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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. In specific, we recently used covariance structure analysis as a new solution for action assignments. 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, hemodynamic data, from cardiac catheterization examinations and treatments in patients with ischemic heart disease, into our large, precise database. Using this database, we have been performing a study comparing risk factors, clinical outcomes, and other data. We have recently reported 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. In the analysis, we reported a possible risk of low-reactivity of natriuretic peptide. Furthermore, since fractional flow reserve (FFR) is reportedly a good method for evaluating significant coronary stenosis, we have been collecting and analyzing information about the clinical data of FFR. The studies of ischemic heart disease have been performed with the group of heart failure in many circumstances.

Arrhythmia Research Group
In our arrhythmia team, we have been focusing on the curative treatment of arrhythmia, especially for atrial fibrillation (AF). Our research activities include the comparison of efficacy and safety of AF catheter ablation, among different ablation methods (conventional Radiofrequency vs Cryoballoon ablation vs Hotballoon ablation vs Lazer Balloon ablation), factors associated with the occurrence of pulmonary vein stenosis following balloon ablation and the association of ablation methods with the asymptomatic cerebral infarction.

Heart Failure Research Group

1. Study group on heart failure

Since last year, we have constructed and updated a database of approximately 4,800 patients who have been hospitalized for cardiac catheterization and treatment. Regarding this database, analysis is conducted using the Structural Equation Modeling (SEM) or Covariance Structure Analysis by adjusting the statistical analysis method, AMOS (Analysis of Moment Structures), which has been previously known but the use of which has been rarely reported in the cardiovascular field. In particular, we analyze the interrelationships of clinical factors that cannot be expressed by multivariate statistical analysis alone, focusing on statistical analysis research on clinical data including plasma BNP. Using a path diagram, it is easier to have a visual understanding of the relationships between each factor, and to perform multiple regression analysis and path analysis (repetition of multiple regression analysis) using factors and confirmatory factor analysis. In addition, Bayesian structure equation modeling successfully gave a description of these results, and it is expected to be a next-generation statistical procedure for mega trials. Two years ago, with respect to the relationship between obesity and BNP, we reported the relationship between the change in BNP concentration before and after treatment along with the change in body weight. This spring, we published an article on the influence of remodeling changes in the left ventricular cavity on BNP concentration. By publishing articles on wide-ranging analysis results including detailed data analysis of the disease state of chronic heart failure along with the relationships between various valvular diseases and atrial fibrillation, we will continue to promote a wide range of clinical studies based on the experience gained from daily clinical practice. We are also continuing our efforts to clarify the mechanism of these findings via fundamental research.

Imaging Research Group

1. Study group on imaging

With the increasing number of cases involving transcatheter aortic valve replacement (TAVR), cardiac CT and echocardiograms are also vital as preoperative examinations for evaluating the aortic valve. From this valuable case information, we are seeking research agendas for clinical studies. Through other imaging modalities such as cardiac MRI and myocardial isotope tests, we are continuing to seek research agendas for clinical studies and conduct analyses on cardiomyopathy and arrhythmias. Also, we have been investigating the cardiac function in patients with lysosome diseases, especially Fabry's disease as a collaboration with the department of pediatrics.

Molecular Biology Research Group

In addition to the various effects of natriuretic peptides (NPs) on cardiovascular systems, increasing attention is being paid to the possibility that NPs induce adipose tissue browning and activate thermogenic program. We established a direct intracellular temperature measurement system using a fluorescent thermoprobe and investigated the thermogenic effects of A-type NP (ANP) on brown adipocytes. The thermoprobe was successfully introduced into rat brown adipocytes, and the temperature dependent change in fluorescence intensity ratio was significantly higher in ANP-treated adipocytes compared to

untreated controls. The ANP treatment increased uncoupling protein-1 (UCP1) levels in p38MAPK-dependent manner. Intriguingly, these thermogenic actions of ANP were more prominent when brown adipocytes were incubated at 35°C than at 37°C. These findings reveal a previously under-appreciated role for NPs in the compensatory thermogenic action when the core body temperature fall due to unfavorable hemodynamic conditions in a state of severe heart failure.

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 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.

For the purpose of investigating the hemodynamics of thrombin, HiLyte-thrombin was administered to perform whole in vivo imaging. The HiLyte-thrombin was internalized to heart and liver, which indicates the tissue thrombin is not derived from heart (namely internal prothrombin) but blood.

Publications

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