学位論文の要旨

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学位論文名　Prognostic Impact of B-Type Natriuretic Peptide in Elderly Patients with Severe Aortic Stenosis

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論文内容の要旨

INTRODUCTION

Aortic stenosis (AS) is one of the most prevalent forms of valvular disease. As the growth rate of the elderly population continues to increase, AS prevalence is dramatically increasing. Although the therapeutic management of patients with AS relies heavily on the onset of symptoms, elderly patients may be difficult to assess symptoms due to their low level of physical activity.

Several studies have reported that plasma B-type natriuretic peptide (BNP) levels are correlated with symptom severity. Although AS is a common cardiovascular disease and plasma BNP level is frequently measured in outpatient clinic, study focused on the relation between plasma BNP levels and clinical outcomes in elderly patients with severe AS remains scarce.

This study aimed to evaluate the relationship between plasma BNP and outcomes in elderly patients with severe AS.

MATERIAL AND METHODS

In this study, we retrospectively reviewed data of 166 patients with severe AS (aortic valve area <1.0 cm^2 on echocardiography) between January 2008 and December 2013. Patients who were 75 years or older, had severe AS, and were not initially planned to undergo surgery were included. Patients with a significant valve disease (severe aortic regurgitation, severe mitral regurgitation, moderate or severe mitral stenosis, or prior valve replacement surgery), decompensated heart failure (HF), prior cardiac operation, missing laboratory tests, or were undergoing hemodialysis were excluded. We defined valve-related events (VRE) as a composite of cardiac death, aortic valve replacement (AVR), and hospitalization due to heart failure.

We divided the study population into two groups based on the presence of VRE and compared the clinical and echocardiographic characteristics of patients between the two groups. receiver operating characteristics (ROC) curve was generated and the area under the curve calculated to determine the optical cut-off value of BNP predicting the VRE. Survival analysis was performed using a Kaplan-Meier analysis and differences between groups were calculated with the log-rank test. To identify predictors of VRE at 2 years, we used Cox proportional hazard analysis. In univariable analysis, significant different variables based on the presence of VRE (P values of <0.05) were includes. Variables with P values of <0.05 in the univariable analysis were included in the multivariable analysis.

The study protocol was approved by the Research Ethics Committee of Shimane University.

RESULTS AND DISCUSSION

The mean age of the cohort was 84 ± 4 years with 29 (33%) men included on baseline characteristics. The mean peak velocity was 4.1 ± 0.8 m/s, mean pressure gradient was 40 ± 17 mmHg, and mean AV area was 0.73 ± 0.19 cm^2. The median plasma BNP level was 211 (69–353) pg/mL. The mean duration of follow-up was 596–730 days with a 94% follow-up rate at 2 years. At the 2-year follow-up, 27 patients had VRE. There were no significant differences between the VRE group and non-VRE group with regards to sex; BSA; presence of hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, prior cerebral infarction; use of β-blockers and ACE inhibitors/ARBs; LV dimension; LVEF; and moderate aortic regurgitation. Patients in the VRE group were older, presented with worse symptoms, and received diuretics more frequently (P <0.05 for all) than those in the non-VRE group. Biological and echocardiographic data indicated that patients in the VRE group had more severe aortic valve stenosis, concomitant mitral regurgitation and pulmonary hypertension.

A plasm BNP cut-off value of 234 pg/mL was used to detect the presence of VRE with a sensitivity, specificity, and accuracy of 74%, 67%, and 69%, respectively. The area under the curve (AUC) was 0.74 (p <0.001).

During the 2-year follow-up, 27 patients had VRE. AVR was observed in 8 patients, hospitalization for congestive HF in 23 patients, and cardiac death in 11 patients (8 patients died due to heart failure, while 3 patients had sudden death). VRE was significantly higher in patients in the high BNP group (plasma BNP levels ≧234 pg/mL, n=40) at the 2-year follow-up (p <0.001). The outcomes of patients in the high BNP group were significantly different from those of patients in the low BNP group (plasma BNP levels <234 pg/mL, n=48). The 1-year and 2-year event-free survival rates of patients in the low BNP group were 96 ± 3% and 84 ± 6%, respectively, whereas those of patients in the high BNP group were 58 ± 8% and 46 ± 8%, respectively (p <0.001).

The univariable analysis showed that age, use of diuretics, LVEF, E/E' , TRPG, concomitant moderate mitral regurgitation, AVA, prior HF hospitalization, New York Heart

Association (NYHA) function class, concomitant anemia, and plasma BNP levels ≧234 pg/mL were significant predictors of VRE. Multivariable analyses revealed that a plasma BNP level of ≧234 pg/mL was an independent predictor of VRE.

BNP is a cardiac hormone that is released in response to intracardiac pressure increase. In patients with moderate to severe AS, chronic pressure overload on the LV leads to progressive LV hypertrophy, diastolic dysfunction, and left atrial dilatation, which can subsequently lead to a rise in BNP levels due to the increased wall stress and filling pressure. Several studies have shown different natriuretic peptides cutoff values were associated with cardiac death, the need for AVR, and onset of symptoms. However, they were not adjusted according to age. Age-adjusted BNP was highly predictive of outcomes in asymptomatic patients with moderate to severe AS. The present study showed that an increased BNP level is an important independent predictor of outcomes in elderly patients with severe AS.

Our study had several limitations. First, it was a retrospective study with a relatively small sample size. Second, although follow-up mortality data were collected, frailty and quality of life was not assessed. Finally, the study was not designed to assess and compare the mortality rates between patients who had surgical interventions and those who received medical treatments.

CONCLUSION

Elderly patients with severe AS and high plasma BNP levels had a significantly worse prognosis than those with low BNP levels. Our results suggest that the plasma BNP level may provide significant incremental prognostic information in elderly patients with severe AS.