Gender differences in bed rest: preliminary analysis of vascular function
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Orthostatic intolerance is a recognized consequence of spaceflight. Numerous studies have shown that women are more susceptible to orthostatic intolerance following spaceflight as well as bed rest, the most commonly used ground-based analog for spaceflight. One of the possible mechanisms proposed to account for this is a difference in vascular responsiveness between genders. We hypothesized that women and men would have differing vascular responses to 90 days of 6-degree head down tilt bed rest. Additionally, we hypothesized that vessels in the upper and lower body would respond differently, as has been shown in the animal literature. Thirteen subjects were placed in bedrest for 90 days (8 men, 5 women) at the Flight Analogs Unit, UTMB. Direct arterial and venous measurements were made with ultrasound to evaluate changes in vascular structure and function. Arterial function was assessed, in the arm and leg, during a reactive hyperemia protocol and during sublingual nitroglycerin administration to gauge the contributions of endothelial dependent and independent dilator function respectively. Venous function was assessed in dorsal hand and foot veins during the administration of pharmaceuticals to assess constrictor and dilator function. Both gender and day effects are seen in arterial dilator function to reactive hyperemia, but none are seen with nitroglycerin. There are also differences in the wall thickness in the arm vs the leg during bed rest, which return toward pre-bed rest levels by day 90. More subjects are required, especially females as there is not sufficient power to properly analyze venous function. Day 90 data are most underpowered.
Gender differences in bed rest: preliminary analysis of vascular function

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ABSTRACT

Orthostatic hypotension is a recognized consequence of spaceflight. Numerous studies have shown that women are more susceptible to orthostatic intolerance following spaceflight as well as bed rest, the most common model of spaceflight for terrestrial research. The purpose of this study was to compare the vascular responses of men and women during short-duration bed rest. Subjects were pre-screened for arterial and venous measurements were maintained with ambulatory monitors to evaluate changes in baseline vascular function during bed rest. Venous function was measured using timed venous occlusions in the dorsal hand and foot veins during the day and night. Arterial function was assessed using ultrasound imaging of the brachial and anterior tibial arteries. Venous and arterial responses to nitroglycerin did not change over the course of bed rest (day effect) in either the brachial or anterior tibial artery, however, the anterior tibial artery dilated more than the brachial artery (p < 0.001). There was a marked decrease in intimal-medial thickness in the anterior tibial artery at days 21 (10.3%), 35 (20.6%) and 49 (24%). We were unable to detect any differences in the dorsal hand or foot vein responses to pharmacological agents during bed rest.

INTRODUCTION

• Orthostatic hypotension continues to be a problem following spaceflight, especially long duration spaceflight.
• Females are more susceptible to orthostatic hypotension and presyncope.
• Numerous citations in the literature point to a venous return issue, this may include differences in arterial or venous function.
• Animal literature shows a differential remodeling of vasculature that leads to structural and functional changes. There is also bed rest evidence for increased arterial dilator function.
• The study evaluated arterial and venous function in subjects confined to bed rest for 90 days (in-bed down bed rest).

HYPOTHESIS

We hypothesized that gender will influence the vascular responses to bed rest.

We also tested the hypothesis that arteries in the arm and leg would remodel during bed rest. Additionally, we tested the hypothesis that there would be differences in arterial and venous responses that would lead to structural and functional changes.

RESULTS I: Reactive Hyperemia

Brachial Artery

Figure 1. Reactive hyperemic responses (flow-mediated dilation) during bed rest for all subjects. These ultrasound images of dorsal veins pre BR7 BR21 BR35 BR49 BR60 BR75 BR90 BR+3 Bed Rest Day. Brachial Artery

Anterior Tibial Artery

Figure 2. Reactive hyperemic responses (flow-mediated dilation) during bed rest for all subjects. These ultrasound images of dorsal veins pre BR7 BR21 BR35 BR49 BR60 BR75 BR90 BR+3 Bed Rest Day. Anterior Tibial Artery

RESULTS II: Sublingual Nitroglycerin

Brachial Artery

Figure 3. Direct arterial dilation with nitroglycerin. These graphs show the difference between pre and post-drug ingestion (delta) for each timepoint for all subjects separated by gender. There were no statistical differences in the brachial artery, left panel, or in the anterior tibial artery, right panel.

Anterior Tibial Artery

Figure 4. Direct arterial dilation with nitroglycerin. These graphs show the difference between pre and post-drug ingestion (delta) for each timepoint for all subjects separated by gender. There were no statistical differences in the brachial artery, left panel, or in the anterior tibial artery, right panel.

RESULTS III: Intimal Medial Thickness

Brachial Artery

Figure 5. Intimal medial thickness. The intimal medial thickness (cm) decreased during bed rest in the anterior tibial artery only (right panel). * = p < 0.05 within group for bed rest day compared to pre bed rest.

Anterior Tibial Artery

Figure 6. Intimal medial thickness. The intimal medial thickness (cm) decreased during bed rest in the anterior tibial artery only (right panel). * = p < 0.05 within group for bed rest day compared to pre bed rest.

RESULTS IV: Venous Function

Figure 7. Ultrasound image of dorsal vein showing venous dilation with acetylcholine, right panel, as compared to baseline pre-constriction, left panel.

Figure 8. Phentolamine pre-constriction (10 μg/0.1 ml) by gender.

CONCLUSIONS:

These data show that some arterial and measures change during bed rest, while others do not. The challenge is to elucidate which parameters may translate into functional decrements on long duration spaceflight. Flow-mediated dilation and intimal-medial thickness has been shown to be clinically relevant indicators of dysfunction in patients exhibiting disease.

We do not have sufficient statistical power to detect any changes in venous function. Twelve more females and 9 more males will be studied.

Further study is needed to determine if these measures can provide any insight into the effects of bed rest, or spaceflight, on cardiovascular performance in otherwise healthy subjects.

LIMITATIONS:

A major limitation for this study is the subject number at the varying time points. This is largely due to the forced evacuation of subjects for Hurricane Rita. These subjects, therefore, only completed 44-03 days of the designed 90-day bed rest protocol. Thus, a subset of subjects completed the full 90 days of bed rest. Due to the relatively small number of women participating, the statistical power was limited.