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Elevated plasma xanthine oxidoreductase activity predicts cardiovascular events in patients with heart failure with preserved ejection fraction

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Background: The pathophysiology of heart failure with preserved ejection fraction (HFpEF) remains poorly understood, although reactive oxygen species (ROS) is reportedly involved in underlying mechanisms. Xanthine oxidoreductase (XOR) is the rate-limiting enzyme of purine metabolism that plays an important role in producing uric acid, and also generates the ROS. However, the impact of plasma XOR activity on the clinical outcomes in patients with HFpEF remains unclear.

Purpose: The aim of this study was to assess whether plasma XOR activity predicts cardiovascular events in patients with HFpEF.

Methods and Results: We measured plasma XOR activity in 257 patients with HFpEF. The patients were divided into 3 groups based on XOR activity: low XOR group (< 33 pmol/h/mL, n = 45), normal XOR group (33 - 120 pmol/h/mL, n = 160), and high XOR group (> 120 pmol/h/mL, n = 52). During a median follow-up period of 809 days, there were 74 major adverse cardiovascular events (MACEs). Kaplan-Meier analysis demonstrated that the patients with high XOR activity were at greatest risk for MACEs. A multivariate Cox proportional hazard regression analysis showed that high XOR activity was significantly associated with MACEs after adjustment for confounding factors. Furthermore, we divided the patients into 4 groups according to the presence of high XOR activity and/or hyperuricemia. Cox multivariate hazard regression analysis revealed that the patients with high XOR activity were associated with cardiovascular events in patients with HFpEF, regardless of whether hyperuricemia was present or not.

Conclusions: Elevated plasma XOR activity is significantly associated with adverse clinical outcomes in patients with HFpEF. Inhibition of XOR could be a potential therapy for HFpEF.