Clinical Implications of Oral Assessment in Elderly Patients with Acute Heart Failure: A Single-center, Retrospective Study

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Abstract

**Background:** Oral health problems are common and are associated with various geriatric conditions in older adults. The importance of oral health has not been fully highlighted in the assessment and management of patients with heart failure. Here, we investigated the clinical implications of oral assessment in elderly patients with acute heart failure.

**Methods:** We evaluated oral health using the revised oral assessment guide in 77 patients aged 65 years or older who were admitted to hospital for acute heart failure. Poor oral health was defined as a revised oral assessment guide score $\geq 9$.

**Results:** Poor oral health was identified in 66.2% of the patients. Patients with poor oral health had high prevalence of decreased physical function, undernutrition, and cognitive impairment. A reduction in the Barthel Index, as an indicator of activities of daily living during hospitalization, was significant in the enrolled patients. The Barthel Index decreased more in patients with poor oral health than those with normal oral health. Furthermore, the revised oral assessment guide score on admission was found to be the only independent predictor of changes in the Barthel Index during hospitalization in the multivariate regression analyses.

**Conclusions:** Oral assessment using the revised oral assessment guide during hospitalization could provide useful information for the management of elderly heart failure patients.

**Trail registration:** Patients were retrospectively registered.

**Background**

The incidence and prevalence of heart failure (HF) increase with age [1] [2] [3] [4]. HF is the most common cause of hospitalization in patients aged 65 years or older. Hospitalization for HF is a significant public health problem, especially in elderly patients, because it is associated with higher rates of mortality, repeated re-hospitalization, and decline in physical activity, compared to that in younger patients [5] [6] [7] [8].

Elderly HF patients generally have complex comorbidity profiles, including not only comorbid diseases but also geriatric conditions [3] [9] [10]. These complex and diverse profiles are associated with poor prognosis of HF and increase the burden on health care services after discharge [11] [12]. Thus, a multidisciplinary approach, as well as medical treatment, is becoming important for the management of elderly patients with HF.

Oral health problems, like dry mouth, periodontal disease, dental caries, and inappropriate dentures, are common health conditions in older adults [13] [14]. Previous studies have demonstrated the association between poor oral health and various geriatric conditions, such as frailty, undernutrition, and cognitive impairment [15] [16] [17] [18]. However, the importance of oral health care has not been fully highlighted.
in the assessment and management of HF patients. In the present study, we investigated the clinical implications of oral assessment in elderly patients with acute HF.

**Methods**

**Study population**

Patients admitted to Anjo Kosei Hospital for the treatment of HF between October 2018 and March 2019 were reviewed. All patients were diagnosed with HF using the Framingham criteria [19]. We enrolled 77 patients aged 65 years and older who underwent oral assessment during hospitalization.

A medical history was obtained to document past medical history, medications, and co-morbid disease. Hypertension was defined as systolic blood pressure (BP) $\geq 140$ mmHg or diastolic BP $\geq 90$ mmHg on repeated measurements, or receipt of antihypertensive treatment. Diabetes mellitus was defined as having a blood hemoglobin A1c $\geq 6.5\%$, 2-hour value $\geq 200$ mg/dL ($\geq 11.1$ mmol/L) on a 75 g oral glucose tolerance test, and/or taking glucose-modulating medication according to the diagnostic criteria of the Japan Diabetes Society [20].

**Oral assessment**

Oral health was assessed by a certified dysphagia nurse using the revised oral assessment guide (ROAG) [21]. ROAG includes eight categories: voice, lips, mucous membranes, tongue, gums, teeth/dentures, saliva, and swallowing. Each category was described and rated from healthy (score 1) to severe (score 3). The total score ranged from eight, representing a normal oral health, to twenty-four, which represents severe oral health problems. The ROAG score was obtained within 1 week of hospitalization when the patient's respiratory state was stabilized without the need for oxygen. In the present study, patients with ROAG scores of 8 were regarded to have a normal oral health and those with higher scores were regarded as having poor oral health.

**Assessments for geriatric conditions**

Physical functional status was evaluated using the Barthel Index (BI), handgrip, and 10-meter gait speed. The BI was obtained by ward nurses at admission and at discharge, as previously reported [8]. Changes in the BI were calculated as the difference between the BI on admission and the BI on discharge. Handgrip and 10-meter gait speed were evaluated by physical therapists before discharge.

Registered dieticians assessed nutritional status. Nutritional status was screened using the controlling nutritional status (CONUT) score and the geriatric nutritional risk index (GNRI) [22] [23]. Laboratory data at admission and body mass index (BMI) at the first measurement within 72 hours of hospitalization were used for calculation of the scores. Dietary energy intake was assessed by the proportion of
nutritional intake from food compared to the predicted calorie requirement. Nutritional intake was calculated based on the food intake for 3 days around the day of oral assessment. The predicted calorie requirement was defined as the total energy expenditure estimated from the Harris-Benedict equation [24].

Pharmacists assessed cognitive function using the mini-mental state examination (MMSE) [25].

**Biomarker analysis and echocardiography**

Blood samples were obtained at the time of hospital admission. Complete blood counts were performed utilizing a Sysmex XE-5000 analyzer (Sysmex, Kobe, Japan). Plasma brain natriuretic peptide (BNP) was measured with the AIA-2000 enzymatic immunoassay analyzer (TOSOH, Tokyo, Japan). Other biomarkers were measured using a LABOSPECT 008 autoanalyzer (Hitachi Co., Tokyo, Japan). Estimated glomerular filtration rate (eGFR) was calculated by the Modification of Diet in Renal Disease formula [26]. Echocardiographic examination was performed by an experienced sonographer using Vivid E9 with XD clear (GE Healthcare, Tokyo, Japan). The images were recorded in a console and analyzed offline. Left ventricular ejection fraction was calculated using the modified Simpson’s rule.

**Statistical analysis**

All analyses were performed using PASW Statistics 21 software (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as the mean ± standard deviation or median (interquartile range). Categorical variables were presented as the count and/or percentage. The student’s t-test or Mann-Whitney U-test was used for group comparisons. Univariate correlations between changes in the BI during hospitalization and other variables were investigated using the Pearson’s rank correlation test, and then a multiple linear regression analysis was performed. Variables with P < 0.05 in the univariate analyses were incorporated into the multivariable model. In all analyses, P < 0.05 was considered statistically significant.

**Results**

**Baseline characteristics**

Baseline characteristics of the patients are shown in Table 1. The mean age of patients was 80.0 ± 9.1 years, and 58.4% of patients were men. The mean ROAG score was 9.9 ± 2.2. Poor oral health (ROAG score ≥ 9) was identified in 66.2% of the enrolled patients. Details of ROAG evaluations are shown in Table S1.

Patients were divided into two groups based on the ROAG score: a normal oral health group (ROAG score = 8, n = 26) and a poor oral health group (ROAG score ≥ 9, n = 51) (Table 1). Patients with poor oral health were older and had lower albumin levels. C-reactive protein levels were higher in patients with poor oral health than in those with normal oral health. There were no significant differences in gender, BMI,
history of HF, etiology of coronary arterial disease (CAD) and stroke, prevalence of hypertension, diabetes and atrial fibrillation, renal function, hemoglobin, sodium, BNP level, left ventricular ejection fraction, and the use of medications on admission between two groups (Table 1).
Table 1
Baseline characteristics of enrolled patients

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 77)</th>
<th>Normal oral health (n = 26)</th>
<th>Poor oral health (n = 51)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROAG score</td>
<td>9.9 ± 2.2</td>
<td>8</td>
<td>10.9 ± 2.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>80.0 ± 9.1</td>
<td>73.8 ± 8.3</td>
<td>83.1 ± 7.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>45 (58.4%)</td>
<td>19 (73.1%)</td>
<td>26 (51.0%)</td>
<td>0.063</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>22.2 ± 3.9</td>
<td>23.1 ± 4.6</td>
<td>21.7 ± 3.5</td>
<td>0.159</td>
</tr>
<tr>
<td>History of admission due to HF</td>
<td>35 (45.5%)</td>
<td>14 (53.8%)</td>
<td>21 (41.2%)</td>
<td>0.291</td>
</tr>
<tr>
<td>History of CAD</td>
<td>26 (33.8%)</td>
<td>8 (30.8%)</td>
<td>18 (35.3%)</td>
<td>0.691</td>
</tr>
<tr>
<td>History of stroke</td>
<td>11 (14.3%)</td>
<td>3 (11.5%)</td>
<td>8 (15.7%)</td>
<td>0.623</td>
</tr>
<tr>
<td>Hypertension</td>
<td>65 (84.4%)</td>
<td>21 (80.8%)</td>
<td>44 (86.3%)</td>
<td>0.529</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>29 (37.7%)</td>
<td>7 (26.9%)</td>
<td>22 (43.1%)</td>
<td>0.165</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>36 (46.8%)</td>
<td>13 (50.0%)</td>
<td>23 (45.1%)</td>
<td>0.683</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>11.5 ± 2.3</td>
<td>12.1 ± 2.7</td>
<td>11.1 ± 2.0</td>
<td>0.072</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>0.84 (0.17–2.54)</td>
<td>0.25 (0.13–0.86)</td>
<td>1.24 (0.28–4.19)</td>
<td>0.009</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.4 ± 0.5</td>
<td>3.6 ± 0.5</td>
<td>3.3 ± 0.5</td>
<td>0.014</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.60 ± 1.02</td>
<td>1.69 ± 1.20</td>
<td>1.56 ± 0.92</td>
<td>0.580</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>40.0 ± 20.6</td>
<td>42.5 ± 22.7</td>
<td>38.7 ± 19.5</td>
<td>0.446</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
<td>139.9 ± 3.5</td>
<td>139.0 ± 3.7</td>
<td>140.3 ± 3.4</td>
<td>0.128</td>
</tr>
<tr>
<td>BNP (pg/mL)</td>
<td>805.0 (502.4–1304.8)</td>
<td>992.0 (415.5–1687.2)</td>
<td>732.8 (531.9–1101.0)</td>
<td>0.598</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>44.2 ± 17.4</td>
<td>39.7 ± 16.6</td>
<td>46.7 ± 17.5</td>
<td>0.106</td>
</tr>
<tr>
<td>Medications on admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors/ARBs</td>
<td>31 (40.3%)</td>
<td>12 (46.1%)</td>
<td>19 (37.3%)</td>
<td>0.451</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>41 (53.2%)</td>
<td>16 (61.5%)</td>
<td>25 (49.0%)</td>
<td>0.298</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>32 (41.6%)</td>
<td>11 (42.3%)</td>
<td>21 (41.2%)</td>
<td>0.360</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>45 (58.4%)</td>
<td>15 (57.7%)</td>
<td>30 (58.8%)</td>
<td>0.924</td>
</tr>
</tbody>
</table>
Association between oral health and geriatric assessments on admission

We examined the association between oral health and common geriatric assessments on admission. Barthel Index, handgrip strength, GNRI, dietary energy intake, and MMSE were significantly lower in the poor oral health group than in the normal oral health group. The COUNT score was significantly higher in patients with poor oral health than those with normal oral health (Table 2). There were no significant differences between the groups in gait speed for the 10-meter walk. Thus, patients with poor oral health showed a higher prevalence of decreased physical function, undernutrition, and cognitive impairment.

Table 2
Geriatric assessment

<table>
<thead>
<tr>
<th></th>
<th>Normal oral health (n = 26)</th>
<th>Poor oral health (n = 51)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barthel Index at admission</td>
<td>96.0 ± 9.8</td>
<td>76.6 ± 30.8</td>
<td>0.004</td>
</tr>
<tr>
<td>Handgrip (kg)</td>
<td>20.2 ± 8.7</td>
<td>14.5 ± 6.6</td>
<td>0.040</td>
</tr>
<tr>
<td>Gait speed for 10-meter walk (sec)</td>
<td>14.8 ± 6.2</td>
<td>19.5 ± 7.5</td>
<td>0.069</td>
</tr>
<tr>
<td>CONUT score</td>
<td>4.3 ± 2.9</td>
<td>5.7 ± 2.8</td>
<td>0.045</td>
</tr>
<tr>
<td>GNRI</td>
<td>98.1 ± 14.3</td>
<td>87.0 ± 9.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Dietary energy intake (%)</td>
<td>89.6 ± 18.7</td>
<td>67.5 ± 32.3</td>
<td>0.002</td>
</tr>
<tr>
<td>MMSE</td>
<td>27.4 ± 2.4</td>
<td>25.2 ± 3.4</td>
<td>0.047</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation (SD). Bold type indicates statistical significance. CONUT, controlling nutritional status; GNRI, geriatric nutritional risk index; MMSE, mini-mental state examination.
Association between ROAG score and activities of daily living (ADL) preservation

Efforts to preserve patients’ ability to perform ADL during hospitalization are important in the management of acute heart failure. The BI has been reported as a common tool to evaluate the ability to perform ADL. Here, we investigated the changes in the BI during hospitalization. The actual BI values on admission and discharge, and the BI changes in each group are shown in Table 3. Reduction in the BI during hospitalization was significant in the enrolled patients in both the normal oral health group and poor oral health group (P < 0.01). Of note, the BI decreased more in patients with poor oral health than those with normal oral health (P < 0.01).

Table 3
Changes in the Barthel index during hospitalization

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 77)</th>
<th>Normal oral health (n = 26)</th>
<th>Poor oral health (n = 51)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barthel Index at admission</td>
<td>82.9 ± 27.4</td>
<td>96.0 ± 9.8</td>
<td>76.6 ± 30.8</td>
<td>0.004</td>
</tr>
<tr>
<td>Barthel Index at discharge</td>
<td>77.4 ± 32.3</td>
<td>93.5 ± 12.8</td>
<td>67.9 ± 36.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Changes in Barthel Index</td>
<td>-7.4 ± 18.1</td>
<td>-1.2 ± 6.6</td>
<td>-11.0 ± 21.5</td>
<td>0.036</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation (SD). Bold type indicates statistical significance.

Finally, to determine factors associated with ADL preservation during hospitalization in elderly patients with acute HF, we compared the clinical parameters on admission that were associated with the change in the BI during hospitalization using univariate and multivariate regression analyses. Changes in the BI during hospitalization were significantly correlated with age, hemoglobin levels, ROAG score, GNRI, and dietary energy intake on admission in the univariate regression analysis. Of those, ROAG score on admission was the only independent predictor of changes in the BI during hospitalization in the multivariate regression analyses (Table 4).
Table 4
Independent predictors of change in the Barthel index based on linear regression analyses.

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>multivariate</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>P-value</td>
<td>β</td>
<td>P-value</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.357</td>
<td>0.004</td>
<td>-0.175</td>
<td>0.219</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Male sex</td>
<td>-0.150</td>
<td>0.233</td>
<td></td>
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<tr>
<td>Body mass index</td>
<td>0.128</td>
<td>0.327</td>
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<tr>
<td>History of admission due to HF</td>
<td>0.102</td>
<td>0.420</td>
<td></td>
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<tr>
<td>Atrial fibrillation</td>
<td>0.080</td>
<td>0.527</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Hemoglobin</td>
<td>0.249</td>
<td>0.046</td>
<td>0.060</td>
<td>0.629</td>
<td></td>
<td></td>
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<tr>
<td>Log CRP</td>
<td>-0.183</td>
<td>0.165</td>
<td></td>
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<tr>
<td>Albumin</td>
<td>0.114</td>
<td>0.365</td>
<td></td>
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<tr>
<td>eGFR</td>
<td>0.062</td>
<td>0.622</td>
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<tr>
<td>Sodium</td>
<td>-0.034</td>
<td>0.787</td>
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<tr>
<td>Log BNP</td>
<td>0.047</td>
<td>0.710</td>
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<tr>
<td>ROAG score</td>
<td>-0.421</td>
<td>&lt; 0.001</td>
<td>-0.307</td>
<td>0.042</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Barthel Index at admission</td>
<td>0.080</td>
<td>0.524</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Handgrip</td>
<td>0.313</td>
<td>0.087</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gait speed for 10-meter walk</td>
<td>-0.282</td>
<td>0.124</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CONUT score</td>
<td>-0.210</td>
<td>0.098</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GNRI</td>
<td>0.276</td>
<td>0.034</td>
<td>0.106</td>
<td>0.431</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dietary energy intake</td>
<td>0.329</td>
<td>0.008</td>
<td>0.003</td>
<td>0.979</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>MMSE</td>
<td>0.154</td>
<td>0.810</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Bold type indicates statistical significance. HF, heart failure; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; BNP, brain natriuretic peptide; ROAG, revised oral assessment guide; CONUT, controlling nutritional status; GNRI, geriatric nutritional risk index; MMSE, mini-mental state examination.

Discussion

The major findings of this study were as follows: 1) poor oral health, assessed using the ROAG score, is relatively common in elderly patients with acute HF; 2) patients with poor oral health had significantly
more geriatric conditions than those with normal oral health, and 3) the ROAG score was independently correlated with changes in the BI during hospitalization in elderly patients with acute HF.

Oral health problems have been reported as common health conditions in older adults and hospitalized patients [17] [18] [27] [28]. Several points are known about the relationship between oral health problems and heart failure. Chronic inflammation caused by periodontal diseases is a risk factor for cardiac and cerebrovascular diseases, which are the most major comorbidities of HF [29] [30]. General fatigue, dyspnea, delirium, and sleep disturbance accompanied by decompensated HF might contribute to reducing adherence to oral hygiene. In addition, dry mouth is often a consequence of polypharmacy, particularly as a side effect of cardiovascular agents (angiotensin-converting enzyme inhibitors, beta-blockers, and diuretics) [31] [32]. However, oral health has been underrecognized in the assessment and management of patients with HF. Our data suggests the importance of oral assessment in the multidisciplinary management of elderly HF patients because poor oral health is highly prevalent and significantly associated with decline in physical function during hospitalization.

We have previously demonstrated that hospitalization for HF was significantly correlated with decreased BI as an assessment of ADL, and a decreased BI during hospitalization was associated with worse clinical outcomes [8]. It has also been reported that a decline in ADL due to acute HF is an independent risk factor of hospitalization for HF and mortality [33]. Therefore, it is important to identify predictors of ADL decline during hospitalization in patients with HF. It has been demonstrated in elderly patients and patients with HF that age and the nutritional index are associated with ADL decline during hospitalization [33] [34]. Our present study involving elderly patients with HF has shown that the ROAG score serves as a good predictor of changes in ADL, and its predictive ability is comparable to age, nutritional indices, and various other parameters. Therefore, oral assessment of patients with HF using the ROAG score to screen for poor oral health may allow us to provide comprehensive care and rehabilitation to patients with poor oral health at an earlier stage. This may help prevent ADL decline during hospitalization for HF, leading to a better prognosis.

In the present study, nutritional status, assessed by CONUT and GNRI, was worse in the poor oral health group than in the normal oral health group. Furthermore, patients with poor oral health had lower dietary energy intake. Previous studies have demonstrated that poor oral health is associated with periodontal disease, dental caries, hyposalivation, and tooth loss or edentulousness, which pose risks of chewing difficulties, decreased masticatory function, and dysphagia [35] [36]. These oral problems may induce a preference for soft and easily chewable food and a need for changes in food texture to prevent aspiration and choking, leading to poor nutritional intake and undernutrition, and finally to sarcopenia, frailty, and decreased physical function [17] [37] [38].

In the acute setting of decompensated HF, nurses have a pivotal role in oral assessment and care, because of the small number of dentists and oral hygienists. Several oral health assessment tools have been developed for non-dental health care professionals [21] [39] [40]. Among these indices, the ROAG is not only a simple and comprehensive assessment but it also has favorable validity and reliability [41].
Oral assessment in patients with acute HF might have several influences on multidisciplinary disease management. First, patients who require consultation with in-hospital or regional dental health care professionals are screened. Second, nurses receive feedback on oral care from their patients. Third, oral care is one of the fundamental self-care activities after discharge, and thus, the information that an oral assessment provides is useful for educating patients on dental health compliance. Forth, several management strategies could be considered for patients with poor oral health. Nutritionists and dietitians could help to increase the dietary intake of the patients by changing meal content and food texture. Doctors and pharmacists could choose orally disintegrating tablets for the ease of taking medicines. Although the efficacy of multidisciplinary interventions for patients with poor oral health has not been fully elucidated, we believe that oral assessment could provide useful information for the multidisciplinary management of elderly patients with HF.

The present study had several limitations. First, this was a single-center, retrospective study, and the sample size was relatively small. Future prospective studies are necessary with larger patient populations. Second oral health was assessed by only one certified dysphagia nurse. Hence, the results could not be generalized to the routine assessment by ward nurses.

**Conclusions**

Poor oral health, as assessed by the ROAG, is highly prevalent and oral assessment using the ROAG predicts a decline in physical function during hospitalization in elderly patients with acute HF. Thus, oral assessment during hospitalization could provide useful information for the management of elderly HF patients.

**Abbreviations**

HF: heart failure; BP: blood pressure; ROAG: revised oral assessment guide; BI: Barthel Index; CONUT: controlling nutritional status; GNRI: geriatric nutritional risk index; BMI: body mass index; MMSE: mini- mental state examination; BNP: brain natriuretic peptide; eGFR: estimated glomerular filtration rate; CAD: coronary arterial disease; ADL: activities of daily living

**Declarations**

**Ethics approval and consent to participate**

The study was approved by the ethics committee of Anjo Kosei Hospital (Approval No. R19-032). Because of its retrospective nature, informed consent was deemed unnecessary according to the national regulation issued by the Japanese Ministry of Health, Labour and Welfare. However, the present study was carried out by the opt-out method of our hospital website.

**Consent for publication**
Not applicable.

**Availability of data and materials**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Competing interests**

The authors declare that they have no competing interests.

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None.

**Authors' contributions**

Y.U., R.S., K.T., and S.I. conceived the study, designed the protocol, contributed to data collection and preparation, analyzed all data, wrote the manuscript and contributed to the interpretation of the results. H.I., A.N., and Y.K. conceived the study, designed the protocol, and contributed to the acquisition and interpretation of data. M.W. and T.M. were responsible for critical revision of the article for important intellectual content and approval of the final version.

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**References**


Supplementary Files

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