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Research Article

Thermal Disparity among Fingers and Its Amelioration by CO_2-Water Bathing in Connective Tissue Disease Patients

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Objective. Correlation between a low finger temperature and thermal disparity among fingers was studied in connective tissue disease (CTD) patients. Whether the thermal disparity may be ameliorated by hand immersion in a warm carbon dioxide- (CO_2-) water bath was analyzed. *Methods*. CTD patients with suspected peripheral circulation disorder underwent a thermography test. From before to 30 min after hand immersion in CO_2-water (CO_2 bathing; 1000 ppm CO_2, 42°C, 10 min), the nailfold temperatures were measured. The mean temperature (m-Temp) and the coefficient of variation of the temperature (CV = SD/m-Temp of one hand; the mean of CVs of both hands was adopted as the indicator of thermal disparity) were monitored. The correlation between m-Temp and CV was also analyzed. *Results*. Forty-seven (45 females and 2 males) patients were included, 32 of whom had Raynaud's phenomenon. The m-Temp was $30.8 \pm 3.0°C$ at the baseline, increased to $35.3 \pm 1.0°C$ immediately after CO_2 bathing, and remained significantly higher than that at the baseline until 30 min after ($32.1 \pm 1.9°C$). The CV was 0.0291 ± 0.0247 at the baseline, decreased to 0.0135 ± 0.0039 immediately after CO_2 bathing, and remained significantly lower than the baseline until 30 min after (0.0163 ± 0.0143). Between m-Temp and CV, a negative correlation was observed throughout the measurements. *Conclusion*. Thermal disparity was observed at baseline measurement in CTD patients. Warm CO_2 bathing markedly ameliorated the disparity, and this amelioration remained until after 30 min. Throughout the observation, the lower the m-Temp, the more severe the thermal disparity among fingers.

1. Introduction

Peripheral vascular involvement is one of the major features associated with connective tissue diseases (CTDs). We previously reported that thermal disparity among fingers is a characteristic feature of conditions with disturbed peripheral circulation including Raynaud's phenomenon [1]. CO_2 has long been known to improve peripheral circulation, with its effect usually observed after exposure of the whole body for a certain number of days [2]. In this study, we evaluated whether exposure to warm water containing CO_2 may ameliorate the thermal disparity among fingers and whether this amelioration can be achieved after only a short period of exposure. These are intriguing issues, and their clarification might in turn elucidate the pathophysiology of some peripheral vasculature diseases.

2. Patients and Methods

Patients who visited the Japanese Red Cross Medical Center, were diagnosed as having a CTD, and were suspected of having peripheral circulation disorder as determined by their doctors in charge were included. They underwent a thermography test before and after immersing their hands in CO_2-water. The test was performed within the routine clinical setting under the public health insurance system, and the results were retrospectively analyzed.

After acclimatization to room temperature (25°C) for 15 min, both hands were immersed into a 42°C CO_2-water bath for 10 min (CO_2 bathing). The water contained 1,000 ppm CO_2 (Carbothera Onpar™, Mitsubishi Rayon Cleansui Co., Ltd., Japan). Before (-10 min) and 0, 3, 5, 10, 15, 20, and 30 min after CO_2 bathing, nailfold temperature (Temp) of the ten fingers was measured by thermography (INFRAEYE3000™, Nihonkoden, Japan). CO_2 bathing and Temp measurement were carried out in a sitting position with the hands placed at a level below the heart throughout the test.

As an indicator of thermal disparity among fingers, the coefficient of variation (CV) was adopted. CV was calculated as SD/mean temperature (m-Temp). In this study, the mean of right and left hand CVs was used throughout. The correlation between m-Temp and CV was also examined. Results were statistically analyzed by the paired t-test.

This work was supported by Research Award, Japanese Society of Balneology, Climatology and Physical Medicine, 2016. This study was approved by the Ethics Committee, Chiba Central Medical Center: H30-R19.

3. Results

Forty-seven (45 females and two males) patients aged 59.5 ± 18.4 were included. Thirty-two had Raynaud's phenomenon. The underlying CTDs were primary Sjögren disease in nine, pernio in nine, primary Raynaud disease in eight, systemic lupus erythematosus in five, systemic sclerosis in two, mixed connective tissue disease, calcinosis–Raynaud phenomenon–esophageal dysmotility–sclerodactyly–telangiectasia syndrome, polyarteritis nodosa, and Hashimoto disease in one each, and undifferentiated connective tissue disease in 10. Five were taking prednisolone (5 ± 0 mg/day), and 34 a PGI2 derivative (beraprost Na, 60 μg/day).

The time-course changes in Temp of each finger of one hand of a patient are shown in Figure 1 as a representative case. In this patient, the baseline Temp varied from finger to finger, resulting in a high CV at baseline. Then, after CO_2 bathing, the thermal disparity disappeared, and CV diminished.

In Figure 2(a), the m-Temp at each measurement of each patient is plotted in a single line. In Figure 2(b), the changes in the mean and SD of the m-Temps of the 47 patients enrolled are shown. The means and SDs of the m-Temps were 30.8 ± 3.0°C at the baseline, 35.3 ± 1.0°C at 0 min, 32.6 ± 0.9°C at 3 min, 32.6 ± 1.0 at 5 min, 32.5 ± 1.4 at 10 min, 32.4 ± 1.6 at 15 min, 32.4 ± 1.8 at 20 min, and 32.1 ± 1.9°C at 30 min after CO_2 bathing ($p < 0.001$, baseline vs. each measurement after CO_2 bathing; $p < 0.001$, immediately after vs. 5 to 30 min after; ns, 3 min vs. 5 to 20 min after; and $p < 0.05$, 3 min after vs. 30 min after).

The time-course changes in the CV in each patient are plotted in a single line in Figure 3(a). Figure 3(b) shows that the means and SDs of CVs were 0.0291 ± 0.0247 at the baseline, 0.0135 ± 0.0039 at 0 min, 0.0147 ± 0.0058 at 3 min, 0.0145 ± 0.0075 at 5 min, 0.0150 ± 0.0115 at 10 min, 0.0156 ± 0.0126 at 15 min, 0.0164 ± 0.0129 at 20 min, and 0.0163 ± 0.0143 at 30 min after CO_2 bathing ($p < 0.001$, baseline vs. each measurement after CO_2 bathing; ns, 3 min vs. 5 to 30 min after).

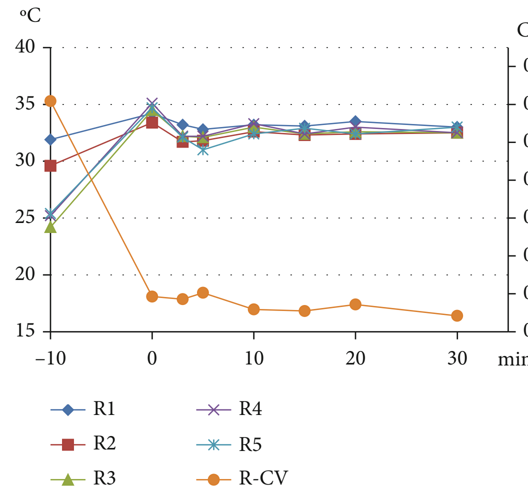

Figure 1: Time-course changes in Temp of each finger of the right hand (R1–5), before and after CO_2 bathing, in a 59-year-old female patient with Raynaud disease. Change in CV is also plotted. Temp: nailfold temperature; CV: coefficient of variation.

When dividing the patients into two groups with a baseline CV lower and higher than the mean, 30 patients showed a lower CV. In these 30 patients, their mean CVs were similar in all the measurements and no significant difference was observed between the baseline CV and each CV after CO_2 bathing (data not shown). On the other hand, in all of the 17 patients with a CV higher than the mean at the baseline, CV decreased significantly after CO_2 bathing, and a statistically significant decrease from that at the baseline was observed in all the measurements. In this latter group, after the initial CV decrease, CV reincreased gradually, and from 15 min after CO_2 bathing until the last measurement, CV became significantly higher than that immediately after CO_2 bathing (data not shown).

The correlation between m-Temp and CV is shown in Figure 4 for each measurement. At the baseline, both m-Temp and CV differed from patient to patient; CV showed a tenfold difference. Patients with a higher CV showed a wide range of m-Temps. In patients with a lower CV, mostly a higher Temp was observed. Immediately after CO_2 bathing, data points appeared clustered; the patients with a lower Temp and/or a higher CV at the baseline showed a higher Temp and a lower CV. Then afterward, the data points gradually returned to their original positions prior to CO_2 bathing. However, Temp increase and CV decrease were still preserved 30 min after. Between m-Temp and CV, a significant correlation was observed in all the measurements ($p < 0.05$, at any measurement).

4. Discussion

Disturbed peripheral circulation is one of the major features of CTDs. Not only the extremities but also internal organs including the lungs and intestines may also be involved in it, sometimes resulting in severe diseases such as pulmonary

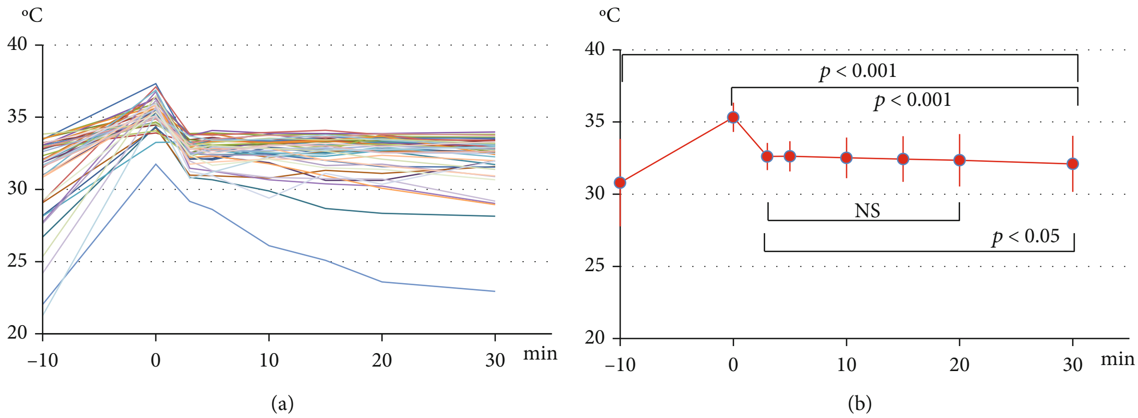

Figure 2: (a) Time-course changes in m-Temps of both hands in 47 patients. The m-Temp of each patient is plotted in a single line. (b) Means and SDs of m-Temps. m-Temp: mean nailfold temperature.

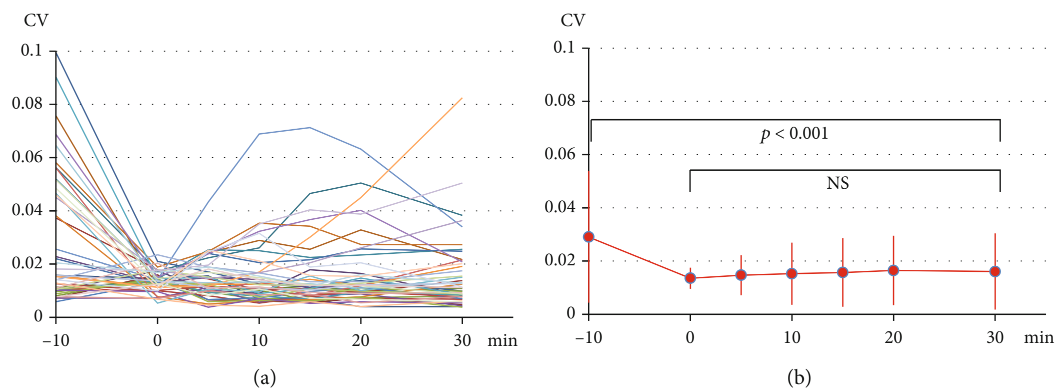

Figure 3: (a) Time-course changes in the mean CV of both hands in 47 patients. The mean of each patient is plotted in a single line. (b) Means and SDs of CVs. CV: coefficient of variation.

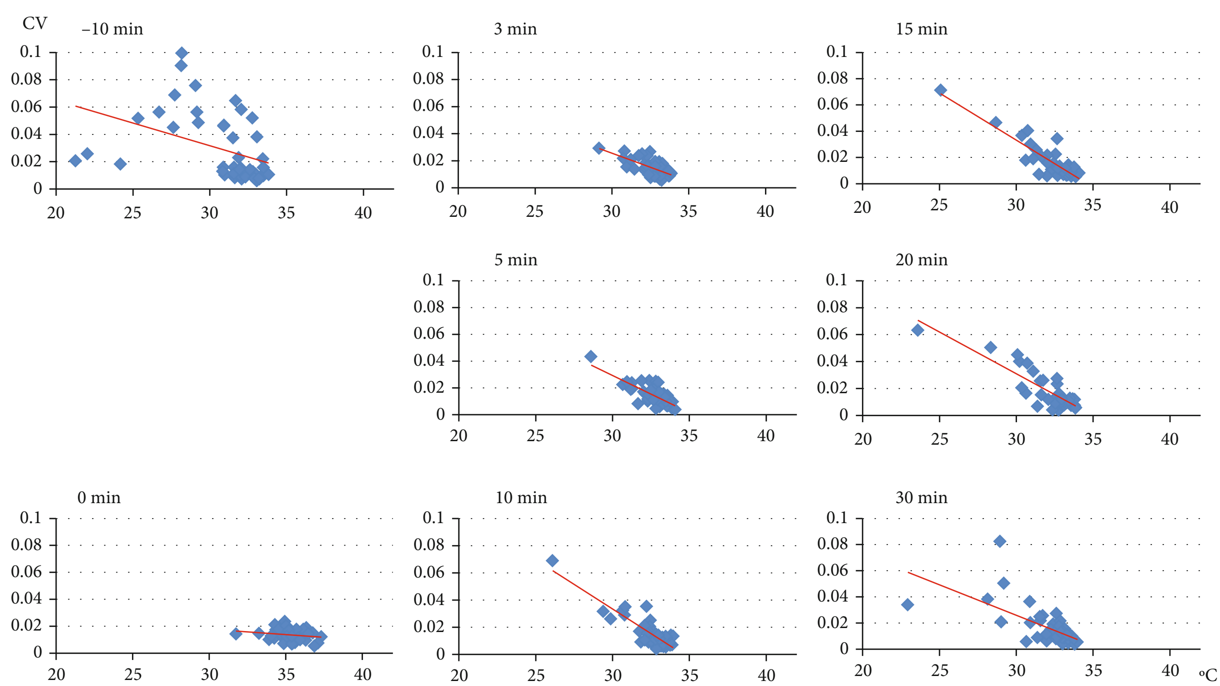

Figure 4: Correlation between m-Temp (X-axis) and CV (Y-axis) at each measurement in 47 patients. $p < 0.01$ for all of the measurements. m-Temp: mean nailfold temperature; CV: coefficient of variation.

hypertension and pseudoileus. Recurrent vasoconstriction, narrowing, or obstruction may develop in small-caliber peripheral vasculatures; the possible pathogenetic mechanisms of which include autonomic nerve system dysfunction, vasculitides, and remodeling of the vascular structure. They are thought to develop usually unevenly from vessel to vessel. A notable case is Raynaud's phenomenon, in which the skin surface color and temperature differ markedly among fingers, not only at an attack but also even at the time without an attack (Figure 1). We have observed a thermal disparity in patients with Raynaud's phenomenon [1]. As an indicator of this thermal disparity, CV would be appropriate to be adopted.

In this study, we focused on thermal disparity. Here, we basically determined whether a low m-Temp, which is due to poor peripheral perfusion, is associated with a high CV. This association is clearly shown in Figure 4; at each measurement, a statistically significant negative correlation was observed between m-Temp and CV. An additional noteworthy observation is that at the baseline, three patients with a substantially low m-Temp did not show a very high CV (Figure 4, -10 min); it is considered that long-standing invasion might have led to diffuse vascular remodeling, resulting in a markedly low temperature in all fingers and consequently in a rather low CV. As far as we know, no study focusing on thermal disparity as an indicator of disturbed perfusion has been reported except for our previous report [1].

When adopting CV change to evaluate an effect of CO_2 bathing, only a 10 min exposure clearly decreased CV. Immediately after CO_2 bathing, simultaneously with an m-Temp increase, CV markedly decreased, as shown by the clustered data points in Figure 4. This likely reflected a greater increase in blood flow in fingers with disturbed perfusion. Another possible explanation is that cooling to the baseline Temp level after warm CO_2 bathing easily occurs in fingers with well-maintained perfusion. However, this is not likely because that as is shown in Figure 1, fingers with a primarily low Temp did not show a higher temperature than others with a primarily high Temp after CO_2 bathing. If flowmetry was also carried out in addition to thermometry, it might be helpful in analyzing the flow [3–6], although flowmetry has not been widely used in a routine clinical setting. The CV decrease was sustained until 30 min after CO_2 bathing (Figures 1 and 3). This sustained CV decrease was in contrast to the Temp increase; m-Temp finally decreased significantly 30 min after CO_2 bathing not only from m-Temp immediately after but also from m-Temp 3 min after bathing (Figure 2). Amelioration of thermal disparity by CO_2 bathing was outstanding.

Therapies that can ameliorate the disparity would be beneficial and should be applied. Natural spring of CO_2-water has long been known to have a warming effect and to cure vascular disorders ever since the Middle Ages [5]. In recent investigations, not only long-term but also short-term exposure to CO_2-water has been examined. Ogoh et al. showed that lower-leg immersion in 38°C water containing 1000 ppm CO_2 for 20 min enhanced skin blood flow, possibly through endothelial-cell-mediated vasodilatation [7]. Finzgar et al. reported that 35 min gaseous CO_2 exposure of a lower limb increased laser Doppler flux [8]. Nishimura et al. showed cutaneous blood flow increase with repeated CO_2-water bathing [9]. Some of the studies compared the effect of CO_2-water to tap water. Regarding the pathological aspect, Akahane et al. showed that a significantly larger number of capillaries were formed four weeks after muscle injury in rats with transcutaneous CO_2 therapy than in rats without it [10].

To the best of our knowledge, this is the first report of an effect of CO_2 bathing focusing on thermal disparity. Although infrared thermography has long been used in various studies, it has never been applied to study from this point of view [11–15]. As a limitation of this study, only a single exposure to CO_2 was carried out. Repeated bathing for a substantial duration might potentially reverse remodeling, resulting in recovery from vascular involvement that frequently develops in CTDs. Comparison to the effect with tap water will show a difference, as studies adopting both CO_2 and tap water have shown a better effect with the former.

5. Conclusion

In conclusion, this study showed that thermal disparity among fingers is a characteristically important finding of disturbed peripheral perfusion in CTD, that the lower the finger temperatures, the higher the thermal disparity, and that CO_2 bathing ameliorated the thermal disparity until after 30 min.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors have no conflict of interest related to this study and no related exclusive license.

Authors' Contributions

Both authors contributed to conception and design. Yasuo Kijima mainly collected the data. Analysis and interpretation of data were mainly by Shigeko Inokuma.

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