The First 10 Years of Aerobic Exercise Responses to Long-Duration ISS Flights

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INTRODUCTION: Aerobic deconditioning may occur during International Space Station (ISS) flights. This paper documents findings from exercise testing conducted before, during, and after ISS expeditions.

METHODS: There were 30 male and 7 female astronauts on ISS missions (48 to 219 d, mean 163 d) who performed cycle exercise protocols consisting of 5-min stages eliciting 25%, 50%, and 75% peak oxygen uptake ($\dot{V}O_{2peak}$). Tests were conducted 30 to 90 d before missions, on flight day 15 and every 30 flight days thereafter, and on recovery (R) days +5 and +30. During pre- and postflight tests, heart rate (HR) and metabolic gas exchange were measured. During flight, extrapolation of the HR and $\dot{V}O_2$ relationship to preflight-measured peak HR provided an estimate of $\dot{V}O_{2peak}$, referred to as the aerobic capacity index (ACI).

RESULTS: HR during each exercise stage was elevated ($P < 0.05$) and oxygen pulse was reduced ($P < 0.05$) on R+5 compared to preflight; however, no other metabolic gas analysis values significantly changed. Compared to preflight, the ACI declined ($P < 0.001$) on R+5, but recovered to levels greater than preflight by R+30 ($P = 0.008$). During flight, ACI decreased below preflight values, but increased with mission duration ($P < 0.001$).

CONCLUSIONS: Aerobic deconditioning likely occurs initially during flight, but ACI recovers toward preflight levels as flight duration increases, presumably due to performance of exercise countermeasures. Elevated HR and lowered oxygen pulse on R+5 likely results from some combination of relative hypovolemia, lowered cardiac stroke volume, reduced cardiac distensibility, and anemia, but recovery occurs by R+30.

KEYWORDS: spaceflight, aerobic capacity, exercise.

Moore AD Jr, Lynn PA, Feiveson AH. *The first 10 years of aerobic exercise responses to long-duration ISS flights*. Aerosp Med Hum Perform. 2015; 86(12, Suppl.):A78–A86.

Continuous human presence aboard the International Space Station (ISS) began in November 2000. The ISS expedition crews have typically remained aboard 4 to 6 mo. Crew health maintenance and preservation of physical capabilities are primary goals for the ISS medical operations practitioners and support scientists. Thus, exercise has been used to counteract microgravity-induced deconditioning of the cardiovascular and musculoskeletal systems. Exercise was first extensively used as a countermeasure to deconditioning during the pioneering flights of the Skylab Program in the 1970s.[40] Although the exercise countermeasure regimen was progressively increased over the course of the three Skylab missions, heart rates (HR) measured at cycle ergometer power levels designed to elicit 75% of their peak oxygen uptake ($\dot{V}O_{2peak}$) were not significantly different from preflight values for eight of nine crewmembers. Thus, the cardiovascular response to aerobic exercise appeared well maintained during these missions. However, the HR response to exercise was markedly elevated in the early days following flight, gradually returning to preflight levels by approximately 24 d postflight.[25]

The longest Skylab mission was 84 d in duration. The typical ISS stay was planned to be about 180 d in duration and the ISS assembly would involve multiple extravehicular activities (EVAs); with some occurring months into an expedition, it was thus deemed prudent to monitor cardiovascular fitness throughout the course of the ISS flights. Although the risk of serious cardiac dysrhythmia during flight was believed to be low,[9,38] at least one case of ventricular tachycardia had been reported during long-duration spaceflight on the Russian Mir

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DOI: 10.3357/AMHP.EC10.2015

space station.[15] Therefore, electrocardiographic (ECG) monitoring was incorporated into the routine exercise monitoring proposed for the ISS missions. In addition, postflight testing was proposed as an aid to determine appropriate exercise levels for rehabilitation. The purpose of this retrospective analysis is to document cardiovascular responses to exercise that were collected during routine medical testing of the astronauts throughout the first 10 yr of ISS operations.

METHODS

The preflight subject characteristics for the 30 male (M) and 7 female (F) (2 men and 1 woman participated in two flights each) astronauts were: age (yr), M 46.2 $\pm$ 4.4, F 42.4 $\pm$ 2.6; height (cm), M 175.5 $\pm$ 6.5, F 169.3 $\pm$ 2.7; weight (kg), M 81.6 $\pm$ 9.1, F 65.0 $\pm$ 4.1; peak exercise HR (bpm), M 174.2 $\pm$ 13.4, F 177.6 $\pm$ 10.7; and $\dot{V}o_{2peak}$ (ml $\cdot$ kg^{-1} $\cdot$ min^{-1}), M 43.4 $\pm$ 7.8, F 40.5 $\pm$ 7.0. Test sessions for crewmembers followed the schedule outlined in SSP 50667 – Medical Evaluation Documents, Volume B, Section 4.1 – Cycle Ergometer Test/Aerobic Functional Capacity (http://lsda.jsc.nasa.gov/lsda_data/MRID_Docs/MEDB41SMCCBfinal2.pdf). The test sessions and equipment used are fully described below.

Preflight Testing

Each crewmember performed an initial cycle ergometer test at approximately 270 d before launch (L-270). The continuous graded exercise test protocol consisted of 3-min stages at 50, 100, and 150 W, followed by stepwise increases of 25 W $\cdot$ min^{-1} until the crewmember reached symptom-limited maximum (volitional fatigue). If the crewmember weighed $<$ 65 kg and reported they performed minimal routine cycle exercise training, the first three stages were 50, 75, and 100 W, followed by stepwise increases of 25 W $\cdot$ min^{-1}. Crewmembers were instructed to maintain a constant pedaling cadence of 75 rpm. Following the test, subjects pedaled the cycle ergometer at a low level ($\sim$25 W) for 5 min to recover.

Each astronaut subsequently performed a submaximal cycle ergometer test, commonly referred to by NASA as the Periodic Fitness Evaluation (PFE) protocol, before flight. This test was originally scheduled and performed at L-30, but the preflight schedule was altered to accommodate Soyuz vehicle training in Russia after the STS-107 Columbia accident. The preflight test date was moved to be within the last period that the crewmember was in the U.S. before a Soyuz launch, typically in the L-60 to L-90 time frame. The PFE protocol consisted of three stages, lasting 5 min per stage, at exercise power levels designed to elicit 25%, 50%, and 75% of their L-270 $\dot{V}o_{2peak}$. This was followed by a 5-min cool-down stage at same level as the first exercise stage.

The cycle ergometer used for the ground-based tests was electronically braked (Lode Excalibur Sport; Lode B.V., Groningen, The Netherlands). The HR and rhythm were monitored continuously (with either a Q-5000 or a Q-Stress ECG monitor, both manufactured by Quinton Instruments, Seattle, WA). The ground-based metabolic gas analysis system for preflight testing changed over the first 10 yr of ISS operations. For ISS Expeditions 1–14, the metabolic measurement device was a MAX-II system (Physiodyne, Quogue, NY). For ISS Expeditions 15 to the present, the metabolic gas analysis system has been a TrueOne® 2400 metabolic gas analysis system (ParvoMedics, Sandy, UT). Unpublished data collected in the Exercise Physiology Laboratory at NASA-Johnson Space Center did not reveal any differences in the metabolic gas analysis data between the two devices. Blood pressure was obtained by auscultation of the brachial artery with a stethoscope using a standard sphygmomanometer. Ratings of perceived exertion (RPE) were obtained using the 6 to 20 scale developed by Borg.[4]

Testing During Flight

The first cycle exercise test during flight was scheduled for flight day (FD) 15, with subsequent evaluations to be repeated every 30 FDs thereafter; however, the testing days were often modified due to real-time mission constraints. For example, testing was not performed during periods of "docked operations" when either the Shuttle or a Russian Soyuz vehicle was present at the ISS and crew transfers were taking place. Evaluations also were not performed around the time of scheduled EVAs.

The cycle ergometer with vibration isolation system (CEVIS; Danish Aerospace Company, Odense, DK) was used for PFE tests conducted during flight. Blood pressure, HR, and rhythm were measured during the in-flight tests using the NASA Crew Health Care System blood pressure and electrocardiograph (BP/ECG) equipment. The BP/ECG system is an EASI™ electrocardiograph system[13] (Royal Phillips Electronics, Amsterdam, The Netherlands) interfaced with an exercise blood pressure monitoring device (SunTech Tango™ system, SunTech Medical Instruments, Raleigh, NC). The BP/ECG system data were recorded electronically and downlinked to biomedical personnel following the test. Metabolic gas analysis data were originally planned to be collected during the ISS exercise tests. However, technical development and budgetary issues prevented a metabolic gas analysis system from being flown to the ISS to support the PFE tests. Therefore, the in-flight exercise test data were constrained by interpretation without the benefit of complementary metabolic gas analysis data.

Testing Following Flight

Postflight PFE tests were scheduled for recovery day 5 (R+5) and R+30. The majority of postflight tests were conducted on or near these days ($\pm$1 d for R+5 and $\pm$5 d for R+30). The postflight testing was conducted either at Johnson Space Center in Houston, TX, or at the Gagarin Cosmonaut Training Center in Star City, Russia—both of these sites employed identical exercise test hardware to that used before flight.

Interpretation of Cardiovascular Exercise Data to Estimate Aerobic Capacity

The HR response to standardized cycle ergometer workloads during submaximal exercise tests may be used to provide an index of aerobic conditioning. Extrapolation of the HR and either workload or $\dot{V}O_2$ data collected during such testing has been used to estimate $\dot{V}O_{2peak}$.[29] Although this technique is commonly used in field testing,[3,39] it has not been validated during spaceflight. Furthermore, while this technique has been found to be a good indicator of the mean $\dot{V}O_{2peak}$ for a group of subjects, considerable variation from true $\dot{V}O_{2peak}$ may occur in individuals.[20,39] As noted above, $\dot{V}O_2$ data were not collected aboard ISS, resulting in a degree of uncertainty in the interpretation of the in-flight graded exercise test results. For the linear extrapolation estimates of aerobic capacity during flight, the assumption was that $\dot{V}O_2$ for each submaximal exercise stage during flight was similar to that measured during preflight testing. This assumption of equivalent mechanical efficiency was based upon the Skylab observations that submaximal $\dot{V}O_2$ at any given exercise stage was similar pre- and in-flight.[24] The present paper contains the cardiopulmonary responses to exercise as they were measured; however, we also report changes in aerobic capacity that have been derived using the linear extrapolation technique. Within this paper we refer to the linear extrapolation derived estimates of aerobic capacity as "aerobic capacity index" (ACI) to avoid confusion with actual measurements of either peak or maximum $\dot{V}O_2$. The ACI results are reported in absolute $\dot{V}O_2$ ($L \cdot min^{-1}$) units since the timing of body mass measurements during flight did not match the PFE dates. In addition, no direct ground-based vs. spaceflight comparisons of ACI are reported as no $\dot{V}O_2$ measurements were made during flight and those comparisons would be tenuous.

Sample Size/Data Acquisition

The number of long-duration NASA, CSA, ESA and JAXA crewmembers flown in the first 10 yr of ISS operations is 40, which is the full potential sample size for the analyses in this paper. However, the number of astronauts for whom we obtained acceptable data was less than the full complement of individuals. The exercise testing protocols for ISS had not been fully defined before the preflight period of the first mission and the CEVIS was not in place during ISS-1. Thus, the first ISS crewmember performed testing that differed from the remaining ISS astronauts. In the aftermath of the Columbia accident, the early postflight test location was switched from Houston, TX to Star City, Russia. Crewmembers from two ISS expeditions returned to Earth before a laboratory was established in Russia to support full acquisition of data. Finally, the metabolic gas analysis equipment located in Star City malfunctioned for one subsequent crew return. The statistical analyses selected for reporting these results in the current manuscript are robust with respect to the problem of unequal sample sizes across the test periods; the resulting sample sizes are reported for each analysis.[8]

Statistical Methods

Pre- vs. postflight descriptive analysis. We used mixed-model regression analyses to estimate means and 95% confidence limits for HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), $\dot{V}O_2$, carbon dioxide production ($\dot{V}CO_2$), respiratory exchange ratio (RER), expired ventilation ($\dot{V}_E$), tidal volume (V_T), breathing frequency (f_b), and RPE during three phases of spaceflight (pre-, early post-, and late postflight) and at each of three exercise stages (25%, 50%, and 75%). For purposes of these analyses, the "early" postflight phase was defined as R+5. The "late postflight" test sessions were on R+30.

Pre- vs. postflight analysis. In support of our study hypotheses using mixed models for oxygen pulse ($\dot{V}O_2$, $ml \cdot min^{-1} \cdot HR^{-1}$), submaximal $\dot{V}O_2$, and HR, we further investigated the effects of flight phase, exercise stage, gender, and their interactions while using bodyweight as a covariate. Applying these mixed models for inference allowed us to properly analyze data from the unbalanced design (preflight $N = 38$; early postflight $N = 33$; late postflight $N = 36$ observations) and account for possible unequal between- and within-subject error variances, depending on exercise stage.

In-flight trend model—aerobic capacity index. The ACI data resulting from all submaximal exercise test sessions were obtained for $N = 37$ long-duration astronauts using the linear extrapolation method described above. The in-flight ACI data were then fitted to a mixed-effects regression model with flight day and gender established as predictors. The model also allowed for subject-specific random intercepts and slopes with respect to flight day, which is an important feature for this analysis as the flight test days varied due to mission constraints. After fitting available data to this model, we calculated estimates, standard errors, and 95% confidence intervals for mean ACI and mean change in ACI over a typical flight of 180 d. Statistical inference was limited to evaluating the presence or absence of a mean trend in ACI during spaceflight. No statistical comparisons of in-flight data to pre- or postflight were made because of the dependence of such inference on the assumption that $\dot{V}O_2$ for a particular subject is the same for a given cycle ergometer whether it is in space or on the ground. Similarly, the L-270 data were not formally compared to the other time points, as $\dot{V}O_{2peak}$ was measured at L-270 versus being estimated at subsequent time points.

RESULTS

Pre- versus Postflight Data

The cardiorespiratory and perception-of-effort responses to the graded exercise tests performed preflight, early postflight, and late postflight are presented in **Table I** and **Table II** for men and women, respectively. On average, all responses, regardless of the time relative to flight, demonstrated the normally expected trends elicited by exercise of increasing effort (that is, HR, SBP, $\dot{V}O_2$, $\dot{V}CO_2$, RER, $\dot{V}_E$, V_T, f_b, and RPE increased with increasing load). Of these measures only average HR increased above preflight levels during the early postflight period and it recovered by the late postflight test.

The pre- to postflight ACI data ($L \cdot min^{-1}$) are shown in **Fig. 1**, with 95% confidence limits for men and women.

Table I. Cardiorespiratory and Perceptual Responses of Male Astronauts ($N = 30$) to Submaximal Exercise Testing by Stage and Time Relative to Flight (Mean ± SD).

	EXERCISE STAGE (% OF L-270 PEAK $\dot{V}O_2$)								
	25%			50%			75%		
MEASURE	PREFLIGHT	EARLY POSTFLIGHT	LATE POSTFLIGHT	PREFLIGHT	EARLY POSTFLIGHT	LATE POSTFLIGHT	PREFLIGHT	EARLY POSTFLIGHT	LATE POSTFLIGHT
HR (bpm)	88 ± 12	95 ± 12*	89 ± 11	112 ± 15	122 ± 15*	112 ± 15	140 ± 18	151 ± 17*	139 ± 17
SBP (mmHg)	138 ± 11	139 ± 14	138 ± 9	163 ± 16	162 ± 16	160 ± 14	193 ± 19	189 ± 16	187 ± 19
DBP (mmHg)	79 ± 7	74 ± 11	75 ± 8	78 ± 6	72 ± 9	76 ± 7	78 ± 7	72 ± 10	75 ± 9
$\dot{V}O_2$ ($L \cdot min^{-1}$)	1.04 ± 0.12	1.02 ± 0.10	1.06 ± 0.17	1.76 ± 0.24	1.70 ± 0.19	1.76 ± 0.21	2.61 ± 0.42	2.49 ± 0.32	2.60 ± 0.33
$\dot{V}CO_2$ ($L \cdot min^{-1}$)	0.90 ± 0.12	0.90 ± 0.09	0.93 ± 0.13	1.66 ± 0.28	1.66 ± 0.20	1.69 ± 0.21	2.68 ± 0.53	2.67 ± 0.43	2.68 ± 0.37
RER	0.87 ± 0.06	0.90 ± 0.05	0.89 ± 0.05	0.94 ± 0.06	0.98 ± 0.07	0.96 ± 0.06	1.02 ± 0.07	1.06 ± 0.06	1.03 ± 0.07
$\dot{V}_E$ ($L \cdot min^{-1}$)	28.0 ± 3.3	28.1 ± 3.7	29.8 ± 5.5	47.2 ± 7.3	47.2 ± 6.3	50.0 ± 8.0	77.2 ± 16.8	77.5 ± 13.8	80.1 ± 12.4
V_T (L)	1.4 ± 0.26	1.4 ± 0.24	1.4 ± 0.35	2.1 ± 0.34	2.2 ± 0.35	2.0 ± 0.49	2.8 ± 0.56	2.8 ± 0.53	2.8 ± 0.67
f_b (breaths/min)	20.7 ± 4.4	20.8 ± 4.9	20.7 ± 3.8	22.9 ± 4.3	22.4 ± 3.8	23.9 ± 4.2	27.9 ± 7.2	28.2 ± 4.3	27.9 ± 4.6
RPE	8.4 ± 1.4	8.4 ± 1.6	8.1 ± 1.2	10.9 ± 1.0	10.9 ± 1.5	10.8 ± 1.3	13.3 ± 1.2	13.9 ± 1.7	13.1 ± 1.3

* Greater than either preflight or late postflight ($P < 0.05$).

During early recovery, ACI was lower ($P < 0.001$, both genders combined) than before flight. Although the mean ACI for women was significantly lower (about 1.0 $L \cdot min^{-1}$) than for men ($P = 0.002$) even when accounting for body-weight differences, there was no evidence of a gender/flight interaction ($P = 0.46$). During the late recovery test (~R+30) the mean ACI for the combined groups was approximately 0.2 $L \cdot min^{-1}$ higher than the preflight level ($P = 0.008$).

Submaximal estimates of mean HR, oxygen pulse, and measured $\dot{V}O_2$ by exercise stage along with 95% confidence limits are shown in **Fig. 2** for a person of average weight for each gender. HR was increased early postflight as compared to either pre- or late postflight. Early postflight oxygen pulse was lower than that observed either before or late after flight. Submaximal $\dot{V}O_2$ did not change as a function of flight exposure or recovery. The male subjects did have significantly ($P < 0.01$) higher oxygen pulse and $\dot{V}O_2$ values at any given exercise stage than the female subjects; this was strictly a function of the higher workloads used because of the higher preflight peak absolute $\dot{V}O_2$ levels of the male subjects (due to the weight differences between the subject groups).

In-Flight Data

The primary finding regarding in-flight ACI estimates was that, on average, they tended to increase almost linearly throughout a typical 180-d ISS mission (**Fig. 3**). In particular, the estimated mean slope was about $0.0026\ ml \cdot min^{-1} \cdot d^{-1} \pm 0.0007$ ($P < 0.001$). Also, on average, female subjects had significantly lower ACI values than male subjects (0.73 $L \cdot min^{-1}$ less, $P < 0.001$) throughout flight, but their average slope with respect to flight day was virtually identical to that of the male subjects. Estimated means and 95% confidence limits for ACI responses are shown in Fig. 3 for each gender, with mean preflight levels shown for reference. However, for the reasons mentioned above, we made no formal comparisons between in-flight and preflight ACI estimates.

DISCUSSION

The major findings from the data collected during submaximal graded exercise testing before, during, and after prolonged ISS flights follows: 1) the HR response to exercise is elevated early after flight and oxygen pulse is lowered; these changes indicate

Table II. Cardiorespiratory and Perceptual Responses of Female Astronauts ($N = 7$) to Submaximal Exercise Testing by Stage and Time Relative to Flight (Mean ± SD).

	EXERCISE STAGE (% OF L-270 PEAK $\dot{V}O_2$)								
	25%			50%			75%		
MEASURE	PREFLIGHT	EARLY POSTFLIGHT	LATE POSTFLIGHT	PREFLIGHT	EARLY POSTFLIGHT	LATE POSTFLIGHT	PREFLIGHT	EARLY POSTFLIGHT	LATE POSTFLIGHT
HR (bpm)	94 ± 11	107 ± 12*	95 ± 14	121 ± 14	136 ± 15*	120 ± 18	148 ± 16	165 ± 9*	147 ± 15
SBP (mmHg)	133 ± 11	138 ± 16	124 ± 15	151 ± 13	160 ± 17	145 ± 18	175 ± 20	181 ± 16	163 ± 21
DBP (mmHg)	75 ± 5	80 ± 13	74 ± 6	75 ± 5	78 ± 14	72 ± 5	77 ± 6	79 ± 13	71 ± 8
$\dot{V}O_2$ ($L \cdot min^{-1}$)	0.81 ± 0.06	0.84 ± 0.08	0.85 ± 0.08	1.34 ± 0.17	1.36 ± 0.15	1.40 ± 0.18	1.95 ± 0.26	1.97 ± 0.25	2.02 ± 0.25
$\dot{V}CO_2$ ($L \cdot min^{-1}$)	0.67 ± 0.09	0.70 ± 0.07	0.70 ± 0.06	1.22 ± 0.18	1.26 ± 0.13	1.25 ± 0.14	1.93 ± 0.31	2.02 ± 0.32	1.97 ± 0.23
RER	0.83 ± 0.07	0.83 ± 0.04	0.82 ± 0.06	0.91 ± 0.05	0.92 ± 0.05	0.90 ± 0.05	0.99 ± 0.06	1.02 ± 0.06	0.98 ± 0.05
$\dot{V}_E$ ($L \cdot min^{-1}$)	22.8 ± 3.1	23.5 ± 3.2	23.7 ± 1.6	37.7 ± 4.0	39.4 ± 2.7	38.1 ± 2.8	58.1 ± 6.8	63.7 ± 6.6	59.7 ± 6.6
V_T (L)	1.2 ± 0.22	1.2 ± 0.31	1.2 ± 0.16	1.6 ± 0.25	1.6 ± 0.27	1.6 ± 0.14	2.1 ± 0.31	2.2 ± 0.30	2.1 ± 0.10
f_b (breaths/min)	21.5 ± 4.9	20.9 ± 5.8	21.2 ± 3.6	25.4 ± 5.1	25.0 ± 4.5	25.1 ± 4.4	28.8 ± 4.8	29.4 ± 3.2	28.9 ± 3.4
RPE	7.9 ± 1.0	9.0 ± 1.4	8.6 ± 0.8	10.5 ± 1.6	11.6 ± 1.1	11.0 ± 1.3	13.3 ± 1.7	14.5 ± 1.2	13.6 ± 1.6

* Greater than either preflight or late postflight ($P < 0.05$).

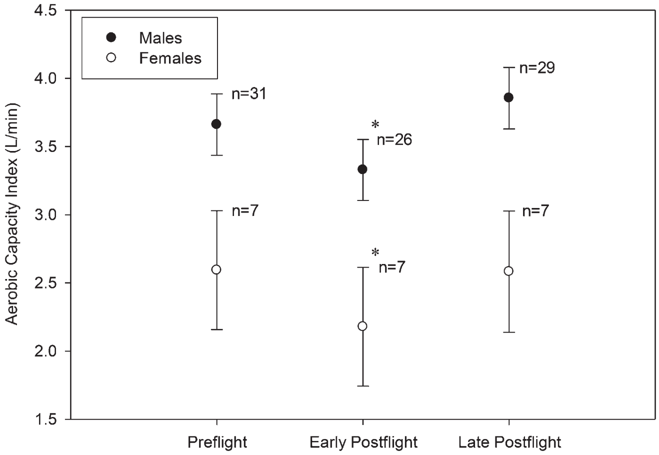

Fig. 1. Pre- and postflight ACI results by gender (means ± 95% CI). * Indicates early (R+5) postflight values being lower than either preflight or late postflight values for both male and female subjects ($P < 0.05$).

that aerobic capacity is likely compromised in this time frame, but the HR and oxygen pulse responses normalized to preflight levels in the month following flight; 2) the HR response to exercise appears increased early during flight, which lowers the ACI; however, as mission duration progresses ACI increases; and 3) although gender was associated with differences in the ACI derived before, during, and after flight, there was no gender/time interaction, thus male and female astronauts did not appear different in their respective responses to prolonged spaceflight. As the number of female subjects was much smaller than the male subjects, this finding should be viewed as tentative.

Preflight versus Postflight

The early postflight elevation in exercise HR accompanied by a decline in oxygen pulse, which is a surrogate measurement of cardiac stroke volume,[42] is similar to observations following the Skylab flights.[24,25,34] The Skylab and ISS exercise tests involved identical stage intensities and durations, but Skylab tests were conducted more frequently during and after flight than our ISS medical operations tests. After flight, the Skylab investigators reported that the elevated HR response to submaximal exercise gradually returned to preflight levels by 24 d following landing. Early measurements of cardiac output following Skylab flights during the third exercise stage (75% of preflight $\dot{V}O_{2max}$) showed declines in both cardiac output (~30%) and stroke volume (~50%).[6] These changes in cardiac output and stroke volume were within 10% of preflight values by 10 d postflight and, similar to the HR response to exercise, had returned to preflight levels by R+24.

The mechanism for decreased oxygen pulse (presumably stroke volume) and elevation in HR early postflight likely involves multiple factors. The cycle exercise testing of the ISS astronauts before and after spaceflight is conducted in the upright position. It has been well documented that both real and simulated microgravity exposure induce lowered total blood volume.[18,32] This

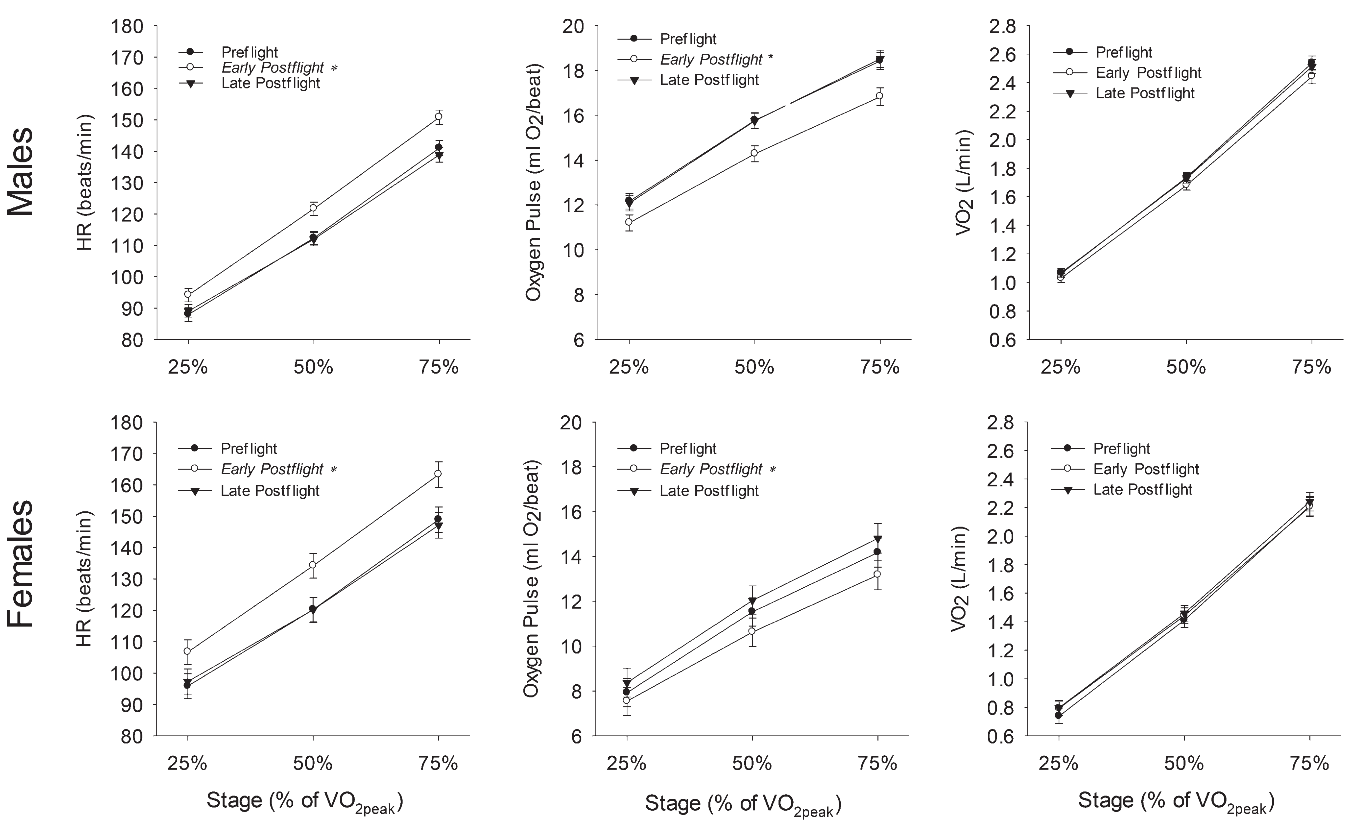

Fig. 2. Preflight, early, and late postflight mixed modeling results, plotted for each gender ($N = 30$ men, 7 women). * Significant main effect $P < 0.05$. Values are means ± 95% CI.

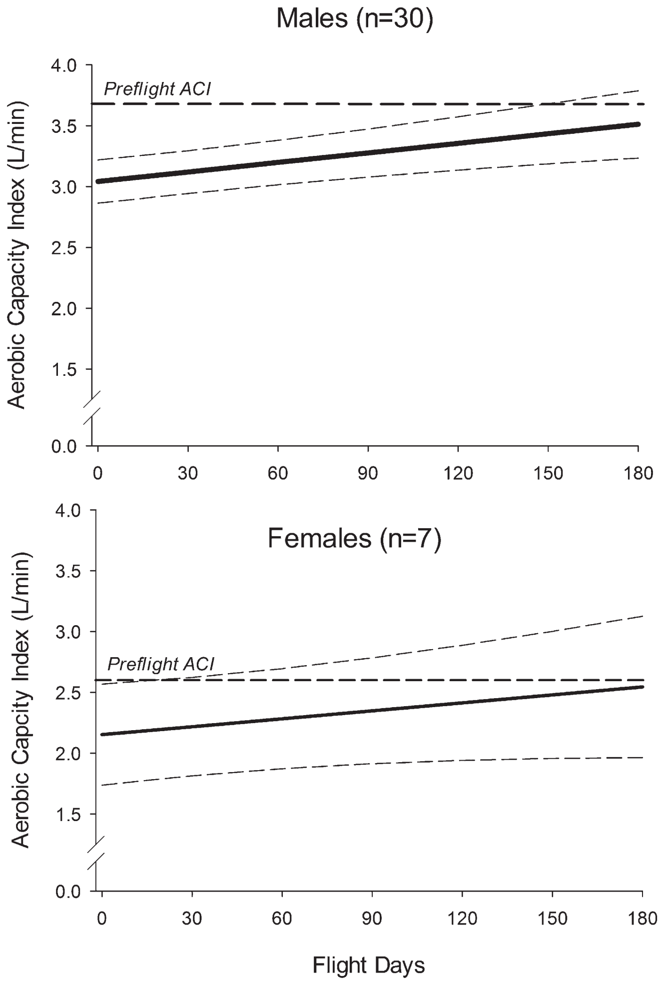

Fig. 3. Mean ± upper and lower 95% CI mixed modeling results of ACI during flight. Solid lines indicate mean ACI, grey dashed lines indicate the upper and lower CIs, and the black dashed lines indicate the mean preflight ACI of each group.

normal adaptation to the cephalic shift of intravascular volume early in flight results in diminished orthostatic tolerance following spaceflight.[5,7] Although not measured during our routine medical operations tests, it is likely that reductions in blood/plasma volume early postflight compromised stroke volume by reducing end diastolic cardiac filling in the upright position.[22] Another potential contributing factor is a loss of left ventricular distensibility due to cardiac atrophy. Cardiac atrophy, with associated losses in left ventricular mass and left ventricular end diastolic volume, has been demonstrated with the bed rest model of spaceflight in both male and female subjects,[12,23] and also in astronauts exposed to short-duration (10 d) spaceflight.[31] Interestingly, exercise training during 18 d of bed rest appeared to preserve left ventricular mass, distensibility, and also upright exercise capacity, but did not preserve orthostatic function without intravenous fluid replacement (IV Dextran).[36] Another factor that may contribute to the postflight exercise tachycardia is potential red cell mass reduction during flight,[1,2,11] which would result in a lowered oxygen carrying capacity per unit of blood. In the present report, it is difficult to determine which mechanisms are the most important contributors to the deconditioning observed as comprehensive blood and exercise cardiac function measurements were not attained.

Increased exercise HR is commonly associated with physical deconditioning[10,30] and it is likely that some portion of our findings are attributable to this. However, our results also indicate that astronauts may not be highly detrained in the early postflight period. Aerobic detraining is typically accompanied by an increased HR response to graded exercise testing as well as other alterations in the submaximal exercise responses. Our subjects did not demonstrate such changes. For example, in a well-controlled experiment designed specifically to study the effects of aerobic detraining in ambulatory subjects, observations in addition to elevated exercise HR included elevated $\dot{V}_E$, RER, and RPE during a submaximal test at workloads eliciting approximately 74% of $\dot{V}O_{2max}$.[10] These findings were evident as early as 12 d following the cessation of training. Studies using bed rest as an analogue to spaceflight deconditioning have demonstrated similar results. Subjects exposed to 15 d of bed rest showed an average 14% decrease in $\dot{V}O_{2peak}$ when no exercise was performed during the bed rest period and this change in $\dot{V}O_{2peak}$ was associated with an elevated HR response to submaximal exercise accompanied by an increase in RER.[41] Similarly, control subjects who performed no exercise with lower body negative pressure countermeasures during 30 d of bed rest experienced a 16% decline in $\dot{V}O_{2peak}$ and exhibited elevations in submaximal HR, RER, and $\dot{V}_E$, although no change in RPE.[21] Within the astronauts returning from flight, other than the elevations observed in exercise HR at R+5, none of the other cardiorespiratory or perception data changed in a manner typically associated with exercise detraining (Tables I and II).

In-Flight Trend Model—Aerobic Capacity Index

Perhaps the most difficult findings to interpret are the changes in ACI during flight. To reiterate a point made in the methods section, $\dot{V}O_2$ measurements were not obtained during the exercise tests conducted aboard the ISS. Therefore, the changes in the ACI are directly proportional to changes in exercise HR. The ACI estimates of $\dot{V}O_{2peak}$ in both the male and female astronaut groups increased during the course of their missions (Fig. 3). Even though we did not make a formal comparison between preflight and flight data, it is interesting to note that the ACI values were low early during flight as compared to preflight. Thus during flight the HR response to exercise was elevated early, but gradually normalized with increasing mission duration.

Submaximal exercise testing of the Russian cosmonauts follows a different protocol than that used by the other ISS International Partners. However, the results from the Russian medical operations testing have yielded results similar to those reported in the current paper. The HR response to 3-min exercise stages of 125, 150, and 175 W is reported to be greatest during testing performed during the first month of flight.[33] The elevations in exercise HR gradually decreased as flight duration increased. The Russian crewmembers typically exercise little during the first 2 wk of flight, which may contribute to this finding.[33] Likewise, the ISS astronauts tend to perform little exercise during the first few days of microgravity exposure due to the activities associated with crew hand-over and unpacking of supplies being transferred to the ISS.[29] They are encouraged to begin exercising starting on FD 5.

No measures of blood/plasma volume have been performed during long-duration spaceflight; however, it is tenable to suggest that these values decrease very early during flight and these changes would contribute to an elevated HR response to exercise. Plasma volume was reduced by an average of 17% during the first day of the Spacelab Life Sciences 2 (SLS-2) mission and remained depressed during flight.[2,19] Long-term bed rest studies conducted without countermeasures to deconditioning induce reductions in plasma volume that, after a period of rapid decline, tends to stabilize at about a 20% loss.[14] However, plasma volume remained unchanged ($-1.5 \pm 2.3\%$) in a group of subjects who performed interval exercise training during a 30 d bed rest study versus either control subjects ($-14.7 \pm 2.8\%$) or those who performed leg strength training ($-16.8 \pm 2.9\%$).[17] As was discussed in the section regarding pre- vs. postflight findings, the adaptive responses to spaceflight may also result in progressive cardiac atrophy, which would contribute to a lowered stroke volume and an increased HR response to exercise, although it appears that these changes can be attenuated by an exercise protocol that exceeds the frequency of that typically prescribed for the ISS crewmembers.[36]

Previous investigations have reported that both $\dot{V}O_{2peak}$ and the maximum workload attained during short-duration flights of up to 13 d did not change during flight.[22,28] Maximal effort exercise sessions were observed in a subset of the Skylab 3 and 4 crewmembers.[35] Although these sessions were not conducted using a standard graded exercise test protocol, these crewmembers were able to attain peak $\dot{V}O_2$ values near those measured preflight.

The linear extrapolated $\dot{V}O_{2peak}$ data for the ISS crewmembers (that is, ACI) appear to be valid when examined in relationship to their performance during routine exercise countermeasure sessions. During the first 10 yr of ISS flight, all U.S., CSA, ESA, and JAXA crewmembers were assigned a series of CEVIS-based exercise protocols to use for physical training purposes.[29] The most intense of these protocols involves interval exercise with workloads up to 90% preflight maximum for 2 min, which is an adaptation of the protocol described by Greenleaf.[16] Crewmembers frequently cannot complete this high intensity protocol early in flight (Moore AD. Unpublished observations. 2015). In these cases, the workloads are typically adjusted downwards and then are slowly titrated upwards as the mission progresses.

Perhaps some factor related to the cycle ergometer exercise modality is confounding the in-flight results. For example, if the metabolic cost of exercise on the CEVIS changed over the course of flight, it could explain the findings. Although the metabolic cost of exercise (that is, mechanical efficiency) did not change during the Skylab missions,[25] nor did the submaximal relationship between HR and $\dot{V}O_2$ change during short-duration spaceflight,[37] the Skylab and Shuttle ergometers were "hard mounted" to the structure of their respective spacecraft. The ISS CEVIS is mounted on a frame that is connected to station structure by wire isolators that allow the CEVIS to float loosely tethered to the ISS module. When an individual rides the CEVIS, an observable swaying of the frame occurs and we have speculated that the efficiency of transmission of force to the CEVIS pedals might be reduced; however, this conclusion is not supported by preliminary data from the first seven subjects in an ongoing NASA experiment aboard the ISS that incorporates metabolic gas analysis measurements.[26] These early findings indicate that submaximal exercise $\dot{V}O_2$ at a given cycle work rate does not change over the course of flights. Thus, change in the mechanical efficiency of CEVIS exercise during flight does not appear to offer a plausible explanation.

A logical interpretation of the gradual recovery in ACI is that detraining followed by a "training effect" occurs over the course of the ISS missions. We speculate that, as a result of introduction to microgravity with no or minimal exercise countermeasures performed early during the missions, plasma volume is reduced and cardiac atrophy might occur at a relatively rapid rate. These changes may be at least partially reversed by the initiation and performance of the exercise countermeasures regimen, and would be reflected in an increasing ACI (and presumably $\dot{V}O_{2peak}$). This hypothesis would fit the available data and future research should more fully address this phenomenon.

Limitations

Studies and observations involving spaceflight are best regarded as sophisticated field studies, with limitations that are not present in a ground-based laboratory investigation. With regard to this paper, periodic problems were encountered with the treadmill exercise device (the TVIS – treadmill with vibration isolation system), the resistance exercise device (the IRED – interim resistance exercise device), and the control panel of the CEVIS. These problems caused the normal exercise routines of some of the crewmembers to be temporarily disrupted. Other limitations, such as the change in the prelaunch testing dates, change in recovery sites, and an equipment malfunction in a relatively remote location have been documented earlier in this manuscript. Perhaps the most major limitation influencing this report was the lack of a metabolic gas analysis device on board during the first 10 yr of ISS flight.

Ongoing Work and Recommendations

Essential future work resulting from our observations is the need to establish or refute the validity of using submaximal exercise testing to infer changes in aerobic capacity. Toward that end, a device that can measure $\dot{V}O_2$ on board has been delivered to the ISS. A study of peak oxygen uptake was completed immediately following the first 10 yr of ISS flight and the results of that study were recently published.[27]

A recommendation that requires immediate attention is the relative lack of routine information regarding exercise intensity during flight. Regular and routine HR measurement, in addition to the parameters that CEVIS and the treadmills normally provide, would be a source of such data. However, oftentimes the HR monitoring devices imbedded into the CEVIS and treadmill control panels do not function well and the crewmembers have not been required to wear a recording heart rate monitor during performance of routine exercise. As part of the effort associated with the current paper, we attempted to analyze the influence of exercise countermeasures on the PFE test results. There was no significant correlation of combined CEVIS and treadmill use with changes in ACI; however, we had information regarding only whether or not the crewmember used the devices (modality and frequency) and for how long (duration), but sparse information on intensity or work levels. This situation must be corrected to properly evaluate the effectiveness of exercise countermeasures.

Conclusions

The submaximal graded exercise test data collected at R+5 following long-duration ISS flight suggest that aerobic capacity is decreased, as evidenced by an elevated HR response. A decline in oxygen pulse lends evidence that this change is related to a reduction in stroke volume. However, changes in the metabolic gas analysis data collected during these submaximal tests are not consistent with those observed during ground-based studies of aerobic detraining. It is plausible that changes in HR following flight are most highly related to the adaptation of central blood/plasma volume to microgravity and perhaps some degree of cardiac atrophy. The changes observed in ACI during flight are consistent with detraining or adaptation early on, which appears to be at least partially reversed as flight duration increases; presumably this is related to the performance of exercise countermeasures. Thus, it is possible that the aerobic capacities of some crewmembers are maintained or recovered fairly well during flight, but the relative hypovolemia that exists due to microgravity exposure obscures this upon return to Earth. More definitive research should be conducted regarding the adaptations to flight, including better documentation of the intensities of exercises performed and evaluations of specific exercise regimens.

ACKNOWLEDGMENTS

This report was sponsored by the NASA ISS Program Office with reference to SSP 50260 – ISS medical Operations Requirements Document (MORD) and SSP 50667 – Medical Evaluations Documentation (MED) Volume B. The authors wish to thank the members of the NASA Exercise Countermeasures Project and many of the team members of the NASA Human Health and Performance Directorate at the Johnson Space Center for their support of this manuscript. Specific recognition is deserved for those involved in the aerobic exercise data collection over the first 10 years of ISS flight. These outstanding individuals are: Stuart Lee, Meghan Everett, Jamie Guined, Mark Leach, Kirk English, Roxanne Buxton, Elizabeth Goetchius, Jason Wickwire, Brent Crowell, Frank McCleary, James Loehr, W. Jon Williams, Jason Norcross, Cassie Wilson, and Kristi Blazine.

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