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Novel Biomarkers for the Prevention of Cardiovascular Diseases

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Cardiovascular disease (CVD) is a leading cause of death in Japan. Because the number of elderly persons and the prevalence of lifestyle-related diseases are both increasing in Japan, the prevention of CVD and lifestyle-related diseases has become an important issue. Recently various biomarkers have been developed and applied clinically. Taking these epidemiological changes into account, we have examined the usefulness of several biomarkers for the prevention of CVD and lifestyle-related diseases in the Japanese population.

Inflammation is involved in the development and progression of atherosclerosis. Evidence from Western countries suggests that high-sensitivity C-reactive protein (hsCRP) has a predictive value for CVD. However, whether hsCRP is a cardiovascular risk marker in the Japanese population remains unclear. To address this question, we examined the relationship between serum hsCRP levels and the Framingham Risk Score (FRS), a risk-prediction scoring system for CVD, in Japanese male company workers[1]. Intriguingly, a significant positive correlation was found between hsCRP and the FRS. Moreover, the highest quartile of hsCRP (≥0.6 mg/L) had a significantly increased odds ratio (3.85, $p<0.001$) for an elevated FRS, compared with the lowest quartile of hsCRP (≤0.1 mg/L), even after adjusting for multiple potential confounders. These results suggest that hsCRP is useful for identifying persons at high-risk for CVD in the Japanese population.

A major limitation of hsCRP as a risk marker for CVD is that it is not specific for the cardiovascular system. Troponin T (TnT) is a specific biomarker for myocardial injury which is used for diagnosing acute coronary syndromes. However, data are lacking regarding the significance of measuring TnT in the Japanese general population. To address this issue, we measured serum levels of high-sensitivity TnT (hsTnT) and hsCRP, and their relationships with the FRS were examined in Japanese middle-aged men[2]. The hsTnT levels were positively associated with the predicted CVD risk category as estimated by the FRS. The highest hsTnT group (≥0.005 ng/mL) also showed a significantly increased odds ratio (3.98, $p=0.001$) for high-predicted CVD risk as compared with the lowest hsTnT group (≤0.002 ng/mL), even after adjusting for multiple potential confounders. Importantly, the combination of low hsCRP and high hsTnT, but not the combination of high hsCRP and low hsTnT, had significant odds for having high-predicted CVD risk. These results suggest that measurement of hsTnT in addition to hsCRP successfully addresses the limitation of hsCRP and improves the predictive ability for CVD in the Japanese population.

We have also explored novel biomarkers for predicting incident lifestyle-related disease. To clarify the effect of reduced kidney function on the risk of incident hypertension, we examined the association between serum cystatin C (CysC) levels and the future risk of incident hypertension in a 4-year follow-up study in a Japanese population[3]. A significantly increased hazard ratio (1.89, p=0.002) for incident hypertension was observed in the highest quintile of CysC (≥0.82 mg/L) compared with the other quintiles combined, after adjusting for multiple potential confounders. These findings indicate that serum CysC is not only a biomarker for kidney function but also a risk marker for incident hypertension.

Impaired glucose tolerance (IGT) has been reported to be associated with systemic inflammation. We therefore examined the association between hsCRP and the risk of developing IGT/diabetes in a 5-year follow-up study in Japanese subjects with normal glucose tolerance (unpublished data). The highest quartile of hsCRP (≥1.0 mg/L) was significantly associated with an increased risk of developing IGT/diabetes (adjusted odds ratio 1.96, p=0.042) compared with the lowest quartile of hsCRP (≤0.3 mg/L). These results suggest that hsCRP is predictive of the future development of IGT/diabetes in subjects with normal glucose tolerance.

References

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