CAROTID INTIMA MEDIA THICKNESS IN THE ASTRONAUT CORPS: ASSOCIATION TO SPACEFLIGHT

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ABSTRACT

INTRODUCTION: Carotid Intima Media Thickness (CIMT) has been demonstrated to be predictive of future cardiovascular events. Within various populations, radiation exposure, stress, and physical confinement have all been linked to an increased CIMT. Recent research discovered CIMT was significantly increased in ten long duration astronauts from pre-flight to four days post flight. The relationship between spaceflight and CIMT is not well understood and trends in CIMT within the larger astronaut population are unknown.

METHODS: In 2010, CIMT was offered as part of the astronaut annual exam at the JSC Flight Medicine Clinic using a standardized CIMT screening protocol and professional sonographers. Between 2010 and 2016, CIMT measurements were collected on 213 NASA astronauts and payload specialists. The values used in this retrospective chart review are the mean of the CIMT from the right and left. Spaceflight exposure was categorized based on the total number of days spent in space at the time of the ground-based ultrasound (0, 1-29, 30-200, ≥200). Linear regressions with generalized estimating equations were used to estimate the association between spaceflight exposures and CIMT.

RESULTS: 530 studies were completed among 213 astronauts with a mean of 2.5 studies (range 1-6) per astronaut over the six year period. As in other populations, CIMT was significantly associated with age; however, gender was not. While there was no significant direct correlation between total spaceflight exposure and CIMT found, astronauts with 30-200 spaceflight days and astronauts with greater than 200 spaceflight days had significantly increased CIMT over astronauts who had never flown ($p=0.002$ and $p=<0.0001$ respectively) after adjustment for age.

DISCUSSION: Further work is needed to fully understand CIMT and its association to spaceflight. Current occupational surveillance activities are under way to study CIMT values in conjunction with other cardiovascular risk factors among astronauts as compared to the general population.

INTRODUCTION

The Astronaut Corps is a unique population with occupation exposures and health hazards unlikely any other group. Astronauts have exposure to the microgravity environment, which has been demonstrated to significantly affect human physiology. [1,2] They also have significant exposure to cosmic radiation. [3] The association between ionized radiation and cardiovascular disease burden has been well described in other populations.[4,5,6] A recent study has suggested that lunar mission astronauts, whose deep space missions exposed them to increased rates of cosmic radiation exposure, may have higher rates of cardiovascular disease related mortality. [7] Astronauts also operate in an isolated, confided space with long working hours and significant mental stress. While these risk factors have been linked to increased cardiovascular disease risk burden in other populations, whether the Astronaut Corps is at elevated risk for cardiovascular disease due to these occupational exposures remains an open question. [9,10,11]

Carotid intima media thickness is a well-established tool for evaluating cumulative cardiovascular risk burden and has been frequently applied as a surrogate marker for cardiovascular disease in research studies.[13] It is most often non-invasively measured by ultrasound. Within various populations, radiation exposure, mental stress, and physical confinement have all been linked to an increased CIMT. [6,10,11] Recent research discovered CIMT was significantly increased in ten long duration astronauts from pre-flight to four days post flight. [8] The relationship between spaceflight and CIMT is not well understood and trends in CIMT within the larger astronaut population are unknown.

The objective of this study was to use existing clinical data to identify the general trends of carotid intimal medial thickness within the Astronaut Corps and to determine whether there exists a relationship between spaceflight exposure and CIMT as part of a larger effort to understand the cardiovascular disease burden in this population.

METHODS

This study was designed as a retrospective chart review of JSC Flight Medicine Clinic records. Carotid intima media thickness measurements have been offered to members of the Astronaut Corps has an optional health screening since 2009. These measurements have been performed by a professional sonographer and, since 2010, a standardized CIMT screening protocol and software have been used to perform these measurements. Between 2010 and 2016, 530 CIMT measurements were completed among 213 astronauts with a mean of 2.5 studies (range 1-6) per astronaut over the six-year period. These measurements were obtained from the ultrasound imaging software directly and entered into a secured, de-identified database. CIMT measurements performed prior to standardization of software in 2010 were excluded. All non-astronauts were also excluded. SPSS and Excel Datapack software packages were used to performed statistical analysis. Linear regression was performed to evaluate the relationship between spaceflight exposure and CIMT. The Atherosclerosis Risk in Communities (ARIC) trial was a large scale research study which defined CIMT by age in the general population and was used as a comparison for astronaut data. [13]

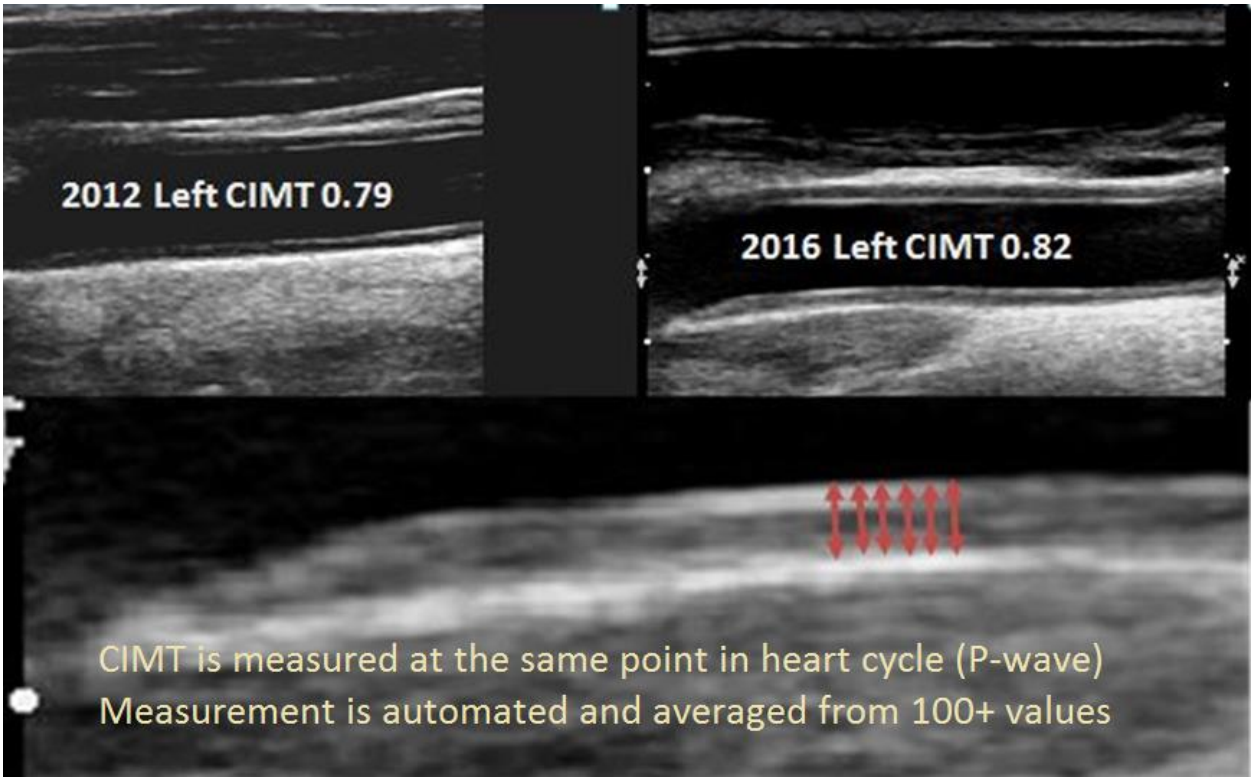

Image 1: Carotid intima media thickness measurement performed by ultrasound.

RESULTS

Astronaut carotid intima media thickness measurements (n=530) were graphed by age to evaluate overall trends. A comparison of ARIC trends and Astronaut Corps trend charts developed from these measurements demonstrated that the Astronaut Corps is trending above the ARIC data at most age ranges (Figure 1). This is particularly pronounced at from ages 35 to 54 and from 70 to 74, and is observed primarily at the 25^{th} and 50^{th} percentiles. Mean year to year progression for all astronauts with 4+ CIMT measurements (n=43, mean age=47.14) was 0.00847mm/year, which is not increased over the typical progression rate observed in general population studies. However, naïve astronauts identified (n=4, mean age=41) in the data set demonstrated a CIMT progression of 0.035mm during the year of their first flight, above the general population and average progression rate for the Corps.

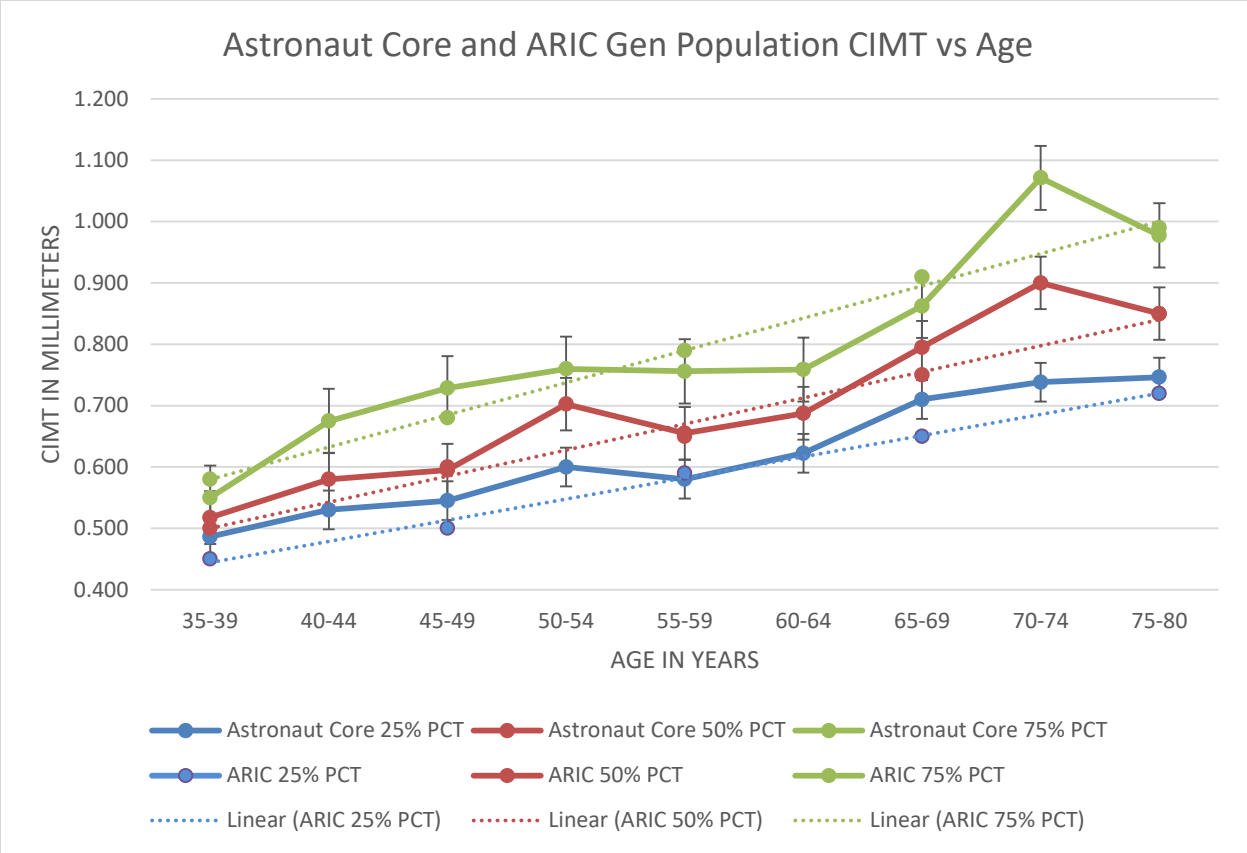

Figure 1 Carotid intima media thickness in the Astronaut Corps by age. The Atherosclerosis Risk in Communities (ARIC) trial defined CIMT by age in the general population and is included for comparison.

In Figure 2 below, astronaut carotid intimal medial thickness measurements grouped by spaceflight exposure are graphed by age. Spaceflight naïve astronauts who were selected and underwent training for the astronaut corps, but never flew in space are included as a comparison population. Atherosclerotic Risk in Communities (ARIC) general population data is also included as a comparison group. Astronaut exposure groups are divided by total cumulative days in space with 1-29 days being designated light exposure (n=176), 30-199 days designated moderate exposure (n=253), and 200+ days designated high exposure (n=52). CIMT in astronauts in all spaceflight exposed groups trended above naïve astronauts without spaceflight exposure. Astronauts in the light and high exposure groups both trended above ARIC general population trend data.

Astronauts in the high and moderate exposure groups had significantly elevated CIMT measurements over the astronauts with no spaceflight exposure ($p<0.0001$ and $p=0.002$) after correction for age. Astronauts in low spaceflight exposure group also had significantly elevated CIMT over astronauts with no spaceflight exposure ($p=0.0113$). However, linear regression analysis did not demonstrate a direct correlation between cumulative spaceflight exposure time and astronaut CIMT ($p=0.2733$).

Mission type also correlated with CIMT results. Within the spaceflight exposed group, lunar mission astronauts had significantly increased CIMT over non-lunar mission astronauts (p=0.0152).

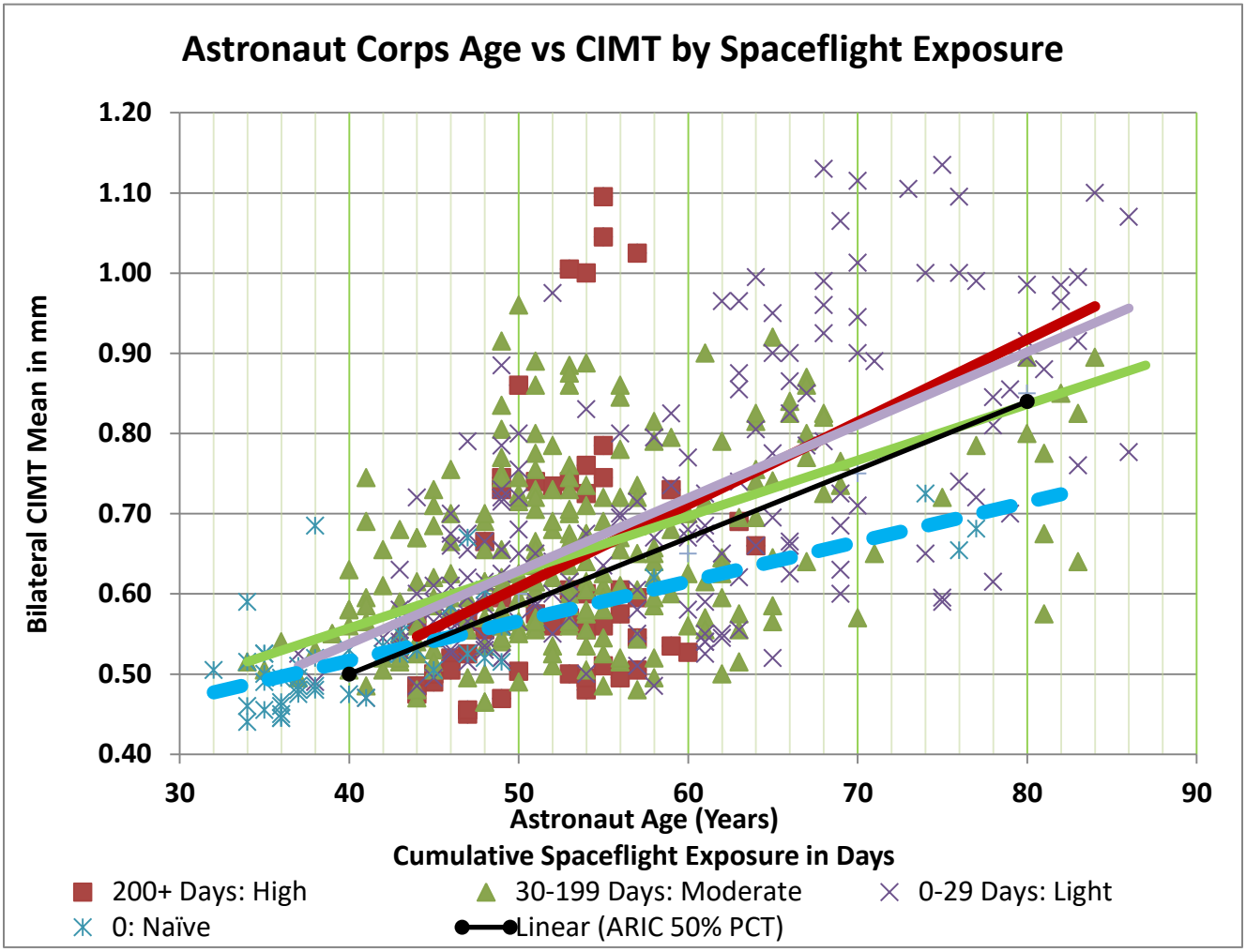

Figure 2 Carotid intima media thickness in the Astronaut Corps grouped by spaceflight exposure vs age.

DISCUSSION

Carotid intimal medial thickness is strongly associated with cardiovascular disease risk burden and progresses with increasing age.[13] Following this trend, the cumulative astronaut data progresses with age similar to the general population data demonstrated in the ARIC population study. However spaceflight naïve astronauts, CIMT age related progression is significantly slower as demonstrated in Figure 2. Astronauts undergo an extensive medical screening process during their selection and must maintain a high level of physical fitness in comparison to the general population. It is likely that the slow age related progression of CIMT in the spaceflight naïve astronauts is consistent with this population's lower baseline cardiovascular disease risk. Despite population's

likely reduced baseline cardiovascular risk, astronaut CIMT in all spaceflight exposure groups trended significantly above spaceflight naïve astronauts CIMT and astronauts in the light and high exposure groups trended above ARIC general population CIMT data. This suggests that astronauts are exposed to some factor during spaceflight that may result in increased CIMT.

Radiation in space has been recognized as a potential health hazard for astronauts that may impact their cardiovascular risk burden.[3] Ionizing radiation results in endothelial cell dysfunction and radiation induced fibrosis in sub-endothelial vascular layers, leading to atherosclerosis.[6] Other studies have established ionizing radiation as a risk factor for cardiovascular disease in the healthcare setting as well as in Japanese nuclear bomb survivors. It has been suggested that cosmic radiation with high energy ions may been more destructive to human tissue than similar exposures to low linear energy transfer radiation commonly used in the healthcare setting. Apollo era astronauts have been found to have an elevated cardiovascular morality rate and this has been attributed to deep space radiation exposure outside of the Earth's protective upper atmosphere and magnetosphere.[7] Apollo astronauts in this dataset had elevated CIMT significantly above both the general population and the rest of the Astronaut Corps, which is consistent with this hypothesis. Astronauts in light spaceflight exposure group, which includes the majority of Apollo astronauts, trended above astronauts with moderate spaceflight exposure. It is possible that their increased cosmic radiation exposure may have increased their CIMT over low earth orbit astronauts. This may also explain why the linear regression model did not find a significant direct correlation between days of exposure and increased CIMT.

The MARS 500 confinement study, which was designed as a ground based model for long duration manned spaceflight, found significant elevation in all subjects CIMT measurements over the course of its 520 day study. The authors speculated whether physical confinement/isolation and mental stress may have contributed to the development of increased artery intima media thickness. Studies performed in combat veterans have shown associations between increased CIMT and mental stress. Similar work has demonstrated a link between social isolation and elevated cardiovascular disease risk. [8]

Arbeille et al found large increases in femoral and carotid intima media thickness over 6 months of spaceflight in 10 astronauts, which persisted 4 days after return to Earth. Our data suggests that increases in CIMT in spaceflight astronauts may persist over many years post-flight and IMT elevations found in that previous study were unlikely to be related to short term fluid shifts associated with microgravity. Although this is not always a direct correlation between cardiovascular disease and carotid intima media thickness, this data may suggest that the Astronaut Corps is at elevated risk for the development of the cardiovascular disease.

This study was limited by several factors, including its retrospective design. There were a limited number of (n=45) measurements of the spaceflight naïve astronaut group, which reduces its utility as a comparison group. The CIMT measurements performed and included in this study are only available from astronauts who volunteered for routine annual screening, which may result in a sample bias. Astronauts who felt they were at higher risk may have volunteered in higher numbers

than lower risk astronauts, which could skew the results of this study. Further data is required to confirm this study's results and determine the wider impact on the Astronaut Corps.

CONCLUSION

While there was no significant direct correlation between total spaceflight exposure and CIMT was identified, astronauts with 30-200 spaceflight days and astronauts with greater than 200 spaceflight days had significantly increased CIMT over astronauts who had never flown after adjustment for age. Astronauts with 1-29 spaceflight days and astronauts with greater than 200 spaceflight days both trended above the general population. Further work is needed to fully understand CIMT in the Astronaut Corps and its association to spaceflight. Current occupational surveillance activities are under way to study CIMT values in conjunction with other cardiovascular risk factors among astronauts as compared to the general population.

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