

## 論文の内容の要旨

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論文題目 The Traditional Japanese Medicine (Kampo) Boiogito has a Dual Benefit in Cardiorenal Syndrome : A Pilot Observational Study (和漢医薬 (漢方薬) 防己黄耆湯は心腎症候群の両面への効果を有する : 試験的観察研究)	
(論文の内容の要旨) <p><b>【Introduction】</b> Cardiorenal syndrome (CRS), a concomitant status of cardiac and renal insufficiency is evolving; however, the consensus to the appropriate management of CRS has not been achieved. This prospective observational study explored a new approach utilizing Boiogito (TJ-20), a traditional Japanese medicine (Kampo), in combination with standard treatment for patients with CRS.</p> <p><b>【Methods】</b> We enrolled patients with chronic heart failure (CHF): New York Heart Association (NYHA) functional class I-III, Stage B or Stage C heart failure, along with renal insufficiency (estimated glomerular filtration rate, eGFR &lt; 65 mL·min<sup>-1</sup>·1.73 m<sup>-2</sup>). TJ-20 treatment was started at the dose of 2.5g, 5.0g, or 7.5g per day on each patient's standard medications and the dose of TJ-20 was modified within the standard dose according to the patient's acceptance and adherence. To evaluate TJ-20 effects on renal function and heart failure status, laboratory parameters were averaged from 2-3 outpatient visits for each 3 points as follows: 1) before initiation of the treatment (3±1.8 months), and followed at mean intervals of 2) 3.5±1.8 and 3) 9.4±2.3 months after starting the treatment.</p> <p><b>【Results】</b> In total, 26 patients (18 men; mean age, 77±8.4 years) were studied. TJ-20 treatment was started at the average dose of 4.6±1.5 g/day, which was increased to 5.2±1.2 g/day at 3.5 months and to 5.9±1.5 g/day at 9.4 months. Mean eGFR levels were significantly increased from 40.02±10.54 to 44.60±10.76 at 3.5 months (P=0.001), and to 45.93±11.57 at 9.4 months (P=0.0004). Brain natriuretic peptide (BNP) levels declined significantly from 241.5±196.6 to 195.5±145.7 pg/mL at 3.5 months (P=0.008), and to 163.3±130.2 pg/mL at 9.4 months (P=0.007). Statistically significant improvement in the NYHA functional class was observed after TJ-20 treatment (P=0.019). The increase in eGFR had no correlation with the decrease in BNP level, indicating independent effects on both renal function and heart failure status.</p> <p><b>【Discussion】</b> Our study demonstrates that addition of TJ-20 on standard treatment improved renal function, decreased BNP levels, and improved NYHA functional class from the baseline. No significant adverse events were observed that resulted in discontinuation of TJ-20 treatment at the end of our study.</p> <p>Standard treatment for CRS with diuretics and inotropes are frequently associated with drug resistance and limited clinical success. Therefore, alternative therapeutic approaches are of major clinical importance. It is widely known that many heart failure medications may also worsen renal function. As a result, it is difficult to maintain optimal fluid balance in CHF patients, while preserving renal function. Importantly, patients with renal dysfunction are often excluded from clinical heart failure trials; therefore, evidence based therapies for CRS patients are lacking.</p> <p>Interesting fluid control effect of TJ-20 has been described previously. TJ-20 elicits moderate diuretic effects in patients with excess body</p>	

water but not in euvoletic patients. Therefore, addition of TJ-20 has the potential to optimize diuresis and prevent renal dysfunction. In this study, we propose that the moderate diuretic effects of TJ-20 adding on standard treatment for heart failure may benefit CRS patients, who require maintaining optimal fluid balance.

Furthermore, we measured changes in eGFR and BNP levels at baseline, 3.5 and 9.4 months between patients with and without receiving angiotensin II receptor blockers, angiotensin-converting enzyme inhibitors,  $\beta$ -blockers, or diuretics to determine effects of these background treatment agents on eGFR and BNP levels. No significant changes in eGFR and BNP levels were observed, in the presence or absence of these background agents. These results suggest that addition of TJ-20 on standard medication benefited both renal function and heart failure status in CRS patients.

In conclusion, the observations of this study, utilizing traditional Japanese medicine (TJ-20), may provide a novel and useful strategy for the difficult management of CRS patients.