Department of Internal Medicine
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General Summary

We have 6 research groups for covering the broad field of cardiology. We perform studies from both clinical and basic standpoints in each research group. We aspire to achieve a greater understanding of the pathogenesis of cardiovascular diseases and to establish or improve clinical diagnostic methods and therapies.

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 (IHD), into a database. Using this precise database, we have been performing a study comparing risk factors, clinical outcomes, and other data. In addition, we have participated in nationwide clinical studies, such as J-LESSON (Japan Unprotected Left Main Coronary Artery Disease Percutaneous Coronary Intervention Strategy On New Generation Stents), PROPEL (A Prospective Multicenter Post-Approval Study to Evaluate the Long-Term Efficacy and Safety of the Resolute Integrity in the Japanese All-Comers Patients with Coronary Artery Disease), and NIPPON (Nobori Dual Antiplatelet Therapy as Appropriate Duration). In 2014, we reported the following interesting clinical findings. We found that the malondialdehyde-modified (MDA) low-density lipoprotein (LDL) level was affected by multiple factors, such as smoking status, LDL-C, and the male sex. Furthermore, statin therapy might have a beneficial effect on the reduction of the MDA-LDL level. Also, we reported about B-type natriuretic peptide (BNP) in patients with IHD. Although plasma BNP levels are increased in patients with heart failure and acute myocardial infarction, we reported that plasma BNP levels were lower in stable patients with IHD than in stable patients without IHD. Perhaps the low reactivity of BNP is causally associated with IHD.

Arrhythmia Research Group

In our arrhythmia team, we have been focusing on the management of atrial fibrillation (AF) among various types of arrhythmias. Each year we perform ablation for more than 400 patients, including 300 patients with AF. We have reported new findings or new methods of catheter ablation at international conferences or in published journals, such as

factors associated with the recurrence of AF after ablation, better methods for minimizing the recurrence of AF after ablation, and the association of sleep apnea with the outcome of AF ablation. In 2014, we started a new ablation method with cryoballoons for curing paroxysmal AF.

Heart Failure Research Group
We have been examining clinical data related to the plasma levels of BNP, which is a sensitive marker of heart failure. Body mass index is a significant factor that reduces the plasma BNP level. This effect is significantly increased in patients with a high body mass index, even among those with a worsening severity of heart failure. Also, we reported about aldosterone in a collaboration study; the immunolocalization of calcium channels in nonpathological adrenals and idiopathic hyperaldosteronism were detected in the zona glomerulosa, with a predominance of CaV3.2 channels in aldosterone-producing adenoma. These findings suggest that different types of calcium channel can be involved in calcium-related aldosterone biosynthesis.

Imaging Research Group
Multidetector (row) computed tomography (MDCT) has become a reliable method for detecting coronary arterial organic stenosis. We have been studying the possibility that a change in coronary arterial tonus can also be detected with repeated MDCT. In 2014, we confirmed for the first time that coronary arteries can fluctuate substantially and that these changes can be documented with MDCT. Changes in coronary arterial tonus should therefore be considered when reading MDCT.

Molecular Biology Research Group
Although the utilization of fatty acids is the predominant metabolic pathway in the normal adult heart, glucose becomes an important preferential substrate for metabolism and ATP generation under specific pathological conditions, such as ischemia. Therefore, the acceleration of glycolysis and glucose utilization in the ischemic myocardium may be cardioprotective. We found that the sodium-dependent glucose co-transporter (SGLT) 1, a major glucose transporter in the heart, is highly expressed in human hearts. Using the Langendorff heart perfusion system, we demonstrated that cardiac SGLT1 provides an important protective mechanism against ischemia-reperfusion injury by replenishing ATP stores in ischemic cardiac tissues by enhancing the availability of glucose. The present findings provide new insights into the significant role of SGLTs in optimizing cardiac energy metabolism, at least during the acute phase of ischemia-reperfusion injury.

Cardiac Physiology Research Group
We have investigated cardiac physiology and pathophysiology, especially cardiac Ca^{2+} handling and adrenergic signaling related to excitation-contraction coupling. We have also reported the role of thrombin on cardiac disease, leading to a next experiment using a mouse model of dilated cardiomyopathy. The activation of protease activated receptor (PAR) 1 is known to lead to the expression of α-smooth muscle actin and to contribute to atrial pathological fibrosis. We examined which types of PAR contribute to the profibrotic

activity of cultured neonatal rat atrial fibroblasts and demonstrated the profibrotic activity of PAR-1 but not of PAR-2, -3, or -4.

Publications

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