Thromboembolic events can be seen in patients with mitral valve prolapse (MVP). It is unclear whether platelet activation may contribute to these events in patients with MVP. Thus, we aimed to evaluate mean platelet volume (MPV) in patients with MVP and its association with the severity of MVP. This study included 312 patients with MVP and 240 control participants. Mean platelet volume was significantly higher in patients with MVP than in controls (8.9 ± 0.7 vs 7.9 ± 0.6 fL, P = .001). In linear regression analysis, MPV was independently associated with the degree of mitral regurgitation (β = .23, 95% confidence interval (CI): 0.14-0.32, P = .001), maximal leaflet displacement (β = .24, 95% CI: 0.17-0.31, P = .001), and mean thickness of the anterior (β = .47, 95% CI: 0.27-0.61, P = .001) and posterior leaflets (β = .22, 95% CI: 0.03-0.41, P = .02). Our findings show that MPV can be elevated in patients with MVP and may be independently associated with severity of mitral regurgitation, leaflet displacement, and thickness of the leaflets.