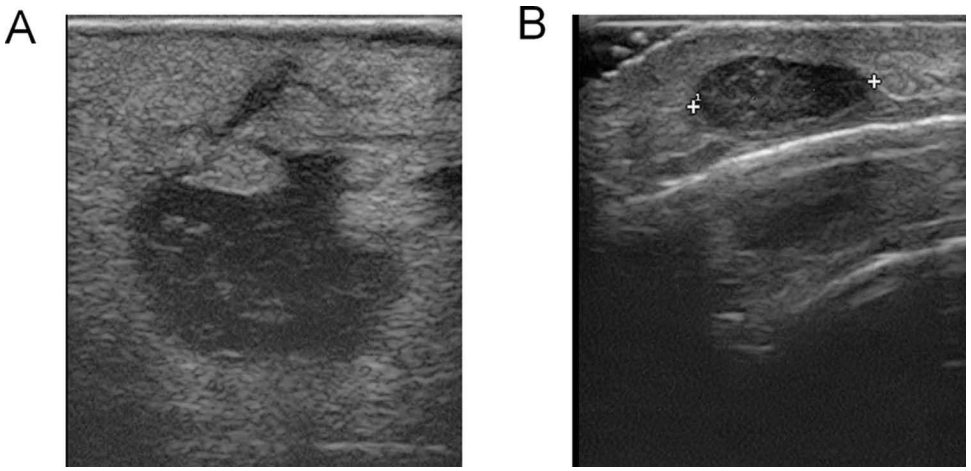

Figure 2 Morphological Comparisons of Trichofolliculoma Lesions: Irregular vs Regular Morphologies. (**A**) Trichofolliculoma lesion with irregular shape. (**B**) Trichofolliculoma lesion with regular shape.

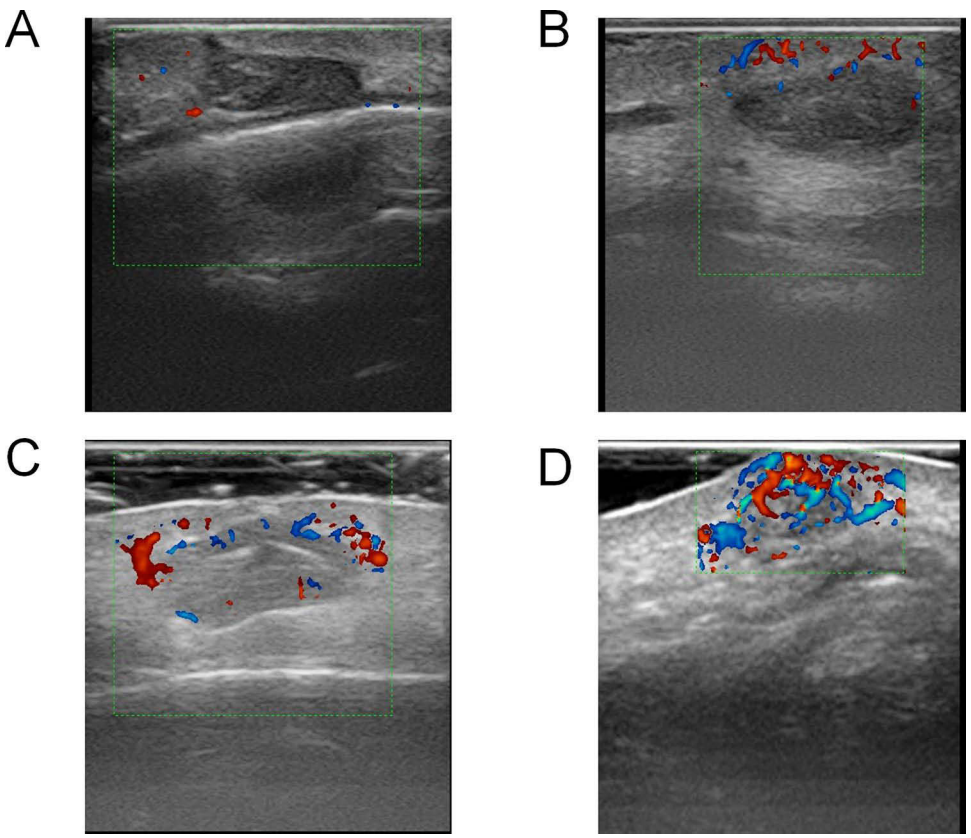

Figure 3 Blood Flow Signal Diversity in Trichofolliculoma Lesions: Range of Presentations from Grade 0 to Grade 3. (**A**) Trichofolliculoma lesion with grade 0 blood flow. (**B**) Trichofolliculoma lesion with grade 1 blood flow. (**C**) Trichofolliculoma lesion with grade 2 blood flow. (**D**) Trichofolliculoma lesion with grade 3 blood flow.

follicles.[14] The cystic structures observed on ultrasound likely correspond to these central keratinous cysts. At the same time, the short linear hyperechoic elements may represent the radiating hair follicles or the fibrous stroma surrounding them.

Additionally, posterior acoustic enhancement of the nodule was noted in over half of the cases, further supporting the diagnostic utility of VHF ultrasound in TF. This acoustic enhancement effect may be attributed to the complex

microstructures within the lesion or the interaction of solid components at the interface between the lesion and the surrounding healthy tissues, which leads to scattering, reflection, and interference of ultrasonic waves during their propagation, thereby enhancing the echo signals behind the nodule.[10]

The morphological diversity of TF lesions was also vividly captured on VHF ultrasound imaging, with lesions exhibiting a wide spectrum of irregular and regular shapes, further emphasizing the heterogeneity of this condition. This variability in lesion morphology is consistent with the clinical presentation of TF. It underscores the importance of considering a broad range of morphological features,[11] including but not limited to shape, size, and internal structure, when evaluating potential cases and formulating diagnostic hypotheses. Such comprehensive consideration of morphological characteristics is crucial for accurate assessment and effective management of TF, particularly in the context of early detection and differential diagnosis.

Blood flow characteristics within TF lesions were also assessed, with peripheral blood flow being the most common pattern observed. This finding suggests that TF lesions may have a distinct vascular pattern that could be useful in differentiating them from other skin lesions. However, it is important to note that a comprehensive review of the current literature did not reveal any reports specifically addressing TF's peripheral blood flow characteristics, highlighting a gap in existing knowledge. Furthermore, many cases did not demonstrate specific blood flow patterns, indicating that the absence of blood flow signals should not exclude the possibility of TF. This underscores the need for further research to fully elucidate the blood flow characteristics of TF lesions and their potential diagnostic implications.

In comparing our findings with the existing literature, we noted a paucity of data on TF's dermoscopic and ultrasonographic features. Our study contributes to the limited pool of knowledge on this rare condition and highlights the potential of VHF ultrasound as a non-invasive diagnostic tool. The high resolution of VHF ultrasound allows for the detailed visualization of superficial tissues, making it a valuable adjunct to clinical examination and histopathology in diagnosing TF.

Conclusion

In conclusion, our study demonstrates that VHF ultrasound exhibits characteristic features of TF, including inhomogeneous low echogenicity, discernible cystic structures, short linear hyperechoic elements, and posterior acoustic enhancement. These findings, coupled with the morphological and blood flow characteristics observed on ultrasound, can aid in the differential diagnosis of TF from other benign and malignant skin lesions. VHF ultrasound as a diagnostic tool for TF holds promise in improving diagnostic accuracy and guiding appropriate clinical management. Further studies with larger sample sizes and comparative analyses with other skin lesions are needed to validate these findings and establish the diagnostic utility of VHF ultrasound in TF. It is important to acknowledge, however, that our study is not without limitations. Given the rarity of TF, our sample size was necessarily limited, which may affect the generalizability of our findings. Therefore, we strongly advocate for further research in this area, including studies with larger sample sizes and comparative analyses with other skin lesions, to validate our findings and establish the diagnostic utility of VHF ultrasound in TF with greater certainty. Moreover, the development of a standard protocol for VHF ultrasound evaluation of TF would facilitate consistent and reproducible assessments, enhancing the practical applications of this diagnostic tool in clinical settings.

Data Sharing Statement

The data set used during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Ethics approval was granted by the Hangzhou Third People's Hospital ethics committee (2024KA113).

Author Contributions

Yu-Ting Zhang wrote the first draft of the manuscript. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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