中文題目：僵直性脊椎炎患者接受腫瘤壞死因子 α 抑制劑後 B 型肝炎再活化之高風險探討

英文題目：High risk of viral reactivation in hepatitis B patients with ankylosing spondylitis undergoing tumor necrosis factor α inhibitor treatment.

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Backgrounds: Hepatitis B virus(HBV) infection poses a public health issue in Taiwan because it accounts for the major cause of chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma. HBV reactivation (HBVr) could be a life-threatening complication in hepatitis B surface antigen (HBsAg)-positive and negative patients whose immune system is deficient or suppressed. Ankylosing spondylitis (AS) is a common systemic rheumatic disease that mainly causes inflammatory back pain, morning stiffness, fatigue, enthesitis and extra-arthritis manifestations. The mainstay treatment used to treat ankylosing spondylitis are NSAIDs and immunosuppressive agents, such as Disease-modifying anti-rheumatic drugs (DMARDs) and tumor necrosis factor α (TNF-α) inhibitors. The incidence of HBVr in AS patients over a long period of time and its association with use of TNF-α inhibitor remains unknown. Here, we determined the incidence of HBVr and its related hepatitis in patients with ankylosing spondylitis (AS).

Methods: In the Taipei Veterans General Hospital cohort, 448 AS cases were retrospectively reviewed for episodes of hepatitis from 2000 to 2017. The clinical feature and cumulative incidence of HBV reactivation in AS patients who stratified by HBsAg positive or resolved hepatitis B (RHB) or by with or without TNF-α inhibitor use were evaluated by Kaplan–Meier analysis. Analysis of risk factors for HBVr was performed using the Cox proportional hazards model.

Results: Among 448 patients who had available HBsAg, 76 (17%) were positive for HBsAg and 105(23.4%) had RHB. In HBsAg positive group, 9 patients who received antiviral prophylaxis before biologic treatment were excluded. During a mean 12 years of follow-up, HBVr developed in 14 (20.9%) of overall 67 HBsAg-positive patients but there was no RHB cased experienced HBsAg reverse seroconversion (RS). The higher proportion of HBVr was noted in HBsAg-positive patient with TNF-α inhibitor use (57.1% vs 30.2%, p = 0.066). AS patients positive for HBsAg had a higher cumulative incidence of HBVr compared to RHB patients. In addition, receiving TNF-α inhibitor was associated with the higher risk of HBVr in HBsAg-positive AS patients. In multivariate analysis, receiving TNF-α inhibitor treatment was an independent risk factor of HBVr in HBsAg-positive group (adjusted hazard ratio = 4.365, 95% CI = 1.366 – 13.944, p = 0.013).

Conclusion: In conclusion, the cumulative incidence of HBVr was high in AS patients who were positive for HBsAg and under TNF-α inhibitor use. Screening of hepatitis B markers, including

HBsAg, anti-HBc, and anti-HBs, prior to biologic therapy may be necessary for AS patients. Our findings suggest that antiviral prophylaxis should be considered for HBsAg-positive AS patients when administrating biologic treatment such as TNF-α inhibitors.