

Cardiovascular Medicine

1. Staffs and Students (April, 2010)

Professor	Mitsuaki Isobe	
Associate Professor	Kenzo Hirao	
Junior Associate Professor	Hitoshi Hachiya	
Assistant Professor	Mihoko Kawabata,	Hiroshi Inagaki,
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	Shunji Yoshikawa,	Koji Higuchi
Graduate Student	Takashi Ishihara,	Masanori Konishi,
	Hirokazu Ohigashi,	Seiji Matsubara,
	Kengo Tanabe,	Manabu Kurabayashi,
	Daisuke Tezuka,	Yoshihide Takahashi,
	Takeshi Sasaki,	Masakazu Ohno,
	Koji Higuchi,	Munehiro Kamimura,
	Taro Sasaoka,	Tatsuya Hayashi,
	Masaaki Shoji,	Shingo Maeda,
	Kiyoshi Ohtomo,	Tetsuo Kamiishi,
	Masahiko Setoguchi,	Susumu Tao,
	Tomoko Manno,	Hiroshi Kawata,
	Yu Hatano,	Daisuke Ueshima,
	Tomoyo Sugiyama,	Kensuke Ihara,
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2. Education

We are dealing with pathophysiology of circulatory system especially cardiovascular diseases. Cardiovascular diseases are principal cause of death in our country. These diseases are categorized into several fields. They include ischemic heart disease, myocardial disease, valvular disease, atherosclerosis, arrhythmia, and infectious disease. The common final figure of these diseases is heart failure leading to patients' death. Based on recent progresses in molecular biology and bioengineering our knowledge on the pathophysiology of these diseases has been expanded rapidly. There are variety of new diagnostic technologies including imaging tests, hematological tests and electrophysiological tests. In addition, development in the treatment of cardiovascular disease is overwhelming. They include intravascular catheter intervention, catheter ablation and operation. Medical treatment has also been progressed rapidly. Further, gene therapy for cardiovascular diseases has started. All of these fields are our focus for education. In this course, students learn about modern knowledge and technologies in cardiovascular diseases, especially in the field of pathophysiology, diagnosis, treatment and prevention.

3. Research Subjects

The purposes of our investigation are to reveal the etiology and pathophysiology of cardiovascular diseases, and to develop new technologies for diagnosis and treatment. For that purpose we investigate clinical cases and model animals. Currently our investigations are focused on arteriosclerosis, atherosclerosis, cardiomyopathy, myocarditis, arrhythmias, cardiac rejection and heart failure. The relationship between gene mutation and cardiovascular disease, electrophysiology, myocardial cell transplantation and myocardial regeneration are also our major subjects of research.

- 1) Clinical study of gene therapy for coronary artery disease (Isobe)
- 2) Clinical study for treatment of acute coronary syndrome (Isobe, Inagaki, Kimura)
- 3) Molecular mechanism and treatment of myocardial ischemia and reperfusion injury (Isobe, Haraguchi)
- 4) Molecular mechanism and treatment of coronary restenosis and vascular disease (Isobe)
- 5) Gene therapy of myocarditis and cardiac chronic rejection (Isobe, Suzuki)
- 6) Cardiac rejection and immunological tolerance (development of safe immunosuppressive therapy) (Isobe, Suzuki)
- 7) Treatment of heart failure and cardiomyopathy by myocardial regeneration (Isobe, Suzuki)
- 8) Regulation of arteriosclerosis by targeting transcription factors (Isobe)
- 9) Gene therapy of vascular disease (Isobe)

- 10) Diagnostic imaging of aortitis (Isobe)
- 11) Molecular mechanism and treatment of aortitis (Isobe)
- 12) Assessment of vascular endothelial dysfunction in vasculitis, heart failure and arrhythmia (Isobe)
- 13) Application in gene therapy for heart failure and cardiomyopathy (Isobe)
- 14) Molecular system of myocardial remodeling in heart failure and ventricular hypertrophy (Isobe)
- 15) Therapy of sleep apnea syndrome with heart failure (Isobe)
- 16) Assessment by imaging of coronary artery and cardiac function (Isobe Tezuka)
- 17) System of origin with tachyarrhythmias (particularly supraventricular tachycardia) (Hirao)
- 18) Medical therapy and ablation for tachyarrhythmias (Hirao)
- 19) Research for the conduction of atrio-ventricular node (Hirao)
- 20) Research and Therapy for arrhythmia by using Cardioendoscope (Hirao)
- 21) Research of atrial fibrillation from origin of pulmonary vein (Hirao)
- 22) Research of genetic factor with atrial fibrillation (Hirao)
- 23) Research of ablation for atrial fibrillation (Hirao Hachiya)

We conduct collaborative researches with not only Medical Research Institute and other facilities in our university but also domestic and foreign institutes according to research projects. Since clinical cases in our hospital are diverse and abundant, clinical investigations are also our major target. Therefore, we can provide many research projects depending on students' need. We encourage and help students to pursue their own original way of investigation.

4. Clinical Services

Students are also encouraged to learn about clinical cardiology. They can participate in any clinical activities underwent in our hospital including cardiac catheterization, electrophysiological study, catheter ablation, various imaging tests, cardiac pathology, and patients care.

5. Publications

Original Article

1. Suzuki J, Isobe M, Morishita R, Nagai R. Characteristics of chronic rejection in heart transplantation –Important elements of pathogenesis and future treatments-. *Circ J*. 74(2):233-239, 2010
2. Suzuki J, Ogawa M, Takayama K, Taniyama Y, Morishita R, Hirata Y, Nagai R, Isobe M: Ultrasound-Microbubble Mediated ICAM-1 siRNA Transfection Attenuates Neointimal Formation after Arterial Injury in Mice. *J Am Coll Cardiol*, 55:904-913, 2010
3. Komura M, Suzuki J, Adachi S, Takahashi A, Otomo K, Nitta J, Nishizaki M, Obayashi T, Nogami A, Satoh A, Okishige K, Hachiya H, Hirao K, Isobe M: Clinical course of arrhythmogenic right ventricular cardiomyopathy in the era of implantable cardioverter-defibrillators and radiofrequency catheter ablation. *Int Heart J*, 51: 34-40, 2010
4. Isobe K, Kuba K, Maejima Y, Suzuki J, Kubota S, Isobe M: Inhibition of endostatin deteriorates left ventricular remodeling and heart failure through matrix proteinases and angiotensin converting enzyme in rat myocardial infarction. *Circ J* 74(1): 109-119, 2010
5. Hachiya H, Hirao K, Sasaki T, Higuchi K, Hayashi T, Tanaka Y, Kawabata M, Isobe M: Novel ECG predictor of difficult cases of outflow tract ventricular tachycardia: Peak deflection index on an inferior lead. *Circ J*, 74(2): 256-261, 2010
6. Kosuge H, Ishihara T, Haraguchi G, Maejima Y, Okada H, Saiki H, Suzuki H, Isobe M: Treatment with telmisartan attenuates graft arteriosclerosis in murine cardiac allografts. *J Heart Lung Transplant* 29(Jan): 562-567, 2010
7. Hishikari K, Watanabe R, Ogawa M, Suzuki J, Masumura M, Shimizu T, Takayama K, Hirata Y, Nagai R, Isobe M. Early treatment with clarithromycin attenuates rat autoimmune myocarditis via inhibition of matrix metalloproteinase activity. *Heart* 96: 523-527, 2010(Apr)
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9. Konishi M, Haraguchi G, Kimura S, Inagaki H, Kawabata M, Hachiya H, Hirao K, Isobe M: Comparative effects of carvedilol versus bisoprolol for severe congestive heart failure: Special reference to atrial fibrillation. *Circ J* 74:

1127-1134, 2010(May)

10. Katsuno T, Hirao K, Kimura S, Komura M, Haraguchi G, Inagaki H, Hachiya H, Isobe M: Diagnostic significance of a small Q wave in precordial leads V2 or V3. *Ann Noninvasive Electrocardiol* 15(2):116-23, 2010 Apr
11. Yonetsu T, Kakuta T, Lee T, Takayama K, Kakita K, Iwamoto T, Kawaguchi N, Takahashi K, Yamamoto G, Iesaka Y, Fujiwara H, Isobe M: Assessment of acute injuries and chronic intimal thickening of the radial artery after transradial coronary intervention by optical coherence tomography. *Eur Heart J* 31(3): 1608-1615, 2010(July).
12. Kawara T, Narumi J, Hirao K, Kasuya K, Kawabata M, Tojo N, Isobe M, Matsuura M: Symptoms of Atrial Fibrillation in Patients With and Without Subsequent Permanent Atrial Fibrillation Based on Retrospective Questionnaire Survey. *Int Heart J*, 51(4):242-246, 2010
13. Miyamoto T, Obayashi T, Hattori E, Yamauchi Y, Niwa A, Isobe M: Pre-hospital physical activity status affects in-hospital course of elderly patients with acute myocardial infarction. *J Med Dent Sci* 57: 119-126, 2010
14. Yamamoto T, Suganami T, Kiso-Narita M, Scherle PA, Kamei Y, Isobe M, Higashiyama S, Ogawa Y. Insulin-induced Ectodomain Shedding of Heparin-binding Epidermal Growth Factor-like Growth Factor in Adipocytes *In Vitro*. *Obesity* 18, 1888-1894 2010
15. Higuchi K, Yamauchi Y, Hirao K, Sasaki T, Hachiya H, Nitta J, Sekiguchi Y, Aonuma K, Isobe M: Superior vena cava as the initiator of atrial fibrillation. Factors related to its arrhythmogenicity and effects of prophylactic isolation. *Heart Rhythm* 7:1186-1191, 2010.
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17. Suzuki J, Ogawa M, Tamura N, Maejima Y, Takayama K, Maemura K, Honda K, Hirata Y, Nagai R, Isobe M. A critical role of sympathetic nerve regulation for the treatment of impaired daily rhythm in hypertensive Dahl rats. *Hypertens Res.* on line publication 29 July, 33: 1060-1065, 2010
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23. Nakajima T*, Hishikari K*, (*equal contribution), Ogawa M, Watanabe R, Suzuki J, Nagashima A, Masumura M, Takayama K, Hirata Y, Nagai R, Isobe M. Clarithromycin attenuates myocardial ischemia reperfusion injury. *Expert Opin Ther Targets*. 14(9):1-13,2010
24. Shoji M, Yamashita T, Uejima T, Asada K, Semba H, Otsuka T, Sagara K, Sawada H, Isobe M, Aizawa T: Electrocardiography characteristics of isolated non-compaction of ventricular myocardium in Japanese adult patients. *Circ J* 74(7): 1431-1435, 2010
25. Maeda S, Iesaka Y, Otomo K, Uno K, Nagata Y, Suzuki K, Hachiya H, Goya M, Takahashi A, Fujiwara H, Isobe M: No severe pulmonary vein stenosis after extensive encircling pulmonary vein isolation: 12-month follow-up with 3D computed tomography. *Heart Vessel*, published on line December 2010
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Effect of High-dose Telmisartan on the Prevention of Recurrent Atrial Fibrillation in Hypertensive Patients. *J Atrial Fibrillation* 2:747-759, 2010

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Book

1. Suzuki J, Isobe M, Morishita R, Nagai R: Antioxidation in prevention of cardiovascular diseases-An effect of polyphenols. *Aging and Age-Related Disorders*. Bondy S (eds.) in the series of Oxidative Stress in Applied Basic Research and Clinical Practice. Armstrong D (eds) Springer /Humana Press. California, pp297-307, 2010
2. Suzuki J, Isobe M, Morishita R, Nagai R: Gene therapy for prevention of acute and chronic cardiac rejection. *Heart Transplantation*. Ed. Catherine T. Fleming, NOVA Science Publishers, 18-23, 2010
3. Hishikari K, Suzuki J, Ogawa M, Isobe M. Roles of Prostaglandins and the Receptors in the Development of Myocardial Ischemia. In press; In *Myocardial Ischemia: Causes, Symptoms and Treatment*. Chaptor 11. Vukovic D, Kiyani V. (eds.) Nova Science, New York, 279-286,2010.