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## Risk of Febuxostat-Associated Myopathy in Patients with CKD

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### Abstract

**Background and objectives** Febuxostat, a nonpurine xanthine oxidase inhibitor, is widely used to treat hyperuricemia. Although febuxostat-associated rhabdomyolysis was reported in some patients with CKD, the association between CKD and febuxostat-associated myopathy remains uncertain.

**Design, setting, participants, & measurements** Our retrospective cohort study included 1332 patients using febuxostat in Taipei Medical University-Wanfang Hospital from February of 2014 to January of 2016. The primary predictor was time-averaged eGFR as calculated by the equation proposed by the 2009 Chronic Kidney Disease Epidemiology Collaboration. The outcome was febuxostat-associated myopathy defined as elevated creatine kinase levels during febuxostat use that were not attributed to other muscular injuries.

**Results** The median duration of febuxostat use was 224 days (25th, 75th percentiles: 86, 441.5 days). Of 1332 study participants, 1222 (91.7%) had CKD; the median eGFR was 20.8 ml/min per 1.73 m<sup>2</sup> (25th, 75th percentiles: 9.0, 35.4 ml/min per 1.73 m<sup>2</sup>). Forty-one of the participants had febuxostat-associated myopathy (3.2%). All patients with myopathy had CKD, and the incident rate was 0.013 (95% confidence interval, 0.01 to 0.02) events per 100 patient-days in patients with CKD. Of 41 patients with myopathy, 37 had myositis, and four had rhabdomyolysis. Myopathy resolved in 17 patients who withdrew from treatment and eight patients who continued febuxostat treatment. Among the evaluated predictors, multivariate analysis showed that only the lowest eGFR tertile was significantly associated with myopathy in febuxostat users. The odds ratio of the lowest eGFR tertile to the highest tertile was 4.21 (95% confidence interval, 1.7 to 10.43). This finding remained consistent among subgroups stratified by age, sex, diabetes status, coronary artery disease, and statin or fibrin use.

**Conclusions** Patients with severely reduced eGFR had higher risk of myopathy with treatment of febuxostat. Regular monitoring of creatine kinase level is suggested for early detection of febuxostat-associated myopathy, particularly in patients with CKD.

chronic kidney disease   febuxostat   myopathy   Confidence Intervals  
coronary artery disease   Creatine Kinase   diabetes mellitus  
Febuxostat   Fibrin Acids   glomerular filtration rate   Gout Suppressants  
Humans   Hyperuricemia   Multivariate Analysis   Myositis   Odds Ratio  
Renal Insufficiency, Chronic   Retrospective Studies   rhabdomyolysis  
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