Coagulation cascade, inflammatory and fibrosis markers in patients with paroxysmal/persistent atrial fibrillation

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Background: Atrial fibrillation (AF) is one of the most common of cardiac arrhythmias and associated with atrial structural changes that may have an inflammatory and fibrosis basis. AF is associated with a prothrombotic or hypercoagulable states, which may be contributed to an increased risk for stroke and systemic embolism. There is a plausible evidence linking inflammation to the initiation and perpetuation of AF and AF-related thrombosis. Transforming growth factor (TGF-β1) is a key cytokine involved in the pathogenesis of fibrosis in many organs, whereas IL-6 plays an important role in the regulation of inflammation. Several prothrombotic factors have been found to be elevated in AF, indicating abnormal thrombogenesis and increasing the risk of stroke and thromboembolism. Tissue Factor (TF) is the principal initiator of the coagulation cascade. It is expressed in response to injury, as well as to a number of different extracellular stimuli, including cytokines IL-6 and TGF-β1. In this way TF is promoted blood coagulation and involved in inflammation and fibrogenesis. The purpose of this study is to evaluate the link between inflammation and fibrosis as well as the prothrombotic state in the setting of AF, including the impact of this relationship on clinical presentation and outcome of AF.

Methods: 165 patients with paroxysmal/persistent AF (mean age 64.6 ± 9.5) where enrolled in this study. After the enrollment the echocardiography examination and 24-hour ambulatory Holter monitoring ECG were registered in each patient. We measured plasma indexes of inflammation (hs-CRP, IL-6) and fibrosis (TGF-β1) as well as the prothrombotic state, including markers of the coagulation cascade such as TF and fibrinogen (F) in all observed patients with AF and 38 healthy subjects as control group. All of blood tests in plasma were determined by ELISA on the analyzer. Studies were conducted on the basis of simple randomized protocols, using the universal statistical packages SPSS 13.0 and EXCEL-2007.

Results: The obtained results showed that AF patients had higher levels of IL-6 (p = 0.014), hs-CRP (p = 0.001), TGF-β1 (p = 0.001), TF (p = 0.016) and F (p = 0.025) compared with controls group. Plasma CRP and TGF-β1 levels were higher among AF patients at high risk of stroke (CHA2DS2-VASc >2) (p = 0.002). Moreover, the levels of hs-CRP, IL-6 and especially TGF-β1 are markedly elevated in patients with dilated left atrium, poorly functioning left atrial appendage and longer duration of AF.

Conclusion: Paroxysmal/persistent AF may trigger an inflammatory response leading to activation of myofibroblasts and to the release of cytokines such as TGF-β1 and platelet-derived TF. Increased plasma levels of IL-6, CRP and TGF-β1 are related to the coagulation cascade indexes and may contribute to structural remodeling of left atrium in patients with AF.