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The Relationship of Central Circulation and Peripheral Circulation During Exercise in Patients With Chronic Heart Failure

Yuichi Ishikawa¹, Nobuhiro Miyazaki², Hiroshi Yamabe³, Yoshio Fujioka³, Takahiro Taniguchi³, and Mitsuhiro Yokoyama³.

The relationships between brachial arterial blood flow (BBF), cardiac output (CO), and pulmonary capillary wedge pressure (PCWP) were studied in 32 patients. The change of BBF was negatively correlated with change of PCWP (r=-0.701, p<0.001). The change of ratio of BBF/CO also significantly correlated with change of PCWP (r=-0.676, p<0.001). The change of forearm vascular resistance was positively correlated with change of PCWP (r=0.656, p<0.001). The peripheral Tarazi's Index (TIP) was correlated with PCWP at peak exercise (r=0.535, p<0.005). The change of BBF was correlated to changes of CO (r=0.470, p<0.01), and patients with small increase of CO showed decreased change of BBF. Patients were divided to two groups; high PCWP (>25 mmHg) and low PCWP (<25 mmHg). At peak exercise, high PCWP group showed small increase of CO, decreased BBF, decreased BBF/CO ratio, increase of FVR and TIP. These results indicated that the vascular compliance at rest was already decreased in patients with high PCWP at peak exercise, that flow redistribution from non-working muscle to working muscle occurred during exercise, and that the extent of blood redistribution was greater in patients with high PCWP.

Key Words
Cardiopulmonary exercise test, Cardiac output, Pulmonary capillary wedge pressure, Brachial blood flow, Vascular compliance.

Introduction

Patients with chronic heart failure (CHF) experience significant morbidity because of dyspnea and fatigue with impaired activities of daily living. Although cardiac pump failure is the hallmark of this disorder, a close relationship between exercise intolerance and left ventricular performance has not been shown¹.²) This suggests that exercise intolerance in patients with CHF is multifactorial, and that research efforts must be made on central and peripheral abnormalities, and alterations on peripheral blood flow and skeletal muscle biochemistry and histology³). Previous studies have shown that blood flow to inactive organ is decreased during exercise in patients with CHF.¹-⁷ However it is not well shown whether there are organic changes in vascular beds. In the present study, we measured vascular compliance in addition to cardiac output, pulmonary capillary wedge pressure and brachial ar-

Faculty of Health Sciences¹, First Department of Internal medicine², Kobe University School of Medicine and Department of Internal Medicine Konan Hospital³.

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terial flow to elucidate the presence of functional vascular changes in patients with chronic heart failure.

Methods

Patients

Thirty-two patients, 26 males and 6 females, were studied. The average age was 56.8 years old, ranging 30 to 71 years old. Clinical diagnose were as follows: ischemic heart disease in 24, idiopathic dilated cardiomyopathy in 3, valvular heart disease in 3 and chest pain syndrome in 3. Patients with acute myocardial infarction, unstable angina pectoris, pulmonary disease, anemia, or obstructive peripheral vascular disease were excluded from this study. NYHA functional classification in patients was class I and class II. The cardiac medications were continued at the time of study, but the use of vasodilators were discontinued at least 36 h before the study. The study protocol was designed to fulfill the regulations of the Institutional Research Committee of the Kobe University School of Medicine. The risks and benefits of the study were explained fully to the patients and a written informed consent for participation was obtained.

Study Design and protocol

The right-side cardiac pressure, arterial blood pressure, and brachial blood flow were measured at rest and during exercise. A multistage exercise test was performed in the supine position using electronically braked bicycle ergometer (Siemens Elema 380 B)\(^9\). The workload was increased by 25 watts every 3 min. The endpoint of exercise was severe fatigue or dyspnea. All subjects underwent exercise testing in the afternoon and at least 4 h after a meal. They had exercised before the study to ensure familiarity with the apparatus.

Subjects were divided into two groups based on the pulmonary capillary wedge pressure (PCWP) at peak exercise. Seventeen patients had more than 25 mmHg of PCWP at peak exercise (H group), 15 had less than 25 mmHg of PCWP at peak exercise (L group).

Measurement of Variables

A 5 lumen 7.5 Fr. Swan-Ganz catheter was inserted and wedged into the pulmonary artery to measure pulmonary capillary wedge pressure and cardiac output (CO) was measured by Fick method. The polyethylene catheter was inserted into radial artery to measure arterial pressure and blood was sampled to measure arterial oxygen content. Brachial blood flow (BBF) was measured by Doppler method using Doppler flow meter (QFM 1000, Nihon Koden). Mean arterial pressure (MAP) was calculated as pulse pressure/3 + diastolic pressure. Forearm vascular resistance (FVR) was calculated as MAP/BBF. Systemic vascular resistance (SVR) was calculated as MAP/CO.

Tarazi's Index was used as the index of vascular compliance and peripheral Tarazi's Index (TIP) was calculated as pulse pressure/ minute BBF/HR and systemic Tarazi's Index (TIS) was calculated as pulse pressure/CO\(^9\). As the index of blood distribution, minute BBF/CO was used. The measurements were performed at rest and at peak exercise during protocol. The differences of each measurements (\(\Delta\)) were calculated and estimated.
Statistical Analysis

Values were expressed as mean ± standard deviation (SD). Relationships were assessed by Pearson's correlation coefficient analysis. The two groups were compared at rest and peak exercise. The significance of difference in each group was determined using non-paired t-test.

P values of less than 0.05 were considered statistically significant.

Results

Relationship between hemodynamic variables

There was a negative correlation between the change of BBF and PCWP at rest and at peak exercise (r=-0.701, p<0.001) (Figure 1). The similar results was obtained in the change between BBF/CO and PCWP (r=-0.676, p<0.001) (Figure 2). These results indicated that the increment of peripheral vascular flow was small in patients with failing heart (the increase of PCWP) during exercise.

There was a positive correlation between the differences of FVR and PCWP at rest and at peak exercise (r=0.656, p<0.001) (Figure 3). There was also the positive correlation between the differences of TIP and PCWP at rest and at peak exercise (r=0.535, p<0.005) (Figure 4). The changes of BBF was correlated to change of CO (r=0.470, p<0.01), and patients with small increase of CO showed decreased changes of BBF (Figure 5).

These results indicated that the increase of peripheral vascular resistance and the decrease of vascular compliance were much more apparent in patients with failing heart (the large increase of PCWP) during exercise.

Comparison of variables in patients with high and low PCWP groups

As shown in Table, there were no differences of PCWP, CO and BBF between H group and L group at rest. At peak exercise, CO and BBF were signifi-
Correlation of $\Delta$ (BBF/CO) with $\Delta$ PCWP

$y = 0.038x + 0.150$ ($r = 0.676$, $p < 0.001$)

Figure 2. Correlation of changes in the ratio of Brachial Blood Flow to cardiac output ($\Delta$(BBF/CO)) with changes in pulmonary capillary wedge pressure ($\Delta$ PCWP).

Correlation of $\Delta$ FVR with $\Delta$ PCWP

$y = 9.200x - 108.1$ ($r = 0.656$, $p < 0.001$)

Figure 3. Correlation of changes in forearm vascular resistance ($\Delta$ FVR) with changes in pulmonary capillary wedge pressure ($\Delta$ PCWP).
Central and Peripheral Circulation

**Figure 4.** Correlation of changes in peripheral Tarazi’s Index (ΔTIP) with changes in pulmonary capillary wedge pressure (ΔPCWP).

**Figure 5.** Correlation of changes in BBF (ΔBBF) with changes in cardiac output (ΔCO).
Table. Changes of hemodynamic variables at rest and at peak exercise

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<tr>
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<th>PCWP (mmHg)</th>
<th>CO (l/min)</th>
<th>BBF (ml/sec)</th>
<th>BBF/CO (%)</th>
<th>FVR (mmHg/ml/sec)</th>
<th>SVR (mmHg/ml/min)</th>
<th>TIP (mmHg/ml)</th>
<th>TIS (mmHg/ml)</th>
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<td></td>
<td>11.1±4.1</td>
<td>4.5±0.9</td>
<td>0.72±0.39</td>
<td>0.90±0.46</td>
<td>182.2±101.8</td>
<td>22.2±3.5</td>
<td>143.1±96.1</td>
<td>1.02±0.24</td>
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<td>at peak</td>
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<td>16.8±4.0</td>
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<td>125.2±55.4</td>
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<td>232.4±106.9</td>
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<td>13.7±5.5</td>
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<td>34.5±8.2</td>
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<td>231.2±115.1</td>
<td>15.7±4.2</td>
<td>442.7±271.9</td>
<td>1.77±0.75</td>
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Abbreviations are shown in text. Values were expressed mean ± standard deviation.

* p<0.05 in comparison between L group and H group at rest.
† p<0.05 †† p<0.01 ††† p<0.001 in comparison between L group and H group at peak exercise.
+ p<0.05 ++ p<0.01 +++ p<0.001 in comparison between values at rest and at peak in L group.
§ p<0.05 §§ p<0.01 §§§ p<0.001 in comparison between values at rest and at peak in H group.

cantly lower in H group (P<0.05, P<0.05). FVR and SVR were significantly higher in H group (p<0.01, p<0.05).

In H group, SVR was significantly decreased at peak exercise (p<0.001) and FVR significantly increased (P<0.05). BBF/CO in H group was decreased from 1.11 ± 0.46 to 0.49 ± 0.21 % (p<0.001). This suggested that the blood redistribution occurred during exercise.

In L group, FVR and SVR were significantly decreased at peak exercise (P<0.05, P<0.001). BBF/CO in L group was not changed during exercise.

Discussion

In present paper we showed that the changes of forearm blood flow was negatively correlated with changes of PCWP. And also we showed that the forearm blood flow at peak exercise in H group was significantly lower than that in L group. These results indicated that the ratio of blood distribution between peripheral and central circulation in L group was maintained during exercise, but that in H group was decreased. During exercise, blood redistribution occurred and blood was diverted from non-working muscle to working muscle\(^7\).

We also showed that the vascular compliance at rest in H group was significantly lower than that in L group. This indicated that vascular compliance was decreased even at rest and also suggested that organic arterial changes already occurred at rest in H group.

Zelis et al.\(^11\) showed that peripheral artery easily contracted as the cardiac performance was decreased. The possible mechanisms are lowered sensitivity of pressure receptor, activation of sympathetic nerve system, elevation of catecholamine, angiotensin II, and vasopressin. He also pointed the increased content of sodium in vascular wall and edematous changes of perivascular region inhibiting vasodilatation. Sullivan et al.\(^3\) histochemically showed the decrease of slow twitch oxidative type I fiber, increase of fast twitch glycolytic type IIb fiber and the decrease of mitochondrial oxidative enzyme such as succinate dehydrogenase.
Morphologically muscle fibers showed atrophic changes and abnormalities of mitochondria. These changes resemble the disuse deconditioning in normal subjects, but deterioration of peripheral circulation and malnutrition may relate to the muscle atrophy. The muscle atrophy occurred not only in leg muscles (deconditioning) but occurred systemically. The elevation of serum tumor necrosis factor is reported to relate to muscle atrophy. Tumor necrosis factor soluble receptor also reported to increase in patients with congestive heart failure. These reports may explain systemic muscle atrophy and vascular changes.

In our study the vascular compliance at rest was already decreased. However, the deterioration of endothelial function may influence on the vascular compliance at rest and at peak exercise. Hornig et al. showed that physical training improved endothelial function in patients with chronic heart failure by up-regulation of nitric oxide synthesis. The vascular compliance might be improved by various interventions such as physical training and angiotensin converting enzyme inhibitor.

References

Y. Ishikawa et al.


