External compression increases forearm perfusion

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Application of compression stockings to the lower extremities is a widely used therapeutic intervention to improve venous return, but there is little information about the effects of compression on local arterial perfusion. Therefore, we tested the hypothesis that a positive external pressure increases forearm perfusion. The relation of increasing external pressure induced by standardized compression to the arterial inflow and arterial flow reserve of the forearm was critically evaluated in a group of healthy young men (n = 9). Flow was measured with venous occlusion plethysmography under baseline conditions. Then the compression sleeve was applied to the right forearm (in general, the dominant arm) for 10 min. At the end of this intervention period (within 10 min), the blood flow was measured again under baseline conditions. The blood flow of both forearms was measured with venous occlusion plethysmography. The cost of compression pressure increasing from 13 to 23 mmHg. During compression, the arterial inflow increased significantly from 3.7 ± 0.85 to 8.8 ± 2.01 ml/min/100 ml tissue−1 (P < 0.001) and the arterial flow reserve increased from 17.7 ± 4.7 to 28.3 ± 7.0 ml/min/100 ml tissue−1. The flow increase was persistent after 3 h of constant application of external pressure and also during simultaneous low-intensity hand grip. Similar results obtained with occlusion plethysmography were seen with MRI. During the interventions, forearm temperature was unchanged, and the volunteers reported no discomfort. In conclusion, 1) arterial perfusion of the human forearm increases more than twofold during application of external compression over a pressure range of 13–23 mmHg, and 2) the result is interpreted as an autoregulatory response following the decrease of the transmural pressure gradient.

METHODS

Measurement Protocol

The effect of compressive pressure on forearm blood flow was tested in a group of nine healthy young men (25 ± 3 yr of age). The study was approved by the ethical committee of the Medical Faculty of the Technical University of Dresden. No subject had diabetes or a history of venous or arterial disease, nor was any subject taking vasoactive medication. Upper arm blood pressures measured with standard blood pressure cuffs verified that subjects were normotensive (117 ± 7 and 76 ± 5 mmHg systolic and diastolic, respectively). Heart rate was 68 ± 8 beats/min. During the experimental sessions, the subjects were seated in an armchair, such that the forearms rested comfortably on wide armrests at heart level, with the wrist slightly elevated above the elbow to promote venous drainage. During the entire session, a light cloth over both forearms prevented cooling. The room temperature was regulated and held constant at 22 ± 2°C.

Study 1. The purpose of study 1 (n = 9) was to determine the forearm blood flow with six compression sleeves exerting an increasing compression pressure. The blood flow of both forearms was measured under baseline conditions. Then the compression sleeve was applied to the right forearm (in general, the dominant arm) for 10 min. At the end of this intervention period (within 10 min), the blood flow of both arms was measured. In the same manner, five other sleeves

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with increasing compression pressure were applied consecutively to the right forearm. Thus the duration of the entire compression protocol was 60 min. Again, after removal of the strongest compression sleeve, the blood flow of both arms was measured twice under baseline conditions: 1) immediately after removal of the last compression sleeve and 2) after an additional 10 min.

**Study 2.** The purpose of study 2 (n = 9) was to determine the effect of an external compression pressure on the arterial flow reserve. **Study 1** was repeated, with the addition of arterial flow reserve measurements 1) after the second baseline measurement, before application of the first compression sleeve; 2) after application of the third compression sleeve (CS3); and 3) at the end of the study, i.e., after the second baseline measurement. After the end of the arterial flow reserve measurement, there was a resting interval of 10 min before the next measurement or before application of compression pressure.

**Study 3.** The purpose of study 3 (n = 5) was to test the duration of the effect of compression on forearm blood flow. After a baseline measurement, compression sleeve CS3 was applied to the test arm, and blood flow measurements were obtained at 10 min, 30 min, and then every 30 min to 180 min. After 180 min, the compression sleeve was removed, and forearm blood flow was determined immediately and after 10 and 30 min. Between flow measurements, that is, from 30 to 180 min, the subjects could move freely and perform laboratory work.

**Study 4.** The purpose of study 4 (n = 5) was to test the hypothesis that the flow augmentation by compressive force was maintained during light exercise or movement. After a baseline measurement, compression sleeve CS3 was applied to the test arm. A first measurement of resting flow was obtained after 10 min. Then the subjects were instructed to carry out rhythmic hand-grip exercise with both hands (5–10% of maximal voluntary contraction in a 1:2-s contraction-relaxation duty cycle) for ~70 min. The low workload of 5–10% maximal voluntary contraction and the relaxation period twice as long as the contraction period were selected to prevent an increase in blood flow by the exercise itself. During handgrip exercise, blood flow was determined every 10 min. During the flow measurements (90 s), the subjects did not exercise.

**Study 5.** The purpose of study 5 (n = 3) was to test the flow augmentation under clinical conditions and to measure the forearm blood flow with the MR technique. With use of the MR technique, the blood flow of the right forearm was determined under normal conditions without compression and again 10 min after the application of compression sleeve. For comparison, the blood flow of the same forearm was measured with venous occlusion plethysmography with and without the compression sleeve. For technical reasons, it was not possible to perform MR and plethysmography simultaneously. The time lag between the measurements was ~180 min.

The temperature of both forearms was controlled using a multichannel measuring system (ALMEMO-1, Ahlborn Mess- und Regelungstechnik, Holzkirchen, Germany).

### Flow Assessment

The arterial inflow and arterial flow reserve of both forearms were measured with venous occlusion plethysmography (COMPACTUS, Gutmann-Medizintechnik, Eursburg, Germany). This method, which is based on measurement of volume changes when venous outflow is blocked, measures arterial inflow. The strain gauge was placed on the proximal end of the forearm. An electrocardiogram probe was positioned near the isocenter of the magnet. A rectangular flexible surface coil (7 cm wide) was placed on the proximal end of the forearm where the circumference is maximal, and during application of the compression sleeve, the strain gauge was placed over the sleeve. The venous occlusion cuff around the upper arm was inflated for 4 s with a pressure of 60 mmHg to ensure venous occlusion. The measurement error in our experiments was ±2 mmHg. The pressure under the stocking was measured at two positions with different winding radii of the circumference of the forearm. According to the law of Laplace, the pressure inside a wall is inversely proportional to the winding radius at a given wall tension. Therefore, the two sensors were placed on the forearm at positions of greatest and least winding radii.

### Compression Sleeves

The force exerted on the skin surface critically depends on the dimensions and elastance of the sleeves as well as individual arm geometries. Thus the compression sleeves were manufactured individually for each volunteer on the basis of six measurements of the circumference of the forearm between wrist and elbow. The increasing level of compression was realized by decreasing the equivalent circumferences of the textile. In this way, the wall tension of the sleeves, when they covered the forearm, was increased according to the stress-strain relation. According to the law of Laplace, this increased wall tension exerted a certain pressure on the tissue of the forearm. Thus, for each subject, a set of six sleeves (CS1–CS6) with decreasing circumferences was designed and manufactured using a knitted fabric that is based on an elastane yarn plated on a cotton yarn. These compression sleeves are similar to the sleeve of a sport tricot, and their thickness is 1.022 ± 0.034 mm. The stress-strain relation of the knitted fabrics was determined, and the textile parameters are summarized in Table 1.

The sleeves were produced in consideration of the textile-physical parameters of the knitted fabrics as usual in clothing manufacturing. The specific stretch factor of the fabrics was determined at six different stresses for manufacture of the sleeves. These factors were multiplied by the corresponding circumferences of the forearm at different cross sections as measured for each subject.

### MR Measurements

MR measurements were performed on a 1.5-T whole body scanner (Magnetom Sonata, Siemens, Erlangen, Germany). The volunteers were positioned in a supine-to-lateral position to locate the forearm near the isocenter of the magnet. A rectangular flexible surface coil was placed on the proximal end of the forearm. An electrocardiogram-triggered FLASH two-dimensional sequence with flow encoding perpendicular to the slice plane (maximum velocity = 100 cm/s) was used.

### Table 1. Textile parameters of the circular knitted fabric

<table>
<thead>
<tr>
<th>Fiber Composition</th>
<th>Yarn Fineness</th>
<th>Cover Factor, γtex/mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coconut (CO)</td>
<td>70/1</td>
<td>80</td>
</tr>
</tbody>
</table>

CO, cotton; EL, elastane; 1 tex = 1 g/1,000 m.
applied (field of view = 220 × 165 mm², matrix = 256 × 192, slice thickness = 5 mm, echo time = 3.9 ms, repetition time triggered to every heartbeat, 5 averages), giving modulus and velocity images every 32 ms. For quantification, the ARGUS software package was used (Siemens). Flow and velocity data were derived from regions that were fitted to the actual vessel size and position for each time point.

Statistics

Sample size was estimated a priori for the primary hypothesis that external compression would result in a vasodilatory response. These calculations showed that a sample size of nine subjects would allow detection of a 50% increase in forearm blood flow under external compression with a power of 80% at α = 0.05. Statistical comparisons were performed by Student’s t-test and ANOVA for repeated measures. Forearm blood flow responses of the test arm to external pressure were compared with the response of the control arm. All calculated probability values were two tailed, and P < 0.05 was considered to indicate statistical significance. All group data are means ± SD.

RESULTS

The effect of a compression pressure of 16 ± 5 mmHg applied to the forearm surface is shown in Fig. 1. Baseline forearm blood flow averaged 2.3 ± 0.2 and 1.9 ± 0.6 ml·min⁻¹·100 ml tissue⁻¹ for test and control arms, respectively (not significant). After application of pressure, blood flow of the test arm increased within 3 min to a new steady state 115% above control (P < 0.001), whereas blood flow of the control arm remained unaffected. After removal of the compression, blood flow of the test arm returned to baseline within 1 min.

Study 1

The effect of increasing compressive force on forearm perfusion is shown in Fig. 2. All six compression sleeves enhanced blood flow of the test arm. The flow increases were significant (P < 0.001) compared with the control arm for CS2, CS3, CS4, CS5, and CS6. The flow increases were completely reversible after 1 min of removal of the compressive force.

Calibration curves for the different constructions of compression sleeves with respect to the surface pressure applied are summarized in Fig. 3. Data are presented with respect to the smallest and largest winding radii. An almost linear relation was found for the largest winding radius, whereas the relation was less consistent for the smaller winding radius. From the data shown in Figs. 2 and 3, the relation of forearm perfusion to compression pressure was calculated (Fig. 4). The largest flow increase was found for an arm surface compression pressure of 19.7 ± 5.8 mmHg. In three subjects, an additional flow measurement was obtained at a compression pressure of 50 mmHg by slight movement of the sleeve upward. Pressures >50 mmHg reduced forearm blood flow considerably.

Study 2

Similar to baseline blood flow, the flow reserve was enhanced during application of compressive force. Peak flow after 5 min of occlusion was nearly five times baseline blood flow (Fig. 5). During application of compression sleeve CS3, peak flow was significantly (P < 0.01) increased to 28.0 ± 6.0 ml·min⁻¹·100 ml tissue⁻¹ compared with 17.4 ± 6.0 ml·min⁻¹·100 ml tissue⁻¹ without compression. These effects were completely reversed after removal of the compression sleeve. In contrast, baseline flow and flow reserve of the control arm remained unchanged over the entire duration of the experiment (Fig. 5B).

Study 3

The effects of compression force on forearm blood flow were also studied for a more extended period of time (Fig. 6).
In five subjects, forearm blood flow remained increased over the entire period of pressure application (3 h). After a slightly higher initial increase of blood flow, the flow response reached a steady state after 60 min. After removal of the compression sleeves, the flow changes were largely reversible after 1 min and fully reversible after 30 min. The forearm blood flow of the control arm remained unchanged during the entire study period.

Study 4

In a further set of experiments, we tested whether the flow augmentation by compressive force was maintained during light exercise. Light hand exercise during continuous application of compression sleeves (CS3) was associated with a trend to a further slight elevation of forearm blood flow in the test arm, but not in the control arm (Fig. 7).

Study 5

In a final set of experiments, forearm blood flow in response to compressive force (CS3) was determined consecutively by venous occlusion plethysmography and MR in three subjects. Both methods revealed increases of blood flow during the application of compression pressure (Fig. 8).

The skin temperatures of the forearms remained unchanged throughout the measurement periods. No differences were found between the test and the control arm before (34.1 ± 0.98°C and 34.1 ± 1.29°C, respectively) and after test series (34.3 ± 1.03°C and 34.5 ± 1.26°C, respectively).

DISCUSSION

The application of increased tissue pressure, known as compression therapy, is the mainstay of physical treatment of venous insufficiency of the legs and prevention of deep vein thrombosis (15, 16). The application of compression therapy increases the healing rate of venous leg ulcer and improves deep vein hemodynamics. However, little is known about the impact of external compression on arterial flow regulation.
With the use of a forearm model, the present study has revealed two major findings. 1) The external pressure application significantly increases forearm blood flow. A clear relation between the increase of external pressure and the increase of blood flow could be established, with a maximal flow effect at a forearm surface pressure increase of \( \frac{1}{20} \) mmHg. The present study extends previous reports in which it was suggested that external compression may not only augment venous return but also affect arterial flow regulation separately. 2) The external compression significantly increases hyperemic peak flow after 5 min of circulatory arrest.

A few previous studies addressed the effects of moderate leg compression on arterial inflow (18, 22, 23, 25). In one of these studies, application of graded compression pressure did not change calf muscle blood flow (18); in this study, muscle blood flow was determined by measuring xenon-133 clearance, and the maximally applied compression pressure was 30 mmHg. In another study (25) conducted on male distance runners, moderate compression (40 mmHg) reduced the muscle blood flow in the thigh by \( \frac{1}{20} \) 50%. The reason for the discrepancy between these two studies (18, 25) is not readily apparent, because the method used to assess changes in leg blood flow was identical. Another previous study comprising 14 healthy subjects reported the effects of leg compression by bandaging on leg pulsatile blood flow using a nuclear MR flowmeter (18, 19). A flow increase of 29% was reported for a pressure increase of \( \frac{1}{20} \) 40 mmHg. Leg compression was produced by wrapping one leg from foot to knee with a four-layer bandaging system. The effect of lower compression pressures was not studied.

In the present study, an individually fitted set of compression sleeves was used to obtain flow measurements over a wider pressure range. To the best of our knowledge, this is the first systematic study performed on the human forearm. The use of elastic sleeves to induce an external compression pressure has two advantages. 1) Blood flow at the forearm can be measured with strain gauge plethysmography with and without the elastic sleeves. The strain gauge must be placed around the outside of the sleeve to detect the expansion of the forearm when the venous outflow is blocked. 2) With use of compression sleeves, it is possible to change or superimpose other conditions, such as hand exercise or free movement. To address the limitation of strain gauge utilization during application of a compression sleeve, the volume expansion during a single measuring cycle under resting conditions is estimated: if the resting blood flow to the forearm is \( \frac{1}{20} \) 3 ml \( \cdot \) min \(^{-1} \) \( \cdot \) 100 ml tissue \(^{-1} \), then the additional blood volume that is pooled in the forearm during

Fig. 6. Effects of external compression on forearm perfusion over 3 h \((n = 5)\). Compression sleeve CS3 was applied from 5 to 180 min. Baseline measurements are set to 100%. •, control arm; *, test arm. \* \( P < 0.01 \) vs. control arm.

Fig. 7. Forearm perfusion of control (○) and test (●) arms during compression and rhythmic handgrip (exercise). Compression sleeve CS3 was applied from 5 to 180 min \((n = 5)\). \* \( P < 0.01 \) vs. control arm.
The relation between compression pressure and flow increase was more consistent for the pressure measured under the sleeve for the larger winding radius (Fig. 3). The larger winding radius was determined over the group of hand flexors, whereas the minimal winding radius was measured over the region of the hand extensors. Both muscle groups differ considerably with respect to their masses. The mass of the group of flexors is considerably greater than that of the extensors. In addition, both muscle groups are compartmentalized and separated from each other by bone and ligament structures. Thus it seems that the true relation between compressive surface pressure and blood flow change of the forearm is best expressed by that determined for the larger winding radius. Additionally, scan of the human forearm shows that most of the cross-sectional area is characterized by a large winding radius. This relation between compressive pressure and blood flow change was almost linear for 0–20 mmHg.

The application of external pressure also increases the peak flow after a 5-min occlusion of the upper arm (Fig. 5). The increase in peak flow is greater than the increase in resting blood flow. In addition to resting blood flow, the present study evaluated flow under stimulated conditions induced by moderate handgrip exercise for 1 h (Fig. 6) or for 3 h, during which the subjects could move freely in the laboratory (Fig. 7). For both conditions, the enhancement of blood flow could be assessed, suggesting that the mechanism that leads to the flow augmentation is robust with respect to the particular condition. The somewhat surprising finding that static compression consistently increases, rather than decreases, blood flow of the human forearm gives rise to the question of the underlying mechanism(s). On the basis of known vascular control features, three mechanisms may be envisioned to account for this: 1) myogenic response, 2) venular-arteriolar communication, and 3) skin vasomotor reflexes.

**Myogenic Response**

It is well established that arteriolar vessels constrict in response to an increase of the vessel transmural pressure gradient and dilate in response to a fall of the pressure gradient (Bayliss effect) (2, 6, 12). The increased external arm compression by the sleeve is transmitted into the tissue and reduces the transmural pressure gradient of the arterial vessels and arterioles (21). The potential importance of transmural vascular pressure is supported by the early study of Greenfield and Patterson (8), who applied subatmospheric pressure (~100 mmHg) to the forearm for up to 1 min. Immediately after pressure release, venous occlusion plethysmography indicated a decrease of blood flow, which may have reflected a vasoconstriction in response to the increase of the vessel transmural pressure during external application of the subatmospheric pressure. In a more detailed study, Lott et al. (20) applied a positive or negative pressure of 50 mmHg to the forearm with an onset time and a reset time of <0.2 s. During the first two heartbeats after the onset of +50-mmHg pressure, a rapid transient decrease of blood flow was followed by a steady increase of flow. This steady increase of flow after a positive-pressure step and the equivalent decrease of flow after a negative-pressure step provide evidence that the myogenic response is normally operative in the forearm circulation of humans.

Our study clearly demonstrates that external pressure increases not only resting blood flow in the forearm but also the peak flow after a 5-min occlusion. The role of nitric oxide (NO)-mediated dilatation in the hyperemic flow response was investigated in two studies (4, 11) and revealed that hyperemic peak flow was not influenced by NO synthase blockade.
Joannides et al. (11) measured blood flow and diameter of the radial artery, and the occlusion cuff was placed distally, around the wrist. Under conditions of NO synthase inhibition with N-monomethyl-L-arginine (L-NMMA), the blood flow increase was unchanged compared with control conditions, but the diameter of the radial artery was reduced. Doshi et al. (4) imaged the brachial artery for diameter measurements 7–10 cm distal to the puncture site for L-NMMA infusion, and the hyperemic response was provoked with occlusion cuffs at two positions: distal to the ultrasound probe for imaging and proximal to the puncture site. When NO production was blocked with L-NMMA, there was no dilatation of the brachial artery with the occlusion cuff around the wrist; with the occlusion cuff around the upper arm, however, initial dilatation of the brachial artery was the same as under control conditions. These two studies demonstrated that the decreasing the transmural pressure alone, as during 3–5 min of circulatory arrest, produces a local dilatation. This dilatation does not require local NO production. In this study, we have demonstrated that external compression increases not only resting blood flow in the forearm but also the hyperemic peak flow. These two facts point to the key role of the transmural pressure and the myogenic response in the underlying processes.

Venular-Arteriolar Communication

Because of the much thicker wall, arterial vessels are considerably more rigid than venous vessels. External pressure application may therefore reduce the venous vessel lumen considerably, whereas the arterial segments dilate, because of the above-mentioned myogenic response. As a consequence of the reduced lumen, blood flow may exert an enhanced shear stress in venous vessel segments, which may trigger the release of endothelial dilators in the venous segments. Besides acting locally and thereby, tending to normalize venous segment resistance in the microcirculation, these compounds (e.g., NO or endothelium-derived hyperpolarizing factors) may reach neighboring arterial vessel segments by diffusion and reduce arteriolar resistance (10). In the arteriolar vessel segments, this communication might act synergistically with the myogenic response in reducing vessel resistance. Within our experimental setup, we cannot exclude the influence of the venular-arteriolar communication under resting conditions. However, as pointed out above, L-NMMA treatment did not diminish the reactive hyperemic response after transient ischemia, which argues against the importance of this mechanism.

Skin Vasomotor Reflexes

The application of pressure to the skin surface may activate nonnociceptive skin receptors or proprioceptors in the underlying tissue layers. The potential importance of such reflexes has been stressed recently (1, 7). After application of increasing (5 mmHg/min) external pressure locally (1 cm²), microcirculatory flow in the same region was measured by laser-Doppler flowmetry. In the range of high compression pressure (>50 mmHg), the laser-Doppler flow signal decreased steadily, whereas at 20 mmHg there was a transient increase in the laser-Doppler flow signal above baseline. However, this result might also be evoked by a myogenic response. More study is required to conclusively discern between these two causal factors.

In conclusion, the present study demonstrates that systematic elevation of forearm external compression results in an increase of resting blood flow and hyperemic peak flow in that region. The maximal flow effect is induced by a pressure increase of 20 mmHg. The flow increase in response to external pressure application is likely mediated by the myogenic response. Future studies are needed to define the limits of the involvement of venous-arterial communication and skin vasomotor reflexes.

REFERENCES


