

A pilot study using high-frequency ultrasound to measure digital ulcers: a possible outcome measure in systemic sclerosis clinical trials?

Sirs,

Digital ulcers (DUs) are often the primary end point in systemic sclerosis (SSc)-related clinical trials; however, the reliability of SSc-interested rheumatologists in grading DUs is only poor to moderate (1-3). DUs commonly occur on the fingertips and over the extensor aspects of the hands, and can occur over subcutaneous calcinosis (4). Despite a number of treatments to prevent and heal DUs (5-6), in some patients recurrent DUs remain a major source of morbidity (7). Therefore, a method of accurately assessing DUs is needed, to facilitate future clinical research. High-frequency ultrasound (HFUS) has been used to measure skin thickness (currently as a research tool only) with reported high intra- and inter-observer reliability (8, 9). Against this background, our primary aim was to examine the feasibility and tolerability of HFUS to measure SSc-related DUs.

Eleven (10 female) patients with SSc-spectrum disorders (5 diffuse and 5 limited cutaneous SSc) and 15 DUs (4 fingertip, 7 extensor, 2 nailbed, 1 lateral and 1 palmar aspect) were studied. One DU occurred in relation to underlying calcinosis. Four patients had two DUs imaged. The mean (SD) age of patients was 55.9 (16.1) years. The majority (n=9) had a history of severe digital vascular disease (DUs and intravenous vasodilator therapy). Mean (SD) Raynaud's phenomenon (RP) and disease duration (from first non-RP clinical manifestation) were 19.9 (15.9) and 14.0 (10.1) years, respectively. Almost all (n=9) patients were receiving drug therapies for digital vasculopathy.

For each DU, HFUS imaging (Episcan I-200, frequency 35MHz) was performed (using sterile ultrasound gel, taking approximately 10 minutes) along the visually apparent 'long' (the longest surface dimension) and 'short' axes (90° perpendicular to the 'long' axis) (Figure 1). The National Research Ethics Service: Committee North West-Preston approved the study, and signed patient consent was obtained.

Patient opinion on the feasibility ('not feasible', 'indifferent', 'very' or 'completely feasible') and amount of time to complete the HFUS ('too little time', 'just the right amount of time', 'too long') were collected. Patient-reported pain on a visual analogue scale (0-100, 100 being the most severe pain imaginable) associated with HFUS was documented.

Three raters (MH, GD and AM) decided by consensus agreement whether the image was 'classifiable' (*i.e.* that a measurement

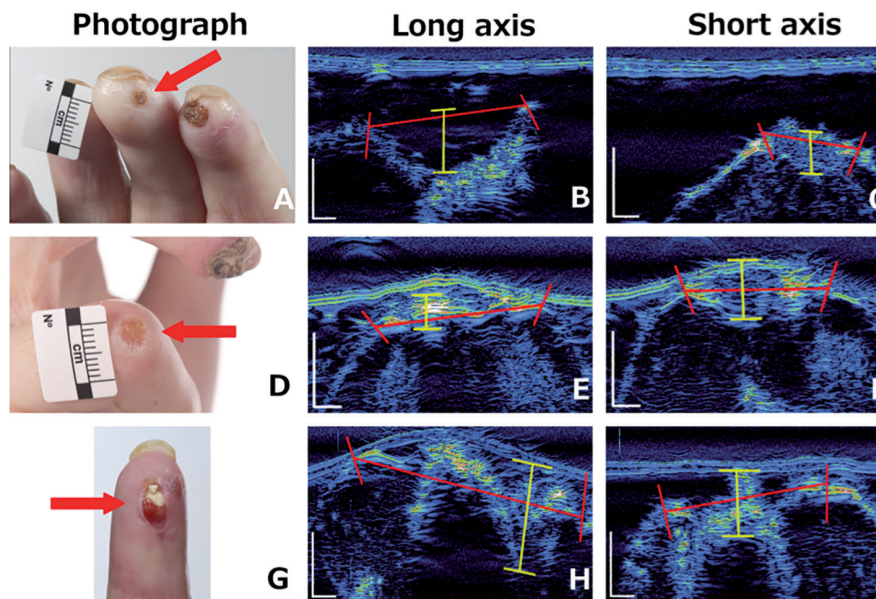


Fig. 1. DU HFUS. Clinical photographs (with the DU indicated by a red arrow) are presented (left column) with the HFUS 'long' (middle column) and 'short' (right column) images for fingertip (A-C) and extensor (D-F) DUs, and ulceration in relation to subcutaneous calcinosis (G-I). The coloured bars on the HFUS images indicate the measured DU width (red) and depth (yellow). The scale bar (bottom left) on the HFUS images represents 1mm in each direction.

of width and/or depth could be made). They then determined the edges of the DU at the surface of the skin by identifying changes in the surface layers or an appreciable change in profile (Fig. 1). Measurement of width and depth is depicted in Figure 1. HFUS was considered by the majority (n=10) of patients to be either 'completely' or 'very feasible', and in most patients (n=7) to take 'just the right amount of time'. The pain VAS (median [IQR]) associated with HFUS was low (0 [0-35]). The majority of DUs (n=13) had at least one image that was considered 'classifiable' with at least one width and depth measurement.

The mean (SD) DU depth was 0.99 (0.45) mm and width was 5.74 (2.16) mm. In conclusion, DU HFUS was considered feasible and was well tolerated in most patients. The majority of DUs had at least one image that was rated 'classifiable', allowing measurement of both width and depth. This was a small pilot study primarily addressing the feasibility and tolerability of DU HFUS. Further research is warranted to develop DU HFUS, with larger numbers of patients with a spectrum of DUs, including examination of validity including technique reliability.

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