

## 9. Cardiovascular Diseases

**Reference**

Katayama K, Matsuda N, Kakuta K, et al. The effect of goreisan on the prevention of chronic subdural hematoma recurrence: multi-center randomized controlled study. *Journal of Neurotrauma* 2018; 35: 1537-42. CENTRAL ID: CN-01611342, Pubmed ID: 2944611, UMIN ID: UMIN000015970

**1. Objectives**

To investigate the preventative effect of goreisan (五苓散) on post-operative recurrence of chronic subdural hematoma.

**2. Design**

Randomized controlled trial (RCT).

**3. Setting**

Five neurosurgical institutions (university hospital and other hospitals)(the author belongs to the Department of Neurosurgery, Hirosaki University Graduate School of Medicine), Japan.

**4. Participants**

Two-hundred and eight patients over 60 years old with chronic subdural hematoma presenting neurological deficits and undergoing burr hole surgery. Exclusion criteria were severe liver dysfunction, severe renal dysfunction, and prior use of goreisan or corticosteroids before surgery.

**5. Intervention**

Arm 1: TSUMURA Goreisan (五苓散) Extract Granules 2.5 g three times daily orally for 12 weeks, starting within 72 hours after surgery (n=104).

Arm 2: Control (without goreisan) (n=104).

**6. Main outcome measures**

Neurological assessment and CT were performed pre-operatively and on Days 1, 7, and 14 and Weeks 4, 8, and 12 post-surgery. These assessments were performed by two site investigators blinded to the allocation. The primary endpoint was recurrence of chronic subdural hematoma, which was defined as increased hematoma volume with neurological deficits and need for re-operation. The secondary endpoint was hematoma volume reduction rate, calculated as  $(1-A/B)*100$  [%] (where A was post-operative hematoma volume and B was the preoperative hematoma volume).

**7. Main results**

Since 12 patients in Arm 1 and 16 patients in Arm 2 were lost to follow-up, the analysis was conducted on 92 patients in Arm 1 and 88 patients in Arm 2. In overall subjects, post-operative recurrence occurred in 9 patients (9.8%) in Arm 1 and 11 patients (12.5%) in Arm 2, without significant difference between the two groups. Among the subjects under 75 years of age, post-operative recurrence occurred in 1 patient (3.0%) in Arm 1 and 6 patients (17.4%) in Arm 2, and in significantly fewer patients in Arm 1 than in Arm 2 ( $P=0.04$ ). Among the subjects over 75 years of age, the number of post-operative recurrences did not significantly differ between the two groups. The hematoma volume reduction rates showed no significant differences between the two groups at any time points of evaluation. Even when the subjects were divided by age (i.e., under or over 75 years), the hematoma volume reduction rate did not significantly differ between the two groups. Multivariate analyses were performed to evaluate factors associated with post-operative recurrence and the preventive efficacy of goreisan. As confounding factors, those reported to have an influence on the postoperative recurrence, such as use of goreisan, age, use of anticoagulant, and bilateral chronic subdural hematoma were selected. Bilateral chronic subdural hematoma was the only independent risk factor for the recurrence.

**8. Conclusions**

This preliminary study showed that goreisan did not reduce the recurrence of chronic subdural hematoma or the hematoma volume reduction rate.

**9. From Kampo medicine perspective**

None.

**10. Safety assessment in the article**

Not stated.

**11. Abstractor's comments**

This was a multicenter randomized study of goreisan in the prevention of recurrence of chronic subdural hematoma, and is unprecedented in that it attempted to determine the effectiveness of goreisan on chronic subdural hematoma. However, the study showed no significant differences compared with the control group. This could be due to the inadequate sample size, as the authors stated. However, the study revealed that goreisan can be effective in patients aged under 75 years with relatively less brain atrophy and patients with unilateral chronic subdural hematoma. Future studies are awaited to collect data from more patients, determine the conditions indicated for goreisan, and characterize the efficacy of goreisan in preventing recurrence of chronic subdural hematoma.

**12. Abstractor and date**

Goto H, 10 September 2019.