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.
RESULTS I: Reactive Hyperemia

Figure 1. Reactive hyperemic responses (flow-mediated dilation) during bed rest for all subjects. These graphs show the difference between pre- and post-occlusion (delta) for each time point. There were no significant differences pre-to post-bed rest. Male and female responders demonstrated similar responses.

Figure 2. Reactive hyperemic responses (flow-mediated dilation) during bed rest for all subjects. These graphs show the difference between pre- and post-occlusion (delta) for each time point. There were no significant differences pre-to post-bed rest. Male and female responders demonstrated similar responses.

RESULTS II: Sublingual Nitroglycerin

Figure 3. Direct arterial dilation with nitroglycerin. These graphs show the difference between pre- and post-occlusion (delta) for each time point. There was no change in the brachial artery. In contrast, the anterior tibial artery dilated more than the brachial artery (p = 0.001).

Figure 4. Direct arterial dilation with nitroglycerin. These graphs show the difference between pre- and post-occlusion (delta) for each time point. There was no change in the brachial artery. In contrast, the anterior tibial artery dilated more than the brachial artery (p = 0.001).

RESULTS III: Intimal Medial Thickness

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 compared to Bed Rest Day 30.

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 compared to Bed Rest Day 30.

RESULTS IV: Venous Function

Figure 7. Changes in venous function. The venous function showed a decrease in venous function during bed rest. Male responders demonstrated a greater decrease in venous function than female responders.

Figure 8. Changes in venous function. The venous function showed a decrease in venous function during bed rest. Male responders demonstrated a greater decrease in venous function than female responders.

SUMMARY

There were no differences in flow-mediated dilation response in the arm at any time point. However, the flow-mediated dilation response in the leg was significantly increased at day 49. There is a trend for a gender difference over the course of bed rest in the anterior tibial artery (p = 0.07). On day 21, there is a significant difference in the anterior tibial artery between men and women.

Arterial responses to nitrroglycerin did not change 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 (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.

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. Those subjects, therefore, only completed 44-53 days of the designed 90 days 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.