TRADITIONAL CARDIOVASCULAR RISK FACTORS AS PREDICTORS OF CARDIOVASCULAR EVENTS IN THE U.S. ASTRONAUT CORPS

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Introduction

The Framingham Risk Score (FRS) assesses the absolute 10-year risk for myocardial infarction (MI) and coronary heart disease (CHD)-related death, using a predictive model developed from data collected during the Framingham Heart Study (FHS). The FRS calculation is dependent upon traditional CHD risk factors: age, total and high - density lipoprotein (HDL) cholesterol, systolic blood pressure and treatment, and smoking status. However, numerous studies have documented that the FRS under- or overestimates CHD in populations exhibiting different demographics than the FHS population (1,2).

NASA currently uses FRS to assess the 10-year risk for CHD in astronauts. However, the demographics of the U.S. astronaut corps differ greatly from the FHS population. Furthermore, astronauts experience unique exposures during space flight training and participation that could affect their cardiovascular health. Currently, it is difficult to determine the accuracy of the FRS in predicting the 10-year CHD risk in the astronaut corps due to the small number of CHD events. However, given the unusual demographic profile and unique exposures of this study population, NASA medical personnel have determined the need to develop a predictive model specific to U.S. astronauts. This presentation provides some evidence that risk factors traditionally used to predict CHD in the general population may lack the ability to predict CHD events in astronauts. Furthermore, the presentation discusses imaging techniques that are being considered for inclusion in the new predictive model in an effort to add sensitivity and specificity.

Methods

Study Population & Data Collection

- All U.S. astronauts (n=321), from the first selection class of 1959 through 2004, were included in this analysis.
  - Although the selection criteria for acceptance into the astronaut corps has evolved since 1959, generally, candidates have been screened for appropriate expertise, education, and overall health (3).
  - Women were first selected in1978.
- Payload specialists, international partners, and other space flight participants were excluded from these analyses due to lack of outcome data.

Acknowledgements

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Methods (cont.)

- Death certificate searches were conducted to ascertain vital statistics and cause of death through April 2009.
- Information on demographic and health characteristics collected at baseline and last physical were obtained from medical records and lifestyle questionnaires.
- The outcome was defined as hard coronary heart disease events, including CHD-related deaths or MIs.

Analyses

- Low-density lipoprotein (LDL) and HDL levels, systolic and diastolic blood pressure, and resting pulse were evaluated as predictors of CHD death or MI using exploratory, multivariable Cox proportional hazards regression modeling.
  - The proportional hazards assumption was checked using log-cumulative hazard plots.
  - Each factor was initially evaluated in a univariable model.
  - A backward, stepwise model-building strategy was utilized to identify significant predictors of CHD hazard over time (α=0.10).

Results

Table 1. Frequency distributions of selected characteristics of astronauts

Variable	Overall (n=321) No. (%)
Age at selection	
<35 years	**176 (54.8)**
≥35 years	**145 (45.2)**
Sex	
Male	**276 (86.0)**
Female	**45 (14.0)**
Race	
Non-Hispanic white	**293 (91.3)**
Other	**28 (8.7)**
Marital Status	
Married	**262 (81.6)**
Unmarried	**59 (18.4)**
Educational Level	
Bachelors	**54 (16.8)**
Masters	**161 (50.2)**
Doctoral	**106 (33.0)**

References

1. Brindle P *et al.* (2003). "Predictive accuracy of the Framingham coronary risk score in British men: prospective cohort study". *BMJ* **327** (7426): 1267.
2. Hense HW *et al.* (2003). "Framingham risk function overestimates risk of coronary heart disease in men and women from Germany- results from the MONICA Augsburg and the PROCAM cohorts". *EHJ* 24:937-45.
3. Hamm PB et al. (2000). Design and current status of the Longitudinal Study of Astronaut Health. Aviation, Space, and Environmental Medicine, 71(6):564-70.

Images from:

CIMT: http://www.medicine.emory.edu/divisions/cardiology/research/

EBCT: http://www.life-enhancement.com/article_template.asp?ID=993

Figure 1. Kaplan-Meier Survival Curves by LDL

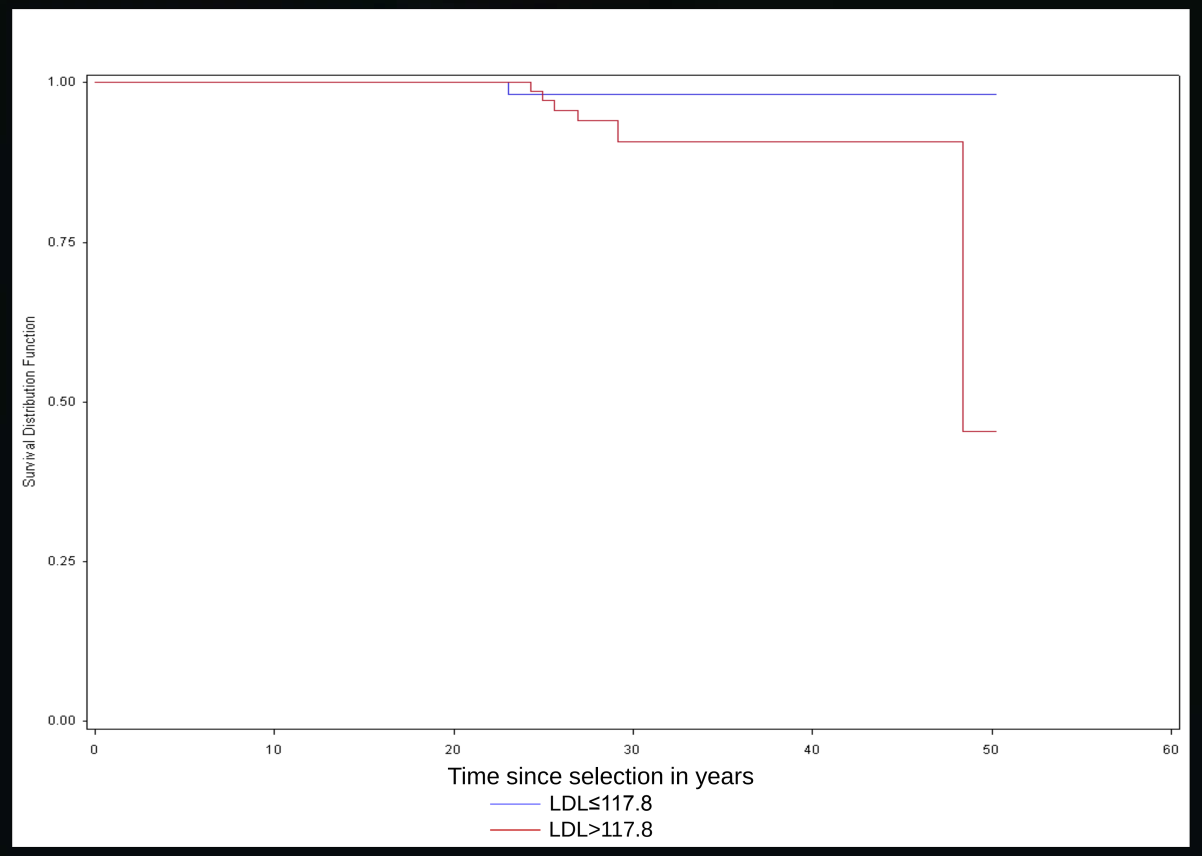


Table 2. Cox proportional hazards regression analysis results showing univariable (A) and multivariable (B) results

Characteristic*	Hazard Ratio (95% CI) (n=321)
Panel A	
Low-density lipoprotein (per 5mg/dl increase)	**1.10 (1.02-1.18)**
High-density lipoprotein (per 5mg/dl increase)	0.80 (0.60-1.06)
Resting pulse (per 5 beat increase)	1.19 (0.81-1.75)
Systolic blood pressure (mmHg)	1.05 (0.98-1.14)
Diastolic blood pressure (mmHg)	1.06 (0.95-1.18)
Panel B	
Low-density lipoprotein (per 5mg/dl increase)	**1.11 (1.03-1.20)**
Resting pulse (per 5 beat increase)	1.29 (0.88-1.91)

Note. Further adjustment for race, education, and sex has no effect on the Hazard Ratios presented; race, education, and sex are not predictive of CHD over time in our study population.
*Characteristic measured at baseline unless otherwise indicated.

Conclusions

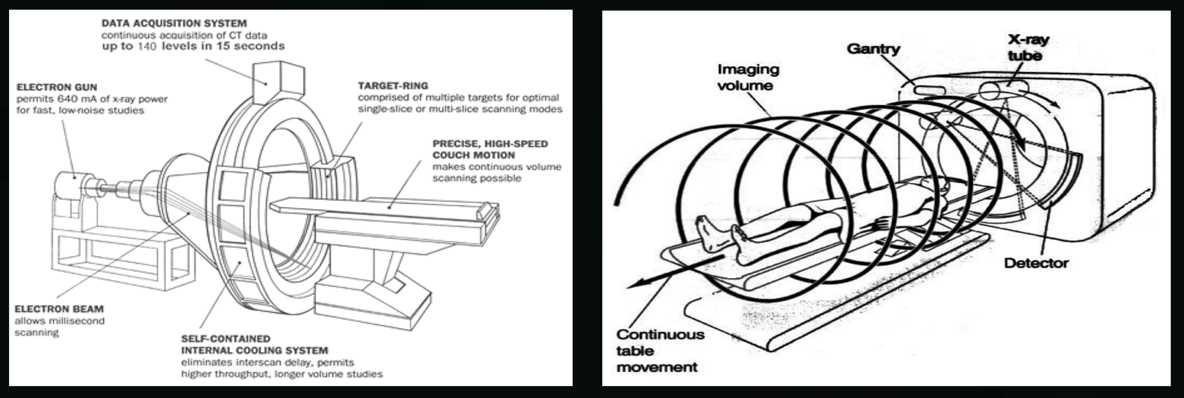
Of all the traditional CHD risk factors examined in this study, only low-density lipoprotein level at baseline is a significant predictor of CHD death or MI in the U.S. astronaut corps. It appears that for every 5mg/dl increase in LDL, there is an approximate 10% increase in CHD death or MI risk over time (HR: 1.10; 95% CI: 1.02-1.18). While these results may be due in part to inadequate statistical power, it is also plausible that the astronaut corps is so different from the general population that more sensitive, nontraditional measures are needed to assess CHD risk appropriately, consequently directing clinical practice guidelines.

Future Directions

Further collection of data on CHD risk factors and outcomes in the astronaut corps is vital both for the development of a new predictive model to assess CHD risk and for increasing the statistical power of existing risk assessments. Moreover, including imaging measures as part of the astronauts' standard clinical care regimen will provide more comprehensive information for use in the development of new CHD risk assessment strategies.

Developing a very sensitive and specific predictive model using traditional and nontraditional risk factors to assess astronaut CHD risk is a high priority for space medicine. This new model will be developed specifically for use in the U.S. astronaut corps and can thus maximize predictive accuracy in this unique population, potentially incorporating occupational exposures and other specific factors that may not necessarily be relevant to the general public. The importance of such a model would be that it could help determine the healthiest astronauts for participation in long-duration missions (including missions to the moon and Mars) and thus, could help prevent CHD events from occurring in space during such missions.

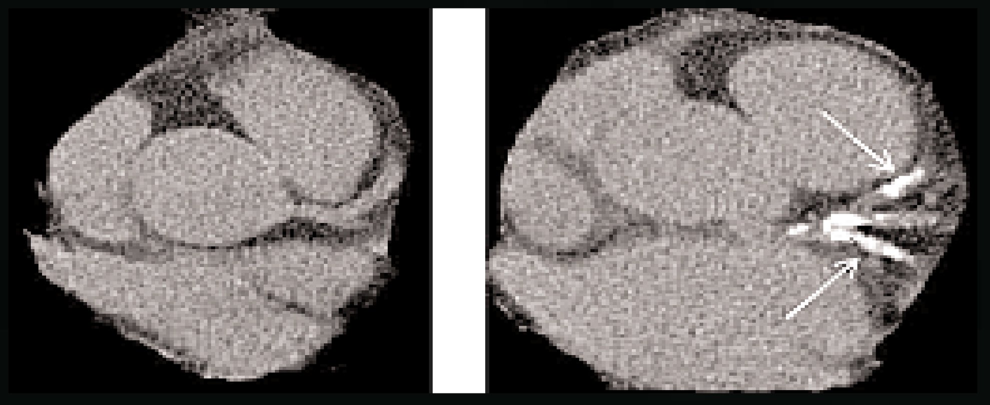
Electron Beam Computed Tomography



EBCT (shown above) can be used to detect artery calcification in asymptomatic people to identify those at high risk for developing coronary heart disease and cardiac events.

Coronary Artery Calcium by EBCT

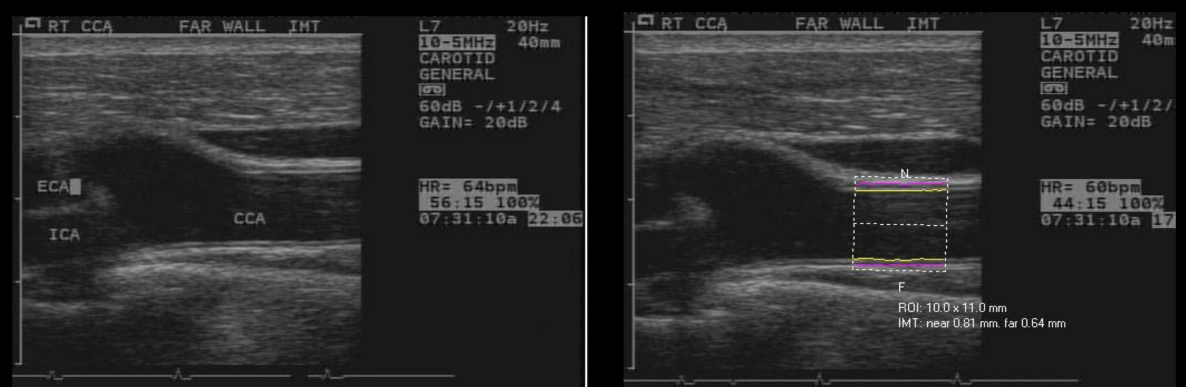
Normal Calcium | **Extensive Calcium**



Calcification is shown in the right artery, as detected by EBCT; the severity of calcification is known to be associated with risk of coronary events.

Carotid Intima Media Thickness

Without Reading | **With Reading**



CIMT (shown above) provides a reading of the thickness of the carotid artery and is an imaging technique that can be used to aid in evaluating risk of CHD in asymptomatic people.