

# Enhancement of muscle deoxygenation in ischemic heart disease

Dr Shun Takagi



# ENHANCEMENT OF MUSCLE DEOXYGENATION IN ISCHEMIC HEART DISEASE

Dr Shun Takagi investigates exercise muscle physiology in patients who have recently suffered from heart attack. Furthermore, he studies the maximum oxygen uptake by skeletal muscle as a measure of the aerobic capacity in these patients.

**Can you start by telling us about your research background and when you began your focus on patients with ischaemic heart disease?**

When I was PhD student at Tokyo Medical University, I was interested in skeletal muscle oxygen dynamics during exercise. Some researchers in our laboratory managed the cardiac rehabilitation centre at Tokyo Medical University Hospital. Approximately half of our patients had ischemic heart disease, and ischemic heart disease is a primary disease of chronic heart failure. So, I began to examine whether the peripheral factors are impaired in early post ischemic heart disease patients.

It is well known that heart disease patients suffer from limited oxygen supply, caused by a suppression of the heart pump function. Recently, it has been established that not only central function (i.e. heart function), but also peripheral function (i.e. muscle blood flow and/or muscle metabolism) is impaired, especially in chronic heart disease patients. In contrast, in ischemic heart disease patients, it is generally believed that exercise tolerance is limited by heart function (i.e. ischemia of the heart), but it is unclear whether ischemic heart disease patients have impaired muscle function because of muscle deconditioning, which is considered to be one of the main reasons of impaired muscle function in chronic heart disease patients.

**In your research, why did you choose to measure muscle oxygen dynamics and maximum oxygen uptake in these patients?**

Increasing aerobic capacity is important for ischemic heart disease patients to improve their prognosis, and to accomplish this, an

enhancement of muscle oxygen extraction may be needed. That's why we investigated muscle oxygen dynamics during exercise and their relationship to maximum oxygen uptake. We need to monitor the circulation and metabolism in exercising muscle during whole-body exercise and test the direct relationship between peripheral factors and peak aerobic capacity.

**You used the Near Infrared Spatial Resolved Spectroscopy (NIRS) technique to measure certain variables in patients. How does NIRS work and what exactly does it measure?**

The NIRS technique is a way to take measurements non-invasively during whole-body exercise, and it is widely used in exercise physiology, sports science and clinical science. To explain briefly, NIRS technique uses a wavelength in the range of 700–900nm to penetrate biological tissue. It reflects the oxygen dynamics in the arterioles, capillaries, and venules in exercising muscles. Muscle oxygen dynamics by near infrared spectroscopy reflects the balance between oxygen supply and utilization, and it estimates muscle oxygen extraction.

**What effects of exercise did you observe regarding the maximum amount of oxygen in heart disease patients?**

We observed that maximum oxygen uptake was heightened by aerobic training. Increased maximum oxygen uptake reduces cardiovascular-associated morbidity and mortality. Therefore, aerobic exercise training is an effective way for patients with heart disease to increase maximum oxygen uptake.

**Based on your research, can you make recommendations for aerobic exercise in patients with ischaemic heart disease?**

In our study, even though the amount of aerobic training was low (30 minutes of cycling at moderate intensity, 1 or 2 times a week for 12 weeks), aerobic training certainly improved maximum oxygen uptake safely in early after ischemic heart disease patients. It has also been reported that, in patients after onset of heart attack, early enrolment in aerobic exercise training is more effective for improving exercise capacity than later enrolment. From these findings, for early after ischemic heart disease patients, 2 times/week aerobic training (such as 30 minutes of cycling at moderate intensity) seems to be one of the best and safest options to improve aerobic capacity.

**This appears to be a promising area of research. What further studies, if any, will you be working on?**

We have some plans to look deeper into muscle oxygen dynamics and the relationship to peak aerobic capacity. In the subjects of our previous study, heart pump function, such as left ventricular ejection, was relatively preserved. There may be an interaction between muscle oxygen dynamics and preserved heart pump function. Also, to some extent, the preserved heart pump function may be related to improving peak aerobic capacity. Trainability for muscle oxygen dynamics may also be different, compared to ischemic heart disease patients who have reduced heart pump function.



## IMPROVING POST HEART ATTACK OUTCOMES THROUGH AEROBIC EXERCISE

Dr Shun Takagi is conducting research trials to determine the effects of exercise on muscle oxygen uptake in patients who recently suffered from myocardial infarction (heart attack). The results point to the benefits of initiating aerobic exercise early after a heart attack.

In individuals battling long-term heart disease, the heart pump activity is profoundly affected. Hence, they exhibit a limited supply of oxygen. Also, their skeletal muscle function is impaired, which could be attributed to either reduced blood flow to the skeletal muscles or less metabolism taking place in the muscles. These patients also have muscle deconditioning, which may contribute to muscle physiology abnormalities. Likewise, those with ischemic heart disease also have altered muscle physiology as well as poor exercise tolerance resulting from suppressed heart function.

Dr Takagi hypothesises that a higher aerobic capacity results in better medical results in individuals with ischemic heart disease. Peak aerobic capacity is defined as the maximum amount of oxygen utilised by the muscles. He further speculates that increased muscle deoxygenation, or muscle usage of oxygen, will help achieve an improvement in aerobic capacity.

To aid the research studies, Dr Takagi and his team employ a non-invasive technique, referred to as Near Infrared Spatial Resolved Spectroscopy (NIRS). This method evaluates the balance between oxygen supply and use, as it assesses how much oxygen was removed from the blood. The NIRS technique measures the vastus lateralis muscle in the thigh for haemoglobin and myoglobin bound to oxygen, haemoglobin and myoglobin unbound to oxygen, the total concentration of these proteins, and oxygen levels in muscle. It utilises a wavelength in the range of 700 to 900 nanometres, which enters the tissue to specifically measure the oxygen levels attached to blood haemoglobin and myoglobin of the individual at rest in comparison to the levels during exercise. Haemoglobin and myoglobin are proteins that bind oxygen in the blood and muscle, respectively.



**The effects of exercise in patients with myocardial infarction (heart attack)**

In one of his research projects, Dr Takagi investigated the effects of aerobic exercise training and non-training in patients with recent myocardial infarction. The trial was conducted at the cardiac rehabilitation centre affiliated with Tokyo Medical University Hospital. In this study, the enrolled participants met several main criteria. First of all, the patients' myocardial ischemia had occurred less than six weeks prior. Also, the ages of the subjects fell between 40 and 75 years. Finally, the individuals demonstrated a capability of physical exercise. Moreover, they qualified by passing five cycling sessions. The patients were stable and received coronary artery stents. Additionally, they received their appropriate cardiac medications and were watched closely throughout the study. There were two groups of patients: 1) a training group which consisted of 10 patients and

2) a non-training group comprising six patients. Training consisted of moderate intensity cycling for 30 minutes, twice a week, for 12 weeks. The training sessions included warm ups and cool downs with a gradual increase in intensity. Before and after the 12-week period, the patients exercised up to the point of exhaustion. To obtain the required data, the NIRS technique was used to measure important variables.

The important findings demonstrate that the peak aerobic capacity was significantly elevated after 12 weeks in the training group, but remained unchanged in the non-training group. Additionally, the training patients showed enhanced muscle deoxygenation, which means more oxygen was used by the muscles. However, this was not observed in the non-training group. These results exhibit significant implications in terms of improving morbidity and fatality in heart disease. Therefore, it is paramount for patients with cardiac health issues to incorporate aerobic exercise in their course of recovery.

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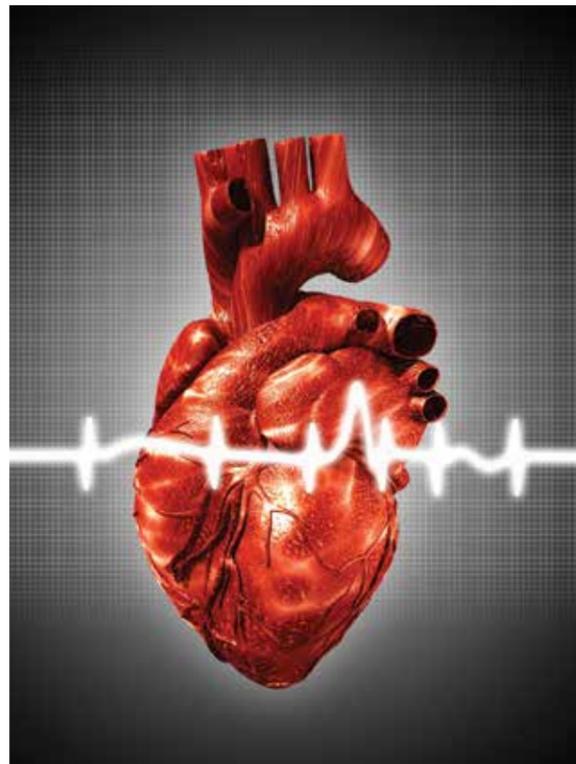
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In another trial, the research team compared the muscle deoxygenation and peak aerobic capacity in two groups: 1) patients who recently suffered a heart attack and 2) normal healthy control subjects who were matched in age, height and weight to those in the first group. Specifically, the first group was made up of 16 patients who had experienced a heart attack 12 to 45 days prior to partaking in the study, while the control group consisted of 18 subjects. All of these subjects underwent ramp cycling until exhaustion. The findings revealed that muscle deoxygenation was blunted and markedly less in the heart attack group versus the healthy control group. These results are likely attributed to the lower use of oxygen, not decreased blood flow.

Collectively, these studies indicate that exercise improved the maximum amount of oxygen uptake in patients with cardiac ischemia. Furthermore, this enhanced muscle deoxygenation is likely correlated to increased peak aerobic capacity in these post heart attack individuals.

#### **The effects of exercise in patients with angina pectoris**

An additional study compared patients with angina pectoris and control patients, and evaluated the before and after effects of training in angina pectoris patients. The trial enrolled seven participants with angina pectoris and seven healthy subjects of similar age, height and weight as the patients in the first group. As for those with angina pectoris, they all had recently undergone coronary artery bypass grafting; specifically, their post-surgery timing ranged from 18 to 42 days. These enrollees trained with cycling activities for 10 to 20 half-hour sessions over 12 weeks. Before and after training, they performed a ramp bicycle exercise until exhaustion. Furthermore, the NIRS method was employed in this trial to take key measurements. The investigators observed that diminished muscle deoxygenation occurred in patients with angina pectoris compared with healthy matched controls. Furthermore, the investigators concluded that low volume aerobic exercise enhanced muscle deoxygenation and extraction in training angina pectoris.



#### **Future research prospects**

Dr Takagi and his colleagues have future plans to examine the relationship between muscle oxygen dynamics and the peak aerobic capacity in further depth. For example, based on the fact that the heart pump function is preserved in the patients previously studied, it would be beneficial to find its association with the oxygen dynamics.

Another aspect worthy of assessment is the occurrence of muscle deconditioning and when this happens in the heart attack timeline. Taking this a step further, he questions whether deoxygenation results from post heart attack deconditioning of muscles or if it develops prior to the heart attack.

Another important consideration for future projects is the expansion of the research trials described above. Enrolling a larger volume of subjects, especially women, will be pertinent to corroborate the findings yielded in those studies.

#### **Applying these results in a healthcare setting**

In one of Dr Takagi's main research studies, positive outcomes were observed in post myocardial infarction patients participating in cycling at moderate intensity for a duration of 30 minutes once or twice a week. Since this exercise regimen enhanced oxygen uptake by the muscles, it can be recommended as an option for patients who have recently experienced a heart attack. Moreover, it is better to begin physical exercise soon after a heart attack as opposed to later. While more frequent training with or without increased intensity can boost the aerobic capacity, this may not be feasible or convenient for the patient's schedule or health. In conclusion, there is promise for successful healthcare in patients who recently suffered a heart attack.

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Dr Shun Takagi is currently a researcher at the Faculty of Sport Sciences at Waseda University. He received a PhD from Tokyo Medical University. His focus is on exercise physiology with emphasis on muscle circulation and metabolism in relation to aerobic capacity. He was recognized with the Mishima Award and the Dietrich W. Lübbers Award for his excellent work. With funding from the Japan Society for the Promotion of Science, Dr Takagi is conducted research trials in skeletal muscle oxygen dynamics during exercise in patients with heart disease.

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#### **FUNDING**

Grant-in-Aid for scientific research from the Japan Society for the Promotion of Science

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