

## BIOMECHANICAL INSIGHTS INTO THE MAINTENANCE OF ORTHOSTATIC TOLERANCE: WHEN CARDIAC REPLACEMENT AND SPACE FLIGHT FLY TOGETHER

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Two early observations of cardiovascular function from the use of pneumatically powered total artificial hearts (TAH) and orbital space flight provide insights into biomechanical factors involved in the maintenance of orthostatic tolerance. In bed-ridden, end-stage heart disease patients being supported to cardiac transplantation by an implanted TAH, it was observed that reduced cardiac output in the presence of mild hypovolemia could be reversed by adding a few mmHg of vacuum to the air side of the pumping diaphragm during diastole. The addition of the diastolic vacuum increased the cardiac transmural pressure, promoting increased filling and stroke volume in the presence of a reduced intraventricular pressure which served to augment venous return to the TAH. As TAH patients recovered to the point where they could become ambulatory, it was observed that transitioning from the supine to the upright posture, the cardiac output may drop 25%, presumably the result of venous pooling due to a down-regulation of vascular tone as a part of the chronic disease process. The cardiac output could be restored by adding 3 to 5 mm Hg of diastolic vacuum again to increase cardiac transmural pressure resulting in augmented venous return and filling.

The initial measurement of central venous pressure (CVP) and cardiac dimensions on SLS-1 and SLS-2 revealed a seemingly paradoxical finding of increased cardiac size and stroke volume in the presence of a reduced CVP. It was proposed that, like in the pneumatic TAH patients, there had been an increase in the cardiac transmural pressure in this case mediated via a drop in the intrapleural pressure (IP) as the elastic rib cage expanded slightly due to the unloading with entry into microgravity. This phenomenon could be demonstrated with an instrumented left ventricular model pumping on a mock circulatory system and later in instrumented human test subjects where intraesophageal pressure (IEP) and CVP were measured during parabolic flight. Ground-base measurements associated with the human test subjects also revealed that the IEP may drop by as much as 5 to 7 mm Hg when transitioning from the supine to the upright posture. Hence, the normally existing biomechanical interaction of the heart, lungs, chest wall, and abdomen result in a naturally occurring “countermeasure to increase cardiac transmural pressure and promote venous return when transitioning from the supine to the upright posture.

The previous observations pose an interesting challenge when considering the control of an electrohydraulic TAH that may not be responsive to changes in IP. The AbioCor™ completely implantable artificial heart system provides total circulatory support while operating by manual or automatic control. The left and right ventricles operate at 180° out-of-phase, hence the motor speed used to eject blood from one ventricle is the same motor speed used to draw blood into the opposite ventricle. While the AbioCor™ operated in the automatic motor speed and fixed beat rate control modes, the hemodynamic response during changes in posture in the first two patients was measured on 27 occasions during the first three weeks of implantation. Arterial and central venous pressure (AP, CVP) were continuously measured with clinical, fluid-filled catheters; left atrial pressure (LAP) was measured with a gravity-insensitive catheter (Millar Instruments). Cardiac output (CO), left and right systolic motor speed (LMS, RMS), and other control parameters were recorded simultaneously. The patients had acceptable circulating volume status as indicated by the CVP preceding the change in posture. Patient transition from supine (SUP) to upright-seated (UPS) posture resulted in no reduction in AP (SUP=84±9, UPS=87±12 mm Hg) and CO (SUP=7.0±0.5, UPS=7.1±0.4 l/min) while the LAP always dropped (SUP=17±4, UPS=12±4 mm Hg). The LMS increased in 56% of the observations (LMS: SUP= 6911±273, UPS=6995±323) and the RMS increased in 85% of the observations (RMS: SUP=6925±418, UPS=7071 ±469) indicating some level of increased transmural pressure being implemented to maintain CO. The integration of all of these observations suggest that in addition to the maintenance of peripheral vascular tone and resistance, transitioning from the supine to the upright posture also requires an increase in cardiac transmural pressure to promote diastolic filling for the successful maintenance orthostatic tolerance.