Circulation Journal Award of the Year 2008

Dear Colleagues:

On behalf of the Editorial Team of Circulation Journal, I am pleased to announce the Circulation Journal Award of the Year 2008.

The aim of this Award is to give recognition to the best papers published in 2008, both clinical and experimental investigations, as rated by the Editorial Team. The selection process consisted of two steps. The first step involved an initial screening of the 360 original papers published in 2008. Thirty-four Associate Editors (AE) from the previous Editorial Team (prior to 2008) and current Editorial Team (2008 onwards) selected highly scientific papers in their respective research fields. In the second step, the 2 AE Teams (each with 17 AE) evaluated the selected papers on the basis of originality, contribution to the field of cardiovascular science, presentation, and future potential.

The following 4 papers from 2008 were selected for the Circulation Journal Award.

<Clinical Investigation Papers—First Place>

Practical Risk Prediction Tools for Coronary Heart Disease in Mild to Moderate Hypercholesterolemia in Japan–Originated From the MEGA Study Data–[1]

Tamio Teramoto, Yasuo Ohashi, Noriaki Nakaya, Shinji Yokoyama, Kyoichi Mizuno and Haruo Nakamura, for the MEGA Study Group

Background: A simple and practical risk prediction tool for coronary heart disease (CHD) to determine the specific risk level in each patient that fits the true clinical practice setting is needed and would be valuable in Japan.

Methods and Results: A 5-year risk prediction score and chart for CHD based on the MEGA study data was developed in the present study. The MEGA risk prediction score and chart were constructed based on the coefficient of each risk factor. The risk factors included in these risk prediction tools were: treatment (diet, diet plus pravastatin), sex, age, baseline high-density lipoprotein-cholesterol, baseline low-density lipoprotein-cholesterol, glucose abnormality (diabetes and impaired fasting glucose), hypertension, and smoking. The MEGA risk prediction score comprised the risk score for each risk factor, and it can predict 5-year risk for CHD with 5 levels of risk, based on the total risk score. The MEGA risk prediction chart more accurately predicts risk, by reflecting the accumulation of risk factors and using an 8-color visual chart.

Conclusions: The MEGA risk prediction score and chart, developed from the MEGA study data, more easily and accurately assesses the 5-year CHD risk in mild to moderate hypercholesterolemic patients in the usual clinical practice setting in Japan. (*Circ J* 2008; **72:** 1569–1575)

[Comment] The MEGA study is one of several large-scale clinical trials in Japan conducted to evaluate the efficacy of a statin (pravastatin) for the primary prevention of cardiovascular events in patients with mild to moderate hypercholesterolemia. In this study, the authors developed a risk prediction score and chart for accurate assessment of 5-year CHD risk of hyperlipidemia in clinical practice, further enhancing the clinical importance of the MEGA study.

<Clinical Investigation Papers—Second Place>

Adipokines and the Prediction of the Accumulation of Cardiovascular Risk Factors or the Presence of Metabolic Syndrome in Elementary School Children[2]

Masao Yoshinaga, Koji Sameshima, Yuji Tanaka, Akihiro Wada, Jun Hashiguchi, Hirofumi Tahara and Yasuko Kono

Background: Information is limited about how adipokines predict the accumulation of cardiovascular (CV) risk factors or the presence of metabolic syndrome (MS) in children.
Methods and Results: The subjects were 321 children (200 boys and 121 girls; 109 normal and 212 obese) aged 6–12 years. Obesity was defined as a body mass index of ≥ the 95th percentile for age and sex. MS was defined by using the newly established Task Force criteria. The levels of the adipokines – adiponectin, leptin, ghrelin, high sensitive C-reactive protein (CRP) and resistin – were measured. Regression analyses revealed that high leptin levels were predictive of the accumulation of CV risk factors in normal weight, obese, and entire (normal weight and obese) group of subjects. High CRP in the normal weight group and low adiponectin in the obese and the entire groups were also independently predictive of the accumulation of risk factors. A high leptin level was solely predictive of the presence of MS in obese and entire groups.
Conclusions: Leptin was the most sensitive marker for predicting the accumulation of CV risk factors and the presence of MS in elementary school children. Primary prevention is important because both leptin and adiponectin levels abruptly worsened when children obtained any 1 risk factor. (*Circ J* 2008; **72:** 1874 – 1878)

[Comment] In this unique study, the authors examined the potential of metabolic biomarkers for predicting cardiovascular risk in obese elementary school children. They found leptin to be the most sensitive of the tested biomarkers for predicting cardiovascular risk factor accumulation and the presence of metabolic syndrome. This study provides important information for the primary prevention of cardiovascular disease, which is required from elementary school age.

<Experimental Investigation Papers—First Place>

Effect of Pioglitazone on Nitroglycerin-Induced Impairment of Nitric Oxide Bioavailability by a Catheter-Type Nitric Oxide Sensor[3]

Hideyuki Ikejima, Toshio Imanishi, Hiroto Tsujioka, Akio Kuroi, Yasuteru Muragaki, Seiichi Mochizuki, Masami Goto, Kiyoshi Yoshida and Takashi Akasaka

Background: We examined whether nitroglycerin (NTG)-induced impairment of nitric oxide (NO) bioavailability could be modified by a peroxisome proliferator-activated receptor (PPAR) γ agonist.
Methods and Results: Male New Zealand White rabbits were treated for 7 days with NTG patches, either alone or in combination with pioglitazone. Plasma NO concentration was measured with the catheter-type NO sensor located in the aorta. N^{G}-methyl-L-arginine and acetylcholine (ACh) were infused into the aortic arch to measure the basal and ACh-induced plasma NO concentrations. Vascular nitrotyrosine and tetrahydrobiopterin (BH_4) concentrations were measured by enzyme-linked immunosorbent assay and high-performance liquid chromatography with fluorescence detection, respectively. The negative effects of NTG, that is, the decrease in basal and ACh-induced NO production, were significantly suppressed by co-treatment with pioglitazone. NTG-induced increases in vascular nitrotyrosine and BH_4 concentrations were significantly decreased with co-treatment with pioglitazone.
Conclusions: NTG-induced impairment of basal and ACh-stimulated NO production might be prevented by the co-treatment with a PPAR γ agonist, pioglitazone through suppressions of nitrosative stress. (*Circ J* 2008; **72:** 998 – 1002)

[Comment] The authors' group has recently developed a unique catheter system that can be used to measure plasma levels of NO in vivo. They used this NO-sensing catheter in an experimental study on rabbits to demonstrate that tolerance to nitroglycerin can be prevented via co-treatment with the PPAR-γ agonsit pioglitazone, in vivo. This study demonstrates the validity of the NO-sensing catheter and suggests that a PPAR-γ agonist may have potential for the prevention of tolerance to nitroglycerin in humans.

<Experimental Investigation Papers—Second Place>

High-Dose Granulocyte-Colony Stimulating Factor Promotes Neointimal Hyperplasia in the Early Phase and Inhibits Neointimal Hyperplasia in the Late Phase After Vascular Injury[4]

Makoto Shoji, Yoshitaka Iso, Taro Kusuyama, Yasutoshi Omori, Teruko Soda, Fumiyoshi Tsunoda, Takatoshi Sato, Shinji Koba, Eiichi Geshi, Youichi Kobayashi, Takashi Katagiri and Hiroshi Suzuki

Background: Granulocyte-colony stimulating factor (G-CSF) affects injured arteries through early endothelialization. Some reports, however, have cautioned that the restenosis rate may increase after G-CSF injection. In the present study, high-dose G-CSF was administered to mice with vascular injury to clarify its effect.
Methods and Results: Mice were received daily subcutaneous injections of saline or a high dose (300μg/kg) of G-CSF for 5 days after vascular injury. In the FACS analysis, CD34-/Sca-1-positive progenitor cells were more abundant in the G-CSF group ($p<0.05$). Neointimal hyperplasia was more evident in the G-CSF group at 1 week ($p<0.05$), whereas at 4 weeks it was more evident in the control group ($p<0.01$). TUNEL-positive cells in the arterial wall were more numerous in the G-CSF group at day 1 ($p<0.01$). CD34-positive cells were observed in the G-CSF group at 1 week. Re-endothelialization appeared earlier in the G-CSF group (at 4 weeks; $p<0.01$). An increased number of 1A4-positive smooth muscle cells were found in bone marrow cell culture treated with G-CSF.
Conclusions: High-dose G-CSF induced neointimal proliferation through excessive inflammation and bone marrow cell mobilization in the early phase. In the late phase, however, it induced early re-endothelialization and thereby inhibited neointimal hyperplasia. (*Circ J* 2008; **72:** 1885–1893)

[Comment] Granulocyte-colony stimulating factor (G-CSF) is a hematopoietic cytokine that is widely used in the treatment of various forms of hematological disorders. In this study, the authors used a mouse model of vascular injury to demonstrate the biphasic effects of high-dose G-CSF, which promotes neointimal hyperplasia in the early phase through inflammation and bone marrow cell mobilization, while inhibiting it in the late phase through accelerated re-endothelialization. This study provides useful insights into the time-dependent effects of the hematopoietic cytokine in clinical practice.

The 4 research groups will be presented with their awards at the 73rd Annual Scientific Meeting of the Japanese Circulation Society. The awards will also be announced on the website of the Society.

We look forward to receiving manuscripts with high scientific impact for publication in Circulation Journal in 2009.

Hiroaki Shimokawa, MD, PhD
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Circulation Journal

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