Summary of Research

Modeling of Cardiovascular Response to Weightlessness

PI: M. Keith Sharp

Department of Bioengineering
50 South Central Campus Drive, Room 2480
University of Utah
Salt Lake City, UT 84112
Phone: 801-581-6955
Fax: 801-585-5361
Email: m.k.sharp@m.cc.utah.edu

Grant number NAGW-4338

1 Jan 95 - 31 Dec 98

ABSTRACT

It was the hypothesis of this project that the simple lack of hydrostatic pressure in microgravity generates several purely physical reactions that underlie and may explain, in part, the cardiovascular response to weightlessness. For instance, hydrostatic pressure within the ventricles of the heart may improve cardiac performance by promoting expansion of ventricular volume during diastole. The lack of hydrostatic pressure in microgravity might, therefore, reduce diastolic filling and cardiac performance. The change in transmural pressure is possible due to the difference in hydrostatic pressure gradients between the blood inside the ventricle and the lung tissue surrounding the ventricle due to their different densities. On the other hand, hydrostatic pressure within the vasculature may reduce cardiac inlet pressures because of the typical location of the heart above the hydrostatic indifference level (the level at which pressure remains constant throughout changes in gravity). Additional physical responses of the body to changing gravitational conditions may influence cardiovascular performance. For instance, fluid shifts from the lower body to the thorax in microgravity may serve to increase central venous pressure (CVP) and boost cardiac output (CO). The concurrent release of gravitational force on the rib cage may tend to increase chest girth and decrease pericardial pressure, augmenting ventricular filling. The lack of gravity on pulmonary tissue may allow an upward shifting of lung mass, causing a further decrease in pericardial pressure and increased CO. Additional effects include diuresis early in the flight, interstitial fluid shifts, gradual spinal extension and movement of abdominal mass, and redistribution of circulatory impedance because of venous distention in the upper body and the collapse of veins in the lower body. In this project, the cardiovascular responses to changes in intraventricular hydrostatic pressure, in intravascular hydrostatic pressure and, to a limited extent, in extravascular and pericardial hydrostatic pressure were investigated. A complete hydraulic model of the cardiovascular system was built and flown aboard the NASA KC-135 and a computer model was developed and tested in simulated microgravity. Results obtained with these models have confirmed that a simple lack of hydrostatic pressure within an artificial ventricle causes a decrease in stroke volume. When combined with the acute increase in ventricular pressure associated with the elimination of hydrostatic pressure within the vasculature and the resultant cephalad fluid shift with the models in the upright position, however, stroke volume increased in the models. Imposition of a decreased pericardial pressure in the computer model and in a simplified hydraulic model increased stroke volume. Physiologic regional fluid shifting was also demonstrated by the models. The unifying parameter characterizing the three mechanisms of cardiac response was diastolic ventricular transmural pressure (DVΔP). The elimination of intraventricular hydrostatic pressure in 0-G decreased DVΔP and stroke volume, while the elimination of intravascular hydrostatic pressure increased DVΔP and stroke volume in the upright posture, but reduced DVΔP and stroke volume in the launch posture. The release of gravity on the chest wall and its associated influence on intrathoracic pressure, simulated by a drop in extraventricular pressure, increased DVΔP and stroke volume.

Methods

Hydraulic model - The hydraulic model [Gillars, et al. 1999a] incorporated left and right ventricles of a pneumatic artificial heart, left and right atria, a peripheral venous pool (PVP), three systemic vascular sections (cephalic, central and caudal) and a pulmonary

section. Each vascular section comprised a proximal resistor, proximal compliance, peripheral resistor and peripheral compliance. A small amount of inertance was also introduced in connecting tubing. The resistors were made from open-cell foam compressed by a motorized piston. Each compliance unit incorporated a coil spring-loaded piston moving inside a cylinder sealed with an elastomeric diaphragm [Woodruff, et al. 1997]. Non-linear compliance was provided by both high pressure and low pressure limits on the displacement of the piston and diaphragm. The peripheral venous pool (PVP) consisted of a spring-loaded bellows designed to mimic the human blood vessel pressure-volume relationship corresponding to vessel cross sectional shapes of 1) collapsed, 2) partially filled elliptical, and 3) inflated circular and the blood volume displacements due to gravity measured by previous investigators. An extensive computer model, which incorporated over 1000 elements (lumped resistance, compliance and inertance), was used to choose values of the elements in the regional mock circulation units most closely approximating the input impedance of the human system. Tests were performed to find and adjust the hydrostatic indifference level (HIL) of the hydraulic model to be just below the ventricles as in the natural cardiovascular system. The hydraulic model was flown in simulated 0-G aboard the NASA KC-135, with a different posture being tested each flight day and a different cardiac output for each set of ten parabolas.

Computer model – The computer model [Petersen, et al. 1999] consisted of a distributed parameter systemic arterial system with 28 tapered elastic segments representing the large arteries and lumped parameter terminal Windkessel elements representing the small arteries, along with resistive elements representing minor artery branches off the main systemic tree. The ventricles were modeled with time-dependent elastance. Added were a three-region lumped parameter systemic venous system with non-linear compliance, lumped parameter pulmonary circulation and Windkessel left and right atria. Energy losses were included in the unsteady Bernoulli equations describing flow from parent to daughter branches across systemic arterial bifurcations. The influence of hydrostatic pressure was included in the ventricular response, as well as in the systemic venous volume calculations. The quasi-one-dimensional unsteady equations of momentum and continuity modeled the flow in each artery segment. A third equation, the tube law relating pressure and cross-sectional area of the tube was used to describe arterial wall behavior, including wall viscoelasticity. The MacCormack finite difference predictor-corrector scheme was used to solve the non-linear partial differential equations.

Results and Discussion

Hydraulic model - (see Gillars, et al. [1999b]) A shift to the right of the cardiac performance curve (cardiac output [AOQ] versus left atrial pressure [LAP]) was evident with decreasing gravity, as noted by the investigators in previous experiments. This drop in cardiac performance at low LAP is attributed to the decrease in effectiveness of cardiac filling by the lack of hydrostatic pressure within the ventricle [Pantalos, et al. 1998]. AOQ converged for all gravitational conditions to the Starling limit at high LAP. Note that in the recumbent positions (launch and supine), the intraventricular hydrostatic pressure (IVHP) is smaller (along the anterior-posterior axis) than in the upright position, but does not disappear. Diminished filling was seen in the supine posture, though less than in the upright posture. Cardiac performance was similar for all postures in 0-G.

Because of the large compliance of the PVP when elevated to model the launch posture, LAP, aortic pressure (AOP) and AOQ dropped sharply from 1-G to 0-G. The large PVP compliance raised the HIL significantly above the heart, resulting in drops in pressures at the level of the heart in 0-G. This phenomenon was not evident in the supine posture, because of the minimal hydrostatic gradient for fluid shifting among G levels. The smaller compliance of the PVP for further volume reduction between 1-G and 1.8-G in the launch posture was clearly reflected in the limited increases in LAP, AOP and AOQ (AOQ actually decreased slightly). With the HIL slightly below the heart in the upright posture, increases in LAP, AOP and AOQ would be expected upon entry into weightlessness from 1-G. These changes, however, were moderated by the elimination of the beneficial effects of the IVHP. In these results, it appeared that the intraventricular hydrostatic pressure was the more important factor, since only AOP rose with entry into weightlessness, while LAP and AOQ decreased slightly.

The change in right atrial pressure (RAP) in the model from 10.1 mmHg in 1-G to 4.1 mmHg in 0-G at the nominal 6.0 l/min set point in the launch posture compared favorably with measurements by Buckey, *et al.* [1996], who found that central venous pressure (CVP) dropped in three astronauts from 11 mmHg in 1-G to 1.8 mmHg in 0-G. The lower CVP in 0-G in humans has been attributed to decreased intrathoracic pressure due to unweighting of the thorax and abdomen, which acts to augment diastolic filling by decreasing extraventricular pressure and ,therefore, increasing ventricular transmural pressure.

Computer model – (see Petersen, et al. [1999]) Simulated arterial pressure and flow waveforms resembled those of the human. Because the model included hydrostatic gradients only in the superior/inferior direction, supine results for all G levels and 0-G results in all postures were computationally equivalent. Peak systolic pressure, peak left ventricular volume and peak aortic pressure were all increased in the numerical model output for 0-G as compared to 1-G standing posture. These results are in agreement with the results for left ventricular pressure and aortic pressure for the hydraulic model, which increased in 0-G as compared to 1-G standing due to the cephalad shifting of blood even though cardiac output decreased. Systemic venous volume shifts in the computer model followed expected trends, with caudal fluid shifting into the central and cephalic regions with entry into weightlessness.

Small changes were seen in the launch posture as well. Most notably, caudal venous volume increased in 0-G as compared to 1-G and was shifted from both the cephalic and central regions. Stroke volume and left ventricular end-diastolic pressure decreased in 0-G as compared to the 1-G launch posture, due to the absence of hydrostatic augmentation of diastolic filling. Central venous pressure (right atrial pressure) decreased in 0-G as compared to the 1-G launch position, consistent with the hydraulic model and with human data [Buckey, *et al.* 1996]. Since both models neglect at this stage body structural interactions [Buckey, *et al.* 1996], this decrease was expected. Fluid shifts footward decrease volume and therefore pressure at the level of the right atrium [Watenpaugh and Hargens 1995].

Conclusions

The findings from these models lend support to the notion that the purely biomechanical response to weightlessness, *i.e.*, the direct response of the heart, blood and blood vessels to the elimination of hydrostatic pressure, motivates the many other changes in the cardiovascular system observed in astronauts. In these models, changes in cardiac filling and flow and vascular pressures and fluid shifting have been documented in the absence of all controls and adaptation mechanisms, including neurohumoral influences. The important parameter in determining the influence of hydrostatic pressure on cardiac performance was DVΔP. Intraventricular hydrostatic pressure increased DVΔP and, therefore, reduced cardiac filling resulted from its absence in 0-G. The elimination of intravascular hydrostatic pressure increased DVΔP in the standing posture, but decreased DVΔP in the launch posture because of the relative position of the heart to the HIL, producing the expected effects on cardiac filling. A decrease in intrathoracic pressure, representative of the unloading of the chest wall, increased DVΔP and cardiac filling. The role of these phenomena in causing subsequent changes in circulating fluid volume, blood chemical and cellular composition and cardiac and vascular properties, including peripheral resistance, remains to be investigated. A striking phenomenon evident in the flow and pressure data from both models was the dependence of the results on the state of each compliance relative to its pressure-volume relationship. The compliances in both models are adjustable and may be designed to a wide variety of compliance curves, however, there is a general lack of data in humans for matching, as well as potential variations among humans and between rest and exercise conditions. Measurements of vascular compliance are needed to improve the accuracy of the models. Refinements are planned in both models for monitoring cranial arterial pressure and flow so that postflight orthostatic intolerance can be predicted and candidate countermeasures evaluated.

References

Buckey JC, Gaffney FA, Lane LD, Levine BD, Watenpaugh DE, Wright SJ, Yancy CW, Meyer D & Blomqvist CG, 1996, "Central venous pressure in space," *J Appl Physiol*, 81(1):19-25.

Gillars KJ & Sharp MK, "The evaluation of characteristic values for components of a three-region hydraulic model of the human systemic circulation," in preparation, 1999a.

Gillars KJ, Sharp MK & Pantalos GM, "Response of a hydraulic model of the cardiovascular system to simulated microgravity," in preparation, 1999b.

Pantalos GM, Sharp MK, Woodruff SJ, O'Leary DJ, Lorange R, Everett SD, Bennett TE & Schurfranz T, 1998, "The influence of gravity on cardiac performance," *Ann Biomed Eng*, 26:6:931-943.

Peterson K, Sharp MK & Pantalos GM, "A numerical simulation of the cardiovascular system to microgravity," in preparation, 1999.

Watenpaugh DE & Hargens AR, 1995, "The cardiovascular system in microgravity," Chap 29 in Handbook of Physiology-Environmental Physiology.

Woodruff SJ, Sharp MK & Pantalos GM, "Compact compliance chamber design for the study of cardiac performance in microgravity," *ASAIO J* 43:4:316-320, 1997.

BIBLIOGRAPHY

The following publications have so far resulted or are in preparation from this research project:

1. Pantalos GM, Sharp MK, Woodruff SJ, O'Leary DS, Lorange RD, Bennett TE, Dussack LG & Charles JB, "Cardiovascular response to gravitational and postural changes," AIAA/NASA Life Sciences & Space Med Conf & Exhib, Houston, TX, Apr 3-5, 1995.

2. Sharp MK, "Cardiovascular function in zero-gravity," Presentation to University of Toronto Department of Mechanical Engineering, Oct 10, 1995.

3. Sharp MK, Pantalos GM, Bennett TE, Woodruff SJ, O'Leary DS & Charles JB, "Modeling of the cardiovascular response to microgravity," BMES Fall Meeting, Boston, MA, Oct 6-8, 1995.

4. Pantalos GM, Sharp MK, Woodruff SJ, O'Leary DS & Gillars KJ, "Simulation of cardiovascular adaptation to weightlessness," Am Soc Grav & Space Biol Conf, Washington DC, Oct 26-28, 1995.

5. Pantalos GM, Sharp MK, Woodruff SJ, O'Leary DS & Gillars KJ, "Simulation of cardiovascular adaptation to weightlessness," AIAA/NASA Life Sciences & Space Med Conf & Exhib, Houston, TX, Mar 5-7, 1996.

6. Pantalos GM, Mathias J, Sharp MK, Watenpaugh D, Buckey J, Parnis S, Hargens A & Thornton W, "Variations in esophageal and abdominal pressure in humans during parabolic flight," Am Soc Grav & Space Biol Conf, Charlotte, NC, Oct 23-26, 1996.

7. Sharp MK , Pantalos GM, Gillars KJ , O'Leary DS & Woodruff SJ, "Modeling of cardiovascular response to weightlessness," ASME Summer Bioengineering Conf, Sun River, OR, Jun 11-15, 1997.

8. Pantalos GM, Bennett T, Sharp MK , Woodruff SJ, O'Leary DS, Gillars KJ , Lemon M &Sojka J, "The role of gravitational acceleration in cardiac diastolic function," 13th Ann meeting Am Soc Gravitational & Space Biol, Washington DC, Nov 19-22, 1997.

9. Woodruff SJ, Sharp MK & Pantalos GM, "Compact compliance chamber design for the study of cardiac performance in microgravity," *ASAIO J* 43:4:316-320, 1997.

10. Sharp MK, "Cardiovascular function in zero-gravity," Presentation to Florida International University Department of Mechanical Engineering, Apr 18, 1997.

11. Pantalos GM, Bennett T, Sharp MK , Woodruff SJ, O'Leary DS, Gillars KJ , Lemon M &Sojka J, "The role of gravitational acceleration in artificial heart diastolic function," 44th Ann conf ASAIO/CVST, New York, NY, Apr 23-25, 1998.

12. Pantalos GM, Sharp MK, Woodruff SJ, O'Leary DJ, Lorange R, Everett SD, Bennett TE & Schurfranz T, "The influence of gravity on cardiac performance," *Ann Biomed Eng*, 26:6:931-943, 1998.

13. Sharp MK & Dharmalingam RK, "Development of a hydraulic model of the human systemic circulation," accepted for publication, *ASAIO J*,1998.

14. O'Leary DJ, Pantalos GM, Sharp MK, "Feedback control of mean aortic pressure in a dynamic model of the cardiovascular system," accepted for publication, *ASAIO J*,1998.

15. Sharp MK, Pantalos GM, Gillars KJ & Peterson K, "Hydraulic and computer modeling of cardiovascular response to weightlessness," NASA Space Biomedical Investigators Workshop, League City, TX, Jan 11-13, 1999.

16. Sharp MK, Pantalos GM, Gillars KJ & Peterson K, "Physical and computer modeling of the influence of hydrostatic pressure on cardiovascular performance," Summer Bioengineering Conf, Big Sky, MT, Jun 16-20, 1999.

17. Gillars KJ & Sharp MK, "The evaluation of characteristic values for components of a three-region hydraulic model of the human systemic circulation," in preparation, 1999a.

18. Gillars KJ, Sharp MK & Pantalos GM, "Response of a hydraulic model of the cardiovascular system to simulated microgravity," in preparation, 1999b.

19. Peterson K, Sharp MK & Pantalos GM, "A numerical simulation of the cardiovascular system to microgravity," in preparation, 1999.