Association between C-reactive Protein and Incidence of Type-2 Diabetes in a Japanese Worksite-based Cohort

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Background/Objective

Chronic inflammation is suggested to exist in the pathogenesis of type-2 diabetes (T2D). Relationships of inflammatory markers with diabetes risk or insulin resistance have been shown. However, the causality of the relationship is still under debate. We examined whether C-reactive Protein (CRP) is a risk factor to predict T2D incidence.

Method

We studied 3,371 civil servants in Aichi prefecture without diabetes aged 35 to 66 at baseline (2002) for whom high-sensitivity C-reactive protein (CRP) were obtained. Subjects with CRP value 10 mg/L or higher were excluded from the analysis. T2D incidence was defined as the year when annually-assessed fasting blood glucose level first exceeded 126 mg/dl, or self-reported initiation of medication through 2007. Cox proportional hazards regression was used to estimate hazard ratios (HRs) for the incidence of T2D adjusted for sex, age, body mass index (BMI), alcohol intake, smoking status, physical activity, and family history of diabetes according to the CRP quartiles (Q1: 0.02-0.18, Q2: 0.18-0.34, Q3: 0.34-0.69, Q4: 0.69-10).

Results

The mean (standard deviation) age of subjects was 47.9±7.1 years old. The numbers of male, and premenopausal and postmenopausal women were 2,582 (77.3%), and 560 (16.8%) and 229 (6.9%), respectively. The mean BMI was 22.8±2.7 kg/m^2. The geometric mean and the 95% confidence interval (CI) of CRP was 0.35 mg/L (0.12-1.03). During the follow-up, 177 developed T2D. The crude HRs (95% CIs, p-value) for CRP quartiles Q2, Q3, and Q4 groups against Q1 were 0.89 (0.54-1.47, p=0.65), 2.10 (1.39-3.20, p<0.01), and 2.32 (1.53-3.52, p<0.01), respectively. Multivariate-adjusted HRs were 0.72

(0.43-1.21, p=0.22), 1.50 (0.96-2.33, p=0.07), and 1.45(0.92-2.27, p=0.11), respectively (p for trend=0.011). Stratified analysis by smoking status (nonsmokers and current smokers) revealed that statistically significant association was observed only in the nonsmokers: multivariate-adjusted HRs being 0.75 (0.37-1.49, p=0.41), 1.91 (1.07-3.37, p=0.027), 1.93 (1.07-3.48, p=0.029) for Q2 to Q4 compared to Q1, respectively. Among current smokers who had significantly higher risk of T2D as well as CRP compared to nonsmokers [HR: 1.56(1.13-2.15, p=0.007), geometric mean of CRP: 0.45 vs.0.32], they were 0.62 (0.29-1.36, p=0.24), 0.95 (0.47-1.93, p=0.47), and 0.90 (0.45-1.79, p=0.45).

Discussion

Chronic low-grade inflammation represented by higher CRP was related to T2D incidence in nonsmokers. The finding of the present study implied that inflammation precedes T2D.

- ◆ Among nonsmokers, baseline blood CRP level was positively associated with T2DM incidence but not in smokers.
- ◆ The reason why non-significant result was found among smokers might be as follows:

Current smokers might develop T2DM through much more complicated pathways (such as: not ideally life-styles; cigarette damaging β-cell function; oxidative stress, etc.) than nonsmokers, hs-CRP represented inflammation pathway might contribute little in the pathogenesis of the development of T2DM in smokers.

- ◆ Compare with previous studies this cohort have relatively higher proportion of men (76.6%) and younger age that might lead to non-significant result in smokers in present study.
- ◆ The findings of the present study implied that low-grade inflammation precedes type-2 diabetes in nonsmokers.