**Low Systolic Blood Pressure on Admission Predicts Mortality in Patients With Acute Decompensated Heart Failure Due to Moderate to Severe Aortic Stenosis**

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**Background:** We investigated the relationship between admission systolic blood pressure (SBP) and all-cause mortality in patients hospitalized for acute decompensated heart failure (ADHF) due to aortic stenosis (AS).

**Methods and Results:** We retrospectively reviewed the data for 71 consecutive patients (mean age 85±7 years) who had been hospitalized for ADHF due to AS between January 2006 and August 2012. The primary endpoint of the study was the 1-year all-cause mortality. Clinical outcomes of patients who survived and those who died during a 1-year period were compared. Low admission SBP was defined as <120 mmHg. During the 1-year period, 26 (37%) of the 71 patients died, including 16 (57%) of 28 patients with low SBP and 10 (23%) of 43 patients with normal or high SBP (log-rank P=0.0065). Between the patients who survived and those who died, there were significant differences in admission SBP (152±43 vs. 116±32 mmHg, P<0.001), estimated glomerular filtration rate on admission (43.2±20.3 vs. 28.2±22.2 ml·min⁻¹·1.73 m⁻², P=0.005), and left ventricular ejection fraction <50% (33% [15/45] vs. 65% [17/26], P=0.013). Low admission SBP independently predicted 1-year all-cause mortality (adjusted hazard ratio: 2.41, 95% confidence interval: 1.04–5.57, P=0.033).

**Conclusions:** Low admission SBP is associated with significantly higher 1-year all-cause mortality in patients hospitalized for ADHF due to AS. (Circ J 2014; 78: 2455–2459)

**Key Words:** Acute decompensated heart failure; All-cause mortality; Aortic stenosis; Blood pressure

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Systolic blood pressure (SBP) on admission has emerged as a predictor of outcomes in patients with acute decompensated heart failure (ADHF). Most studies have shown an inverse relationship between SBP and mortality. Aortic stenosis (AS) is a major cause of ADHF and the most common valvular heart disease in elderly patients; it affects 4.6% of adults older than 75 years of age. However, the relationship between admission SBP and outcomes in patients hospitalized for ADHF due to AS is unclear, and we aimed to clarify that relationship in this study.

**Study Population**

A total of 107 consecutive patients were evaluated. They had been admitted to the coronary care unit of Kurashiki Central Hospital to be treated for ADHF due to moderate to severe AS (maximal jet velocity ≥3 m/s or aortic valve area [AVA] <1.5 cm²) between January 2006 and May 2012. We excluded 21 patients with ADHF due to acute coronary syndrome, 21 patients who had undergone aortic valve replacement, and 7 patients who were lost to follow-up during the 1-year study period. A total of 71 patients were included in the final analysis (Figure 1).

**Echocardiographic Evaluation**

All patients underwent 2-dimensional echocardiography and Doppler color flow imaging during the index hospitalization. Maximal jet velocity was recorded using the apical, right parasternal or suprasternal window that yielded the highest velocity signal. AVA was obtained by the standard continuity equation or planimetry. Moderate AS was defined as maximal jet velocity of 3–4 m/s or AVA of 1–1.5 cm² and severe AS was defined as maximal jet velocity ≥4 m/s or AVA ≤1 cm² based on the ACC/AHA guidelines. For the present analysis, we used a left ventricular ejection fraction (LVEF) cut-off of 50% to...
differentiate reduced LVEF from preserved LVEF.\textsuperscript{9–13}

Clinical Data and Follow-up

Demographic clinical data were obtained from medical records and included age, sex, New York Heart Association (NYHA) functional class, admission and discharge vital signs (heart rate, SBP, and diastolic blood pressure [DBP]), concomitant diseases (hypertension [blood pressure ≥140/90 mmHg or a history of hypertension and being on antihypertensive medications], dyslipidemia, diabetes mellitus, atrial fibrillation/flutter, ischemic heart disease [history of angina pectoris, myocardial infarction, angiographic evidence of coronary artery disease, coronary intervention, or coronary artery bypass surgery], chronic obstructive pulmonary disease, cancer, history of hemodialysis, history of cerebral infarction), and admission laboratory values (hemoglobin level and serum sodium level) on admission. For chronic kidney disease, the estimated glomerular filtration rate (eGFR) was calculated on the basis of serum creatinine level on admission, age, and sex using the simplified Modification of Diet in Renal Disease equation.\textsuperscript{14} We used the Society of Thoracic Surgeons (STS) risk score for risk quantification. The clinical characteristics and concomitant diseases were assessed on the basis of independent physician assessment. The patients were followed up with clinical follow-up data being obtained either in person or by telephone interviews. The primary endpoint of the study was 1-year all-cause mortality.

Statistical Analysis

Categorical variables are presented as number or percent, and they were compared by $\chi^2$ test or Fisher’s exact test as appropriate. Continuous variables are presented as mean±standard deviation for variables with a normal distribution and as median and interquartile range for variables with a non-normal distribution. Comparisons between groups of continuous variables were made on the basis of the distribution using the t-test or Wilcoxon’s rank-sum test. Low admission SBP was defined as <120 mmHg in several previous studies, and the cut-off value of admission SBP calculated using the receiver-operating characteristic curve (area under the curve [AUC]=0.75) was 121 mmHg.\textsuperscript{1,3,4} Therefore, low admission SBP in this study was defined as <120 mmHg. Survival analysis was performed using the Kaplan-Meier method, and differences between groups were tested using the log-rank test. To determine the independent predictors of all-cause mortality during the 1-year period, a Cox proportional hazards model was used to estimate the risk associated with the following variables: low admission SBP, admission DBP, admission eGFR, STS risk score, and reduced LVEF. Variables for which probability values were

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Patient population. ADHF, acute decompensated heart failure; AS, aortic stenosis.}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Kaplan-Meier curve of cumulative survival based on the admission systolic blood pressure in patients with acute decompensated heart failure due to moderate to severe aortic stenosis.}
\end{figure}
Low Admission SBP in ADHF Due to AS

### Results

**Baseline Patient Characteristics**
The patients included 50 women (70%) and 21 men (30%), with a mean age of 85±7 years. All patients were in NYHA functional class III (13 patients) or IV (58 patients). There were 16 patients (23%) with moderate AS and 55 patients (77%) with severe AS. The median STS risk score was 11.9 (7.4; 16.6), which is a high value. Mean admission SBP was 139±42 mmHg, admission DBP was 75±24 mmHg, and 75±13 beats/min, respectively, and low admission SBP was recorded for 28 patients (39%). The most common concomitant diseases were hypertension (62 patients, 87%) and ischemic heart disease (31 patients, 44%). Mean admission hemoglobin level was 10.9±2.2 mg/dl, mean admission serum sodium level was 138±4 mmol/L, and mean admission eGFR was 37.7±22.1 ml·min⁻¹·1.73 m⁻². Reduced LVEF was observed in 26 patients (39%). Average maximal jet velocity was 3.6±0.9 m/s and mean AVA was 0.79±0.28 cm². Reasons for nonsurgical management were difficult to establish for many of the patients in view of the retrospective nature of the study. Some of the prominent reasons included patient refusal, high surgical risk, and noncardiac comorbidities such as dementia, cancer, and physical debility.

### Survival Analyses: (1) Admission SBP <120 mmHg or ≥120 mmHg and (2) Survival Difference During the 1-Year Period

During a median follow-up period of 491 (148; 1019) days, 46 (62%) of the 71 patients died. During the index hospitalization, 8 of the 71 patients died. During the 1-year period, 26 (37%) of the 71 patients died; 10 (23%) of the patients with SBP ≥120 mmHg and 16 (57%) of the patients with SBP <120 mmHg died (log-rank P=0.0065, Figure 2). Table I shows the results of a comparison of the patients who survived and those who died during the 1-year period. Univariate analysis showed that there were significant differences between patients who survived and those who died in STS risk score (10.5 [6.4; 15] vs. 13.5 [11.5; 20.8], P=0.008), admission SBP (152±43 vs. 116±32 mmHg, P<0.001), admission DBP (80±26 vs. 67±17 mmHg, P=0.026), admission eGFR (43.2±20.3 vs. 28.2±22 ml·min⁻¹·1.73 m⁻², P=0.005), and reduced LVEF <0.10 in the univariate analysis and for which proportional assumptions were generally fair were included in the multivariate analysis. Differences were considered statistically significant at P<0.05. All analyses were performed using a statistical software package (JMP 7, SAS Institute, Cary, NC, USA).
Causes of Death

Table 4 shows the causes of death; cardiac-related causes in 73% of the patients who died during the 1-year period and non-cardiac causes in 12% of the patients. For the remaining 15%, the cause was unknown. Thus, cardiac death accounted for nearly three-quarters of the total deaths.

Discussion

The results of our analysis indicated that low admission SBP is a strong and independent predictor of all-cause mortality in patients hospitalized for ADHF due to AS. Earlier studies conducted in patients with chronic and acute HF suggested an inverse relationship between low admission SBP and outcomes.1–3 However, there have been few studies in which the relationship between admission SBP and mortality in patients with ADHF due to AS was analyzed. In the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) registry, low admission SBP was identified as a predictor of short-term mortality despite medical therapy in patients with HF.3 Fonarow et al reported a lower risk of in-hospital mortality in patients with ADHF who had admission SBP >115 mmHg from the Acute Decompensated Heart Failure National Registry (ADHERE).2 However, which factor led to a better prognosis – onset with etiology of SBP elevation on admission or capability of SBP elevation in the acute phase – remained to be elucidated. Admission SBP can effectively identify a group of patients that differ with respect to clinical characteristics, prognosis, and perhaps underlying pathophysiology. On the other hand, it is noteworthy that there was no difference in discharge SBP between patients who survived and those who died during the 1-year period. It remains unclear why patients with both ADHF due to AS and low admission SBP have a dismal prognosis. 

(33% [15/45 patients] vs. 65% [17/26], P=0.013). There was no difference in admission SBP between the reduced LVEF and preserved LVEF groups (134±40 vs. 143±44 mmHg, P=0.36). In addition, there was no difference in reduced LVEF between patients with SBP ≥120 mmHg and those with SBP <120 mmHg (16/28 [57%] vs. 16/43 [37%], P=0.14). There were no significant differences in discharge SBP (117±19 vs. 110±18 mmHg, P=0.15), AVA (0.8±0.3 vs. 0.76±0.24 cm², P=0.58), maximal jet velocity (3.7±0.9 vs. 3.5±1 m/s, P=0.47), and concomitant diseases. Multivariate adjustment analysis showed that low admission SBP (hazard ratio [HR], 2.41; 95% confidence interval [CI] 1.07–5.67, P=0.033), admission eGFR (HR, 0.97; 95% CI 0.95–0.99, P=0.008), and reduced LVEF (HR, 3.24; 95% CI 1.44–7.77, P=0.004) were independent predictors of all-cause mortality during the 1-year period (Table 2). There was no difference in medications at discharge between patients with SBP ≥120 mmHg and those with SBP <120 mmHg (Table 3).

Abbreviations as in Table 1.

Table 2. Univariate and Multivariate Analyses of Predictors of 1-Year All-Cause Mortality in Patients With ADHF Due to Moderate to Severe AS

<table>
<thead>
<tr>
<th>Cause</th>
<th>Univariables</th>
<th>Multivariables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low SBP on admission (&lt;120 mmHg)</td>
<td>3.37 (1.55–7.71) 0.002</td>
<td>2.41 (1.07–5.67) 0.033</td>
</tr>
<tr>
<td>DBP on admission</td>
<td>0.98 (0.96–0.997) 0.023</td>
<td>0.97 (0.95–0.99) 0.008</td>
</tr>
<tr>
<td>eGFR on admission</td>
<td>0.97 (0.95–0.99) 0.004</td>
<td>0.97 (0.95–0.99) 0.008</td>
</tr>
<tr>
<td>STS risk score</td>
<td>1.05 (1.01–1.09) 0.009</td>
<td>1.05 (1.01–1.09) 0.009</td>
</tr>
<tr>
<td>Reduced LVEF (&lt;50%)</td>
<td>3 (1.35–6.97) 0.007</td>
<td>3.24 (1.44–7.77) 0.004</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

Table 3. Medications at Discharge of Patients With ADHF Due to Moderate to Severe AS

<table>
<thead>
<tr>
<th>Medications</th>
<th>All patients (n=63)</th>
<th>&lt;120 mmHg (n=23)</th>
<th>≥120 mmHg (n=40)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI, n (%)</td>
<td>10 (16)</td>
<td>2 (9)</td>
<td>8 (20)</td>
<td>0.47</td>
</tr>
<tr>
<td>ARB, n (%)</td>
<td>24 (39)</td>
<td>6 (27)</td>
<td>18 (45)</td>
<td>0.19</td>
</tr>
<tr>
<td>β-blocker, n (%)</td>
<td>11 (18)</td>
<td>3 (14)</td>
<td>8 (20)</td>
<td>0.73</td>
</tr>
<tr>
<td>Spironolactone, n (%)</td>
<td>27 (44)</td>
<td>11 (50)</td>
<td>16 (40)</td>
<td>0.59</td>
</tr>
<tr>
<td>Furosemide-equivalent diuretic, n (%)</td>
<td>51 (82)</td>
<td>19 (86)</td>
<td>32 (80)</td>
<td>0.73</td>
</tr>
<tr>
<td>Statin, n (%)</td>
<td>19 (31)</td>
<td>6 (27)</td>
<td>13 (33)</td>
<td>0.78</td>
</tr>
</tbody>
</table>

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker. Other abbreviations as in Table 1.

Table 4. Causes of Death During the 1-Year Study Period of Patients With ADHF Due to Moderate to Severe AS

<table>
<thead>
<tr>
<th>Cause</th>
<th>No. of deaths (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>19 (73)</td>
</tr>
<tr>
<td>Congestive HF</td>
<td>15 (58)</td>
</tr>
<tr>
<td>Sudden cardiac death</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Noncardiac</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Infection</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Cancer</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (15)</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.
al suggested that patients with greater functional cardiovascular reserve (ie, “vascular failure”) have increased sympathetic tone and fluid redistribution, and they usually present with high SBP, abrupt onset of symptoms, and pulmonary congestion. On the other hand, patients with “cardiac failure” have low or normal SBP on admission, progressive onset of symptoms, and significant systemic congestion. In the present study, patients with low admission SBP might have had low cardiac output. Left ventricular systolic dysfunction with reduced LVEF or small ventricular volumes with left ventricular hypertrophy and preserved LVEF may contribute to low cardiac output in patients with ADHF due to AS. However, there was no difference in the admission SBP between the reduced LVEF and preserved LVEF groups. If cardiac output could be compared, there might be a difference; however, it was not clarified in the present retrospective study. In order to clarify why higher admission SBP leads to lower mortality in patients with ADHF due to AS, more detailed examination by using an index obtained from right heart catheterization or echocardiographic examination is needed.

Earlier studies conducted in patients with AS suggested that the mortality rate in this cohort dramatically increases after the onset of HF. In our study, which was conducted in patients with ADHF due to AS, the mortality rate during the 1-year study period (37%) was considerably high. Our results might have been affected by the characteristics of the patients, who were elderly (mean age 85 ± 7 years) with various concomitant diseases. However, nearly three-quarters of the patients died of cardiogenic causes. Therefore, appropriate selection of treatment modalities for AS may reduce the mortality rate of patients with ADHF due to AS. Although low SBP on admission is a simple prognostic predictor, it is useful.

Study Limitations
The main limitation of the present study is its retrospective design, which is prone to inherent bias. In addition, the number of patients was small.

Conclusions
Low SBP (<120 mmHg) on admission is associated with significantly higher 1-year all-cause mortality in patients hospitalized for ADHF due to AS.

Acknowledgments
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Disclosures
None.

References