

Acute haemodynamic response to carbon dioxide hand immersion in patients with systemic sclerosis evaluated by Doppler ultrasonography

Sirs,

Secondary Raynaud's phenomenon (sRP) is a frequent manifestation of systemic sclerosis (SSc) causing pain and digital ulcers. In SSc, small digital arteries are narrowed and constricted by concentric intimal hyperplasia, overproduction of collagen and dysregulation of vasoconstrictive and dilating molecular mechanisms (1).

Carbon dioxide (CO₂) hand immersion is applied as a component of the physical medicine regimen for sRP in SSc (2, 3) to increase distal digital blood flow. Immersion of the body into CO₂-enriched water has a long history in the treatment of peripheral vascular disorders based on the vasodilatory effects of CO₂. In patients with peripheral arterial occlusive disease, CO₂ baths can mobilise capillary perfusion (4) and serial application in primary and secondary Raynaud's syndrome can improve tolerance to cold (5).

In a small pilot study, we used color Doppler ultrasound with measurements of the resistance index (RI) of digital arteries (6–8) to quantify treatment effects of CO₂ hand immersion supplementing our previous work on synovial perfusion in wrist arthritis after local cryotherapy (9).

In the present study, twenty-one patients (19 females; mean age 58±12.4 years, range 23–73; mean disease duration 10±8 years, range 1–31) fulfilling the American College of Rheumatology criteria for SSc were compared with ten controls (8 females, mean age 49±12.8 years, range 28–67). Exclusion criteria were the presence of concomitant vascular disease, vasoactive medication and digital ulcers.

All examinations were performed in compliance with the Helsinki Declaration and approved by the local ethics committee. Written informed consent was obtained from each patient.

After the baseline ultrasound examination of the ulnar artery of the right index finger using a Logiq 7 Pro ultrasound machine (General Electric Medical Systems, USA) with a wide-band linear transducer (4.7–13 MHz), a standard hand immersion was performed using Bastian baths (2 g/l CO₂, 35°C; Bastian-Werk-GmbH, Munich, Germany) for 15 minutes. Further measurements and RI calculations were performed at 0, 5, 10 and 20 minutes after the hand bath (Fig. 1). RI values were calculated from a spectral Doppler curve using the following formula: $RI = (S-D)/S$, in which S is the peak systolic and D the end-diastolic velocity. The Wilcoxon signed-rank test was used for statistical analysis.

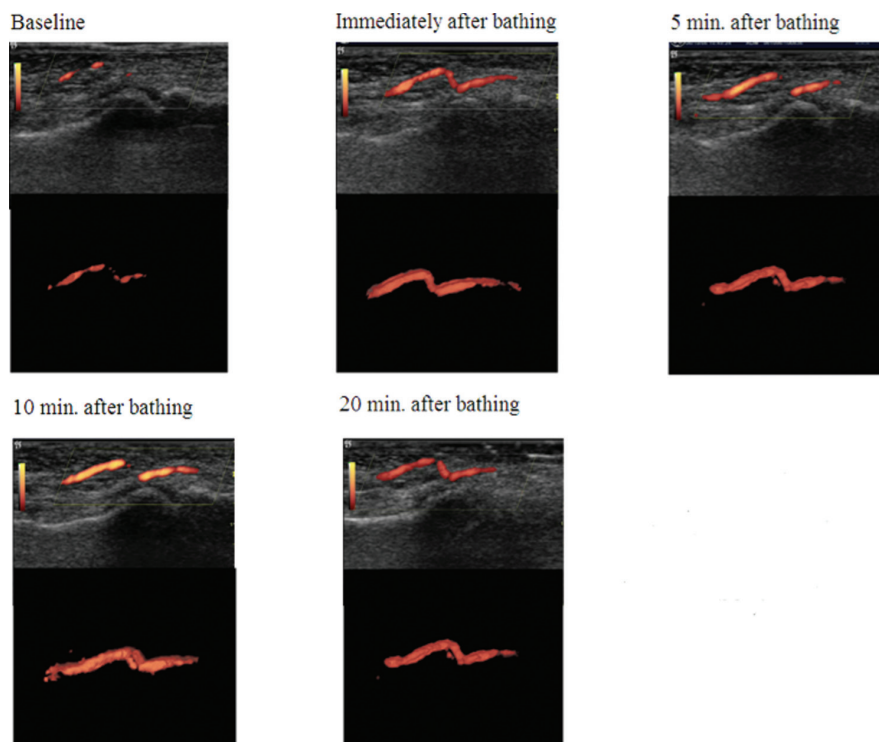


Fig. 1. 2D (upper images) and 3D (lower images) Doppler sonographic images of the ulnar artery of the index finger of a patient with SSc before (baseline) and at consecutive timepoints (0, 5, 10 and 20 minutes) after carbon dioxide hand immersion. The ulnar artery was scanned in the region of the proximal interphalangeal joint.

The mean RI at baseline (0.85 vs. 0.82) as well as the RI values over time after treatment were higher in SSc (0.73, 0.68, 0.68 and 0.75 at 0, 5, 10 and 20 minutes, respectively) than in controls (0.71, 0.7, 0.66 and 0.7, respectively). The difference in RI between the two groups was not significant. However, in keeping with the aim of the study, the achieved reductions in RI (delta-RI of 0.12, 0.17 and 0.17, respectively, at 0, 5 and 10 minutes, respectively) were significant ($p < 0.01$) in SSc, whereas in the controls (delta-RI of 0.11, 0.12, 0.16, respectively) they were not.

The higher baseline RI values in SSc are most likely due to structural changes in the vasculature, while higher levels compared to controls over time are probably due to reduced vascular dilative capabilities. These functional alterations most likely are modulated by CO₂, leading to a more significant decrease of the RI compared to controls. Of note, the investigated single CO₂ immersion shows considerable short-term improvement of acral perfusion, with the RI values not returning to baseline values after 20 minutes. Based on these results of a single CO₂ hand immersion, we suggest that regular application of this treatment modality may lower the RI consecutively and thus facilitate improvement of acral perfusion in the long term.

CO₂ hand immersion is a simple, inexpensive way for SSc patients to improve distal digital blood flow without notable adverse effects. Special equipment or experience

are not required, so that it can be used easily by physiotherapists and patients for the treatment of sRP.

In summary, this study for the first time shows the value of short-term CO₂ immersion baths on acral perfusion in SSc and the capability of Doppler ultrasound to visualise the respective treatment effects.

M. MÜLLER-ESCHNER^{1,2}

K. ALBRECHT³

I.H. TARNER⁴

U. MÜLLER-LADNER⁴

J. STRUNK⁵

U. LANGE⁶

¹Department of Diagnostic and Interventional Radiology, University Hospital Heidelberg;

²Dept. of Radiology, German Cancer Research Center (DKFZ), Heidelberg;

³German Society of Rheumatology, Berlin;

⁴Department of Internal Medicine and Rheumatology, Justus-Liebig-University, Giessen,

Department of Rheumatology, Clinical Immunology, Osteology and Physical Medicine, Kerckhoff-Klinik, Bad Nauheim;

⁵Department of Rheumatology, Porz Hospital, Cologne;

⁶Professorship of Rheumatology, Osteology and Physical Medicine, Department of Internal Medicine, Justus-Liebig-University Giessen, Department of Rheumatology, Clinical Immunology, Osteology and Physical Medicine, Kerckhoff-Klinik, Bad Nauheim, Germany.

Address correspondence to: Prof. Uwe Lange, MD, Department of Internal Medicine and Rheumatology, Justus-Liebig-University Giessen Kerckhoff-Klinik, Benckestrasse 2-8, D-61231 Bad Nauheim, Germany.

E-mail: u.lange@kerckhoff-klinik.de

Competing interests: none declared.

References

- MÜLLER-LADNER U, DISTLER O, IBBA-MAN-
NESCHI L, NEUMANN E, GAY S: Mechanisms of
vascular damage in systemic sclerosis. *Autoimmun-
ity* 2009; 42: 587-95.
- MEYER MF, DAIGELER A, LEHNHARDT M, STE-
INAU H, KLEIN HH: Therapeutic management of
acral manifestations of systemic sclerosis. *Med Klin*
2007; 102: 209-18.
- LANGE U, UHLEMANN C, BERG W, FETAJ S,
ENGEL JM: Physical medicine in rheumatology –
differential indicative prescription in collagen dis-
eases and vasculitides. *Akt Rheumatol* 2007; 32:
281-6.
- HARTMANN BR, BASSENGE E, HARTMANN M:
Effects of serial percutaneous application of carbon
dioxide in intermittent claudication: results of a
controlled trials. *Angiology* 1997; 48: 957-63.
- SCHMIDT J, MONNET P, NORMAND BB, FABRY
R: Microcirculatory and clinical effects of serial
percutaneous application of carbon dioxide in pri-
mary and secondary Raynaud's phenomenon. *Vasa*
2005; 34: 93-100.
- KEBERLE M, TONY HP, JAHNS R, HAU M,
HAERTEN R, JENETT M: Assessment of micro-
vascular changes in Raynaud's phenomenon and
connective tissue disease using colour doppler ul-
trasound. *Rheumatology* 2000; 39: 1206-13.
- KEBERLE M, TONY HP, HAU M, KESSLER C,
JAHNS R, JENETT M: Colour doppler ultrasound
of the nailbed: an objective tool for monitoring re-
sponses to vasodilatory treatment of connective tis-
sue disorders? *Rheumatology* 2001; 40: 954-5.
- BREGENZER N, DISTLER O, MEYRINGER R,
SCHÖLMEICH J, MÜLLER-LADNER U, LOCK
G: Doppler ultrasound identifies increased resistive
indices in SSc. *Ann Rheum Dis* 2004; 63: 109-10.
- STRUNK J, STRUBE K, KLINGENBERGER P,
MÜLLER-LADNER U, LANGE U: Two- and three-
dimensional doppler sonographic evaluation of the
effect of local cryotherapy on synovial perfusion in
wrist arthritis. *Rheumatology* 2006; 45: 637-40.