



## OPEN **Determining minimum cuff pressure required to reduce arterial blood flow at rest**

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The aim of our study was to determine the minimum cuff pressure to induce alterations in the brachial and popliteal blood flow (BF). Forty-two healthy men underwent an incremental cuff pressure protocol at rest. The cuff was positioned at the proximal part of the right arm (9 cm width, brachial artery) and thigh (13 cm width, superficial femoral artery) in a randomized order. Pressure increments started at 0 mmHg, increased by 20 mmHg up to 100 mmHg, and then by 10 mmHg until total occlusion of BF. Each pressure was held for 30 s to stabilize BF and measurements were carried out on brachial (BA) and popliteal (PA) arteries using a 2-D B-mode ultrasound. Mean arterial occlusion pressure (AOP) was  $161 \pm 18$  mmHg in BA and  $150 \pm 15$  mmHg for the PA. At 20–100 mmHg, the mean BF changes were 4% (BA) and 11% (PA), without significant BF reductions compared to baseline values. Reductions in BF vs. baseline ( $p < 0.05$ ) were found from 120 mmHg (BA) and 110 mmHg (PA) cuff pressures. Calculations of the minimal clinically important differences showed meaningful changes beginning at 110 mmHg for BA and 100 mmHg for PA. Experimental approaches requiring BF restriction should use cuff pressures greater than 69% (BA) and 67% (PA) of AOP to promote significant reductions in blood flow.

**Keywords** Arterial occlusion pressure, Ischemia, Reperfusion, Tourniquets

A large body of evidence demonstrates that ischemic preconditioning (IPC) before exercise and blood flow restriction training (BFRT) during exercise provide significant health and performance benefits<sup>1–7</sup>. IPC has shown to reduce myocardial injury in patients undergoing coronary artery bypass surgery<sup>5,8</sup> and improve exercise performance, such as the time to complete a set distance<sup>1,2,9,10</sup> or time-to-exhaustion<sup>3,11</sup>. Similarly, BFRT has demonstrated benefits in post-surgery rehabilitation by mitigating muscle atrophy<sup>6</sup>, preserving strength and facilitating recovery. Additionally, it counteracts sarcopenia in older adults<sup>12</sup> and enhances hypertrophic and strength adaptations during low-load resistance exercise<sup>7</sup>. Both interventions use a pneumatic cuff, with IPC inducing complete occlusion and BFRT inducing partial restriction of arterial and venous blood flow.

Identifying the appropriate cuff pressure is critical for these interventions, regardless of whether the goal is to achieve arterial occlusion pressure (AOP) or partial blood flow restriction. BFRT, requires cuff pressures that are sufficiently high to occlude venous return from the muscles while remaining low enough to allow arterial inflow<sup>7</sup>. Pressures outside this optimal range may significantly alter the effectiveness of the intervention by changing the performance of physiological parameters during interventions. Furthermore, excessively high cuff pressures can lead to limb discomfort, injury, or reduced adherence to the protocol<sup>13</sup>. Determining the minimal cuff pressure to alter blood flow (BF) and understanding how different percentages of AOP affect blood flow is therefore essential, as using a given percentage of AOP doesn't necessarily result in a proportional reduction in blood flow. Inter-individual differences in upper and lower limb circumferences directly influence the pressure applied to the cuff<sup>7</sup>. As a result, conflicting results in BFRT studies may arise from variations in blood flow changes despite using the same cuff pressure<sup>14–16</sup>, which can be influenced by factors such as cuff specifications, body position<sup>16</sup> and time of measurements (e.g., at rest or during exercise)<sup>15</sup>. Similarly, IPC exhibits heterogeneous results, with applied pressures for both the upper and lower limbs often varying widely, ranging from 10 mmHg above systolic

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blood pressure to over 300 mmHg<sup>17</sup>. This variability may contribute to inconsistencies in protocols, potential placebo effects<sup>18</sup>, and limited observations of IPC-induced changes in blood flow<sup>19</sup>.

For researchers and practitioners aiming to identify specific cuff pressures that effectively restrict blood flow in both the upper and lower limbs, determining the optimal cuff pressure is essential. Therefore, our study aimed to assess the relationship between blood flow and cuff pressure in these limbs and to identify the minimum pressure that significantly alters blood flow.

## Methods

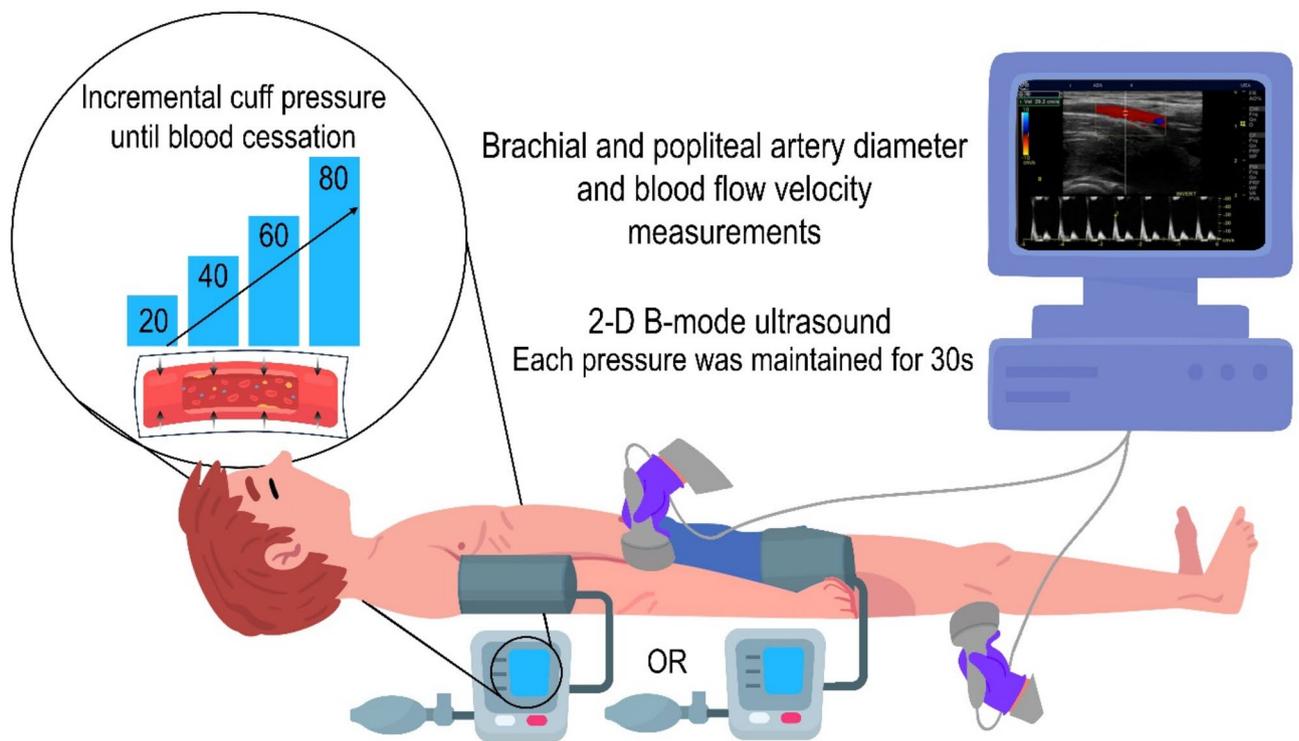
### Participants and procedures

We used a prospective, within-participant design to examine brachial and popliteal artery diameter and blood flow velocity. Based on an a priori sample estimation (G\*Power 3.1.9.2, Heinrich-Heine Universität Düsseldorf, Düsseldorf, Germany; <http://www.gpower.hhu.de>) using one group, repeated measures design with a medium effect size ( $f=0.25$ ),  $\alpha=0.05$ , power  $(1-\beta)=0.8$  and correlation of 0.5 indicated a minimum sample size of 34 subjects. Thus, 42 healthy men were recruited. Inclusion criteria stipulated that participants were: (1) male subjects with 18 years or older, (2) reported no known medical problems (e.g., cardiovascular, or cerebrovascular disease); and (3) abstinent of medications or drugs that affect systemic hemodynamics (e.g.,  $\beta$ -blockers, calcium antagonists, renin-angiotensin system inhibitors). All participants provided written informed consent for this study, which was approved by the Local Institutional Ethics Committee (n. 4.120.625) and was conducted in accordance to the Declaration of Helsinki<sup>20</sup>.

Participants arrived at the laboratory at 08:30 a.m. in a fasted state, having abstained from caffeine, nicotine, alcohol, and moderate or intense exercise for 24 h. After a 10-min supine rest, resting blood pressure was measured. The incremental cuff pressure intervention was then administered, along with concurrent measurements of blood flow velocity and the diameter of either the brachial or popliteal arteries, in a randomized order. Following a 10-min rest where participants lay supine the remaining artery was measured. All assessments were conducted by the same researcher in a temperature-controlled room ( $22 \pm 1$  °C;  $77 \pm 10\%$  humidity). Figure 1 illustrates the data collection procedures with participants.

### Measured parameters

Our primary outcome measures were systolic and diastolic blood pressure, brachial and popliteal artery diameter, and blood flow velocity. Blood pressure was measured twice, using an automatic oscillometric device (model ABPM50; cuff size: 51 cm length  $\times$  14 cm width; bladder size: 13.1 cm length  $\times$  23.5 width cm; Contec Medical Systems Co., Ltd., Qinhuangdao, China) placed 2–3 cm above the antecubital fossa of the right arm, with a 3–5-min interval between measurements. The selected cuff size is recommended for arm circumferences between 27 and 34 cm<sup>21</sup>, and all participants in our sample fell within this range. Given the relative homogeneity of the



**Fig. 1.** Schematic setup of blood flow measurement during incremental cuff pressures administration. Measurements of brachial or popliteal arteries were performed from 0 until AOP, during the same session, 10 min apart, in a randomized order.

sample's anthropometric characteristics, the cuff was appropriate for all individuals and allowed for accurate blood pressure measurements. The mean value was used for analysis.

For artery diameter and blood flow velocity, a 2-D B-mode ultrasound (Voluson™ S6, 12L-RS probe, 4–12 MHz) was used. Measurements were taken on the right side for both upper and lower limbs in a randomized order, with participants in a supine position. To standardize measurements, the ultrasound probe's position was marked on the skin, and a consistent insonation angle of < 60° was maintained (between 55 and 59°)<sup>22</sup>. Doppler window width encompassed the entire vessel (to ensure accurate detection of flow cessation during AOP determination, a broader window minimized missed residual flow and improved measurement consistency), and 30-s measurements were taken 2–3 cm proximal to the brachial bifurcation assessing brachial blood flow or popliteal fossa assessing the downstream popliteal artery blood flow.

Blood flow calculations were performed after data collection by an experienced, blinded physician (G.B.C) using a software (GE Healthcare, Milwaukee, WI, USA) that automatically detected the inner-lumen diameter. Blood flow was calculated in milliliters per minute using a standardized Eq. (1)<sup>22</sup>:

$$\text{Blood flow} = \pi \left( \frac{\text{arterial diameter}}{2} \right)^2 \times \text{time-averaged velocity} \times 60 \quad (1)$$

<sup>1</sup>where arterial diameter is in cm and time-averaged velocity is in cm/s.

Skinfold thickness at the biceps, triceps, and thigh of the right arm and thigh were measured using Lange caliper (Beta Technology Inc., Houston, TX, USA). The biceps skinfold was measured over the midpoint of the biceps muscle belly on the anterior arm, the triceps skinfold on the posterior midline, and the thigh skinfold on the anterior midline. Measurements were taken in duplicate, with retests if differences exceeded 1–2 mm, and the mean value of the two measurements was used for analysis. Arm and thigh circumferences were measured at the same sites as the biceps and thigh skinfold, respectively. All anthropometric measurements were completed before resting blood pressure assessments.

### Cuff intervention

After 5 min of supine rest, a pneumatic cuff (9 cm for the arm, 13 cm for the thigh) was positioned on the axillary arm (occluding brachial artery) and inguinal region of thigh (occluding superficial femoral artery), both on the right side. Cuff pressure increments began at 0 mmHg, increasing by 20 mmHg up to 100 mmHg, then by 10 mmHg until arterial flow was undetectable. Each pressure level was maintained for 30 s to stabilize blood flow and measurements were taken during the last 5 s of this 30-s period to ensure that blood flow has stabilized at each pressure<sup>15</sup>.

### Statistical analysis

The normality of data distribution was assessed using the Shapiro–Wilk test. For comparisons among the incremental cuff pressures, a nonparametric ANOVA (Friedman test) followed by a post hoc Dunn's test was used. A line chart was generated to depict the relationship between mean cuff pressure (expressed as a percentage of each participant's AOP) and mean percentage blood flow. The minimal clinically important difference (MCID) was determined using a distribution-based approach, based on the upper limit of Cohen's small effect size classification (0.3 × group standard deviation of resting blood flow values) to identify the minimal meaningful change in blood flow, considering the probability that the change occurred by chance<sup>23,24</sup>. The MCID was then compared to the mean difference (MD) between resting and applied pressure values, with changes deemed meaningful if the MD exceeded the MCID. Additionally, correlation analyses and linear regression were performed to explore potential associations between skinfold thickness, limb circumference, resting blood pressure, and AOP. The significance level was set at 0.05, and the software used for data analysis was GraphPad (Prism 8.0.0; San Diego, CA, USA).

### Results

All 42 participants completed the study without adverse events. Their physiological and hemodynamic characteristics are presented in Table 1.

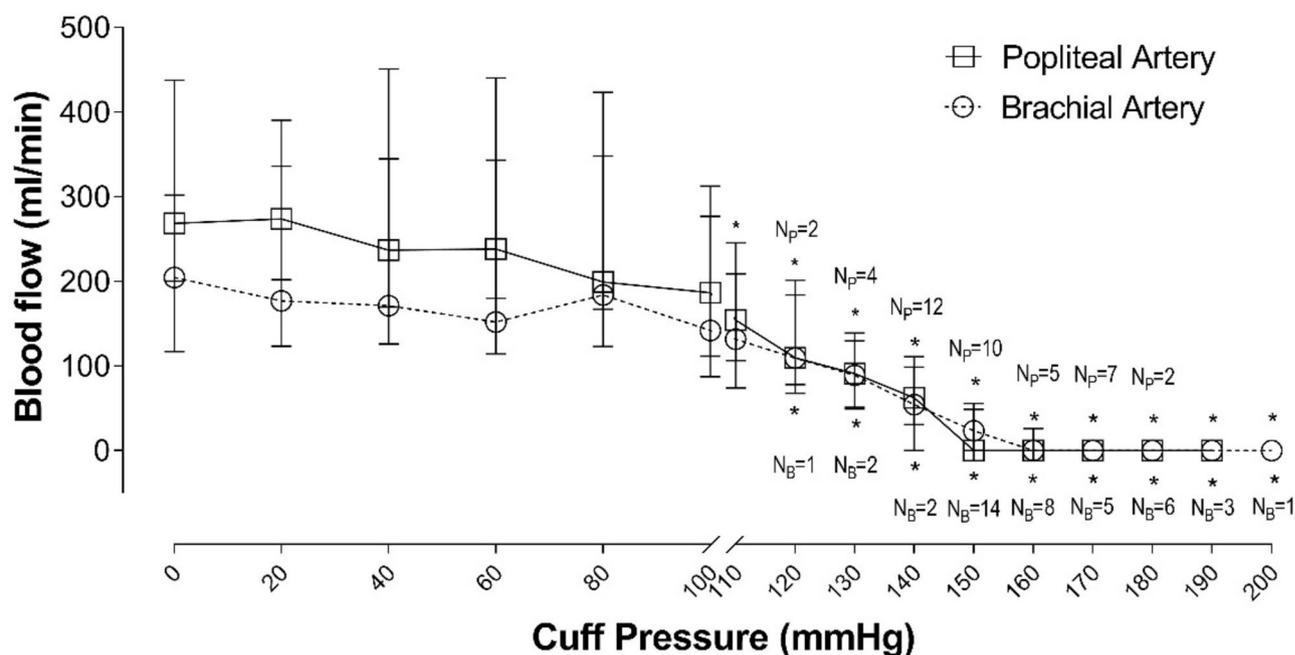
The mean AOP was 161 ± 18 mmHg for the BA and 150 ± 15 mmHg for the PA, with the lowest AOP recorded at 120 mmHg for both arteries. Blood flow did not decrease statistically significantly until cuff pressures reached 120 mmHg (~75% of AOP) for the BA and 110 mmHg (~74% of AOP) for the PA (Fig. 2). Pressures up to 100 mmHg led to only minor, non-significant reductions, averaging 4% in the BA and 11% in the PA ( $p > 0.05$ ).

Based on the MCID, cuff pressures up to 80 mmHg did not produce meaningful reductions in blood flow. The first meaningful decrease was observed at 110 mmHg for the BA (~69% of AOP), followed by a reduction at 100 mmHg for the PA (~67% of AOP). Figure 3 illustrates the relationship between the percentage of AOP and the corresponding blood flow for both the brachial (A) and the popliteal (B) arteries.

We examined the relationship between resting brachial blood pressure (Table 1) and AOP in the upper and lower limbs. A weak-to-moderate positive correlation was observed in the upper limb ( $r = 0.35$ , 95% CI 0.050–0.590,  $R^2 = 0.12$ ,  $p = 0.02$ ) and a slightly stronger association in the lower limb ( $r = 0.39$ , 95% CI 0.097–0.631,  $p = 0.01$ ). Linear regression confirmed these trends, with a significant slope in the upper limb (slope = 0.72, 95% CI 0.103–1.34,  $p = 0.02$ ,  $R^2 = 0.12$ ), while the lower limb relationship did not reach significance (slope = 0.49, 95% CI –0.059 to 1.046,  $p = 0.07$ ,  $R^2 = 0.07$ ). Further analyses revealed no significant associations between brachial blood pressure and potential confounders, including limb circumference and skinfold thickness (all  $p > 0.10$ ). These findings suggest that these anthropometric variables do not notably influence AOP in our study.

| Parameters                             | Mean $\pm$ SD   |
|--|-----------------|
| Age (years)                            | 24 $\pm$ 6      |
| Weight (kg)                            | 73.1 $\pm$ 11.6 |
| Height (cm)                            | 175.9 $\pm$ 7.4 |
| BMI (kg/m <sup>2</sup> )               | 23.5 $\pm$ 2.7  |
| Biceps skinfold (mm)                   | 4.7 $\pm$ 1.9   |
| Triceps skinfold (mm)                  | 11.7 $\pm$ 5.1  |
| Thigh skinfold (mm)                    | 17.0 $\pm$ 6.9  |
| Arm circumference (cm)                 | 30.4 $\pm$ 3.4  |
| Thigh circumference (cm)               | 50.7 $\pm$ 5.2  |
| Resting brachial artery diameter (mm)  | 3.7 $\pm$ 0.6   |
| Resting popliteal artery diameter (mm) | 5.6 $\pm$ 1.0   |
| rSBP (mmHg)                            | 120 $\pm$ 9     |
| rDBP (mmHg)                            | 69 $\pm$ 9      |

**Table 1.** Participant's anthropometric characteristics and hemodynamic profile (n = 42). Data are presented as mean  $\pm$  SD. BMI, body mass index; rSBP, resting systolic blood pressure; rDBP, resting diastolic blood pressure.

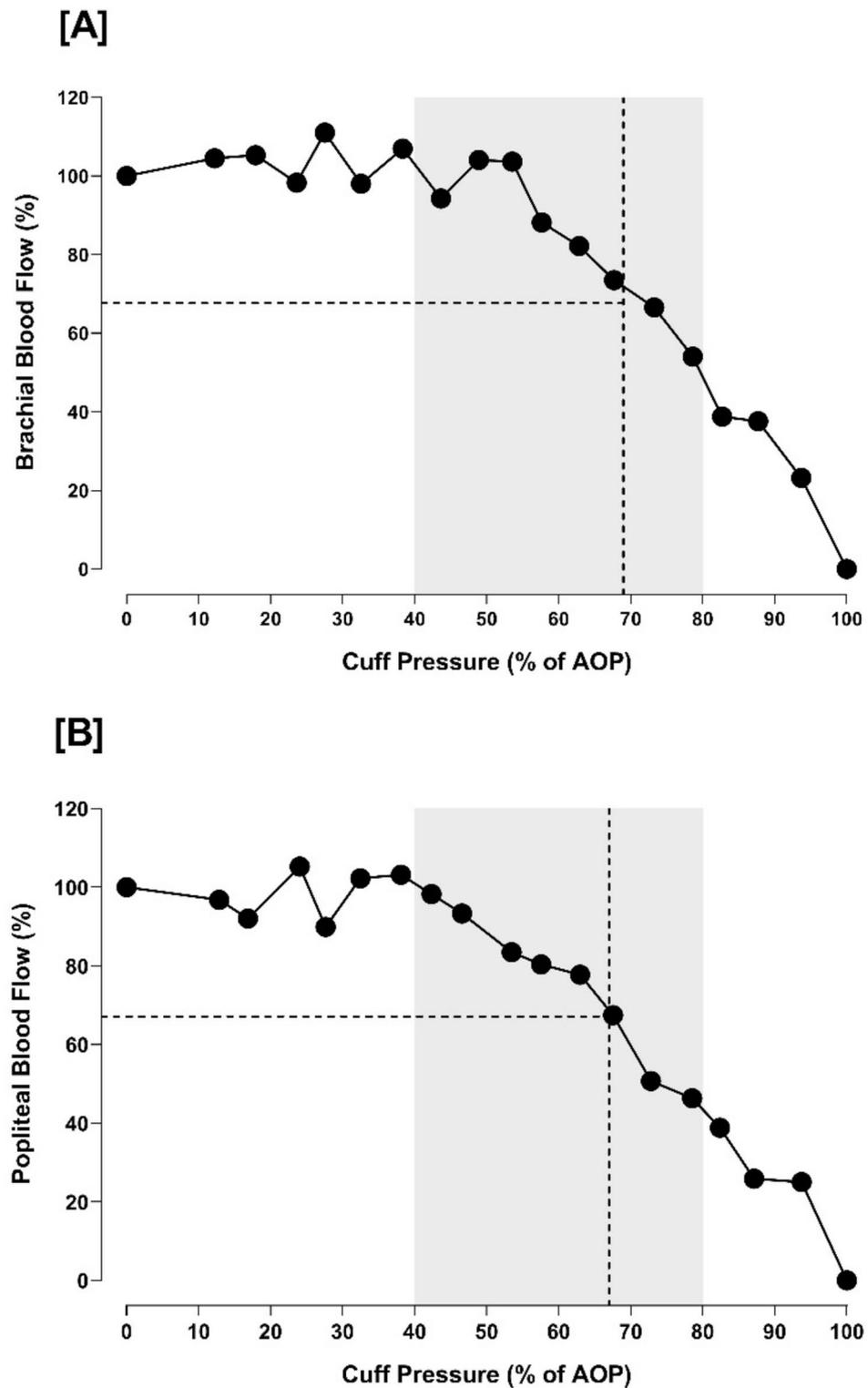


**Fig. 2.** Blood flow response related to cuff pressure increments. \*Denotes significant reductions compared to baseline (0 mmHg), starting at 120 and 110 mmHg for brachial and popliteal arteries, respectively. N<sub>p</sub> and N<sub>b</sub> represent the number of subjects who had achieved AOP at each cuff pressure for brachial and popliteal arteries, respectively. Data are expressed as median  $\pm$  interquartile range.

## Discussion

Our study aimed to assess the relationship between blood flow and cuff pressure in upper and lower limbs and identify the highest pressure that maintains normal blood flow and the lowest pressure that diminishes it. Based on MCID calculations, cuff pressures between 20 and 80 mmHg did not produce meaningful reductions in blood flow. In contrast, the first physiologically relevant changes were observed at 110 mmHg for the BA (~69% of AOP) and 100 mmHg for the PA (~67% of AOP). These thresholds mark the onset of meaningful blood flow restriction and help distinguish between sham and effective occlusion pressures. Therefore, the 20–80 mmHg range appears suitable for sham conditions in IPC and BFRT studies, as it did not alter arterial blood flow according to both statistical and MCID criteria. These findings are important for optimizing cuff-pressure protocols and enhancing the reproducibility of studies evaluating the efficacy of these interventions.

The ergogenic effects of IPC may involve hemodynamic responses through humoral or neural signaling, triggered by substance release during reperfusion or synthesis during ischemia, activating afferent pathways<sup>28,29</sup>. These mechanisms are hypothesized to occur under the condition of occlusion and reperfusion of BF. Such effects do not appear to occur with a low pressure of 20 mmHg, although other signaling pathways related to



**Fig. 3.** The relationship between the percentages of individual cuff pressure and the percentage of blood flow in the brachial (A) and popliteal (B) arteries. Cuff pressure is expressed as a percentage of each participant's arterial occlusion pressure (AOP). The shaded area represents the recommend cuff pressure range for blood flow restriction training guidelines (40–80% of AOP)<sup>7,25–27</sup>. Vertical lines indicate the minimum cuff pressures observed in the present study that significantly reduced blood flow in the arm and thigh, while horizontal lines represent the percentage of baseline blood flow at which minimal important differences were observed (~67%). Each point in the figure corresponds to the respective percentage of cuff pressure relative to AOP and mean blood flow percentage.

the use of IPC, such as psychobiological factor and pain perception triggering neural afferent-efferent pathways increasing the motor drive may still have an influence<sup>30</sup>. Regarding BFRT, evidence has suggested restricted pressures should range from 40 to 80% of AOP<sup>7,25,26,31,32</sup>. According to our results, these recommendations may overestimate hemodynamic modifications to some extent, as blood flow remains largely unchanged across most of this percentage range compared to the resting value (0 mmHg). This suggests that if protocols employ up to ~69% of AOP for BA and ~67% of AOP for PA, there would be no meaningful reduction in BF, potentially mischaracterizing its relation to BFRT. A comparison between the most commonly used BFRT cuff pressure recommendations guidelines and our findings are shown in Fig. 3. To ensure greater effectiveness of BF restriction, it is important to test the recommended pressure ranges while measuring blood flow, emphasizing that the efficacy of BFRT depends on the precise regulation of blood flow.

Given that studies report a wide range of cuff pressures, describing percentages between 40 and 80% of AOP<sup>7,25–27</sup>, percentages of systolic blood pressure (40%) and also absolute cuff pressure values<sup>25</sup> our results highlight a need to measure the blood flow and standardize the cuff pressure used in future research. Compared to our results, the most typical percentage values of cuff pressure are below the minimum limits necessary to promote BF reduction. However, when analyzing the absolute cuff pressures, it is possible to find values (120–240 mmHg) that would promote significant restrictions or even occlusion of blood flow<sup>33,34</sup>. In this context, considering that cuff width directly affects the minimal pressure needed for blood flow occlusion, showing an inversely proportional relationship between them<sup>35</sup>, a relationship between applied pressure and cuff width should be considered. It should be noted that we used cuff width of 9 cm and 13 cm for the upper and lower limbs, respectively. For narrower cuffs, the minimum pressure must be increased and recalculated to effectively restrict BF<sup>35</sup>. In this way, the differences in cuff width in our study directly influenced the AOP required for full occlusion in both the upper and lower limbs, with lower pressures being necessary for 13 cm cuff.

For IPC, there has been increasing evidence supporting the significant contribution of placebo effects when employing a low-pressure sham cuff intervention alongside with the active IPC condition<sup>36–38</sup>. However, as previous research had not validated whether the sham intervention elicited changes in blood flow, it is difficult to infer whether changes are due to hemodynamic or placebo responses. The use of sham-IPC protocols with varying pressures is common in IPC studies<sup>18,39</sup>, typically employing cuff pressures below diastolic blood pressure values<sup>40–42</sup> or using protocols alternating with high and low pressures<sup>43,44</sup>. If the applied cuff pressures exceed the MCID threshold of 80 mmHg for PA and 100 mmHg for BA observed in the present study (e.g., pressures near diastolic blood pressure), the BF may be affected, and the sham intervention could then produce effects related to BF changes. Our results indicate that using a cuff pressure range of 20–80 mmHg (equivalent to approximately 13–50% of the AOP for the arm and 13–53% of the AOP for the thigh) is appropriate as a standardized sham-IPC condition from a hemodynamic perspective, as it does not alter arterial BF. The administration of a 20 mmHg cuff pressure is unlikely to induce changes in venous BF, and any observed improvements in outcomes are likely due to placebo effects. However, in a crossover experimental design, participants are likely to recognize that 20 mmHg is a sham, causing the blind to fail in randomized controlled trials. As such, future research should utilize a cuff pressure of up to 80 mmHg, which could be more effective in blinding participants to the intervention they received.

Our findings corroborate previous research indicating that AOP is modulated not only by systemic blood pressure but also by factors such as limb circumference and tissue composition<sup>45</sup>. However, in our study, no significant associations were observed between AOP and limb circumference or skinfold thickness, indicating that these anthropometric variables did not notably impact AOP in our sample. These results suggest that, while interindividual variability in occlusion pressures exists, it may stem from a broader range of vascular and anatomical factors beyond the scope of brachial blood pressure or the variables we assessed. Given the lack of significant findings in this regard, we have chosen to focus the discussion on the primary physiological mechanisms that govern AOP regulation, particularly the role of systemic hemodynamics in shaping individualized occlusion pressures, rather than exploring the potential influence of these anthropometric variables on BFR-related outcomes.

Our results should be interpreted in light of the following limitations. Our measurements were conducted in the supine position, consistent with IPC interventions typically administered before exercise. Extrapolating our results to seated or standing position, or during BFRT protocols, requires consideration of orthostatic and exercise-induced changes in arterial pressure<sup>46,47</sup>, which may necessitate higher cuff pressures or wider cuffs to achieve the same magnitude of BF reduction<sup>35</sup>. The most significant factor affecting BF is cuff width. Wider cuffs promote greater restriction or occlusion of BF, thereby modifying BF responses relative to cuff pressure. Our results are applicable to 9 cm and 13 cm cuff widths for the upper and lower limbs, respectively, which are significantly larger than the commonly used 5 cm cuff width in BFRT studies<sup>25,48</sup>. In such, achieving similar BF responses would require much higher cuff pressures, potentially exceeding 80–90% of the AOP. Finally, we only included healthy men, emphasizing the need to replicate findings in women, obese subjects, and the elderly. These populations may benefit from IPC and BFRT but may experience different blood flow responses. Obese subjects may require specially sized cuffs, while the elderly and those with hypertension need careful monitoring due to altered vascular compliance and increased cardiovascular risk.

## Conclusion

The use of a 9 cm cuff on the arms or a 13 cm cuff on the thighs did not significantly alter blood flow or induce arterial ischemia up to 100 mmHg. Cuff pressures between 20 and 80 mmHg may serve as valid sham interventions in IPC and BFRT performance studies, as indicated by MCID calculations. For effective blood flow restriction, cuff pressures above 69% of AOP for the arm and 67% for the thigh are recommended.

## Data availability

The database that supports the conclusions of this study is available from the corresponding author Moacir Marocolo upon request (via the Email: isamjf@gmail.com), without any restrictions.

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## Author contributions

H.L.R.S. and M.M. conceived and designed the study. H.L.R.S., G.T.O., B.P.B., E.O.P. and G.B.C. collected the data. H.L.R.S., G.T.O. and M.M. performed formal analyses. H.L.R.S., M.W., MBP and M.M. drafted the manuscript. P.H., M.W. and MBP reviewed the manuscript and contributed technically to the quality of the manuscript. M.M. provided supervision and administrative support. All authors reviewed and approved the final manuscript text.

## Declarations

## Competing interests

The authors declare no competing interests.

## Additional information

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