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General Summary

We have 6 research groups for covering the broad field of cardiology. In respective study groups, we have been studying the problems that face us in clinical practice. Our research is based on clinical studies that use the large database we have been developing. Basic research is also performed to solve clinical questions.

Research Activities

Ischemic Heart Disease Research Group
We have converted patients' data, including risk factors and coronary lesion morphology, from catheterization examinations and treatments in patients with ischemic heart disease, into our large and precise database. Using this database, we have been performing a study comparing risk factors, clinical outcomes, and other data. We have recently been studying the differences of risk factors between coronary organic stenosis and acute coronary syndrome by using covariance structure analysis. We have been using a similar method to study a contributing pattern of obesity to ischemic heart disease. Furthermore, since fractional flow reserve is reportedly a good method for evaluating significant coronary stenosis, we have been collecting and analyzing information about the clinical data of fractional flow reserve.

Arrhythmia Research Group
In our arrhythmia team, we have been focusing on the curative treatment of atrial fibrillation. Our research activities include the comparison of efficiency and safety among different ablation methods (radiofrequency vs. cryoballoon ablation), factors associated with the occurrence of pulmonary vein stenosis following balloon ablation, and the association of ablation methods and asymptomatic cerebral ischemia.

Heart Failure Research Group
A database has been established with respect to the clinical data of approximately 3,000 cases of patients admitted to hospital for the purpose of cardiac catheter examination and treatment, and the relationships among factors, which are difficult to analyze with standard multivariate analysis alone, are being analyzed with a highly statistical analysis.

Currently, covariance structure analysis is used for ongoing research related to the plasma concentration of B-type natriuretic peptide (BNP). Regarding BNP, detailed analytic results have been acquired from various areas, such as the relationship between the change in BNP concentration and the change in body weight before and after the treatment of acute hear failure and also the relationship between BNP concentration and anemia in patients with heart failure. These results are promoting the publication of articles. Moreover, we are continuously trying to elucidate the mechanism of the clinical findings through basic research.

Imaging Research Group

As for coronary artery spasm, which are common in ischemic heart disease in Japanese patients, vascular tonus changes in coronary arteries were studied through image pathognomy by coronary computed tomography (CT). In addition, since CT is becoming more valuable as a test for evaluating the aortic valve condition before transcatheter aortic valve replacement (TAVR), a recently-stated approach to treatment of aortic stenosis, we have been aggregating the valuable information. In other imaging methods, such as echocardiography, heart magnetic resonance imaging (MRI), and myocardium isotope testing, clinical research topics are still being searched and analyzed with other subjects, such as cardiac myopathy and abnormal cardiac rhythm.

Molecular Biology Research Group

Glucose becomes an important preferential substrate for cardiac metabolism and ATP generation during ischemia-reperfusion injury (IRI). A series of our recent studies on insulin signaling indicated that a transient increase in glucose uptake into myocardium is protective against IRI. The study from the clinical database showed a transient decrease in the serum potassium level during acute coronary syndrome (ACS) attack, the degree of which is positively correlated with the plasma glucose level but not with homeostasis model assessment insulin resistance or HbA1c, as the indicators of insulin resistance. These data suggest the presence of endogenous glucose-coupled potassium lowering mechanisms, other than insulin, promoting glucose metabolism during ACS. The coupling of sodium-glucose co-transporter 1 (SGLT1) and Na^+/K^+ ATPase is a potential mechanism. In fact, a study of Langendorff heart perfusion demonstrated that the inhibition of SGLT1 during IRI reduces glucose uptake into the myocardium, leading to a decrease in the cardiac tissue ATP content. As a consequence, cardiac functional recovery after IRI was impaired by SGLT1-inhibition. The present findings provide new insight into the significant role of SGLT1 in optimizing cardiac energy metabolism during IRI.

Cardiac Physiology Research Group

We have demonstrated that thrombin, the final product of the coagulation cascade, in present in the heart. Coagulability is increased in patients with dilated cardiomyopathy (DCM). Using knock-in mice that have a cardiac troponin T deletion mutation that causes human DCM (ΔK210 knock-in mouse) (B6;129-$Tnnt2^{tm2Mmto}$), we investigated how thrombin is involved in the development of DCM. We observed that thrombin expression was stronger in mice with DCM than in wild-type mice. We assessed the effects of a

direct thrombin inhibitor, dabigatran, in ΔK210 knock-in mice. Dabigatran significantly improved fractional shortening in echocardiographic findings and survival outcomes. In conclusion, tissue thrombin is involved in the pathogenesis of DCM, and thrombin inhibition can be beneficial for the treatment of DCM.

Publications

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