学 位 論 文 の 要 旨

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学　位　論　文　名	Factors Influencing the Prognosis of Octogenarians with Aortic Stenosis in the Advanced Aging Societies
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論 文 内 容 の 要 旨

INTRODUCTION

Aortic valve stenosis (AS) is now the most common form of native heart disease. The growth rate of the elderly population has continued to increase and the prevalence of AS sharply increases with age. The therapeutic management of AS patients depends on the hemodynamic severity of the stenosis and the presence of symptoms (angina, syncope, dyspnea), as the onset of symptoms and left ventricular (LV) systolic dysfunction are associated with a poor prognosis. However, it is difficult to use these variables to assess the risks of AS patients who are 80 years of age or older. The decision to operate raises specific problems in the elderly, because of higher incidence of operative mortality and morbidity, particularly in those who are deemed to be at high surgical risk. Although AS is common, little data is available regarding the factors that influence the natural history of AS patients of 80 years of age or older in advanced aging societies. To address this issue, this study investigated the natural history and the indications for valve procedures in AS patients who were 80 years of age or older.

MATERIALS AND METHODS

All of the patients who were 80 years of age or older, who were examined at our outpatient clinic for valvular heart disease between 2006 and 2012 and who were found to have a stenotic native aortic valve (AV) area of $\leq$ 1.5 cm^2 were included in the present study. This study protocol was approved by the ethical committee of Shimane University Faculty of Medicine. Patients with significant associated valve disease (aortic or mitral regurgitation of a grade higher 2/4 or mitral stenosis with a valve area of $\leq$ 1.5 cm^2 and prior valve replacement surgery) were excluded from the study. According to these criteria, 108 patients (mean age, 84.2 $\pm$ 3.9 years; female, 65 patients; average AV area, 0.85 $\pm$ 0.27 cm^2; average AV peak velocity, 4.1 $\pm$ 0.9 m/s) were identified.

The clinical data included age, gender, body surface area, body mass index, smoking history, documented diagnosis of atrial fibrillation, diabetes mellitus, hypertension, dyslipidemia, hemodialysis, coronary artery disease (history of myocardial infarction, coronary artery stenosis on coronary angiography), and pertinent current and past medical and surgical history. Special attentions was paid to the documented symptoms that were potentially associated with AS, including angina, chest pain, syncope and dyspnea or other evidence of heart failure. Our echocardiographic database was searched for patients with moderate and severe AS (defined as a valve area $\leq$ 1.5 cm^2). All of the patients underwent standard echocardiographic examinations which that included comprehensive 2-dimensional and Doppler echocardiography.

All study patients were followed up after their initial examination for moderate and severe AS. The follow-up information was obtained by a detailed review of all medical records. For the assessment of the outcome, the end points were death (all cause death) or AVR during the follow-up period.

RESULTS AND DISCUSSION

Eighty patients were symptomatic at the time of their enrollment: chest pain (n = 26), dyspnea (n = 47), and syncope (n = 7). The asymptomatic and symptomatic groups were defined

according to baseline clinical characteristics. The median duration of follow-up was 9 months (interquartile range, 2 to 25 months).

There was no significant difference in the AV area of the symptomatic and asymptomatic patients (0.85 ± 0.28 cm^2 vs. 0.88 ± 0.25 cm^2, P = 0.59). Thirty-eight events were observed, including AVR in 26 patients and death in 16 patients (including 4 patients who died after AVR). The rates of event free survival were 70 ± 5% at 1 year, 62 ± 6 % at 2 years, 47 ± 8% at 3 years, 43 ± 8% at 4 years, 43 ± 8 % at 5 years, and 29 ± 13% at 6 years. The AV area index and AV velocity were found to be the most powerful predictors of outcome (P < 0.05). In this study, neither a symptomatic nor asymptomatic status was found to be a significant independent predictor of mortality.

In many patients, the development of symptoms is clear, but some asymptomatic patients are difficult to assess due to inactivity or under-reporting. Although a watchful waiting approach is generally justified in asymptomatic patients with severe AS, due to the high event rate and the possibility of rapid deterioration in patients who are 80 years of age or older, the consideration of early elective surgery might be worthwhile, even when patients are still asymptomatic.

CONCLUSION

The severity of AS affected the prognosis of even asymptomatic patients who were 80 years of age or older. Thus the frequent monitoring of their subjective symptoms combined with the objective measurement of AV area is necessary.

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論文審査の結果の要旨

大動脈弁狭窄症は弁膜症の中で最も頻度の高い疾患であり、高齢化に伴い急速に増加している。重症化により狭心痛、失神、心不全症状が出現すれば予後不良のため外科的手術が勧められるが、高齢者に対する手術タイミングの決定は、加齢に伴う手術リスクの増加から判断が難しくなる。本研究では80歳以上の大動脈弁狭窄症患者の自然歴に影響を与える因子について検討した。対象は80歳以上で、心エコー検査にて大動脈弁口面積1.5cm^{2}以下の108例である。平均年齢は84.2±3.9歳、男性43例、女性65例で、初診時の大動脈弁口面積は0.85±0.27cm^2、大動脈弁血流速度は4.1±0.9m/secであった。80例に初診時より自覚症状があり（有症状群）、狭心痛が26例、失神が7例、心不全症状が47例に認められ、28例は無症状であった（無症状群）。追跡期間は中央値で9か月（四分位値は2～25か月）であった。有症状群と無症状群で大動脈弁狭窄症の重症度に差は認めなかった。追跡期間中に38のイベント（大動脈弁置換術あるいは死亡）が発生し、26例に大動脈弁置換術が施行され、16例が死亡した。イベントフリー生存率は1年で70±5%、2年で62±6%、3年で47±8%、4年で43±8%、5年で43±8%、6年で29±13%であった。有症状群と無症状群でイベントフリー生存率に差は認めなかった。Cox回帰分析によると、イベントフリー生存率に関与する独立因子は大動脈弁口面積係数（体表面積で補正した大動脈弁口面積）、大動脈弁血流速度であった。高齢者においては症状の有無ではなく、大動脈弁狭窄症の重症度自体が予後に関係した。これらの結果は超高齢者の大動脈弁狭窄症に対する治療法を選択する上で臨床的に重要な成果である。