## **How Is Uric Acid Related to Atrial Fibrillation?**

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ric acid (UA) is an end product of purine metabolism in humans, produced in the liver, muscles, and intestines. Xanthine oxidoreductase (XO) is the enzyme responsible for UA production. Under normal conditions its serum level is lower than 6 mg/dL in women and 7 mg/dL in men because of homeostatic regulation carried out mostly by the kidney. Dietary factors may influence serum UA, increasing its levels (meat, seafood, alcohol etc.) or decreasing them (coffee, ascorbic acid etc.). In addition, high cellular turnover conditions, such as in

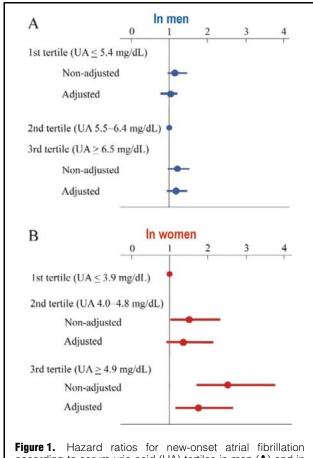


Figure 1. Hazard ratios for new-onset atrial fibrillation according to serum uric acid (UA) tertiles in men  $(\mathbf{A})$  and in women (B). Reproduced with permission from reference 4.

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neoplastic disease, may increase the UA concentration. When the serum UA concentration is higher, the condition is defined as hyperuricemia. UA may have an opposite role to oxidative stress, according to its intracellular (antioxidant) and extracellular (pro-oxidant) localization.1 UA acts as an antioxidant and accounts for 50% of the total antioxidant capacity of biological fluids in humans. When present in the cytoplasm of cells or in the acidic/hydrophobic milieu of atherosclerotic plaques, UA converts to a prooxidant and promotes oxidative stress, participating in the pathophysiology of human disease, including cardiovascular disease (CVD), through this mechanism. Most epidemiological studies suggest the existence of an association between elevated serum UA level and CVD, including

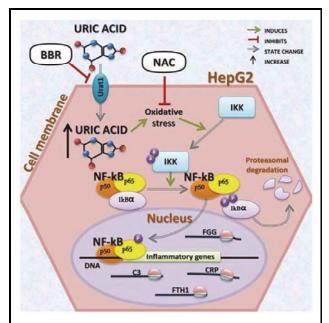


Figure 2. Mechanisms of uric acid-induced inflammation of cardiomyocytes possibly related to atrial fibrillation. Excessive uric acid might induce the expression of inflammatory molecules by activating the proinflammatory NF-kB signaling cascade. Reproduced with permission from reference 14.

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