Effects of Depressed Myocardial Contractility Induced by Microgravity on Cardiovascular Response to Orthostatic Stress: A Computer Simulation

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Abstract

The aim of present study is to investigate the role played by the depression of myocardial contractility in the mechanism of cardiovascular deconditioning and orthostatic intolerance (OI) induced by space weightless-ness. Based on our previous model, which was used to simulate cardiovascular response to lower body negative pressure (LBNP), we incorporated the factor of changes of myocardial contractility into the model by multiplying a coefficient to the time-varying elastance that represents the changes of cardiac contractility. By decreasing the coefficient progressively, we simulated the changes of heart rate (HR), blood pressure (BP), and cardiac output (CO) during LBNP after 0~30% of myocardial contractility depression combined with 12% decrease of the total blood volume. Simulation results indicate that depressed myocardial contractility induces more augment of HR, and more decrement of BP and CO during LBNP and suggest that the depression of myocardial contractility degenerate cardiovascular response to orthostatic stress.

1. Introduction

Cardiovascular acclimation to weightless-ness of spaceflight is inappropriate for return to Earth gravity. Even after short flights, most astronauts experience some postflight reduction of orthostatic tolerance and upright exercise capacity[1, 2]. Orthostatic tolerance is the ability of an organism to function normally while immobile with its long axis parallel to the gravity vector[2]. Reduced orthostatic tolerance and upright exercise capacity pose serious hazards during re-entry and during emergency egress of crewmembers immediately after landing of spacecraft. After spaceflight, astronauts suffer presyncope or syncope during exposure of orthostatic stresses, such as standing, head-up tilt or lower body negative pressure (LBNP). Heart rate might exceed 160 beats/min (bpm) and systolic pressure decrease 25 mmHg upon first standing after landing[1]. This symptom is called as orthostatic intolerance (OI) or cardiovascular deconditioning [1, 2]. Although hypovolemia is considered as the primary cause of OI, the role played by other factors, such as the lowered vasoconstrictor responsiveness of resistance vessels, the enhanced vasoconstriction response of cerebral vessels, and the depressed myocardial contractility need to be elucidated[1, 3, 4, 5]. It is difficult to assess experimentally how each of these changes would affect orthostatic tolerance and how these factors interact with each other. An alternative approach is to conduct simulation studies by use of mathematical models of cardiovascular system capable of simulating the cardiovascular response to orthostatic stress. This presentation describes the construction of the model used, and presents the preliminary simulation results illustrating the effects of varying depression of myocardial contractility on responses to orthostatic stress. The ultimate goal of our work was to integrate the new experimental findings and to simulate the complexity to get a thorough understanding of the mechanism of postflight cardiovascular dysfunction and orthostatic intolerance.

2. Model description & simulation procedure

Based on the previous work of Melchior et al[6], we have developed a mathematical model (Fig 1) by incorporating some more detailed sub-models to describe blood redistribution, cardiac contractility, peripheral circulation, local vascular tone changes, and baroreflex control mechanism[7]. The detailed descriptions of the model have been given in previous work [6, 7] and the model have been validated for simulation of the cardiovascular system (CVS) response to exposure of LBNP, or head up tilt by the data obtained from human experiment and published data[5,7]. Here we briefly review the main points and then focus on the establishment of the method for simulating varying level of depressed myocardial contractility.

Because the arteries and capillaries are much less compliant than the veins, we assumed that blood volume redistribution during LBNP takes place only in the venous beds. Venous blood volume is considered to be

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stored in seven different compartments representing the head and up-limbs, thoracic region, abdomen region, pelvis and buttocks, thigh, calf and foots (Fig 2). In the model, HR and venous tone are modulated by the carotid baroreceptors (denoted by mean arterial pressure, MAP), whereas the peripheral resistance is regulated by both carotid and cardiopulmomary baroreceptors (denoted by MAP and central venous pressure, CVP). The left ventricle end-diastolic volume can be compute based on the work of Melchior et al.[6], which consider the elastic properties of left ventricle and preload of heart (CVP).

$$\Delta CVP = \lambda \cdot [\exp\beta \cdot V_{LVED}) - \exp\beta \cdot V_{0LVED})] \quad (1)$$

where λ is a constant and β is left ventricular elastic stiffness.

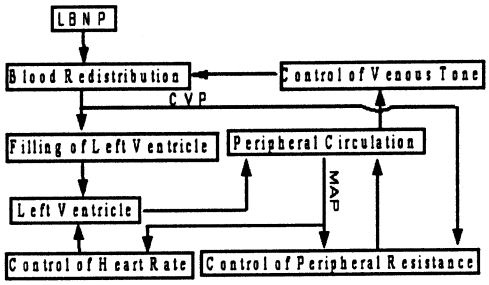

Fig 1. Block diagram of the cardiovascular model

Because our purpose of modeling the interaction between left ventricle and peripheral circulation is to simulate the effect of depressed myocardial contractility on CVS response to LBNP, three-element windkessel mode to represent the arterial system is adequate and has be modified for our special use[6, 7]. *Eqn.*2 is model for contracting of left ventricle, which is based on the work of Suga and Sagawa [8].

$$P_{LV}(t) = E(t)[V_{ED} - \int_{ED} Q_{LV}(\tau)d\tau - V_0] \quad (2)$$

where $P_{LV}(t)$ and V_{ED} are pressure and end-diastole volume of left ventricle, ventricle volume and V_0 is the volume axis intercept of the line connecting maximum elastance P/V points for differently loaded beats. $Q_{LV}(\tau)$ is flow rate of left ventricle. $E_t(t)$ is time-varying elastance that represents the changes of cardiac contractility. According to work of Sunagawa et al[8, 9], the maximum elastance E_{max}, peak value of function E(t), reflects the contractility of myocardia. The factor of changes of myocardial contractility has been incorporated into the model by multiplying a coefficient μ to E(t), and then

$$P_{LV}(t) = \mu \cdot E(t) \cdot [V_{ED} - \int_{ED} Q_{LV}(\tau)d\tau - V_0] \quad (3)$$

By decreasing the coefficient progressively, we simulated the changes of heart rate (HR), blood pressure (BP), and cardiac output (CO) during LBNP after 0~30% of myocardial contractility depression (μ=1~0.7) combined with 12% decrease of the total blood volume.

3. Results

Dynamic simulation process indicated that CVS reached to steady state after 3 min application of LBNP, and HR, SBP, DBP and CO were recorded (Fig 3). As shown in Fig 3, the augment of HR is increased significantly as LBNP and myocardia contractility is decreased. The decrement of SBP is reduced progressively with the decrement of myocardia contractility. However, DBP is increased slightly when myocardia contractility is decreased slightly with low level LBNP. But if the decrement of myocardia contractility is over 10%, DBP decreases sharply with the increment of LBNP exposure, and the system seemed to run into collapse. Also CO is decreased with the decrement of myocardia contractility and increment of LBNP. It is obvious that CO tends to a steady level when both the decreases of myocardia contractility and LBNP are high.

4. Discussion

LBNP is a well-established technique in the study of orthostatic stresses. The advantage of LBNP compared with passive tilt is that the subject remains at rest in the supine position, which facilitates physiological measurements and minimizes the likelihood of confounding activity in skeletal muscle. Another advantage of LBNP is that it is not limited by gravity, and so is widely used in space microgravity environment [1, 2]. Using the model developed, we simulated the effects of depression of myocardia contractility on cardiovascular response to LBNP in order to investigate the role played by depression of myocardia contractility in postflght OI. The simulation results indicated that the cardiovascular responses to orthostatic stress changed significantly with decrement of myocardia contractility. Simulation results suggest that depression of myocardia may be a factor in the cause of orthostatic intolerance induced by weightlessness [1, 2].

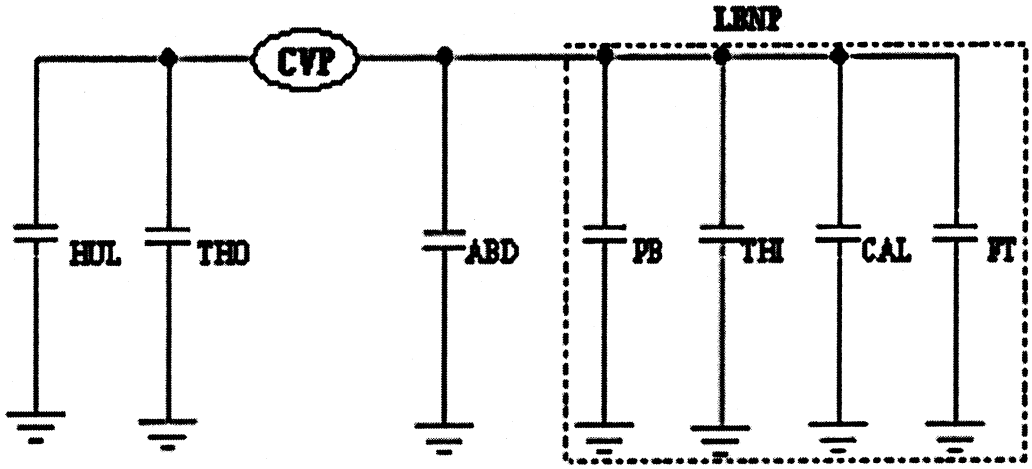

Fig 2. Compartments model for blood redistribution during LBNP. The Compartments represents the head and up-limbs (HUL), thoracic region (THO), abdomen region (ABD), pelvis and buttocks (PB), thigh (THI), calf (CAL) and foots (FT)

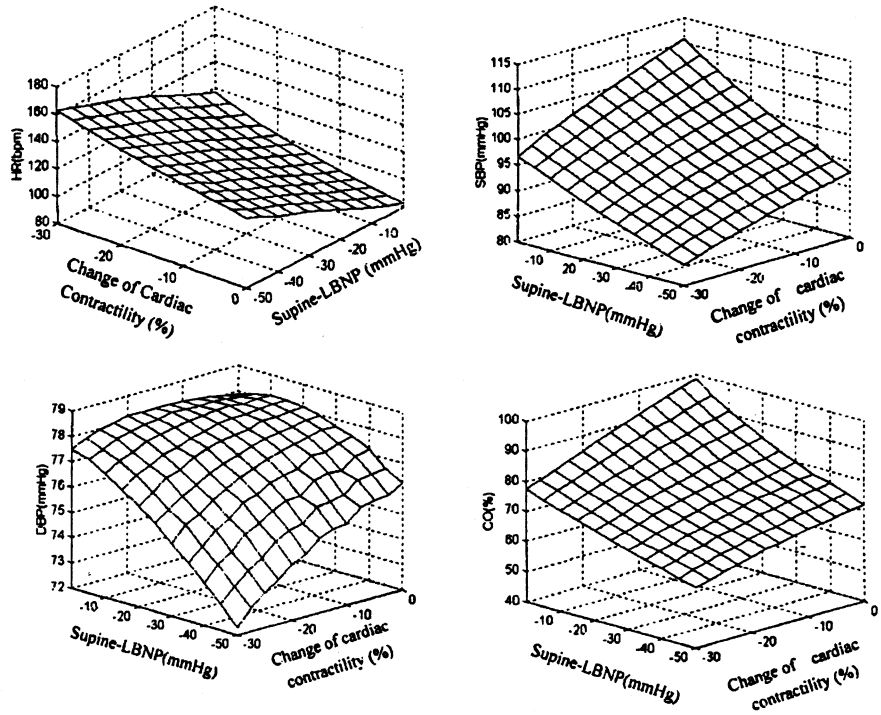

Fig 3. Effect of depressed myocardia contractility on heart rate (HR), systole blood pressure (SBP), diastole blood pressure (DBP) and cardiac output (CO) response to supine-LBNP

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