ORIGINAL ARTICLE

Use of Short-Radius Centrifugation to Augment Ankle–Brachial Indices

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Background: Peripheral arterial disease is mainly caused by atherosclerosis and is characterized by decreased circulation, lower blood pressure, and insufficient tissue perfusion in the lower extremities. The hemodynamics of standing and altered gravity environments have been well studied relative to arm blood pressures but are less well understood for ankle pressures.

Methods: Because regional blood pressure depends, in part, on the gravitational pressure gradient, we hypothesized that artificial gravity exposure on a short-arm centrifuge with the center of rotation above the head would increase blood pressure in the lower extremities. Cardiovascular parameters for 12 healthy subjects were measured during exposure to supine short-arm centrifugation at 20, 25, and 30 revolutions per minute (rpm), corresponding to centripetal accelerations of 0.94, 1.47, and 2.11 Gz at the foot level, respectively.

Results: Systolic ankle blood pressure significantly increased at all levels of centrifugation. Ankle–brachial indices (the ratio of systolic ankle to arm blood pressures) increased significantly from 1.17 ± 0.03 to 1.58 ± 0.03 at 0.94 Gz ($P < 0.005$), 1.74 ± 0.02 at 1.47 Gz ($P < 0.005$), and 1.89 ± 0.06 at 2.11 Gz ($P < 0.005$). Systolic arm blood pressure significantly increased at 2.11 Gz, but heart rate did not change significantly. All parameters returned to normal after cessation of centrifugation.

Conclusions: We demonstrated that short-radius centrifugation leads to an increase in ankle–brachial indices. This could have potential implications for the treatment of peripheral arterial disease.

Key Words: blood pressure, artificial gravity, ankle–brachial index, short-arm centrifuge

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The hemodynamics of standing and exposure to altered gravitational environments have been relatively well studied, with blood pressure (BP) typically being measured at the arm. However, BP changes in the lower extremities have not been widely studied. The Bernoulli principle is a fundamental formula providing a relation between hydrostatic pressure, gravitational potential energy, and kinetic energy. Changes in BP as a function of the longitudinal component of the gravitational acceleration are well known.[1] We can maximize the effect of gravity on BP in the lower extremities by standing; this results in all of the gravitational acceleration acting along the body's longitudinal axis. One way to potentially increase BP is to use artificial gravity (AG) via short radius centrifugation. Other hemodynamic factors also come into play, such as the hydrostatic indifference level.[2,3] For the purpose of this study, we assume that the hydrostatic indifference level remains constant while subjects remain supine.

Artificial gravity, when applied along the longitudinal axis, alters the hydrostatic pressure gradient such that a further increase in fluid pressure will result in the lower extremities. The hydrostatic pressure gradient is calculated in equation (1.1).

$$\Delta \mathrm{P} = \rho \mathrm{a} \Delta \mathrm{h} \tag{1.1}$$

where a is the component of acceleration (gravitational and inertial) acting along the body's longitudinal axis, ρ is the fluid density, Δh is the distance between 2 reference points across which the pressure difference is being measured, ΔP is the pressure difference between the 2 reference points.

However, in our situation, a is not constant but is a function of the centripetal acceleration. The centripetal acceleration in a rotating environment is a function of both the rate of rotation and the radius, and can be calculated as in equation (1.2),

$$\mathrm{a} = \omega^2 \mathrm{r}$$

where a is the centripetal acceleration, at a distance r from the center of rotation, ω is the rotational velocity of the centrifuge, r is the radius from the center rotation.

So, substituting equation (1.2) into equation (1.1) and integrating over the radius, we obtain

$$\Delta \mathrm{P} = \rho \omega^2 \int_{\mathrm{r}_1}^{\mathrm{r}_2} \mathrm{r} \cdot \mathrm{dr} = \rho \omega^2 \left[\frac{\mathrm{r}_2^2}{2} - \frac{\mathrm{r}_{\mathrm{head}}^2}{2} \right] \tag{1.3}$$

where r_{head}: is the radius of rotation at the level of the head, r_2: is the radius at the level of the body part in question.

Equation (1.3) can be used to calculate the expected change in pressure because of the hydrostatic pressure gradient induced by the centrifugal force. The expected total pressure at any radius can then be predicted by adding the change in pressure as calculated in equation (1.3) to a baseline (supine, nonrotating) BP measurement for any subject.

The goal of the present experiment was to study the effects of short-radius centrifugation on the upper and lower extremity BP in healthy subjects. We hypothesized that short-radius centrifugation applied along the longitudinal axis would increase BP preferentially in the legs compared with the arms and result in an increase in ankle–brachial index (ABI), the most widely used parameter to assess patients with peripheral arterial disease (PAD).[4–6] The ABI is calculated by dividing the ankle systolic BP by the arm systolic BP. In addition to further our

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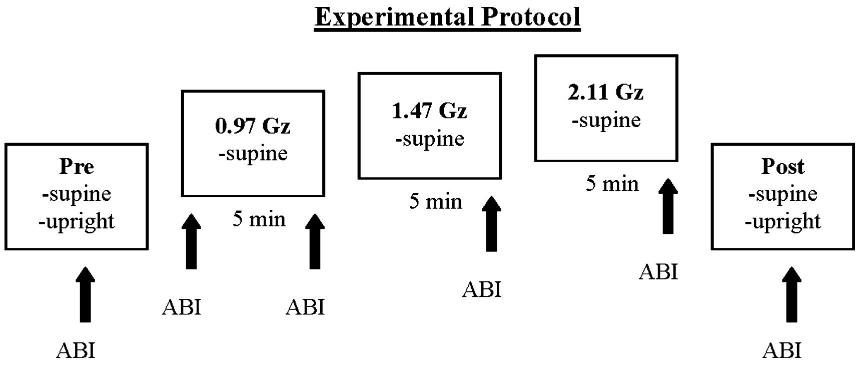

FIGURE 1. Experimental design. ABI indicates ankle-brachial index.

understanding of the effects of AG on the cardiovascular system, the motivation for this experiment was to investigate whether increasing the gravitational pressure gradient could be used to increase BP in the feet, with a potential clinical application in patients with PAD.

METHODS

Twelve healthy subjects, 4 females, 8 males (26 ± 1 years, weight 70 ± 3 kg, height 177 ± 2 cm) completed the study. Screening procedures included a medical history and bilateral arm BP measurements to ensure no significant BP difference between the 2 arms. The subjects were all nonsmokers and were taking no medications before the study. The exclusion criteria included a history or evidence of hypertension, coronary artery disease, diabetes, renal insufficiency, thyroid disease, hepatitis, anemia, psychiatric disorder, alcohol or drug abuse, or present pregnancy. Subjects had to abstain from using caffeine 24 hours before the study but were not kept post-prandial before testing. The study protocol was approved by the Massachusetts Institute of Technology Committee on the Use of Humans as Experimental Subjects, and written informed consent was obtained from all subjects.

Subjects began testing at 9:00 AM or 14:00 PM according to the protocol shown in Figure 1. For all sessions, heart rate (HR) and BP measurements from the arm and ankle were measured by a sphygmomanometer using the oscillometric method (Blood Pressure Sensor; Vernier Software and Technology, Beaverton, OR). To measure the BP in the ankle, an appropriate sized BP cuff was placed (up to 40% of calf circumference) above the ankle. Measurements were performed initially in the supine position after an equilibration period of 2 minutes, then in the upright standing position, also after an equilibration period of 2 minutes (control: "Pre"). Arm and ankle BP measurements were always performed simultaneously. Following this, the subjects were placed in the short-arm horizontal centrifuge lying supine with head near center and were spun at 20 revolutions per minute (rpm), 25 rpm, then 30 rpm (the subjects were instructed to keep their head stable to decrease risk of motion sickness and possible influence of vestibulosympathetic reflexes). This results in a centripetal acceleration of 0.94 G (0.97 Gz), 1.47 G (1.47 Gz), and 2.11 G (2.11 Gz) at the foot level, respectively. Because of the varying height of the subjects and the fact that we designed the experiment to keep the G-level constant at the foot to evaluate the effects on ankle BP, the G-levels experienced at heart and head levels were different for each subject. Each centrifugation period was maintained for 5 minutes, after which BP and HR measurements were repeated. Additional measurements were performed immediately after reaching the 20-rpm level. Two minutes after centrifugation was completed, post-BP measurements were performed in the supine position and were then repeated in the upright position 2 minutes after standing (post). Ankle–brachial indices were calculated by dividing the right ankle systolic BP by the right arm systolic BP.

Means and SE of HR, BP, and ABI across all times were calculated and were analyzed using analysis of variance. The Levine statistic for equality of variance was used and the null hypothesis was rejected if $P < 0.05$. When variances were assumed to be equal between groups, the Bonferoni post hoc test was used to further detect differences between groups. When variances were assumed to be nonequal, then the Tamhane post

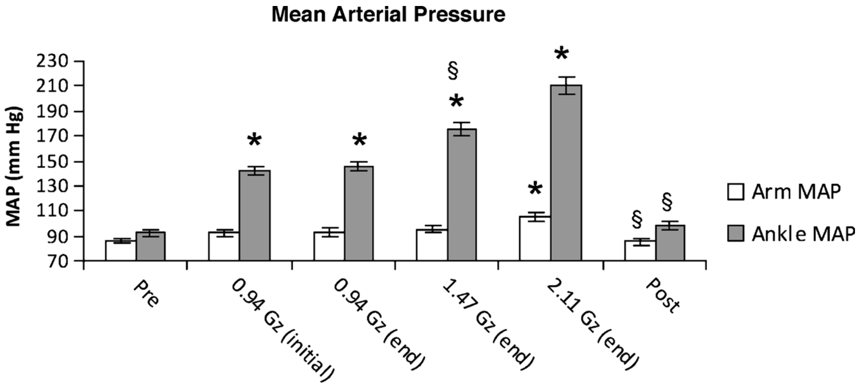

FIGURE 2. Mean arterial pressure (MAP) in the arm and ankle at different level of short-radius centrifugation. *$P < 0.05$ compared with supine "Pre"; §$P < 0.05$ compared with previous Gz level. Data are presented as means ± SE.

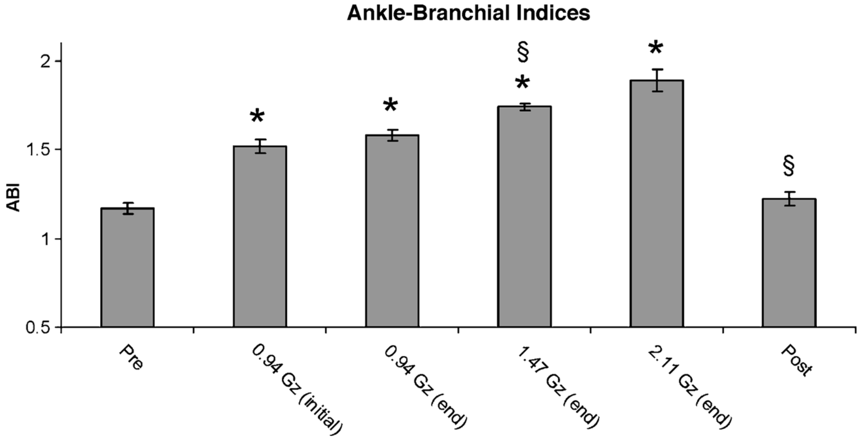

FIGURE 3. Ankle–brachial indices (ABI) at different level of short-radius centrifugation. *$P < 0.05$ compared with supine "Pre"; §$P < 0.05$ compared with previous Gz level. Data are presented as means ± SE.

hoc test was used to detect differences between groups. The prior hypotheses for the study also involved pairwise contrasts between 2 prespecified conditions (supine and standing measurements) and were analyzed with paired *t* tests. Data were analyzed using SPSS statistical software (SPSS Inc., Chicago, IL).

RESULTS

Fourteen subjects were recruited and 12 successfully completed the study. One subject experienced presyncope upon standing before centrifugation, and no further testing was done. The other subject experienced severe motion sickness at 2.11 Gz, and no further data were collected from him. There were no presyncopal or syncopal episodes among the subjects at 0.94, 1.47, and 2.11 Gz.

Effect of Centrifugation on Hemodynamic Parameters

Figure 2 shows the mean arterial pressure (MAP) at different g-levels. Mean arterial pressure was significantly increased at all levels of centrifugation for the ankle, but only at 2.11 Gz for the arm.

Figure 3 summarizes the calculated ABIs for the different G-levels. As shown, the ABIs increased significantly with centrifugation, which corresponds to the changes noted in ankle BP. The ABI was significantly higher at 2.11 Gz (1.89 ± 0.06) compared with the upright position (1.70 ± 0.07; $P = 0.045$).

Table 1 displays hemodynamic parameters with short-radius centrifugation. As shown, arm BP increased significantly only at 2.11 Gz. There were no significant changes in HR with centrifugation. In addition, it appears that very little time was needed for the BP parameters to change significantly. For example, we can see that the arm and ankle parameters are very similar at the beginning and the end of the 0.94-Gz level.

Table 2 displays hemodynamic parameters with assuming the upright position before and after a period of centrifugation. Note the significant increase in leg systolic and diastolic pressure with standing both before and after short-radius centrifugation. There was also a significant increase in HR with standing before and after centrifugation, which is expected.

Figure 4 shows the relation between predicted and measured systolic BP values in the ankle based on equation (1.3), with a correlation coefficient of 0.832.

DISCUSSION

The present study allowed us to characterize the responses of different cardiovascular parameters to AG. We demonstrated that short-radius centrifugation leads to an increase in ankle–brachial indices.

Comparison With Other AG Studies

Only a limited number of studies have investigated the cardiovascular effects of AG. In 1997, Hastreiter and Young[7] at Massachusetts Institute of Technology studied the effects of 1-hour centrifugation (2-m radius with top of head at the center of rotation) with 0.5 to 1.5 g at the foot level in the Gz axis. Responses at 0.5 g demonstrated no significant effects. At 1.5 g, HR and BP were comparable to standing. This is characterized by an increase in HR, increase in diastolic pressure, and decrease in pulse pressure relative to supine.

TABLE 1. Hemodynamic Parameters With Short-Arm Centrifugation

Parameters	Pre	0.94 Gz (Initial)	0.94 Gz (End)	1.47 Gz (End)	2.11 Gz (End)	Post
Arm systolic pressure, mm Hg	121 ± 3	131 ± 4	129 ± 3	132 ± 3	148 ± 5*	121 ± 4§
Arm diastolic pressure, mm Hg	69 ± 2	73 ± 3	75 ± 3	77 ± 3	85 ± 5*	67 ± 2§
Heart rate, bpm	64 ± 3	67 ± 3	67 ± 3	72 ± 3	89 ± 8	59 ± 3
Ankle systolic pressure, mm Hg	141 ± 3	197 ± 3*	203 ± 4*	229 ± 4*§	271 ± 3*§	147 ± 7§
Ankle diastolic pressure, mm Hg	68 ± 3	114 ± 5*	118 ± 5*	149 ± 6*§	181 ± 10*	73 ± 2§

Data are presented as means ± SE.

*$P < 0.05$ compared with supine "Pre."

§$P < 0.05$ compared with previous Gz level.

TABLE 2. Orthostatic Vitals Before and After Short-Arm Centrifugation

Parameters	Pre-Supine	Pre-Upright	Post-Supine	Post-Upright
Arm systolic pressure, mm Hg	121 ± 3	130 ± 6*	121 ± 4	141 ± 4*
Arm diastolic pressure, mm Hg	69 ± 2	73 ± 3	67 ± 2	80 ± 3*
Heart rate, bpm	64 ± 3	77 ± 4*	59 ± 3	75 ± 4*
Ankle systolic pressure, mm Hg	141 ± 3	218 ± 6*	147 ± 7	238 ± 4*
Ankle diastolic pressure, mm Hg	68 ± 3	133 ± 6*	73 ± 2	148 ± 9*
Ankle–brachial index	1.17 ± 0.03	1.70 ± 0.08*	1.22 ± 0.04	1.70 ± 0.05*

Data are presented as means ± SE.

*$P < 0.05$ compared with supine level (pre-upright vs pre-supine; post-upright vs post-supine).

Also using a short-arm centrifuge, Edmonds et al.[8] demonstrated an increase in HR at 30 rpm, which is consistent with a trend (although not statistically significant) seen in our study.

Earlier, Cardus and McTaggart[9] found that 2 g at the feet induced syncope in 2 out of 6 subjects. They also demonstrated a decrease in systolic and diastolic pressure, although the longitudinal force applied was 0.38 Gz, which is different from our protocol. They reported a significant decrease in HR after AG exposure, but no significant changes in BP. Iwasaki et al.[10] also report the usefulness of AG in preventing the alterations in HR caused by bed rest and concluded that 1 hour of daily +2 g (at the foot level) along the longitudinal axis might eliminate the changes in autonomic cardiovascular control during simulated microgravity, although the exposure was not sufficient to prevent decreases in exercise capacity. Iwase et al.,[11] in a study investigating the effects of exercise with exposure to graded G loads (centrifuge was 4 m diameter), reported increases in HR and MAP during centrifugation with up to 2 G at the heart level. The authors' explanation for the HR increase suggested that this may be due to a baroreflex response to blood volume displacement in the lower extremities and MAP elevation from an increase in peripheral resistance as a result of sympathoexcitation. Another study by Watenpaugh et al.[2] assessed the changes in hemodynamics with short-arm centrifuge, long-arm centrifuge, and lower-body negative pressure. They reported no changes in HR with short-arm centrifuge, and there were no increase in BP with short-arm or long-arm centrifugation.

Physical Contribution to Increase in BP and Microvascular Circulation

We described in the Introduction the equations used to predict BP under AG conditions where centripetal acceleration and centrifugal forces are present. Incompressible fluid flowing along a streamline in a frictionless system can be described by Bernoulli's equation. In our case, we need to adapt Bernoulli's equation to a rotating environment by taking into account the centripetal acceleration, resulting in

$$P + \frac{1}{2}\rho v^2 + \rho g z - \frac{1}{2}\rho \omega^2 r^2 = \text{ constant} \qquad (1.4)$$

where P is the fluid pressure, ρ is the fluid density, v is the fluid velocity, g is the gravitational acceleration (=9.82 m/s^2), ω is the rotational velocity of the centrifuge, r is the radius of rotation.

The fourth term in equation (1.4) will increase in magnitude when moving toward the lower extremities because the radius is increasing while the rotational velocity and fluid density remain constant. The third term represents gravitational acceleration and remains constant because our subjects are lying supine. Therefore, according to Bernoulli principle as blood flows from the upper body toward the lower extremities, either the flow velocity increases, or the pressure increases, or both increase. In this experiment, we have only measured the increase in BP and have not measured changes in the flow velocity. Our study has shown that BP increases in both the arm and ankles during centrifugation.

Orthostatic challenges are known to add a hydrostatic pressure gradient to leg arterial and venous pressures by translocation of blood.[12–14] In addition, these orthostatic changes also result in peripheral vasoconstriction and subsequent decrease in microvascular circulation which is mediated centrally by adrenergic activation in response to unloading of arterial and cardiopulmonary baroreceptors,[15,16] myogenic autoregulation,[17,18] and the cutaneous venoarteriolar reflexes.[19,20] The goal of these mechanisms is to withstand the orthostatic challenge. Interestingly, these normal reflexes may be attenuated based on the stimulus type (centrifugation[5]) or may be altered in disease states.[21] For the former case, Watenpaugh et al.[2] studied human cutaneous vascular responses to whole-body testing and Gz centrifugation and demonstrated that centrifugation produced less vasoconstriction than tilt.

In the case of diseased states, it has been noted that skin blood flow (measured with laser Doppler flowmetry) and its postural auto-regulation, the venoarteriolar reflexes, are significantly decreased in patients with PAD.[21] This may partly explain why patients with ischemic rest pain in the foot tend to dangle it over the edge of the bed[22] to benefit from a hydrostatic increase

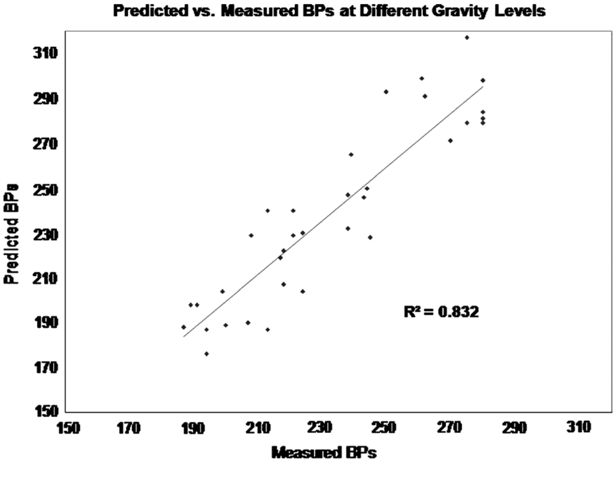

FIGURE 4. Predicted versus measured hemodynamic parameter at different artificial gravity levels. BPs indicate blood pressures.

in BP due to gravity. Hence, although gravitational hemodynamics predict that an increase in leg BP (such as with standing) would lead to vasoconstriction and decrease in microvascular blood flow, this may not necessarily apply to short-term centrifugation or PAD patients and were not measured in the present study.

Implications for Peripheral Arterial Disease

Although we recognize that an increase in pressure at the ankles alone does not ensure a desired increase in blood flow and perfusion as reviewed in the previous section, there is still a reason to believe that an increase in pressure is beneficial. Patients instinctively make use of gravitational pressure gradients to relieve their symptoms, typically by lying on a bed with their legs dropping off the edge of the bed.[22] This reportedly reduced the pain and discomfort associated with critical limb ischemia. Although we have not measured blood flow directly, it is likely that the large increases in pressure also correlate to increases in blood flow through the lower leg, which would further aid the treatment of PAD.

Although this could translate into important clinical advantages, some important issues need to be addressed which represent limitations of the present study. First, although arterial BP and venous pressure are key to perfusion, the perfusion pressure was not measured in this investigation, hence, the next steps will be to study actual tissue perfusion. Future studies should aim to directly measure changes in blood flow to the lower leg resulting from exposure to short-radius centrifugation, as well as further investigate the effects of large and prolonged increases in BP to the leg. Finally, although an increase in ABIs was noted in healthy subjects, this may not be the case in patients with PAD in the presence of atherosclerotic lesions and would also need to be evaluated.

CONCLUSIONS

Short-radius centrifugation leads to an increase in ankle–brachial indices characterized by changes in ankle systolic BP greater than arm systolic BP. This could have potential implications for the treatment of PAD.

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