

Department of Internal Medicine

Division of Cardiology

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General Summary

Research in every field, both clinical and basic, is being propelled daily on the basis of reliable results.

Research Activities

Clinical research

In clinical research, we have been participating in multicenter collaborative studies, including large-scale clinical studies, and conducting research during routine clinical practice. In large-scale clinical studies, we have collaborated in subanalyses in the Japanese Investigation of Kinetic Evaluation in Hypertensive Event And Remodeling Treatment (JIKEI HEART) study, whose results were reported last year, and in such studies as the Japanese Rhythm Management Trial for Atrial Fibrillation (J-RHYTHM: upstream drug therapy for atrial fibrillation associated with hypertension by means of a multicenter study, a study related to and comparative study of calcium antagonists and angiotensin receptor blocker [ARB]), the Assessment of β -Blocker Treatment in Japanese Patients with Chronic Heart Failure (J-CHF: a large-scale clinical study to establish a β -blocker treatment method in chronic heart failure), the Pitavastatin hEARTt gaiLure (PEARL) study (multicenter cooperative study to investigate the ameliorative effect of hydroxymethyl glutaryl coenzyme A reductase inhibitors on chronic heart failure), the Combination of OLMesartan and CCB or Low-Dose Diuretics in High-Risk Elderly Hypertensive Patients study (COLM study: comparing a calcium antagonist and low-dose diuretic as combination drugs for use in ARB therapy of elderly hypertension patients at risk of cardiovascular disease), and the Nationwide Gender-specific Atherosclerosis Determinants Estimation and Ischemic Cardiovascular Disease Prospective Cohort Study (NADESICO Study: multicenter cooperative prospective cohort study on sex differences in risk factors for arteriosclerotic diseases and prevention), which used computed tomography examinations of the coronary arteries. We performed subanalyses in the JIKEI HEART Study (Mochizuki S. et al., *Lancet*, 2007) which were related to background factors (sex, age, ischemic heart disease, diabetes, and hyperlipidemia) and left ventricular mass index. The results of these subanalyses were presented at meetings of the Japanese Circulation Society, the Japan Geriatric

Society, the Japanese Society of Hypertension, the European Society of Cardiology, and the American College of Cardiology.

We have converted patient data, including risk factors, lesion morphology, during catheter examinations and treatment in various clinical research divisions into a database and performed a study comparing risk factors, outcome, and other variables in ischemic heart disease, cardiomyopathy, and other conditions. In addition, we have participated in nationwide clinical studies (the Japan-Drug Eluting Stents Evaluation; a Randomized Trial [J-DESsERT], the Coronary Spasm Association [CSA]), investigating treatment with drug-eluting stents and the diagnosis of coronary vasospasm, which is closely related to the etiology of ischemic heart disease.

With regard to heart failure, which is an extremely common form of circulatory pathology, we have been assessing data related to serum concentrations of brain natriuretic peptide, which is an index of pathology, and have been investigating standard values that will be useful in clinical practice. In addition, we are investigating the pathology of heart failure before and after hospital admission and are assessing clinical data that will serve as a new index.

We have been aggressively treating atrial fibrillation by means of catheter ablation, and in this fiscal year we treated a total of 232 patients. In addition, in clinical research we have 1) investigated the usefulness of the pulmonary vein antrum isolation procedure by voltage mapping and 2) presented papers on the suppression of re-conduction after pulmonary vein-antral isolation procedures by abolishing adenosine triphosphate re-conduction.

In research on human lipoprotein metabolism we performed a tracer experiment with stable isotopes in patients with autosomal recessive hypercholesterolemia, a rare condition everywhere in the world, in cooperation with Kanazawa University. In addition, we are analyzing the effect of ezetimibe, an inhibitor of cholesterol absorption in the small intestine, on lipoprotein metabolism.

Basic research

Our research activities include study at other institutions in Japan and abroad by graduate students in basic sciences and clinical sciences and the presentation of the results of many studies. In the field of arrhythmia, we have studied the effects of inflammatory cell invasion mechanisms and myocardial fibrosis on the development of atrial fibrillation in various experimental models. In the field of cardiomyocyte physiology, we have investigated the physiological and pathophysiological regulatory mechanisms of myocardial contraction and relaxation by means of both molecular biologic techniques and physiologic techniques. We have also investigated a new signal transmission system in the α -receptor stimulation effect in relation to L-type Ca channels in the rat myocardium, the effects of β -receptor stimulation in sarcoplasmic reticulum function, and cardiomyocyte intracellular Ca kinetics in mice with dilated cardiomyopathy due to troponin T mutations. In the field of myocardial metabolism, we have investigated the association between ischemia-reperfusion damage and intracellular ion kinetics in isolated perfused hearts of mice with type 2 diabetes.

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