

## Impact of baroreflex on venous return surface

Takafumi Sakamoto, Yoshinori Murayama, Atsushi Tanaka, Kazuo Sakamoto, Tomoyuki Tobushi, Keita Saku, Kazuya Hosokawa, Ken Onitsuka, Takeo Fujino and Kenji Sunagawa, Senior Member, IEEE

**Abstract— Background:** Although Guyton's concept of venous return (VR) revolutionized circulatory physiology, the pulmonary circulation is invisible in its original framework. Since the pulmonary circulation is critical in left heart failure, we characterized the VR as a surface described by right ( $P_{RA}$ ) and left atrial ( $P_{LA}$ ) pressures and demonstrated that the VR surface was capable of representing mechanics of pulmonary as well as systemic circulation. However how baroreflex impacts the VR surface remains unknown. **Methods/Results:** In 8 dogs, we isolated the carotid sinuses and replaced both ventricles with pumps. We varied cardiac output, shifted blood distribution between the systemic and pulmonary circulation at carotid sinus pressures (CSP) of 100 or 140 mmHg. The coefficient of determination of the VR surface ranged 0.96-0.99 indicating how flat the surface is. Increasing CSP decreased maximum VR ( $233\pm 27$  vs.  $216\pm 33$  ml/kg/min,  $p<0.05$ ), whereas did not change the slopes of VR along  $P_{RA}$  or  $P_{LA}$  axes. **Conclusions:** Baroreflex parallel shifts the VR surface, thereby stressed volume, without changing its slopes.

### I. INTRODUCTION

Guyton's classic concept of circulatory equilibrium [1] revolutionized circulatory physiology. Guyton's classic concept, however, was not intended to represent the circulatory equilibrium of left ventricular failure because neither left ventricular mechanics nor pulmonary circulation is explicitly incorporated. To overcome such a limitation of Guyton's classic concept, we previously developed a framework of circulatory equilibrium [2, 3] where, as shown in Fig. 1, we defined the cardiac output curve and venous return curve as functions of both right atrial pressure ( $P_{RA}$ ) and left atrial pressure ( $P_{LA}$ ). We denoted the venous return curve as the venous return surface. A theoretical analysis using a distributed vascular model indicated that venous return (VR) of the total circulatory system can be described as

$$VR = VR_{max} - (G_P P_{LA} + G_S P_{RA}) \quad (1)$$

where  $VR_{max}$  is maximum venous return and is a function of stressed blood volume [2, 3, 4],  $G_P$  and  $G_S$ , conductance of pulmonary and systemic venous return, respectively. We demonstrated that the venous return surface was remarkably

flat and the slopes toward the  $P_{LA}$  and  $P_{RA}$  axes did not differ among animal preparations [2, 3].

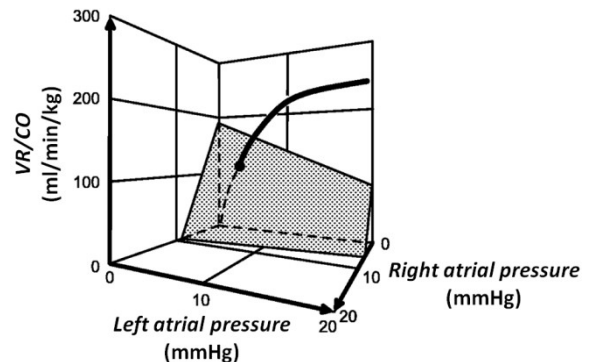


Figure 1 Proposed framework of circulatory equilibrium consists of integrated cardiac output curve and venous return surface.

Since baroreflex is a powerful physiological modulator of mechanical properties of cardiovascular system and thereby capable of changing circulatory equilibrium, we investigated how baroreflex impacts on characteristics of venous return surface.

### II. METHODS

#### A. Animal preparation

Eight mongrel dogs were anesthetized with pentobarbital sodium and ventilated artificially. We isolated the bilateral carotid sinuses from the systemic circulation and connected them to a servo-controlled piston pump to control intra-carotid sinus pressure (CSP). We cut the bilateral vagosympathetic trunks to eliminate other reflexes. After median sternotomy, the heart was suspended in a pericardial cradle. Fluid-filled catheters were placed in the right and left atrium to measure pressures.

To examine the venous return surface, we performed total heart bypass. Two roller pumps were used to control systemic and pulmonary flows. A systemic perfusion cannula was placed in the right common carotid artery. A draining cannula for the systemic circulation was inserted into the right ventricle through its free wall. A pulmonary perfusion cannula was placed in the pulmonary artery. A draining cannula for pulmonary circulation was inserted into the left ventricle via the apex. The flow rate (i.e., cardiac output) was measured by an in-line ultrasonic flow probe. After starting two roller pumps at a matched rate, we tied an umbilical tape around pulmonary artery, clamped the ascending aorta and thus established the total heart bypass.

#### B. Protocol

For a given CSP, we waited for several minutes until the

Manuscript received September 15, 2011. This work was supported in part by Health and Labour Sciences Research Grant for Research on Medical Devices for Improving Impaired QOL from the Ministry of Health Labour and Welfare of Japan, Health and Labour Sciences Research Grant for Clinical Research from the Ministry of Health Labour and Welfare of Japan, and Grant-in-Aid for Scientific Research(S) (18100006) from the Japan Society for the Promotion of Science

All authors are with Kyushu University, Fukuoka 8128582 Japan. (corresponding author Takafumi Sakamoto to provide phone: +81-92-642-5360; fax: +81-92-642-5357; e-mail: tsaka@cardiol.med.kyushu-u.ac.jp).

hemodynamic conditions reached a steady state. We then simultaneously changed the flow rate of both pumps stepwise between 40 and 100 ml/min/kg in an increment of 20ml/min/kg. In each step, we varied the blood volume distribution between the pulmonary and the systemic circulations by transiently unbalancing the flow rates of the two pumps. We conducted the protocol at CSP of 100 and 140 mmHg.

### III. RESULTS

We applied multivariate regression analysis and determined  $VR_{max}$ ,  $G_P$  and  $G_S$ . Shown in the left panel of Fig. 2 is a representative venous return surface. All data points appear to be distributed on a flat surface. The fact that all points are distributed around a single line if they are viewed from a direction parallel to the surface indicated how flat the surface is (not shown). Baroreflex did not affect the flatness of the venous return surface. The multiple correlation coefficient was close to unity ( $r^2=0.96-0.99$ ) suggesting that the venous return surface is reasonably flat in every animal.

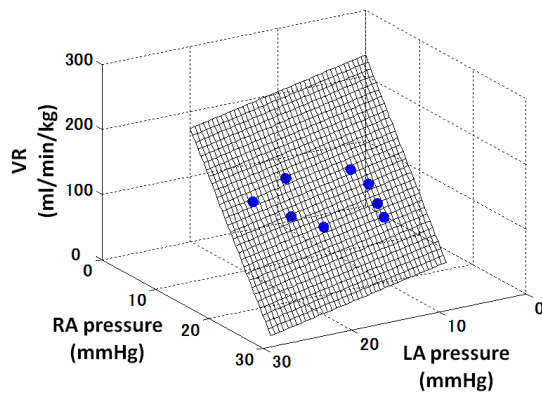


Figure 2 Representative venous return surface at CSP 140mmHg

Illustrated in Fig. 3 are the impact of baroreflex on  $VR_{max}$ ,  $G_S$  and  $G_P$ . Increasing CSP significantly decreased  $VR_{max}$  ( $233 \pm 27$  vs.  $216 \pm 33$  ml/kg/min, data were means  $\pm$  SD,  $p < 0.05$ , paired t-test) whereas it did not change  $G_P$  or  $G_S$ . This is to say that baroreflex shifted the VR surface along the vertical axis without changing the slopes. Since the  $VR_{max}$  reflects stressed blood volume [2, 3], baroreflex in turn changed stressed blood volume.

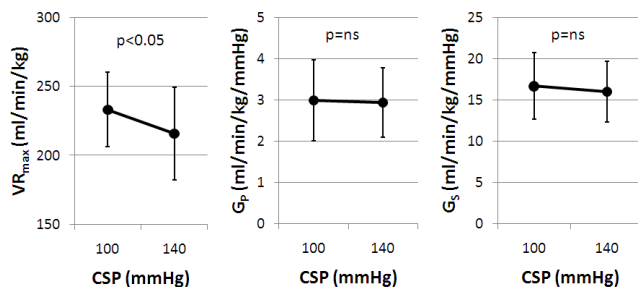


Figure 3  $VR_{max}$ ,  $G_P$ , and  $G_S$  obtained at CSP 100 and 140 mmHg

### IV. DISCUSSION

Uemura et al [2, 3] have demonstrated that VR surface was

remarkably flat and the slopes toward  $P_{LA}$  and  $P_{RA}$  axes did not differ among animal preparations. But the impact of baroreflex on VR surface remained unknown. We reconfirmed that the venous return surface is reasonably flat over a wide range of cardiac output and venous pressures. Baroreflex did not affect the flatness of the venous return surface. Baroreflex markedly changes the maximum venous return, thereby stressed volume, but did not change the slopes of the venous return surface.

### V. CONCLUSION

We conclude that baroreflex modulates the circulatory equilibrium by changing the stressed blood volume without affecting the slopes of venous return.

### ACKNOWLEDGMENT

This study was supported in part by Health and Labour Sciences Research Grant for Research on Medical Devices for Improving Impaired QOL from the Ministry of Health Labour and Welfare of Japan, Health and Labour Sciences Research Grant for Clinical Research from the Ministry of Health Labour and Welfare of Japan, Grant-in-Aid for Scientific Research(S) (18100006, 23220013) from the Japan Society for the Promotion of Science.

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