Abstract: P2861
Elevated cc chemokine receptor 2 expression and higher migratory activity of monocytes in atrial fibrillation patients with progressive structural remodeling

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Topic(s):
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Background: Inflammation in atrial tissue underlies structural remodeling of left atrium, which is a hallmark of atrial fibrillation (AF). Activated monocytes mediate inflammation; however, the role of monocytes in AF pathogenesis has not been extensively examined. In this study, we thus investigated the association between structural remodeling of left atrium, represented by left atrial dimension (LAD), and characteristics of peripheral monocytes in patients with AF.

Methods: Blood samples were collected from patients undergone catheter ablation between July 2017 and October 2018, including AF patients (n=152) and paroxysmal supraventricular tachycardia (PSVT) patients, which serves as a control non-AF group (n=22). AF patients were further divided into two groups by the median of LAD (normal LAD group: LAD <40 mm, n=77, large LAD group: LAD ≥40 mm, n=75). Peripheral blood mononuclear cells (PBMC) were isolated to analyze monocyte subsets by flow cytometry. In a subset of patients, we further isolated monocytes from PBMC by using magnetic bead-based negative selection method then gene products associated with inflammation or monocyte functions were evaluated. We also examined migratory activity of monocytes toward monocyte chemotactic protein-1, a ligand for CC chemokine receptor 2 (CCR2), using a modified Boyden chamber method. Finally, we performed immunofluorescence staining of monocytes and macrophages in left atrial appendages resected from patients underwent coronary bypass graft surgery (CABG) complicated by AF.

Results: There were no differences in age, body mass index and high-sensitivity C-reactive protein levels among three groups, including non-AF, normal LAD and large LAD groups, except that more female subjects were included in non-AF group. We found that proportions of classical CD14++CD16- and nonclassical CD14+CD16++ monocytes were higher (non-AF: 71.2±7.3% vs. AF: 75.5±8.3%, p<0.05) and lower (non-AF: 16.4±5.9% vs. AF: 13.2±5.5%, p<0.05), respectively, in all AF patients compared with those in non-AF group, while no significant difference was observed between normal and large LAD groups. In monocytes from large LAD group, mRNA levels of CCR2, a receptor to mediate monocyte chemotaxis, were significantly higher compared to those in normal LAD group (Figure A, p<0.05). Furthermore, monocytes isolated from large LAD group exhibited higher migratory capacity compared to normal LAD group (Figure B, p<0.01). Finally, higher monocyte/macrophage infiltrations to left atrial appendages were implicated in patients with large LAD, shown by immunofluorescence staining.

Conclusions: Monocytes in AF patients with enlarged left atrium expressed higher CCR2 mRNA and were more active in chemotaxis to MCP-1, suggesting the proactive roles of activated monocytes in the pathogenesis of arterial remolding in AF.
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A) CCR2 mRNA in monocytes

B) Migratory activity of monocytes