There is considerable variability among astronauts with respect to changes in maximal aerobic capacity (VO₂peak) during International Space Station (ISS) missions, ranging from a 5% increase to 30% decline. Individual differences may be due to in-flight aerobic exercise time and intensity. **PURPOSE:** To evaluate the effects of in-flight aerobic exercise time and intensity on change in VO₂peak during ISS missions. **METHODS:** Astronauts (N=11) performed peak cycle tests ~60 days before flight (L-60), on flight day (FD) ~14, and every ~30 days thereafter. Metabolic gas analysis and heart rate (HR) were measured continuously during the test using the portable pulmonary function system. HR and duration of each in-flight cycle ergometer and treadmill (TM) session were recorded and averaged in time segments corresponding to each peak test. Mixed effects linear regression with exercise mode (TM or cycle) as a categorical variable was used to assess the contributions of exercise intensity (%time >70% peak HR or %time >90% peak HR) and time (min/wk), adjusted for body weight, on %change in VO₂peak during the mission, and incorporating the repeated-measures experimental design. **RESULTS:** 110 observations were included in the model (4-6 peak cycle tests per astronaut, 2 exercise devices). VO₂peak was reduced from preflight throughout the mission (FD14: 13±13% and FD 105: 8±10%). Exercise intensity (%peak HR: FD14=66±14; FD105=75±8) and time (min/wk: FD14=82±46; FD105=158±40) increased during flight. The models showed main effects for exercise time and intensity with no interactions between time, intensity, and device (70% peak HR: time [z-score=2.39; P=0.017], intensity [z-score=3.51; P=0.000]; 90% peak HR: time [z-score=3.31; P=0.001], intensity [z-score=2.24; P=0.025]). **CONCLUSION:** Exercise time and intensity independently contribute to %change in VO₂peak during ISS missions, indicating that there are minimal values for exercise time and intensity required to maintain VO₂peak. As the FD105 average exercise intensity and time did not prevent a decline in VO₂peak from preflight, astronauts’ exercise prescriptions should target at least 160 min of weekly aerobic exercise at an average above 75% peak HR with increased time at intensities above 90% of peak HR starting early in the mission.