## Effects of Heart Rate Variability Biofeedback to Improve Autonomic Nerve Function, Inflammatory Response and Symptom Distress in Patients with Chronic Kidney Disease: A Randomized Control Trial

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Abstract : The prevalence and incidence of end-stage renal disease in Taiwan ranks the highest in the world. According to the statistical survey of the Ministry of Health and Welfare in 2019, kidney disease is the ninth leading cause of death in Taiwan. It leads to autonomic dysfunction, inflammatory response and symptom distress, and further increases the damage to the structure and function of the kidneys, leading to increased demand for renal replacement therapy and risks of cardiovascular disease, which also has medical costs for the society. If we can intervene in a feasible manual to effectively regulate the autonomic nerve function of CKD patients, reduce the inflammatory response and symptom distress. To prolong the progression of the disease, it will be the main goal of caring for CKD patients. This study aims to test the effect of heart rate variability biofeedback (HRVBF) on improving autonomic nerve function (Heart Rate Variability, HRV), inflammatory response (Interleukin-6 [IL-6], C reaction protein [CRP]), symptom distress (Piper fatigue scale, Pittsburgh Sleep Quality Index [PSQI], and Beck Depression Inventory-II [BDI-II] ) in patients with chronic kidney disease. This study was experimental research, with a convenience sampling. Participants were recruited from the nephrology clinic at a medical center in northern Taiwan. With signed informed consent, participants were randomly assigned to the HRVBF or control group by using the Excel BINOMDIST function. The HRVBF group received four weekly hospital-based HRVBF training, and 8 weeks of home-based self-practice was done with StressEraser. The control group received usual care. We followed all participants for 3 months, in which we repeatedly measured their autonomic nerve function (HRV), inflammatory response (IL-6, CRP), and symptom distress (Piper fatique scale, PSQI, and BDI-II) on their first day of study participation (baselines), 1 month, and 3 months after the intervention to test the effects of HRVBF. The results were analyzed by SPSS version 23.0 statistical software. The data of demographics, HRV, IL-6, CRP, Piper fatigue scale, PSQI, and BDI-II were analyzed by descriptive statistics. To test for differences between and within groups in all outcome variables, it was used by paired sample t-test, independent sample t-test, Wilcoxon Signed-Rank test and Mann-Whitney U test. Results: Thirty-four patients with chronic kidney disease were enrolled, but three of them were lost to follow-up. The remaining 31 patients completed the study, including 15 in the HRVBF group and 16 in the control group. The characteristics of the two groups were not significantly different. The four-week hospital-based HRVBF training combined with eight-week home-based self-practice can effectively enhance the parasympathetic nerve performance for patients with chronic kidney disease, which may against the disease-related parasympathetic nerve inhibition. In the inflammatory response, IL-6 and CRP in the HRVBF group could not achieve significant improvement when compared with the control group. Self-reported fatigue and depression significantly decreased in the HRVBF group, but they still failed to achieve a significant difference between the two groups. HRVBF has no significant effect on improving the sleep quality for CKD patients.

**Keywords :** heart rate variability biofeedback, autonomic nerve function, inflammatory response, symptom distress, chronic kidney disease

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