Microcirculation of the Ankle after Cryo/Cuff Application in Healthy Volunteers

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Abstract

The aim of the study was to assess the combination of compression and cryotherapy (Cryo/Cuff ankle device) on parameters of ankle microcirculation in healthy volunteers over 30 min. In 21 volunteers (12 males, 29 ± 10 years [incl. females], BMI 24 ± 3) the Cryo/Cuff ankle device (AIRCAST, Summit, NJ, USA) was applied with continuous assessment of parameters of ankle microcirculation, such as tissue oxygen saturation (SO2), relative postcapillary venous filling pressures (rHb), and microcirculatory blood flow at 2- and 8-mm tissue depths during 30 min with the Oxygen-to-see System, a laser-Doppler-spectrophotometry-system (LEA Medizintechnik, Gießen, Germany). Superficial tissue oxygen saturation (SO2, 48 ± 19%) immediately dropped to 23 ± 15% (– 52%, $p < 0.05$) within the first 2 min after Cryo/Cuff activation with a consecutive slow decrease to 32 ± 23% (– 32%, $p < 0.05$ vs. baseline) after 30 min. Deep SO2 (8 mm, 69 ± 5%) did not change within 30 min of Cryo/Cuff application (70 ± 4%, n.s.). Superficial postcapillary venous filling pressures (61 ± 17 relative units) showed an immediate and sustained decrease after Cryo/Cuff application within four minutes to 37 ± 18 relative units (– 39%, $p < 0.05$). Deep postcapillary venous filling pressures (85 ± 20 relative units) dropped within the first four minutes of Cryo/Cuff application to 68 ± 19 relative units (– 20%, $p < 0.05$). Superficial microcirculatory blood flow (21 ± 36 relative units) decreased significantly to 7 ± 5 relative units after 30 min (– 69%, $p < 0.05$ vs. baseline). Deep microcirculatory blood flow at 8 mm tissue depth (63 ± 43 relative units) significantly decreased over the 30 min to 39 ± 23 relative units (– 47%, $p < 0.05$ vs. baseline). Using the Oxygen-to-see system we could demonstrate significant effects of the Cryo/Cuff device on the ankle level in healthy volunteers with reduced superficial tissue oxygen saturation with preserved deep tissue oxygen saturation, reduced superficial and deep postcapillary venous filling pressures, and reduced superficial and deep microcirculatory blood flow as a function of time. Further clinical studies are mandatory to elucidate the effects of the Cryo/Cuff device on the microcirculatory environment in injured ankles.

Key words
Cryotherapy · sport · ankle · microcirculation · cooling · compression

Introduction

Cryotherapy as part of the RICE therapy regimen with *rest, ice, compression, and elevation* is a basic treatment principle of acute soft tissue injuries. It is thought to reduce swelling and pain by various mechanisms [11]. Cryotherapy reduces deep-tissue temperature both, in animals and in humans, in a time- and application-dependent manner [2,16]. Vasodilatation, increased capillary permeability with fluid extravasation and swelling, metabolic changes, and increased proinflammatory cytokines are associated with soft-tissue injuries.

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Nevertheless, evidence-based data on the crucial effects of cryotherapy and compression regarding physiological parameters such as the tissue temperature decrease, capillary vasoconstriction or metabolic effects are not available. Furthermore, until now, the impact of combined compression and cryotherapy, such as achieved by the AIRCAST Cryo/Cuff system has not been evaluated clinically and time-dependent concerning parameters of microcirculation, such as tissue oxygen saturation, postcapillary venous filling pressures, and capillary flow. This study sought to evaluate their impact in respect of distinct tissue depths on the microcirculatory parameters throughout 30 minutes of combined application of cryotherapy and compression by the AIRCAST CryoCuff ankle device.

Fig. **1** O2C-System of LEA Medizintechnik, Gießen, Germany.

Methods

Twenty-one patients (12 males, 29 ± 10 years, BMI 24 ± 3) were enrolled in this prospective study after informed consent. Regarding the sports history, 14 participants performed endurance training on a regular basis (running, triathlon, median 3.1 h per week [1 – 11.5 h per week]), 7 participated in ball sports (5.6 h per week [0.5 – 14 h per week]), 3 in gymnastics (6.6 h per week [1 – 15 h per week]), 5 performed inline skating (4.2 h per week [1.5 – 6.5 h per week]), 4 performed swimming (2.4 h per week [1 – 4 h per week]), 7 participated in fitness training or power lifting (6.1 h per week [1.5 – 10 h per week]), and 2 did equestrian sports (3.5 h per week [2 – 5 h per week]). One participant had an evident partial Achilles tendon tear, and one had a muscle tear of the gastrocnemius muscle on the other, non-studied side. Two participants smoked less than 5 cigarettes a day, two smoked more than 10 cigarettes a day, 17 participants were non-smokers. Two participants took non-chinolon-antibiotics within the past 6 months, but not within the study interval. Six participants were on oral contraceptives, two took non-steroidal antiphlogistic drugs (aspirin), and one patient was on inhalative salbutamol due to asthma.

Exclusion criteria were open wounds at the ankle level, any history of M. Raynaud or other vasospastic diseases, cold hypersensitivity, or diseases with comprised local circulation, such as diabetes mellitus.

Determination of vital parameters of the microcirculation

The determination of hemoglobin and the principle of blood flow measurement are combined in the *O2 C* system. The local oxygen supply parameters, blood flow, oxygen saturation of hemoglobin SO_2 (%), and amount of local hemoglobin rHb are recorded by an optical fibre probe (O2C – Oxygen to see, LEA Medizintechnik, Gießen, Germany, Fig. **1**). The Oxygen-to-see system has been applied both, in animals and in humans, in the assessment of the microcirculation of different parts of the body, such as the sternum after harvesting of the left internal mammary artery in coronary revascularisation, and palmar microcirculation after harvesting of the radial artery as a coronary bypass graft [12].

Laser Doppler flowmetry

The tissue is illuminated with coherent laser light of 830 nm and 30 mW from a laser diode through a fiber optic light guide. Backscattered light is collected by the same probe and frequency shifted light extracted by heterodyne light beating technique. The power-spectral density of shifted light is a linear function of the average velocity of moving cells within the tissue. As laser doppler flowmetry detects all moving particles of certain velocity, it measures blood flow.

Measurement of volume

Laser Doppler perfusion measurements can increase sampling depth by using near-infrared laser light and changing detector geometry. Although it is commonly accepted that separation and use of light in the near infrared light range increases sampling depth actual measurements and calculations in the range of the used probe (separation 2 – 4 mm) are rare. In the near infrared range a mathematical model for measurements of skin blood oxygenation estimated a fiber separation of 400 – 800 µm for the blood sample. A measurement depth of 3.4 mm was shown with a fiber separation of 6 mm with fiber diameter of 3 mm.

Tissue spectrophotometry

Light of the visible range is irradiated into tissue. Backscattered light spectrum is measured over the whole range from 500 – 630 nm through the same glass fiber probe. Light penetrates into the tissue and is partly absorbed, reflected, and scattered. The main absorber hemoglobin changes its absorption characteristics with oxygen saturation. Fully oxygenated hemoglobin has two absorption peaks at 542 and 577, deoxygenated blood one at 556 nm. By fitting measured spectra with spectra of known oxygen saturation, the oxygen saturation of the microvessel blood is calculated with appropriate algorithms the additional absorption by other tissue chromophores like melanin and cytochrome. Measured spectra is further influenced by the path length of photon through tissue. Different tissue models have been used in the past to simulate the path of a photon through tissue, in order to determine multiple scattering influences on absorbance spectra. Here a modified diffusion approximation to the transport equation is used, that includes changes in the whole spectra to estimate scattering influence and absolute oxygen saturation values are calculated. Information is mainly gathered from small arteries, capillaries, and venules, as light entering vessels larger than 100 µm is completely absorbed [8]. As 85 % of the hemoglobin is in the capillary-venous compartment of the microcirculation, measurements with the spectrophotometer reflect mainly the capillary-venous oxygen saturation.

Oxygen saturation of hemoglobin is calculated in percent SO_2 (%) which is an absolute measure. The local amount of hemoglobin is calculated in relative units rHb (rAU), processed from the spectral absorption of the hemoglobin. The hemoglobin amount (rHb) is measured by the sum of absorption at all wavelengths ("area under the curve") and is corrected by the characteristic differences in absorption; fully oxygenated blood absorbs about 15% more than deoxygenated blood. As with hemoglobin amount measurement volume is changed, the hemoglobin values are relative values and reflect the filling of vessels or vessel density per catchment volume.

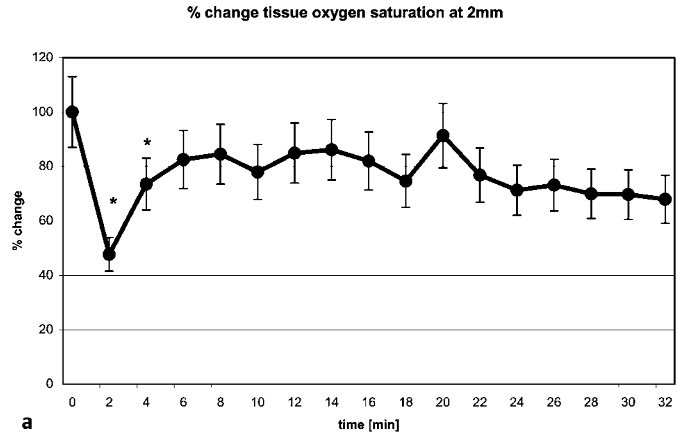

Fig. **2a** Percent change (%) of superficial tissue oxygen saturation at 2 mm tissue depth after cryo cuff ankle application over time in 21 patients.

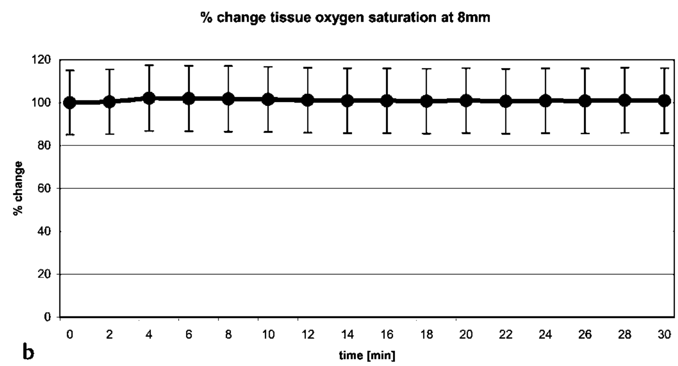

Fig. **2b** Percent change (%) of deep tissue oxygen saturation at 8 mm tissue depth after cryo cuff ankle application over time in 21 patients.

Cryo/Cuff application

A Cryo/Cuff (AIRCAST, Inc., Summit, NJ, USA) cryotherapy device was applied to the right ankle and filled with water of 15 °C temperature according to the manufacturer's recommendation, with additional crushed ice filled in the system. The Oxygen-to-see probe was placed below the Cryo/Cuff ankle bandage at the medial aspect of the ankle before preparing the system with water. After initial baseline assessment of parameters of microcirculation, such as tissue oxygen saturation, relative postcapillary venous filling pressures, and microvascular blood flow at two distinct tissue depths (2 mm and 8 mm), water and ice was filled into the Cryo/Cuff system and measurements were continuously recorded over 30 min of cryotherapy. A 30-min period was chosen to assess possible early and late effects on superficial and deep parameters of microcirculation in a time- and depth-dependent manner.

Statistics

The data is presented as median and range for continuous variables or number and percentages for dichotomous variables. Univariate analysis of categorical data was carried out using the chi-square or Fisher exact tests. A p-value less than 0.05 was considered to indicate statistical significance. The SPSS statistical software package 11.5 for Windows (SPSS Inc., Chicago, Ill, USA) was used for statistical analysis.

Results

None of the enrolled 21 patients had any skin burns or nerve palsies, such as paresthesias or paresis, caused by the Cryo/Cuff ankle device applied for 30 min.

Tissue oxygen saturation

Tissue oxygen saturation was assessed simultaneously at two distinct tissue depths (2 mm and 8 mm, Fig. **2a** and **b**). Superficial tissue oxygen saturation at 2 mm was 48 ± 19% at baseline, immediately dropping to 23 ± 15% (– 52%, $p < 0.05$) within the first 2 min after Cryo/Cuff activation following water inflation, followed by a significant increase vs. the lowest level in the following minutes 4 to 8 (to – 18% vs. baseline, $p < 0.05$), with a consecutive slow decrease to 32 ± 23% (– 32%, $p < 0.05$ vs. baseline) after 30 min of Cryo/Cuff application. Deep tissue oxygen saturation at 8 mm was 69 ± 5% at baseline conditions, with no significant change after inflation of the Cryo/Cuff device nor any further change within 30 min of Cryo/Cuff application (70 ± 4%, n.s.).

Postcapillary venous filling pressures

Superficial postcapillary venous filling pressures at 2 mm tissue depth were 61 ± 17 relative units, with an immediate decrease after Cryo/Cuff application within four minutes to 37 ± 18 relative units (– 39%, $p < 0.05$, Fig. **3a**). Superficial postcapillary venous pressures did not significantly change after minute 4 over the 30 min (– 31%, 42 ± 19 relative units at minute 30, $p < 0.05$ vs. baseline). Deep postcapillary venous filling pressures at 8 m tissue depth were 85 ± 20 relative units at baseline with a significant drop within the first four minutes of Cryo/Cuff application to 68 ± 19 relative units (– 20%, $p < 0.05$) and a tendency to increase over the 30 min of Cryo/Cuff application (78 ± 19 relative units, – 8% vs. baseline, n.s., Fig. **3b**).

Microcirculatory blood flow

Superficial microcirculatory blood flow at 2 mm tissue depth was 21 ± 36 relative units at baseline, decreasing significantly within the first 10 min of Cryo/Cuff application to 9 ± 7 relative units (– 57%, $p < 0.05$) with a consecutive slow decrease to 7 ± 5 relative units after 30 min of Cryo/Cuff application (– 69%, $p < 0.05$ vs. baseline, Fig. **4a**). Deep microcirculatory blood flow at 8 mm tissue depth was 63 ± 43 relative units at baseline, increasing immediately after Cryo/Cuff application to 85 ± 19 relative units (+ 18%, $p < 0.05$), followed by a significant decrease over the

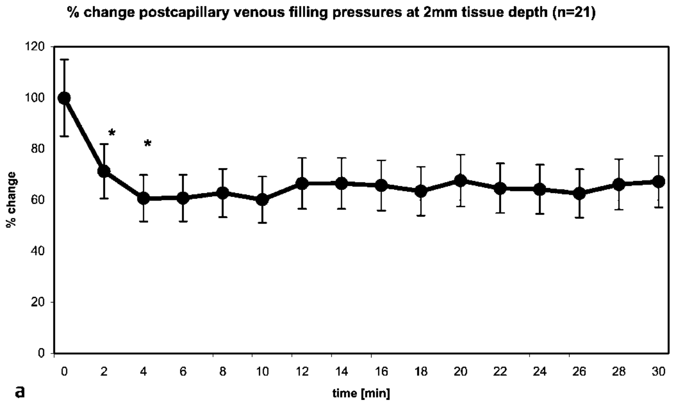

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Fig. **3a** Percent change (%) of superficial relative postcapillary venous filling pressures at 2 mm tissue depth after cryo cuff ankle application over time in 21 patients.

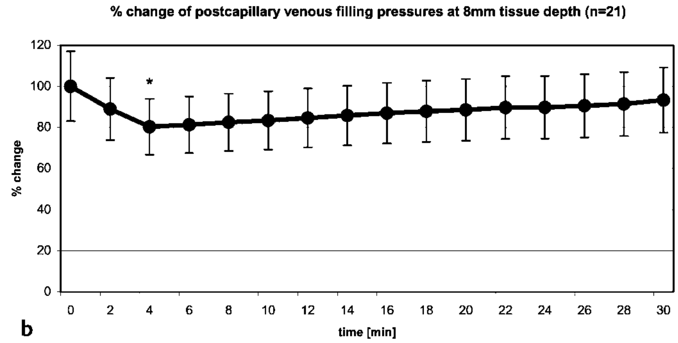

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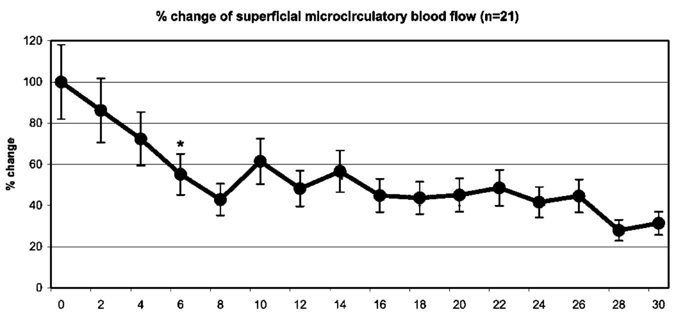
Fig. **3b** Percent change (%) of deep relative postcapillary venous filling pressures at 8 mm tissue depth after cryo cuff ankle application over time in 21 patients.



a

Fig. **4a** Percent change (%) of superficial microcirculatory blood flow at 2 mm tissue depth after cryo cuff ankle application over time in 21 patients.

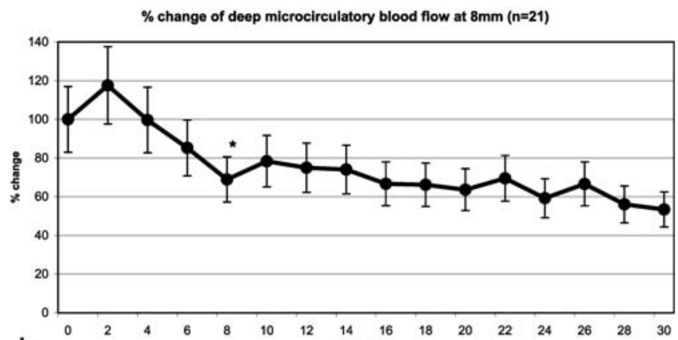


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Fig. **4b** Percent change (%) of deep microcirculatory blood flow at 8 mm tissue depth after cryo cuff ankle application over time in 21 patients.

30 min with 39 ± 23 relative units after 30 min (– 47%, $p < 0.05$ vs. baseline) of Cryo/Cuff application (Fig. **4b**).

Discussion

The crucial findings of our study are:

1. Cryo/Cuff ankle device changes parameters of microcirculation in healthy volunteers within the first 10 min of 30 min application significantly.
2. Different tissue-depths-specific effects of the Cryo/Cuff device could be documented. While superficial tissue oxygen saturation at 2 mm is significantly reduced within the first 6 – 8 min of application, deep tissue oxygen saturation at 8 mm did not alter within 30 min of Cryo/Cuff ankle application. Superficial and deep relative postcapillary venous filling pressures behave similarly, with an immediate drop of 40% vs. 20% within the first four minutes of application and a consecutive further slight increase over 30 min. Superficial and deep microcirculatory flow decreases significantly with a sudden drop within the first 10 minutes of Cryo/Cuff application and a sustained reduction to 60% vs. 40%, respectively.
3. The Oxygen-to-see system is an objective novel method to detect parameters of microcirculation of the soft tissue in different tissue depths.

The RICE therapy regimen with *rest, ice, compression, and elevation* is a basic treatment principle of acute soft tissue injuries. It is thought to reduce swelling and pain by various mechanisms [11]. Vasodilatation, which occurs after soft tissue injuries, as well as the increased hydrostatic pressure in dilated capillaries increases serous fluid extravasation leading to tissue swelling. Cold application may diminish swelling by a time-dependent constriction of superficial cutaneous vessels with consecutive decreased capillary permeability and haemorrhaging [11]. Regarding the metabolic level, cryotherapy reduces cellular respiration and enzyme release of damaged tissue with inflammatory mediators by reducing the energy needs of a cell and thereby decreasing the oxygen consumption [17]. A 10 °C reduction in intraarticular temperature may decrease the local metabolic activity up to 50% [21]. On a collagen level cryotherapy may enhance the elastic properties of collagen by increasing the stiffness and resistance to stretch [14].

Vascular effects of cryotherapy are complex with a decrease of peripheral blood flow of soft tissue up to 26%. To the best of our knowledge only a few working groups examined the microvascular effects of cryotherapy without compression with significant reduction of microvascular perfusion after 20 min of cryotherapy, an effect, which was reversed within 4 h after removal of the ice [5]. Karunakara and coworkes examined different regimens of cold application on forearm blood flow, assessed by a bilateral tetrapolar impedance plethysmograph which was used with venous occlusion to measure changes in local limb blood volume at the forearm for a period of up to 60 min resulting in a significant forearm blood flow reduction when a prolonged intermittent cold application was used compared to a single cryo application [10].

We could demonstrate significant effects of the Cryo/Cuff device on the ankle level with reduced superficial tissue oxygen saturation with preserved deep tissue oxygen saturation, reduced superficial and deep postcapillary venous filling pressures, and reduced superficial and deep microcirculatory blood flow as a function of time especially within the first 10 min of Cryo/Cuff application. These data tie with the results of MacAuley [13] reviewing the physiological effects of ice, demonstrating that 10 min of iced water applied through a wet towel for repeated periods of 10 min are most effective. Based on these data, one could advise to use the ankle Cryo/Cuff device for at least 10 min. If a further intermittent exposure of Cryo/Cuff for at least 10 min would be of further benefical effect has to be proven in prospective clinical trials. Using the identical setting with a plethysmograph applied to the lower limb, data on the ankle could be derived [21,22], demonstrating a maximum decrease of blood volume after cool pack application after 13.5 min, which is in line with our experimental data as well as those of MacAuley [13].

There is accumulating evidence that cryotherapy can reduce deep-tissue temperature in a time-dependent manner in humans [6]. In 12 patients after routine knee arthroscopy with intraarticular placed thermocouple probes in the medial gutter and suprapatellar pouch, the AIRCAST Cryo/Cuff at the knee level used during the first postoperative hour resulted in a significant temperature drop of 6° Celsius vs. control, demonstrating that the entire synovium is cooled after Cryo/Cuff knee application in this patient group [15]. The combination of cryotherapy and compression, such as in the Cryo/Cuff system, seems to reduce the tissue temperature to a greater degree vs. cryotherapy alone [9]. Only one clinical study has yet compared ice and compression vs. ice alone in post-ACL reconstruction patients, with reduced intramuscular and oral analgesia in the ice and compression group [4]. Comparing ice and compression vs. compression alone, only two studies up to now could demonstrate a significant decreased analgesic consumption after ACL reconstruction and a better improvement of postoperative ROM [1,18]. Regarding the postoperative use of cryotherapy and compression, one has to take into account that postsurgical dressings or socks separate the injured area from the cooling device, therefore functioning as a barrier which might mitigate the cryotherapy effects of such devices [3]. We could demonstrate that the effects of the Cryo/Cuff ankle device on parameters of microcirculation are time-dependent with greater effects in the superficial layers immediately within the first 10 min of application, therefore the "barrier theory" seems plausible in this setting. Nevertheless, as analysed by Bleakley et al. in a systematic review of randomized controlled trials on the use of ice in soft-tissue injuries, most of the studies published on this issue lack scientific accuracy and detailed description of the terms and time frames of cryotherapy application. Further, high-quality studies are mandatory to elucidate the value and timing of application of cryotherapy in soft-tissue injuries during immediate and rehabilitative care.

Complications

Deleterious effects of the ice application have been reported, such as skin burns and nerve palsies even after 20 – 30 min of cooling [19,20]. During our 30-min Cryo/Cuff application none of these complications occurred.

Conclusions

Using the Oxygen-to-see system we could demonstrate significant effects of the Cryo/Cuff device on the ankle level in healthy volunteers with immediate reduced superficial tissue oxygen saturation with preserved deep tissue oxygen saturation, reduced superficial and deep postcapillary venous filling pressures, and reduced superficial and deep microcirculatory blood flow as a function of time. The crucial effects on parameters of microcirculation were evident within the first 10 min of Cryo/Cuff ankle application. Further clinical studies are mandatory to elucidate the effects of the Cryo/Cuff device on the microcirculatory environment in injured ankles as well as the timing of the Cryo/Cuff device, such as in intermittent sessions at 10-min intervals.

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