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General Summary

We are actively engaged in research activities associated with daily clinical practices, including large-scale clinical trials and multicenter trials. We have been participating in and cooperating with several large-scale clinical trials, notably the Japanese Investigation of Kinetic Evaluation in Hypertensive Event And Remodeling Treatment (JIKEI HEART) study, the Japanese Rhythm Management Trial for Atrial Fibrillation (J-RHYTHM) study, the Assessment of β-Blocker Treatment in Japanese Patients with Chronic Heart Failure (J-CHF) study, the Pitavastatin hEARt faiLure (PEARL) study, and the Combination of OLMesartan and Calcium channel blocker or diuretics in high risk elderly hypertensive patients Study (COLM) study. The JIKEI HEART Study, is a voluntary physician-oriented study initiated by our chairperson. It is the first clinical-outcome cardiology study in Japan to demonstrate that an angiotensin II receptor blocker administration significantly reduces risks. The study results were reported in *The Lancet* (Mochizuki S, et al. Lancet 2007; 369: 1431–9).

Research Activities

Clinical research

1. Ischemic heart disease

Individual clinical research sections have been compiling subject data, such as risk factors and lesional morphology collected through catheterization tests or treatments, into a database that can be used to compare risk factors and prognosis for ischemic heart diseases, such as cardiomyopathy. Furthermore, we have been carefully examining treatments, mainly those using drug-eluting stents, and diagnoses of vasospasm, which is intimately associated with the development of ischemic heart diseases. We have also been participating in nationwide clinical research activities. Coronary artery computed tomographic scanning using dual-source computed tomography started this May, and we are accumulating visualization exposures at a rate of 950 cases per year. Temporal resolution capacity of our current system is greater than that of our former one, enabling us to provide more accurate diagnoses and detailed examinations for cases of arrhythmia or high cardiac pulsation.

2. Heart failure

We have been examining the serum level of brain natriuretic protein as an indicator of heart failure and investigating reference values that can be used in clinical practice. Also, we are now making detailed examinations of the pathological condition of heart failure, both before and after hospital admission, to obtain clinical data for establishing new indicators.

3. Arrhythmia

We used catheter ablation to treat 232 cases of atrial fibrillation this year. In clinical research, we published papers on the following topics: 1) examining the usefulness of pulmonary vein antral isolation using a potential indicator, and 2) suppression of reentry into the signaling pathway by annihilation of reentry into ATP signaling after pulmonary vein antral isolation.

4. Lipid metabolism

With regard to human lipoprotein metabolic research using a stable isotope, we collaborated with Kanazawa University to perform tracer experiments on patients with autosomal recessive hypercholesterolemia, which is an extremely rare condition. Additionally, we examined the effect of ezetimibe, an inhibitor of cholesterol absorption from the small intestine, on lipoprotein metabolism and are now analyzing the data.

Basic research activities

Basic research activities include domestic and international exchanges of graduate students in basic or clinical courses and the publication of the results of their studies. For research into the cause of atrial fibrillation, we are now observing changes in the expression of connexin, which controls intracellular signal transduction, and decreases in cardiac function/pressure load in the Dahl model of hypertension-induced heart failure. We are also evaluating the localization of proteins, such as zona occludens 1, associated with connexin. In cardiomyocyte physiology, we are examining the physiological and pathophysiological regulatory mechanisms of myocardial contraction and relaxation, at both molecular biological and physiological levels. We are also examining a new signal transduction pathway and its effects on alpha-adrenergic receptor stimulation in the L-type Ca channel of rat myocardium, the effects of beta-adrenergic receptor stimulation on the sarcoplasmic reticulum function, and Ca handling in the cardiomyocytes of mice with dilated cardiomyopathy induced by troponin T mutation. In myocardial metabolism, we have been evaluating the relationship between ischemic reperfusion injury and intracellular ionic handling using isolated perfused hearts from a mouse model of type 2 diabetes.

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