

## High-Sensitivity C-Reactive Protein Predicts Cardiovascular Risk in Diabetic and Nondiabetic Patients: Effects of Insulin-Sensitizing Treatment with Pioglitazone

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### Abstract

Systemic inflammatory activity has turned out to play a key pathogenic role in vascular atherosclerosis, insulin resistance, and type 2 diabetes mellitus. Inflammatory biomarkers may therefore be a valuable tool for risk evaluation. Among them, the best evidence to date supports the use of high-sensitivity C-reactive protein (hs-CRP) to monitor insulin resistance and cardiovascular risk in diabetic and nondiabetic individuals. Data suggest that hs-CRP may also participate directly in the process of atherogenesis. A growing number of clinical trials tested the hypothesis that antidiabetic drugs specifically targeting insulin resistance could benefit individuals by reducing inflammation, atherogenesis, and thus cardiovascular risk. One such class are the thiazolidinediones (pioglitazone and rosiglitazone). These agents act as selective ligands of the nuclear transcription factor peroxisome proliferator-activated receptor- $\gamma$  (PPAR $\gamma$ ). This article reviewed published data on hs-CRP changes with the thiazolidinedione agent pioglitazone. Here we found pronounced insulin-sensitizing and anti-inflammatory properties in different clinical settings, including diabetic and nondiabetic individuals. Coadministration of pioglitazone to antilipidemic statin therapy resulted in additional effects on low-grade inflammation, and hs-CRP reduction has been demonstrated to occur independently of glucose lowering. The anti-inflammatory effect appeared to be a rapid physiologic reaction on PPAR $\gamma$  activation and could be observed within a short-term interval after starting pioglitazone therapy. In summary, clinical study results underline the benefit of an early insulin resistance treatment to oppose systemic vascular inflammation and cardiometabolic syndrome in patients with elevated levels of high-sensitivity C-reactive protein.

*J Diabetes Sci Technol* 2010;4(3):706-716

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**Abbreviations:** (BMI) body mass index, (CVD) cardiovascular disease, (HbA1c) hemoglobin A1c, (HOMA) homeostasis model assessment, (hs-CRP) high-sensitivity C-reactive protein, (LDL) low-density lipoprotein, (PPAR $\gamma$ ) peroxisome proliferator-activated receptor- $\gamma$

**Keywords:** atherosclerosis, diabetes, hs-CRP, inflammation, insulin resistance, pioglitazone

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