Conflicts of interest: None disclosed.

IRB approval status: Not applicable.

Reprints not available from the authors.

Correspondence to: Alessia Villani, MD, Via Pansini,5, 80131 Napoli, Italy

E-mail: ali.vil@hotmail.it

REFERENCES

1. Krengel S, Hauschild A, Schäfer T. Melanoma risk in congenital melanocytic naevi: a systematic review. *Br J Dermatol*. 2006; 155:1-8.
2. Yélamos O, Arva NC, Obregon R, et al. A comparative study of proliferative nodules and lethal melanomas in congenital nevi from children. *Am J Surg Pathol*. 2015;39:405-415.
3. Illig L, Weidner F, Hundeiker M, et al. Congenital nevi less than or equal to 10 cm as precursors to melanoma. 52 cases, a review, and a new conception. *Arch Dermatol*. 1985;121:1274-1281.
4. Shitara D, Nascimento M, Ishioka P, et al. Dermoscopy of naevus-associated melanomas. *Acta Derm Venereol*. 2015;95: 671-675.
5. Lallas A, Longo C, Manfredini M, et al. Accuracy of dermoscopic criteria for the diagnosis of melanoma in situ. *JAMA Dermatol*. 2018;154:414-419.

https://doi.org/10.1016/j.jaad.2020.07.116

Utility of infrared thermography in differentiating cellulitis from pseudocellulitis of the lower limbs—A diagnostic accuracy study

To the Editor: Infrared thermography has been reported in prior studies as an objective, noninvasive, and less time-consuming method of differentiating cellulitis from its mimics.[1-3]

In the present study, we aimed to assess the diagnostic accuracy of infrared thermography in differentiating cellulitis from pseudocellulitis. The criterion standard was the diagnosis established by a dermatologist through clinical examination and investigations.[1,4]

We recruited participants with predominantly unilateral leg cellulitis and pseudocellulitis from the outpatient clinics of dermatology, surgery, and emergency medicine after informed consent. We classified participants with cellulitis into mild, moderate, and severe disease categories.[5] We excluded children; pregnant women; participants who have received antibiotics in the past 2 weeks; and those with abscess, osteomyelitis, necrotizing fasciitis, recent surgery of the affected part, and septic arthritis.

We calculated sample size based on a mean difference of 1.3°C between the affected limbs[1] in cases of cellulitis and pseudocellulitis with a type 1 error of 5% and type 2 error of 20%. We recruited 158 patients (108 in the development group and 50 in the validation group).

The principal investigator (a dermatology trainee) made the preliminary diagnosis and recorded the skin surface temperatures using a FLIR ONE Pro thermal camera (Generation 3; FLIR Systems, Wilsonville, OR). The senior dermatologist who was blind to the thermal measurements counterchecked the diagnoses. We calculated the temperature gradient by subtracting the peak skin surface temperature of the affected leg from that of the corresponding point of the unaffected leg.[1]

The development group included 65 patients with cellulitis and 43 patients with pseudocellulitis including stasis dermatitis, lipodermatosclerosis, and lymphedema (Supplemental Tables I and II; available via Mendeley at https://doi.org/10.17632/hps33b4t4p.1). There were no significant differences between the 2 groups in age ($P = .07$) or sex ($P = .13$).

The median temperature gradient was significantly ($P < .0001$) higher in the cellulitis group in comparison to the pseudocellulitis group (Fig 1 and Supplemental Table III; available via Mendeley at https://doi.org/10.17632/hps33b4t4p.1).

The receiver operating characteristic curve was plotted to assess the discriminatory ability of the temperature gradient to correctly classify cellulitis and pseudocellulitis (Supplemental Fig 1; available via Mendeley at https://doi.org/10.17632/hps33b4t4p.1). The area under the curve was 0.974 (95% confidence interval, 0.924-0.995). We chose a cutoff of greater than 0.6°C because it had the highest combination of sensitivity (95.4%) and specificity (90.7%).

We noted that a temperature gradient of less than 0.4°C perfectly predicts the diagnosis of pseudocellulitis and that a temperature gradient of greater than 1.7°C perfectly predicts the diagnosis of cellulitis.

The validation group included 25 cases of cellulitis and 25 cases of pseudocellulitis (Supplemental Table IV; available via Mendeley at https://doi.org/10.17632/hps33b4t4p.1). There were no significant differences between the 2 groups in age ($P = .13$) and sex ($P > .99$).

The temperature gradient of greater than 0.6°C had a sensitivity of 100% and specificity of 88% to predict cellulitis in the validation group (Table I).

Strengths of the study were having the diagnoses established by the dermatologist, the broad spectrum of cases of cellulitis and pseudocellulitis, and validation of the cutoff. The temperature gradient of (>0.6°C) could be useful to differentiate cellulitis from pseudocellulitis of the legs in an emergency care setting. The results of this

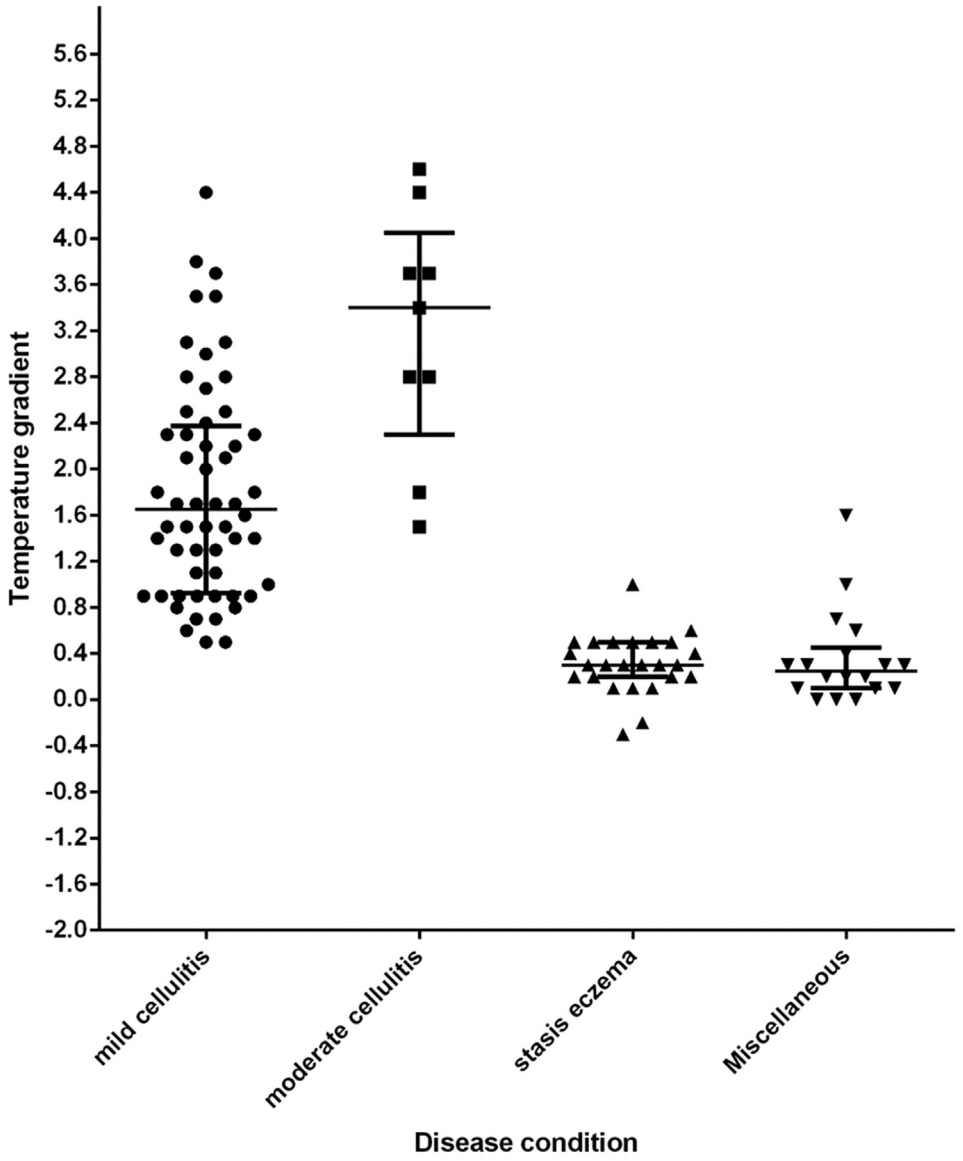

Fig 1. Cellulitis and pseudocellulitis: the median and interquartile range of temperature gradients in the development group among patients with cellulitis and pseudocellulitis.

Table I. Diagnostic accuracy of a temperature gradient of greater than 0.6°C to predict cellulitis in the development and validation data sets

Group	Sensitivity, %	Specificity, %	PPV, %	NPV, %	LR+	LR-	Accuracy, %
Development group	95.4	90.7	91.11	95.16	10.25	0.05	93.04
Validation group	100	88	89.28	100	8.33	0.00	94

LR, Likelihood ratio; *NPV*, negative predictive value; *PPV*, positive predictive value.

study cannot be generalized to participants with symmetric leg involvement and cellulitis of other body parts.

Chethan Rangappa Hanumakka, MBBS,[a] *Nanda Kishor Maroju, MD,*[b] *and Laxmisha Chandrashekar, MD*[a]

From the Department of Dermatology[a] *and Department of General Surgery, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India.*[b]

Funding sources: None.

Conflicts of interest: None disclosed.

IRB approval status: Reviewed and approved by Jawaharlal Institute of Postgraduate Medical Education and Research Institute ethics committee (human studies).

Reprints not available from the authors.

Correspondence to: Laxmisha Chandrashekar, MD, Department of Dermatology, JIPMER, Pondicherry-605006, India

E-mail: laxmishac@gmail.com

REFERENCES

1. Ko LN, Raff AB, Garza-Mayers AC, et al. Skin surface temperatures measured by thermal imaging aid in the diagnosis of cellulitis. *J Invest Dermatol*. 2018;138(3):520-526.
2. Li DG, Dewan AK, Xia FD, Khosravi H, Joyce C, Mostaghimi A. The ALT-70 predictive model outperforms thermal imaging for the diagnosis of lower extremity cellulitis: a prospective evaluation. *J Am Acad Dermatol*. 2018;79(6):1076-1080.
3. Montalto M, Davies F, Marijanovic N, Meads A. Skin surface temperature: a possible new outcome measure for skin and soft tissue infection. *Aust Fam Physician*. 2013;42:653-657.
4. Arakaki RY, Strazzula L, Woo E, Kroshinsky D. The impact of dermatology consultation on diagnostic accuracy and antibiotic use among patients with suspected cellulitis seen at outpatient internal medicine offices: a randomized clinical trial. *JAMA Dermatol*. 2014;150(10):1056-1061.
5. Blumberg G, Long B, Koyfman A. Clinical mimics: an emergency medicine-focused review of cellulitis mimics. *J Emerg Med*. 2017;53(4):475-484.

https://doi.org/10.1016/j.jaad.2020.07.118

Tumor necrosis factor-like weak inducer of apoptosis (TWEAK) in psoriasis and atopic dermatitis: A case-control study

To the Editor: Psoriasis and atopic dermatitis (AD) are common inflammatory, T-cell–mediated diseases. Previous studies suggested a role of tumor necrosis factor–like weak inducer of apoptosis (TWEAK) in psoriasis and AD.[1-5] However, studies are quite limited, with some conflicting results.

This is a case-control study conducted on 90 participants: 30 patients with psoriasis vulgaris, 30 patients with AD, and 30 age- and sex-matched healthy control individuals. All participants were older than 18 years and provided informed consent. Patients were subjected to full history taking and examination of the skin for Psoriasis Area and Severity Index score in patients with psoriasis and EASI score in patients with AD.

Skin biopsy samples were obtained from the lesional skin of patients and normal skin of control individuals. Each skin biopsy sample was weighted and homogenized in phosphate-buffered saline (with a ratio of tissue weight [in grams] to phosphate-buffered saline volume [in milliliters] of 1:9) with a glass homogenizer on ice. The homogenates were then centrifuged for 5 minutes at 5000*g* to get the supernatant. The supernatant was separated to be used for quantitation of TWEAK by using a commercially available enzyme-linked immunosorbent assay kit (catalog No. MBS2511137) provided by MyBiosource, Inc (San Diego, CA.)

Demographic and clinical data of patients and control individuals are summarized in Table I. TWEAK level was significantly higher in patients with psoriasis than those with AD and control individuals ($P = .042$ and $P < .001$, respectively). Also, there was a significant difference between patients with AD and control individuals, with a higher level in AD skin ($P < .001$) (Fig 1).

No significant correlations were detected between the level of TWEAK in patients with psoriasis and each of the age, duration, and Psoriasis Area and Severity Index score ($P = .841$, $r = -0.038$; $P = .64$, $r = 0.089$; and $P = .068$, $r = -0.338$, respectively). Also, there was no relation between TWEAK level and sex ($P = .744$) or family history ($P = .617$).

In patients with AD, the level of TWEAK did not show any association with the measured variables with regard to their age, Eczema Area and Severity Index score, sex, or family history ($P = .736$, $r = -0.064$; $P = .601$, $r = -0.1$; $P = .721$; and $P = .866$, respectively). However, there was a statistically significant positive correlation between TWEAK level and disease duration ($P = .006$, $r = .491$).

TWEAK can have a role in 2 previously known mutually exclusive skin diseases. TWEAK alone cannot produce full AD or psoriasis, but it promotes chemokines common to both diseases from keratinocytes and fibroblasts, in addition to characteristic cytokines of AD and psoriasis such as TSLP and interleukin (IL) 19. Moreover, TWEAK can act in synergy with the disease-specific cytokines IL-13 and IL-17.[5] The absence of correlations with the measured disease variables can be explained by the local production of TWEAK by inflammatory cells. Our demonstration of a positive correlation between the level of TWEAK and duration of AD disease may suggest that persistent activation of TWEAK signaling pathway leads to the harmful effects, causing chronic dermatitis lesions.

In conclusion, TWEAK may have a role in the pathogenesis of psoriasis and AD. Clinical trials studying the blocking of TWEAK signaling in