Gender differences in bed rest: preliminary analysis of vascular function
Steven H. Platts, Michael B. Stenger, David S. Martin, Sondra A. Freeman-Perez, Tiffany Phillips, L.Christine Ribeiro

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.
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**ABSTRACT**
Ketorolac or indomethacin had no differences in flow-mediated dilation (FMD) over the duration of bed rest (day effect) in either the brachial or anterior tibial artery, however, the anterior tibial artery dilated more than the brachial artery with L-NMMA-NO inhibitor.

**INTRODUCTION**

- Chronic hypoperfusion constitutes a problem following spaceflight, especially long duration spaceflight.
- Females are more susceptible to chronic hypoperfusion and plasminogen.
- Numerous citations in the literature point to a remodeling of vasculature that leads to structural and functional changes during spaceflight.
- We studied arterial and venous function in subjects confined to 90 days of head-down tilt bed rest, which is the most widely accepted ground-based analog of spaceflight.

**METHODS**

- Twenty-six subjects were included in this study of men and women from the Flight Analogs Project being conducted at UTMB in conjunction with NASA.
- We determined arterial and venous function and arterial diameter and flows at baseline, during reactive hyperemia, 30 seconds post-occlusion until 5 minutes post-occlusion. For measurements during administration of sublingual nitroglycerin, diameters were measured 5 minutes later.
- There were no statistical differences in the brachial artery, right panel, and in the anterior tibial artery, right panel.

**RESULTS I: Reactive Hyperemia**

- Bed Rest Day 30 Day 60 Day 90

**RESULTS II: Sublingual Nitroglycerin**

- Bed Rest Day 30 Day 60 Day 90

**RESULTS III: Intimal Medial Thickness**

- Bed Rest Day 30 Day 60 Day 90

**RESULTS IV: Venous Function**

- Bed Rest Day 30 Day 60 Day 90

**CONCLUSIONS:**

These data show that some arterial and venous 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. Those subjects, therefore, only completed 44-53 days of the designed 90 day bed rest protocol. Thus, only 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.