URINE 8-HYDROXY-2’-DEOXYGUANOSINE IS A MARKER FOR PREDICTING MORTALITY AND MORBIDITY AS WELL AS EVALUATING THE EFFECTIVENESS OF BETA-BLOCKER THERAPY IN PATIENTS WITH CHRONIC HEART FAILURE

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Authors: Tekehisa Susa, Shigeki Kobayashi, Takeo Tanaka, Shinichi Okuda, Masahiro Doi, Yasuaki Wada, Jutaro Yamada, Takeshi Ueyama, Shuji Kawamura, Masafumi Yano, Masunori Matsuzaki, Yamaguchi University Graduate School of Medicine, Ube, Japan

Background: Oxidative stress is known to play a crucial role in the pathogenesis of heart failure. In our preliminary study, the level of serum 8-hydroxy-2’-deoxyguanosine (8-OHdG: ng/ml), a product of oxidative DNA damage, was higher in coronary sinus than in aorta in CHF, while it was not in normal subjects, indicating that reactive oxygen species is produced in failing cardiac tissue. Based on these findings, we hypothesized that urine (U)-8-OHdG might be a useful biomarker for predicting the prognosis and evaluating the response to the treatment with beta-blocker in patients with CHF.

Methods and Results: We measured U-8-OHdG in 30 control subjects and 120 CHF patients. U-8-OHdG in patients with CHF was significantly higher than that of control subjects (U-8-OHdG(ng/mg): N; 8.1±2.0 vs. CHF; 15.1±9.1, P<0.01). Then, these CHF patients were prospectively followed during a median follow-up period of 670 days with end points of cardiac death or re-hospitalization due to progressive heart failure. From the ROC curve analysis, the cut-off value of U-8-OHdG was determined as 12.5 ng/mg. Kaplan-Meier analysis demonstrated that the high U-8-OHdG group had a significantly higher incidence of cardiac events than those in the low U-8-OHdG group(P<0.0001). In the multivariate Cox analysis, U-8-OHdG level was an independent risk factor for cardiac events (hazard ratio 1.15, 95% confidence interval 1.05-1.13, P<0.005). Furthermore, we investigated whether U-8-OHdG was useful in evaluating the effectiveness of beta-blocker therapy (mean follow-up periods: 12 months) in thirty patients with CHF. The responder was defined as a clinical improvement of either more than 10% in LVEF or more than 1 class of NYHA functional classification before and after addition of beta-blocker. In responder patients (n=17), U-8-OHdG was significantly decreased in parallel with an improvement of NYHA class, LVEF, LV end-diastolic diameter and serum BNP levels after treatment of beta-blocker. On the other hand, in non-responder patients (n=13), it did not.

Conclusion: U-8OHdG might be a useful biomarker for predicting mortality and morbidity as well as evaluating the effectiveness of beta-blocker therapy in patients with CHF.