5-Day Bed Rest: Portal and Lower Limb Veins With and Without Artificial Gravity Countermeasures

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PURPOSE: The objective of the study was to evaluate the effect of short-term, head-down bed rest (HDBR), with and without artificial gravity countermeasures, on splanchnic and lower limb vein properties.

METHODS: Data were collected from 12 men before and after 5 d of continuous −6° HDBR without countermeasures (CON) and with two artificial gravity countermeasure protocols: 30-min continuous centrifugation (AG1), and 30-min intermittent centrifugation (AG2). Portal (PV), tibial (TibV), and gastrocnemius (GastV) veins were investigated by echography supine and after 30 min of head-up tilt.

RESULTS: After HDBR, there was no change in PV, TibV, or GastV cross-sectional area at rest in any of the three conditions. In response to tilt, GastV and TibV area increased (168 ± 141% and 192 ± 124%, respectively) with no change in this response post-HDBR in any of the experimental conditions ($P > 0.05$). PV area decreased with tilt (−33 ± 13%) and was not different pre- to post-HDBR in the CON or AG1 conditions. However, there was a greater reduction in PV area in the AG2 group post-HDBR (−32 ± 10% pre, −49 ± 9% post-HDBR, $P = 0.003$).

CONCLUSIONS: Calf veins were not significantly affected by 5 d of HDBR and did not appear to be negatively impacted by the artificial gravity countermeasures over this time period. In addition, the intermittent protocol resulted in better splanchnic vasoconstriction in response to head-up tilt, which may have contributed to a better maintenance of orthostatic tolerance post-HDBR.

KEYWORDS: bed rest, artificial gravity, centrifugation, portal vein, calf veins.

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Exposure to real or simulated microgravity has been associated with reduced peripheral vascular resistance and smaller vasoconstrictor responses to orthostatic stress, potentially resulting in reduced orthostatic tolerance.[6] Some studies have suggested that this impaired vasoconstrictor response is related to changes in sympathetic nervous system activation;[8] however, other studies have suggested different contributing factors such as smooth muscle atrophy and hyper- or hyposensitivity of adrenergic receptors.[15] Previous work has shown reduced vasoconstriction in response to head-up tilt and lower body negative pressure (LBNP) in both the lower limbs and splanchnic circulation after long-duration, head-down bed rest (HDBR).[2,3] The smaller reduction in portal vein cross-sectional diameter with LBNP or tilt was considered to be a lack of vasoconstriction in the splanchnic territory and was associated with reduced orthostatic tolerance.[2] In addition, it was shown that there was an even greater reduction in orthostatic tolerance when this reduction in splanchnic vasoconstriction was accompanied by reduced vasoconstriction of the lower limbs.[2] Assessments of the lower limb responses to tilt and LBNP with long-duration HDBR have shown increased distensibility of the lower limb veins (the calf veins) and increased fluid stowage in the skin tissue,[5,12,14] but little work has been published examining the responses of leg veins to short-duration HDBR.

The generation of artificial gravity has been proposed as a countermeasure to prevent cardiovascular deconditioning and related orthostatic intolerance induced by bed rest. The use of periods of standing during HDBR has been shown to help maintain orthostatic intolerance and prevent cardiovascular deconditioning.[16] Other studies, using short radius centrifugation to generate artificial gravity, have reported better

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maintenance of orthostatic tolerance post HDBR.[11,17] However, no studies have been published examining the effects of this type of artificial gravity countermeasure on the lower limb or splanchnic venous properties.

The objective of this study was to determine the effects of short-duration HDBR on the veins of the lower limb and splanchnic region with and without artificial gravity countermeasures. It was hypothesized that: 1) 5 d of bed rest would be sufficient to induce splanchnic and leg vein deconditioning similar to that seen with long-duration HDBR; 2) the artificial gravity countermeasure would have a beneficial effect on the splanchnic vascular response to an orthostatic test; and 3) the artificial gravity would have a negative effect on the lower limb veins both at rest (size) and during head-up tilt (distensibility) due to the lower limb being exposed to hypergravity conditions.

METHODS

Procedure

Participating in the study were 12 healthy men (21-42 yr of age). Participants were considered to be recreationally active and without major cardiovascular disease (height: 178 ± 8 cm; body mass: 74 ± 8 kg; maximal oxygen uptake: 39.3 ± 6.5 ml $\cdot$ kg^{-1} $\cdot$ min^{-1}). The study was conducted at the Institute for Space Physiology and Medicine (MEDES) located at Rangueil Hospital in Toulouse, France. All experimental protocols were approved by the Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale, Midi-Pyrénées. Before participation, each subject signed informed consent and was aware of his right to withdraw from the study at any time without prejudice.

The study consisted of 5 d of continuous 6° HDBR with and without artificial gravity countermeasures. It was a crossover design in which each subject participated in a control condition (CON) and each of the two artificial gravity countermeasure conditions with each bed rest session being separated by 1 mo. The countermeasure conditions used a short-arm centrifuge (Verhaert Cie, Kruibeke, Belgium) to generate a force of 1 G at the center of mass of the subject. In the first countermeasure condition, artificial gravity was applied continuously for 30 min (AG1), whereas the second one consisted of six intermittent and consecutive centrifugation steps of 5 min each with 3 min rest in between, for a total of 30 min of artificial gravity (AG2). The artificial gravity countermeasures were applied during the second and fourth day of the bed rest period.

Measurements

Measurements of venous parameters were performed by echography before and after bed rest. These ultrasound examinations took place during an orthostatic tolerance test (head-up tilt). After 5 min of supine rest, subjects were moved to an 80° head-up tilt position for 30 min. Following this, LBNP was progressively applied by steps of -10 mmHg with each step being maintained for 3 min. The test was terminated at the onset of presyncope as indicated by a sudden increase in heart rate (> 15 bpm), a sudden drop in mean arterial pressure (< 70 mmHg), nausea, dizziness, or at the request of the subject. The ultrasound images were collected during the supine rest period (rest) and every 10 min during the 30 min of head-up tilt and before the onset of presyncope if the test was terminated during the 30-min tilt period (tilt).

The portal vein (PV), posterior tibial vein (TibV), and gastrocnemius vein (GastV) cross-sectional areas were measured by echography (Mindray-M5, Beijing, China). For PV measures, the sonographer located the ultrasound probe on the abdomen at the intersection of the right mamilliary and xiphoid lines to obtain a longitudinal view. Portal vein flow volume (ml $\cdot$ min^{-1}) during tilt has been found to be linearly related to changes in portal vein cross-sectional area (cm^2).[1] As it is more complicated and time consuming to measure both portal vein cross-sectional area and Doppler velocity during tilt, we chose to only measure cross-sectional area, which can be used as an indication of portal vein flow. The posterior tibial and gastrocnemius veins were visualized using a flat echography probe (7-MHz linear array) taped to the skin on the posterior face of the calf, providing cross-sectional views of the calf veins. Mean arterial pressure (MAP) was determined continuously throughout the tilt test using finger photoplethysmography (Nexfin, BMEYE BV, Amsterdam, Netherlands). For analysis purposes, values collected at the finger were corrected to heart level during the post processing.

Statistical Analysis

For the statistical analysis, each condition was considered separately with one-way repeated measures ANOVAs with Tukey post hoc testing (SigmaPlot 12.5, Systat Software Inc., San Jose, CA) being used to assess the effects of HDBR. For all tests, significance was set at $P < 0.05$.

Analysis Limitations

The study was originally designed for 12 subjects participating in each of the 3 conditions. However, one subject was excluded from the AG1 group due to difficulties with the countermeasure protocol, and a second subject was excluded from the AG2 group due to illness not related to the study. In addition, in some cases ultrasound images were not of sufficient quality for analysis and were not included in the statistical analysis. The adjusted numbers of participants for each measure have been indicated.

RESULTS

After 5 d of HDBR there was no change in portal, tibial, or gastrocnemius vein cross-sectional area at rest in any of the three conditions (**Table I**). From supine to tilt, TibV and GastV increased (**Fig. 1** and **Fig. 2**), whereas PV decreased (**Fig. 3**). Post-HDBR, there was no difference in the tilt response for TibV or GastV in any of the conditions. Similarly, there was no effect of HDBR on the PV response to tilt in the CON and AG1

Table I. Measurements of Lower Leg Veins and Portal Vein Cross-Sectional Area at Rest Pre- and Post-HDBR.

	PRE-HDBR	POST-HDBR	*P*
PV area (cm^2)			
CON (*N* = 6)	1.15 ± 0.14	1.03 ± 0.18	0.051
AG1 (*N* = 7)	1.03 ± 0.23	0.86 ± 0.30	0.227
AG2 (*N* = 8)	1.15 ± 0.30	1.10 ± 0.30	0.790
TibV area (cm^2)			
CON (*N* = 10)	0.25 ± 0.06	0.29 ± 0.12	0.291
AG1 (*N* = 8)	0.32 ± 0.14	0.32 ± 0.13	0.940
AG2 (*N* = 10)	0.24 ± 0.06	0.25 ± 0.08	0.856
GastV area (cm^2)			
CON (*N* = 10)	0.08 ± 0.03	0.07 ± 0.02	0.431
AG1 (*N* = 8)	0.08 ± 0.04	0.09 ± 0.05	0.773
AG2 (*N* = 11)	0.07 ± 0.03	0.06 ± 0.02	0.456

Values show the cross-sectional area (mean ± SD) of the portal vein (PV), posterior tibial vein (TibV), and gastrocnemius (GastV) vein at rest in the supine position pre- and post-HDBR.

conditions. However, in the AG2 condition there was a greater reduction in PV cross-sectional area with tilt post-HDBR (PV area AG2: −32 ± 10% pre-HDBR vs. −49 ± 8% post-HDBR [$F(1,7) = 19.124$, $P = 0.003$]. In addition, the AG2 condition also showed a better maintenance of orthostatic tolerance post-HDBR (**Fig. 4**) as evident by the smaller reduction in tilt tolerance time in comparison to the CON condition [−25 ± 13 min in the CON condition vs. −7 ± 8 min in the AG2 condition, $F(2,7) = 4.876$, $P = 0.025$].

There was no change in resting MAP after HDBR in any of the three conditions (**Table II**, $P > 0.05$). Similarly, the MAP response to tilt was not changed in the AG1 and AG2 conditions (Table II). However, post-HDBR, the MAP response to tilt was significantly less in the CON condition [9.8 ± 6.0 mmHg pre-HDBR vs. 1.1 ± 5.5 mmHg post-HDBR, $F(1,8) = 12.572$, $P = 0.008$].

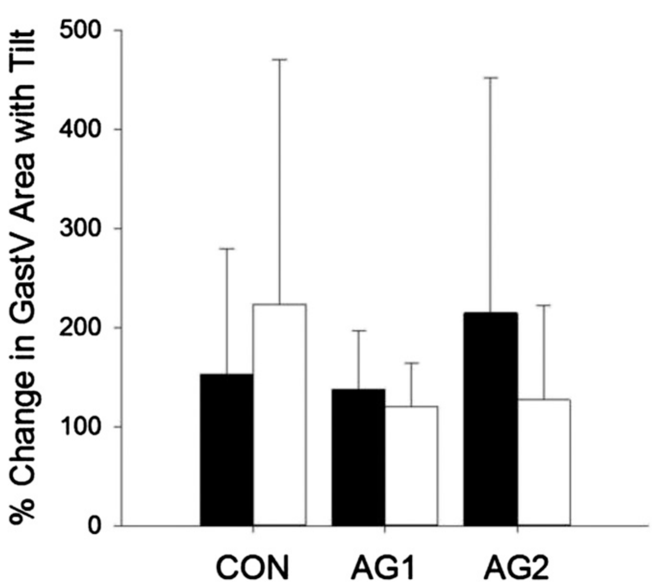

Fig. 1. Percent increase in TibV cross-sectional area with head-up tilt pre-HDBR (black bars) and post-HDBR (white bars) for CON (*N* = 10), AG1 (*N* = 8), and AG2 (*N* = 10).

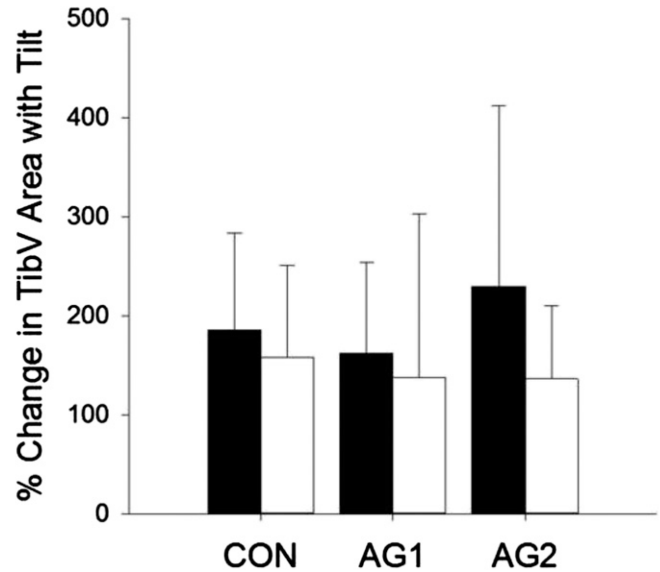

Fig. 2. Percent increase in GastV cross-sectional area with head-up tilt pre-HDBR (black bars) and post-HDBR (white bars) for CON (*N* = 10), AG1 (*N* = 8), and AG2 (*N* = 11).

DISCUSSION

The current study examined the effects of 5 d of HDBR with and without artificial gravity countermeasures on lower limb and splanchnic vein cross-sectional area at rest and in response to head-up tilt. The results showed that 5 d of HDBR did not affect calf vein cross-sectional area at rest or alter the venous response to head-up tilt. Similarly, the PV cross-sectional area was not changed at rest in any of the conditions and the response to head-up tilt was similar pre- to post-HDBR in the CON and AG1 conditions. However, PV vasoconstriction

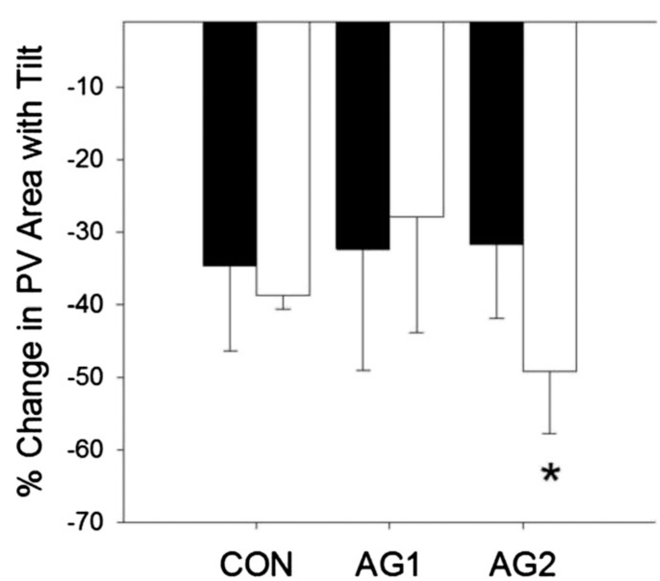

Fig. 3. Percent reduction in PV cross-sectional area with head-up tilt pre-HDBR (black bars) and post-HDBR (white bars) for CON (*N* = 6), AG1 (*N* = 7), and AG2 (*N* = 8). *Post-HDBR values that are statistically different ($P < 0.05$) from pre-HDBR.

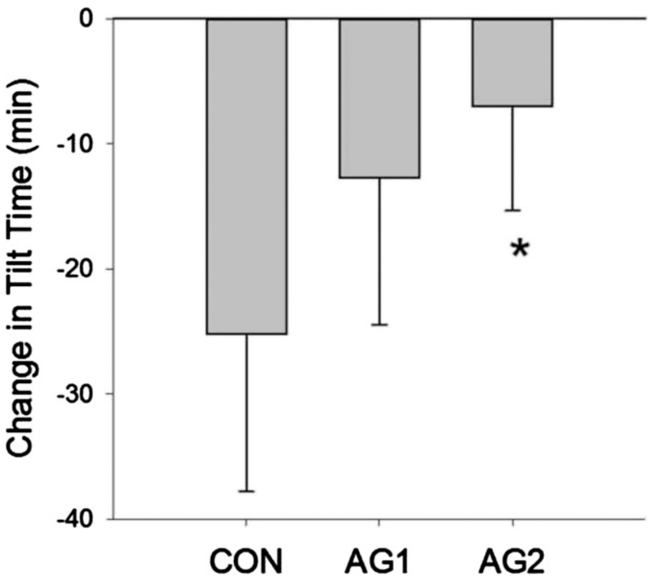

Fig. 4. Difference in tilt duration time from pre-HDBR (an indication of the change in orthostatic tolerance with HDBR). *HDBR values are statistically different ($P < 0.05$) in AG2 when compared to the CON condition.

with tilt was significantly greater in the AG2 condition. These results suggest that the artificial gravity countermeasure may have a beneficial effect on the splanchnic circulation, helping to maintain orthostatic tolerance.

In the current study, no changes were seen in GastV cross-sectional area at rest or in the GastV response to tilt in any of the experimental conditions. Similarly, TibV was unchanged at rest and the response to tilt was unchanged in each of the experimental conditions. These results are in contrast to previous studies of long-duration bed rest, which have shown increased lower leg vein diameter and compliance after HDBR.[2,5,14] Similarly, a study of short-term bed rest found increased femoral vein diameter with LBNP.[4] However, the short-term bed rest study focused on the femoral vein, which may have different responses compared to the veins of the lower legs, and used LBNP to assess the venous response to orthostatic stress, which may produce different results as there is muscle contraction during head-up tilt where the lower limbs are relaxed with LBNP. The results of the current study suggest that 5 d of HDBR may have been insufficient to produce significant changes in lower leg vein properties.

Table II. Mean Arterial Pressure (MAP) Measurement at Rest and in Response to Head-Up Tilt Pre- and Post-HDBR.

	PRE-HDBR	POST-HDBR	*P*
Supine Rest (mmHg)			
CON (*N* = 12)	86.6 ± 9.8	90.0 ± 6.5	0.162
AG1 (*N* = 11)	87.5 ± 10.6	88.0 ± 12.2	0.787
AG2 (*N* = 11)	87.1 ± 7.9	89.3 ± 7.3	0.267
Response to Tilt (mmHg)			
CON (*N* = 9)	9.8 ± 6.0	1.1 ± 5.5	0.008
AG1 (*N* = 10)	5.9 ± 5.7	2.6 ± 5.3	0.138
AG2 (*N* = 9)	7.3 ± 5.6	4.0 ± 5.6	0.166

Values show resting MAP and the percent change with head-up tilt (mean ± SD). The response of MAP to tilt was found to be significantly different post-HDBR compared to pre-HDBR in the CON condition.

The artificial gravity countermeasures used in the current study involved centrifugation to produce a force of 1 G at the center of mass of the participants. Therefore, during the countermeasure sessions, the lower legs of the participants were subjected to hypergravity conditions, which may have altered venous properties independently of the potential effects of HDBR. This does not appear to be the case as the lower leg venous responses to tilt post-HDBR were the same in all experimental conditions.

Previous studies have reported a significant reduction in PV diameter[1,2,10] related to reduced PV blood flow[2,12] and increased splanchnic vascular resistance[9] with orthostatic stress. It has been noted that post-HDBR, PV area was found to decrease less with tilt or LBNP in those individuals who showed greater reductions in orthostatic tolerance post-HDBR.[2] In the present study, PV area decreased more post-HDBR with tilt in the AG2 condition. As the duration of tilt post-HDBR was greater in the AG2 subjects compared to AG1 and CON, indicating better maintenance of orthostatic tolerance, it can be suggested that the better orthostatic tolerance was related at least partially to greater splanchnic vasoconstriction.

Interestingly, the better splanchnic vasoconstriction response was only seen in the AG2 condition and not the AG1 condition. During the AG1 countermeasure, a fluid shift toward the feet occurs at the start of the centrifugation, which may trigger a sympathetic and peripheral vasomotor response that is then sustained for the duration of the countermeasure. In contrast, with the AG2 countermeasure this initial response is repeated for each application of the artificial gravity. Russian medical surgeons have reported using LBNP during the last 2 wk of spaceflight in an effort to re-educate the vasomotor response to orthostatic stress (unpublished data). Similar to the AG2 countermeasure, the application of LBNP is stepped in sessions of 3-5 min, providing multiple stimuli for adaptation, which supports the notion that repetitive application of an orthostatic stress generates greater cardiovascular adaptations when compared to a single sustained stress.

Previous studies have indicated that a transient increase in gravity during even short-duration HDBR can partially prevent orthostatic intolerance after HDBR.[7,16–19] Additionally, it has been suggested that repetitive exposure to hypergravity may improve cardiovascular responses to subsequent hypergravity exposure through better vasoconstriction, increased venous return, and increased baroreflex sensitivity.[13] This could suggest exposure to artificial gravity may be beneficial in preventing cardiovascular deconditioning with HDBR and spaceflight. In the current study it appears that the artificial gravity countermeasure contributed to maintaining orthostatic tolerance through an improved splanchnic vasoconstriction. However, with the artificial gravity countermeasures used in the current study, the lower leg was subjected to hypergravity conditions and it is unclear what effect long-term exposure to this condition may have on the veins of the lower leg.

In conclusion, the results of the current study demonstrated that 5 d of HDBR was insufficient to induce changes in splanchnic or calf veins at rest. In addition, 5 d of HDBR with and without artificial gravity countermeasures did not affect lower leg venous responses to head up tilt. In contrast, intermittent centrifugation (AG2) resulted in statistically significantly greater splanchnic vasoconstriction with tilt post-HDBR, which may have contributed to a better maintenance of orthostatic tolerance. These results suggest that in the future, intermittent centrifugation may be an effective countermeasure to protect splanchnic hemodynamics in astronauts; however, the effects of long-term exposure to hypergravity conditions on the veins of the lower limbs remain unknown and require further investigation.

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