Background

A previous study [1] reported that the instantaneous risk of developing a Herniated Nucleus Pulposus (HNP) was higher in astronauts who had flown at least one mission, as compared with those in the corps who had not yet flown. However, the study only analyzed time to HNP after the first mission (if any) and did not account for the possible effects of multiple missions. While many HNPs occurred well into astronauts' careers or in some cases years after retirement, the higher incidence of HNPs relatively soon after completion of space missions appears to indicate that spaceflight may lead to an increased risk of HNP. In addition, when an HNP occurs after spaceflight, is it related to previous spaceflight exposure? The purpose of this study was to investigate whether multiple missions, sex, age, vehicle landing dynamics, and flight duration affect the risk of developing an HNP using a competing risks model. The outcome of the study will inform the Human System Risk Board assessment of back pain, inform the risk of injury due to dynamic loads, and update the previous dataset, which contained events up to December 31, 2006.

Methods

The study was done using data queried by an epidemiologist from the electronic medical record and provided by the Lifetime Surveillance of Astronaut Health. The data included all 330 United States Astronauts beginning at selection and continuing throughout their life from 1959 through February 2014. HNP diagnoses were confirmed by Magnetic Resonance Imaging, Computed Tomography, Myelography, operative findings, or through clinical corroboration by a neurologist or neurosurgeon. In this analysis, cases of HNP-diagnosed at or before the time an astronaut was selected into the astronaut corps were ignored.

Survival Model. We modeled the distribution of $T_{\text{f}}$, the time from selection into the astronaut corps until first diagnosis of HNP. Exemplary variables fall into two categories:

Flight-related explanatory variables: number and timing of missions, mission duration(s), type of landing vehicle(s), experience as pilot of a high-performance jet aircraft. For purposes of this study, “long-duration” missions were those flown on Skylab, MIR, or ISS. Others were considered “short-duration” missions. Landing vehicles were classified into “STS” (Space Shuttle) or “capsule” (all others).

Demographic explanatory variables: age, gender, weight, height, and BMI.

An important component of the model allows for the possibility that only some astronauts are susceptible to developing a HNP during their active careers or after retirement. For astronauts in the “susceptible” (B) category, if a HNP had not been reported by the time of the last physical exam, $T_{\text{f}}$ was treated as censored at that time, meaning these astronauts would have eventually had a HNP they had been observed longer. On the other hand, nonsusceptible astronauts (A) are those that would never develop a HNP no matter how long they were observed. In practice, susceptibility is treated probabilistically. That is, we cannot tell on an individual basis whether or not a particular astronaut who did not develop a HNP during the study period is in the A or B category, but we can be able to estimate the proportion of susceptible astronauts as a function of how many missions they flew ($0 – 7$).

Analysis goals. The main analysis goal was to separate effects of spaceflight from those of just being in the astronaut corps on the distribution of $T_{\text{f}}$.

Secondary goals were to investigate the degree to which numbers of mission, age, gender, etc. also had an effect on $T_{\text{f}}$.

Survival Model Details. Multiple stochastic processes take place for each astronaut: $T_{\text{f}}$ time from selection to HNP (influenced by astronaut training and lifestyle) and $T_{\text{f}}$ time from selection to the first spaceflight ($j = 1, 2, n$).

Hazard Functions. The distributions of $T_{\text{f}}$ and $T_{\text{f}}$ as well as $P(N)$, the probability that an astronaut is in the A category, are modeled through their hazard functions. A hazard function $h(t)$ is a measure of instantaneous risk of HNP at time $t$ given that one has not occurred previously. For example, in figure 1, the probability of a first HNP occurring in the small time window shown is approximately the value of the hazard function times the width of the window, $h(t) \Delta t$.

In this application, hazard functions are modeled as proportional to Weibull-density functions.

Weibull Density Function

$$w(t, p) = \begin{cases} \lambda p \beta t^{\beta-1} e^{-\lambda t^p} & (t > 0) \\ 0 & (t \leq 0) \end{cases}$$

Hazard Function Components.

Survival Function

$$S_{\text{f}}(t) = \frac{1}{P} \frac{1}{P(N)} \left( \frac{P(N)}{P(N)} \right)$$

Log hazard function

$$h(t) = \lambda \beta t^{\beta-1} e^{-\lambda t^p}$$

Non-susceptibility. The proportion of astronauts that would never develop HNP no matter how long they were observed is given by

$$P(N) = e^{-2\lambda \beta t}$$

where $t$ is the number of space missions. Reflecting the increased cumulative risk as more flights are undertaken, figure 3 shows how the $P(N)$ would decrease if everyone had equally spaced missions 3 years apart. This calculation was made with model parameters estimated from the study data.

Probability that an HNP at time $t$ was caused by Spaceflight

$$P_F(t) = \frac{P(A)t}{P(A)t + P(B)t}$$

(Density functions $f_A(t)$ and $f_B(t)$ are obtained from hazard functions).

Discussion

Analysis of the data revealed clear evidence that spaceflight is associated with increased risk of HNP; thus supporting the conjecture suggested by a higher incidence of HNPs shortly after missions. In arriving at this finding we fit a survival model that took into account differences in type, number, and timing of missions as well as the periods of observation for each astronaut. In addition we allowed for the possibility that a certain proportion of astronauts are not susceptible to HNP and would not develop one no matter how long they were observed. The model-based conditional probabilities that each of the 44 HNPs that occurred after at least one mission were attributable to spaceflight, ranged from 0.07 (shortly after a mission) to about 0.12 (at least 30 years after selection). The average value of these probabilities was 0.44.

Other than a detrimental effect of initial age (i.e. at selection), we did not find evidence that HNP risk was affected by demographic factors such as gender, height, weight, or any astronaut who had experienced a high-performance jet aircraft. It did appear that astronauts from the pre-Shuttle era, were at lower risk of developing an HNP ($p = 0.012$). Finally, we did not find evidence that either mission duration or type of landing vehicle had an effect.

Limitations

Because this was an observational study it is difficult to separate out the effects of the many spaceflight and demographic factors on HNP risk or to claim causality. In particular, we had no control over when long-duration or capsule-landing missions occurred, thus creating substantial confounding factors with HNP reporting and diagnosis practices as well as changing criteria for astronaut selection since the pre-Shuttle era. Also, HNP time of incidence was recorded at the time of diagnosis, not at the time of occurrence.

Because the data span the entire Astronaut Corps, effects from improved spaceflight deconditioning countermeasures may obscure the risk of developing an HNP, particularly related to mission length. A majority of the long-duration missions occurred in the past 25 years, when countermeasures have been implemented. In addition, the relatively low numbers of long-duration flights and female astronauts adversely power the tests for these effects.

Finally, the current study only examines data from U.S. astronauts. Supplementing the data with HNP reports from other Space Agencies could allow more insight into these effects.

Future Work

To better assess the effects of spaceflight on HNP risk, additional crewmember data would be ideal. In addition to the U.S. Astronauts included in this study, additional information may be available from the international partners, which could increase the dataset substantially. Additional countermeasures for crewmembers immediately after landing may also be advised to prevent HNP occurrence in future space missions. Finally, continued surveillance of crewmembers after spaceflight could allow a better understanding of this trend.

These results may also be beneficial to current studies of the intervertebral disc and additional analysis of these data in concert with the data from the current studies may improve our understanding of the mechanism of HNP after spaceflight.

References