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Non-glucose-dependent anti-atherosclerotic effects of pioglitazone: An overlooked phenomenon

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Peroxisome Proliferator-Activated Receptor γ (PPAR- γ). Not only is PPAR- γ involved in the glucose metabolism, but also it is related to Atherosclerosis (AS). Several large prospective randomized controlled clinical trials have intervened diverse crowds (patients with type 2 diabetes and different AS risks, or non-diabetic patients with <u>stroke</u> and insulin resistance, representing primary and secondary prevention of AS respectively) with pioglitazone, and the occurrences of AS-related macrovascular events were observed in them. The results of those trials including the PROactive, IRIS and TOSCA.IT study have been analyzed to evaluate the anti-AS effect of pioglitazone in diverse populations (primary and secondary prevention of AS), and compared with the evidence for the macrovascular protective effects of metformin. The conclusions are that <u>pioglitazone</u> can reduce macrovascular events in AS primary and secondary prevention population, whose evidence is superior to metformin, and at least part of the anti-AS effect of pioglitazone is glucose-independent. Furthermore, we summarize the proposed mechanisms.