

## Easy assessment of the vascular autonomic function

Blood vessels change their diameter to keep a stable blood flow. The diameter of the peripheral arteries is determined by contraction or relaxation of the vascular smooth muscle, by endothelium-dependent and autonomic nerve-dependent mechanisms. Vascular endothelial cells secrete molecules that cause constriction or dilation of the arteries. Although autonomic nerves consist of sympathetic and parasympathetic nerves, sympathetic nerves are mostly distributed to the arteries, working for vasoconstriction (Fig. 1).

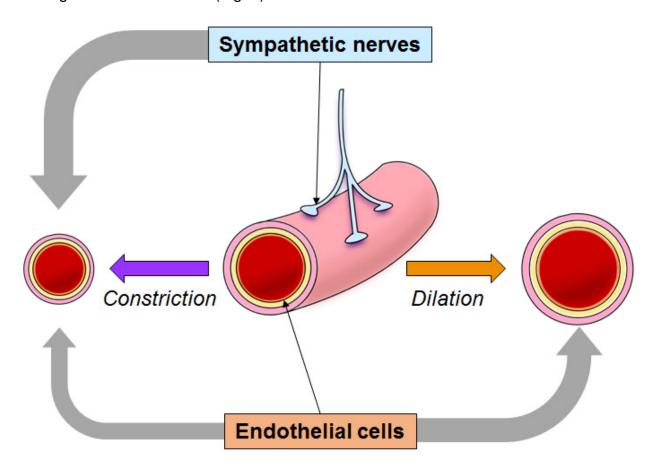


Fig. 1. Regulation of the diameter of the artery.

The autonomic nervous system regulates the entire body, including the heart and blood vessels. It is impaired in some diseases such as diabetes, systemic amyloidosis, and Parkinson's disease. The assessment of the autonomic nervous activity has been established targeting the heart, for example with scintigraphy using radiolabelled neurotransmitters and heart rate variability (HRV) analyses. Regarding the autonomic regulation of the peripheral blood vessels, several modalities have been invented to evaluate it. However, they have not been widely utilized due to their

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invasiveness, technical difficulties, or both.

We focused on reactive hyperemia peripheral arterial tonometry (RH-PAT), one of the non-invasive tests of the vascular endothelial function. For RH-PAT, subjects wear tonometry sensors on both index fingers to record the pulse waves, and a blood pressure cuff on their unilateral arm to occlude the blood flow for 5 minutes (Fig. 2). After releasing the blood flow, the pulse wave amplitude in the occluded arm is increased by secretion of vasodilators from the endothelial cells. RH-PAT also records the pulse wave in the non-occluded arm, which is used as a control to normalize the systemic effect. We observed the change in the pulse amplitude in the non-occluded arm after the blood flow occlusion, hypothesizing that it would reflect the change in the sympathetic activity. From this viewpoint, we tried to establish a novel index for evaluating the vascular sympathetic regulation.

To clarify the relationship between the change in the pulse amplitude in the non-occluded arm and the change in the sympathetic activity, we performed three experiments. First, we performed RH-PAT and examined the temporal change in the pulse amplitude in the healthy subjects and cases who took sympathetic nerve blockers. The pulse amplitude after the blood flow occlusion was decreased from that at baseline in the healthy subjects. This phenomenon disappeared in cases taking sympathetic nerve blockers. Second, to confirm that the 5-minute blood flow occlusion evoked sympathetic activation in the upper arm, we measured the plasma concentration of the catecholamines before and after the occlusion in healthy subjects. The plasma norepinephrine level was significantly increased by the blood flow occlusion. Third, we evaluated the relationship between the change in the pulse amplitude in the non-occluded arm and cardiac sympathetic activity measured by HRV, which showed a significant correlation. Furthermore, we searched for the best timing to measure the pulse amplitude, and found that the pulse amplitude recorded 5 minutes after the end of the occlusion exhibited the strongest correlation to the cardiac sympathetic activity. Based on these results, we defined the novel index, sympathetic hypoemia index (SHI), as the rate of the decrease in the pulse amplitude 5 minutes after the occlusion from the baseline value. Finally, we pursued the potential clinical utility of SHI. We compared SHI in patients who had diabetes, the most common cause of autonomic dysfunction, with matched controls. SHI was significantly lower in the diabetic patients than the controls.

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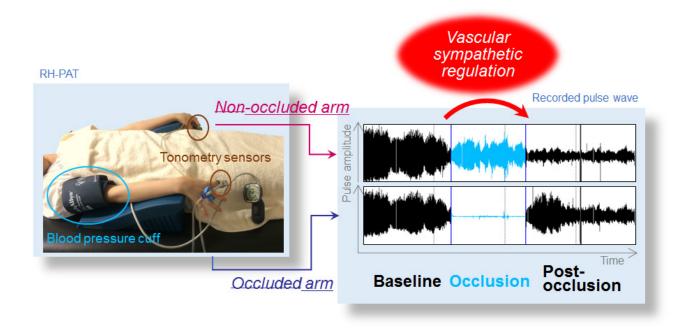


Fig. 2. Change in the pulse amplitude in the non-occluded arm during RH-PAT.

In conclusion, we established a novel index, SHI, which represented the peripheral sympathetic activity. We also demonstrated that SHI had a lower value in diabetic patients. SHI may provide additional information about the vascular autonomic function while patients undergo RH-PAT, without any additional burden.

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## **Publication**

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