

Inflammation, Atherosclerosis and Coronary Artery Disease

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Supplement Aims and Scope

Research into inflammation, atherosclerosis and coronary artery disease, including observational studies, clinical trials, epidemiology, and advances in applied (translational) research. The supplement is intended to include overviews of new concepts in pathophysiology, natural history, diagnostic strategies, and treatment approaches.

Articles should focus on vascular disease may include:

- Diagnosis
- Prognosis
- Treatment
- Screening

- Prevention
- Risk factor modification
- Systematic reviews
- Risk and safety of medical interventions
- Epidemiology and statistical methods
- Evidence-based medicine
- Evaluation of guidelines
- Translational medicine

Article types include original clinical and basic research articles, case reports, commentaries, meeting reports, methodology, perspectives.

Inflammation has been well recognized to play an important role in the development of atherosclerosis.^{1,2} Since chronic infection may lead to chronic systemic inflammation, many studies have investigated the associations between atherosclerotic diseases, such as coronary artery disease (CAD) and chronic infections by various microorganisms, including *Chlamydia pneumoniae*, cytomegalovirus, herpes simplex virus, and hepatitis C virus (HCV). However, these associations and precise mechanisms remain controversial. Several studies have suggested that more infectious pathogens, referred to as the infectious burden, rather than any single pathogen, may be involved in the development of atherosclerosis.³ In this supplementary issue of *Clinical Medicine Insights: Cardiology*, Ishizaka et al.⁴, reviewed the possible association between atherosclerosis and chronic HCV infection. In 2002, Ishizaka et al.⁵, first reported the higher

prevalence of carotid artery plaques in HCV-positive patients than in control subjects, however, the findings of subsequent studies remain controversial, with some studies showing positive results and others negative.

Regarding the associations between inflammatory biomarkers and atherosclerotic diseases, many studies have demonstrated that elevated high sensitivity C-reactive protein (hsCRP) levels, which are one of the biomarkers of systemic inflammation, are a powerful predictor of future cardiovascular events, such as myocardial infarction (MI) and cardiac death.⁶ However, hsCRP levels vary remarkably among different ethnic populations, and hsCRP levels in East Asian populations are much lower in comparison to those in Western populations.⁷ In this supplementary issue of *Clinical Medicine Insights: Cardiology*, Saito et al.⁸, reported a meta-analysis of 8 prospective studies regarding the association



between hsCRP levels and atherosclerotic diseases in East Asians. They demonstrated that East Asians had low hsCRP levels and that, even in East Asians, elevated hsCRP levels were associated with an increased risk of stroke, especially ischemic stroke. Enomoto et al.⁹, also showed hsCRP levels to be associated with all-cause death in 1920 healthy Japanese subjects. In addition to hsCRP levels, some new inflammatory biomarkers related to both metabolic and atherosclerotic diseases have been reported. In this supplementary issue, Furuhashi et al.¹⁰, reviewed the association between atherosclerosis and fatty acid-binding protein 4 (FABP4), one of adipokines, that is mainly expressed in adipocytes and macrophages and may play an important role in the development of insulin resistance and atherosclerosis. Elevated FABP4 levels were reported to be associated with obesity, diabetes mellitus and atherosclerotic diseases.^{11,12}

Notably, there is a male preponderance of death due to atherosclerotic diseases, especially CAD, at a younger age than women, thus suggesting that sex hormones may play a major role in the process of atherosclerotic diseases.^{13,14} Estrogen has anti-inflammatory effects, and such hormones may alter the immune response during the development of atherosclerosis, thereby leading to different disease processes between men and women. In this supplementary issue, Fairweather et al.¹⁵, reviewed sex differences in the inflammatory immune response during atherosclerosis. Moreover, sex hormones are suggested to affect the process of myocardial inflammation and remodeling during myocarditis.

Systemic inflammatory responses are considered to play a major role in the destabilization of atherosclerotic plaques. The presence of inflammation in one artery is highly predictive of inflammation in other arteries.¹⁶ Imaging modalities are expected to noninvasively evaluate atherosclerotic plaques and inflammation within vessel walls. The glucose analogue ¹⁸F-FDG is taken up by metabolically active cells, especially macrophages, thus allowing the detection of inflammatory activity. Using this ¹⁸F-FDG tracer, positron emission tomography (PET) has become recognized as a reliable imaging technique for the detection of metabolic activity of atherosclerosis.¹⁷ Because the most important disadvantage is its limited spatial resolution, PET/computed tomography (CT) combines the excellent spatial resolution of CT with the high sensitivity of PET for the detection of inflammation. In this supplementary issue, Alie et al.¹⁸, reviewed the clinical usefulness of ¹⁸F-FDG-PET/CT for the noninvasive evaluation of atherosclerosis and inflammation in the carotid, coronary arteries and aortas.

A modern lifestyle with high fat diet and lack of physical activity promotes atherosclerosis. Obesity and high fat diet have been shown to be associated with chronic inflammation in human adipose tissues and arteries.¹⁹ Oxidative modification of LDL is an essential mechanism that increases their inflammatory potential, and dietary antioxidants, such as vitamins C and E and polyphenols, are the potential nutrients

leading to the prevention of LDL oxidation and atherosclerosis progression. The inverse associations between the consumption of vegetables, fruits and fish and atherosclerotic diseases have been reported in many epidemiological studies, showing a reduced risk of such diseases. However, there are still many unclear points regarding the contribution of these foods to the prevention of atherosclerosis. In this supplementary issue, Saita et al.²⁰, reviewed the preventative effects of antioxidant foods on atherosclerosis and CAD. In addition to vegetables and fruits, antioxidant polyphenols are rich in beverages, such as wine and black and green tea. Recently, a meta-analysis showed green tea consumption to be associated with a reduced risk of CAD.²¹ Green tea, which is very rich in catechins, is the most popular beverage in Japan. In this supplementary issue, Ohmori et al.²², reported the association between green tea consumption and MI in 725 Japanese patients. Moreover, they demonstrated the inhibitory effect of LDL oxidation and the anti-inflammatory effect of green tea in 22 healthy volunteers.

Inflammation is recognized to play an important role in both the initiation and progression of atherosclerotic diseases, such as CAD, however, the aim to prevent or treat atherosclerosis via modulating inflammation remains challenging. The articles in this supplementary issue of *Clinical Medicine Insights: Cardiology* encompass new research or timely reviews regarding inflammation, atherosclerosis and coronary artery disease.

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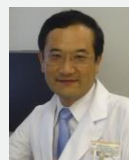
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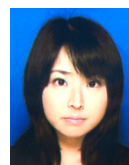
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