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“The Importance of What You Cannot See”

One can easily be influenced by what he or she can see in general, which is also the case in medicine. For instance, in cardiovascular medicine, cardiologists can easily be influenced by what they can see when making a decision; coronary angiogram is a good example, which basically provides information on coronary diameter and flow. However, one should realize that coronary diameter and flow are determined by complex interactions of many regulatory mechanisms. For the last four decades, I performed experimental and clinical studies on coronary artery spasm, endothelial functions, and the therapeutic effects of sound waves, all of which we cannot see but are important players in cardiovascular medicine.

Coronary vasomotion abnormalities play very important roles in the pathogenesis of ischemic heart disease. I have previously demonstrated that vascular smooth muscle hyperconstriction is the central mechanism of coronary artery spasm, for which activation of Rho-kinase is substantially involved. Recently, we were able to demonstrate that adventitial inflammation plays an important role for Rho-kinase activation and resultant coronary spasm. Furthermore, we have recently demonstrated that epicardial coronary spasm is frequently associated with coronary microvascular dysfunction as well.

The endothelium also plays an important role in modulation of vascular tone, by synthesizing and releasing endothelium-derived relaxing factors, including prostacyclin, nitric oxide (NO), and endothelium-dependent hyperpolarizing (EDH) factor. We have previously demonstrated in animals and humans that the importance of EDH factor increases as the vessel size decreases and that endothelium-derived hydrogen peroxide is an EDF factor, for which endothelial NO synthases system plays important roles.

Finally, sound waves could activate the self-healing capability of our body, as we have demonstrated that low-energy shock wave and low-energy pulsed ultrasound (LIPUS) exert effective angiogenic effects, for which mechano-transduction mechanisms mediated by ß1-1-integratin-caveolin-1-endothelial NO synthase axis plays important roles. We are now conducting the randomized control trials with LIPUS for severe angina pectoris and dementia. These findings indicate that we should pay attention not only to what we can see but also to what we cannot see as well.