Impact of CD14++CD16+ monocytes on coronary plaque vulnerability assessed by optical coherence tomography in coronary artery disease patients

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Background:
Diabetes mellitus has been known as an important factor of coronary artery disease (CAD) progression despite of widespread with lipid-lowering therapy. Although we have reported that large glucose fluctuation is associated with the development of cardiovascular disease in both diabetes mellitus (DM) and non-DM patients, the underlying mechanisms remain unclear.

Monocytes play a key role for atherosclerotic plaque formation. Monocytes in human peripheral blood are divided into three subsets: CD14++CD16- monocytes, CD14++CD16+ monocytes, and CD14+CD16++ monocytes. The CD14++CD16+ monocyte subset has recently received attention because it is reported to be associated with future cardiovascular events such as acute myocardial infarction. However, their impact on coronary plaque vulnerability in coronary artery disease (CAD) patients with or without DM remains unclear.

Purpose:
The aim of this study was to investigate the impact of CD14++CD16+ monocyte levels on coronary plaque vulnerability and glucose fluctuation in stable CAD patients with well-regulated lipid levels.

Methods:
This prospective observational study included 50 consecutive patients with CAD (DM [n=22], Non-DM [n=28]), receiving lipid-lowering therapy and undergoing coronary angiography and optical coherence tomography (OCT). Patients were divided into 3 tertiles according to the CD14++CD16+ monocyte percentages assessed by flow cytometry. Standard OCT parameters including lipid arc, lipid length, fibrous cap thickness (FCT) on lipid rich plaque, were assessed for 97 angiographically intermediate lesions (diameter stenosis: 30-70%). The presence of thin-cap fibroatheroma (TCFA), defined as a thin fibrous cap (<65μm) overlying a lipid-rich plaque (>90°), was also assessed. Daily glucose fluctuation assessed by using continuous glucose monitoring system was analyzed by measuring the mean amplitude of glycemic excursion (MAGE).

Results:
CD14++CD16+ monocytes negatively correlated with FCT on lipid rich plaque (r=0.508, p < 0.01) (Figure. 1). The presence of thin-cap fibroatheroma (TCFA) was increased stepwise according to the tertile of CD14++CD16+ monocytes (0 [tertile 1] vs. 5 [tertile 2] vs. 10 [tertile 3], p < 0.01). CD14++CD16+ monocytes were a significant determinant of TCFA (OR 1.279, p=0.001). Although CD14++CD16+ monocytes were not significantly correlated with MAGE in DM patients (r=0.259, p=0.244), a significant relationship was found between CD14++CD16+ monocytes and MAGE in non-DM patients (r=0.477, p=0.018) (Figure 2).

Conclusions:
CD14++CD16+ monocytes were associated with coronary plaque vulnerability in CAD patients with well-regulated lipid levels both in DM and non-DM patients. Cross-talk between glucose fluctuation and CD14++CD16+ monocytes may enhance plaque vulnerability, particularly in non-DM patients.
CD14++CD16+ monocytes could be a possible therapeutic target for coronary plaque stabilization.