Management and 1 Year Outcome of Oldest-Old Hospitalized Heart Failure Patients: A Subacute Geriatric Hospital Survey

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ABSTRACT: Background: Guidelines are frequently under-implemented in older patients with heart failure. Octogenarians are often excluded from clinical trials. Objectives: To characterize the clinical profile of the oldest-old (age ≥ 80 years) heart failure patients hospitalized in a subacute geriatric hospital and to evaluate their management and 1 year outcome. Methods: Patient characteristics and in-hospital course were retrospectively collected. Diagnosis of heart failure was based mainly on clinical evaluation in addition to chest X-ray results and echocardiographic findings when available. Results: The study population comprised 96 consecutive unselected heart failure patients hospitalized from January to June 2003. The patients were predominantly women (67%), aged 85 ± 5 years, fully dependent or frail with a high rate of comorbidities. Adherence to guidelines and use of recommended heart failure medications were poor. Their 1 year mortality was 57%. According to logistic regression analysis the predictor of lower 1 year mortality was higher body mass index (odds ratio 0.86, 95% confidence interval 0.78–0.96), and the predictor of higher 1 year mortality was high urea levels (OR 1.04, 95% CI 1.02–1.06). Conclusions: Our study confirms that the management of oldest-old heart failure patients hospitalized in a subacute geriatric hospital was suboptimal and their mortality was exceptionally high.

KEY WORDS: heart failure, oldest-old, prognosis, mortality

In recent decades people in the western world are getting older and their characteristics are changing [1]. Heart failure is predominantly a disease of older people [1-4]. It is ultimately the most common hospital discharge diagnosis-related group in patients over the age of 65 years [1-4], affecting approximately 7% of those aged 75–84 and 15% of those aged 85 and older [2-5]. A variety of chronic diseases are more prevalent in the aging population than in younger subjects [2,4-6]. In the recent guidelines for diagnosis and management of heart failure, elderly patients were mentioned only briefly [3,7-11]. Older patients and elderly women in particular are often excluded from cardiovascular clinical trials. Therefore, strict application of contemporary evidence-based guidelines to this specific age group may not be appropriate since they do not account for the different characteristics and comorbidities of this population [12,13]. Elderly patients with heart disease and heart failure are frequently frail [14] and cognitively impaired [15], more likely to require home care, hospitalization or institutionalization, and suffer from increased mortality [16].

The diagnosis of heart failure may be more difficult to establish in elderly patients, since the typical symptoms, such as dyspnea and fatigue, may be related to aging, deconditioning, or to other comorbid conditions, such as anemia or depression [3,17,18]. Despite progress in the management of patients with heart failure and the established efficacy of guidelines and recommended medical therapy in reducing mortality and morbidity, data on the clinical characteristics, treatment, and outcome of very old heart failure patients who live in long-term acute care facilities are limited. It seems that in this group of oldest-old (age ≥ 80 years) patients with heart failure, therapeutic modalities are underutilized [1,3,16,18-21].

The purpose of the present study was to characterize the sociodemographic, functional and clinical profile of the oldest-old patients with heart failure hospitalized in a subacute geriatric hospital, and to evaluate their management and 1 year outcome.
PATIENTS AND METHODS

The study population comprised 96 consecutive unselected patients with either stable chronic heart failure or acute exacerbation of heart failure, who were hospitalized from January to June 2003 in the subacute wards of the Shoam Geriatric Hospital in Pardess Hana, Israel. This facility is a large community geriatric LTAC hospital, which includes post-acute care, rehabilitation, nursing, and skilled nursing departments. The study period chosen was in order to compare our results with those of the national survey of hospitalized heart failure patients in Israel (HFSIS 2003) that was conducted during March-April 2003 in all public hospitals [22,23].

Patient characteristics, in-hospital course and therapy details were retrospectively collected for the entire hospitalization period and recorded on prespecified forms. The diagnosis of heart failure was based mainly on clinical evaluation in addition to chest X-ray results and echocardiographic findings when available. The patients were followed for 1 year. Mortality data were obtained from hospital records, by direct telephone contacts with the patient’s families, or by matching their identification numbers with the Israeli National Population Registry.

STATISTICAL ANALYSIS
All variables are presented as mean and standard deviation. For the relationship of 1 year mortality with the various variables we used the independent t-test for continuous variables or Mann-Whitney test for continuous variables with abnormal distribution. For dichotomized variables we used the chi-square test or Fisher’s exact test when expected frequency was < 5. Logistic regression analysis was performed, including the clinical and laboratory variables selected in the univariate procedure which were significantly associated with 1 year mortality (P < 0.05), except for those with many missing values. The results are reported in terms of odds ratio with 95% confidence intervals.

RESULTS
The study population consisted of 96 consecutive patients aged 80 years and older diagnosed with heart failure who were hospitalized in a community geriatric LTAC from January to June 2003.

PATIENT CHARACTERISTICS
The cohort included 31 men (32%) and 65 women (68%). Their mean age was 85.4 ± 4.8 years (86.2 ± 5.7 for men and 85.0 ± 4.4 for women). The majority of them (n=51, 53%) were admitted to our hospital following hospitalization in a general hospital, 32 (33%) arrived from another long-term facility care, and only 13 (13%) from home. Sixty-five patients (68%) were widowed and 27 (28%) were married. In the year prior to the study the patients were hospitalized in a general hospital 1.85 ± 1.2 times [Table 1].

FUNCTIONAL STATUS
Prior to hospitalization most patients were debilitated, fully dependent in their basic activity of daily living, i.e., were chair-bound, incontinent and unable to feed themselves (55 patients, 56%). Additionally, over a third of them were frail and needed mild help in basic activity of daily living (37 patients, 38%). Only 6 patients (6%) were independent.

TYPE OF HEART FAILURE
Most patients had stable chronic heart failure (70 patients, 73%), and the rest experienced acute exacerbation of chronic heart failure (26 patients, 27%). No patient presented with acute de novo heart failure.

ETIOLOGY
As determined by medical evaluation, coronary artery disease was the most common cause of heart failure (55 patients, 57%), 31 (32%) had significant valvular disease, and 7 (7%) had non-ischemic cardiomyopathy.

PRECIPITATING CAUSE OF HEART FAILURE
These were infection (38 patients, 40%), worsening of valvular heart disease (n=28, 29%), arrhythmia (n=25, 26%), post-surgery (non-cardiac) (n=25, 26%), stroke (n=12, 12%), ischemia (n=4, 4%) and deep vein thrombosis/pulmonary emboli (n=3, 3%).
COMORBIDITY
Anemia (defined as hemoglobin ≤ 12 g/dl) (70 patients, 73%), hypertension (n=67, 70%), renal failure (creatinine ≥ 1.5 mg/dl) (n=57, 59%), diabetes mellitus (n=34, 35%), past stroke/transient ischemia attack (n=31, 32%), chronic obstructive pulmonary disease (n=18, 19%) and peripheral vascular disease (n=15, 16%) were the leading comorbidities. Twenty-eight patients (29%) had had prior myocardial infarction, and 13 (13%) had undergone coronary artery bypass graft surgery. Additionally, all patients suffered from cognitive impairment, dementia and/or depression.

KILLIP CLASS
We extended the use of Killip classification, originally applied to clinically characterize the severity of heart failure in acute myocardial infarction patients in their admission phase, and recorded in our heart failure study patients the highest Killip class throughout their entire hospitalization. The majority of patients (n=71, 72%) were classified as Killip class I (without pulmonary rales or third heart sound), 28 patients (29%) as Killip class II (rales < 50% of lung fields and/or third heart sound), 28 patients (29%) as Killip class I (without pulmonary rales or third heart sound), 28 patients (29%) as Killip class II (rales < 50% of lung fields and/or third heart sound), one patient as Killip III (pulmonary edema) and 8 patients (9%) as Killip IV (cardiogenic shock) [Table 2].

WEIGHT AND BMI
Average weight was 65.9 ± 12.9 kg (median 64.7, range 39–95 kg), height 158.1 ± 7.3 cm (median 160, range 138–176 cm) and BMI 26.5 ± 5.6 kg/m² (median 25.3, range 17.6–44.0)

ELECTROCARDIOGRAM
The index ECG of most patients (n=58, 60%) showed sinus rhythm. Atrial fibrillation was recorded on the ECG of 36 patients (37%). An additional 13 patients had intermittent (paroxysmal or persistent) AF. Overall, 49 patients (51%) had AF.

CHEST X-RAY
In 34 patients (35%) the chest X-ray or its interpretation was not available. The main finding among the 62 patients with available X-ray results was cardiomegaly (58 patients, 94%). Other radiographic findings were pulmonary congestion or edema, pleural effusion and pneumonia.

LABORATORY FINDINGS
The average hemoglobin was relatively low (10.8 ± 2.0 g/dl), hematocrit 31.9 ± 6.0%, with low iron level 39 ± 17 mg/dl. Urea 84 ± 51 mg/dl was elevated and creatinine clearance 40 ± 19 ml/min was reduced.

MEDICATIONS
The most frequently used drugs were antidepressants (85%), followed by furosemide (79%), aspirin (50%), enalapril (42%), beta-blockers (mainly atenolol, 36%), tranquilizers (32%), nitrates (30%), digoxin (26%), and spironolactone (21%). Less frequently used medications were anticoagulants (19%), calcium channel blockers (16%), amiodarone (12%), statins (12%), insulin (11%), clopidogrel (10%), thiazides (5%) and oral hypoglycemics (5%).

MORTALITY
Fifty-five patients (57%) died during the first year after their admission. Univariate analysis of patient subgroups showed that 1 year mortality was significantly higher in patients with the following characteristics: admitted from a long-term care facility; fully dependent; acute heart failure exacerbation; lower BMI; higher urea levels; lower hemoglobin, hematocrit, iron and cholesterol levels; and reduced creatinine clearance [Tables 1 and 2].

Logistic regression analysis of laboratory results, including the only significant variables associated with mortality in the univariate analysis, showed that only elevated urea (P = 0.009) and reduced creatinine clearance (P = 0.03) were associated with increased 1 year mortality. When the significant clinical variables (BMI, previous residence, functional status, type of heart failure) and laboratory results (urea, creatinine clear-

### Table 2. One-year clinical and laboratory subgroup mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Deceased</th>
<th>Alive</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>86.2 ± 4.7</td>
<td>79–95</td>
<td>84.7 ± 4.7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63.8 ± 13.6</td>
<td>39–95</td>
<td>68.7 ± 11.5</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>198 ± 7</td>
<td>145–176</td>
<td>157 ± 7</td>
</tr>
<tr>
<td>BMI</td>
<td>25.3 ± 5.3</td>
<td>17.6–41.3</td>
<td>28.0 ± 5.6</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>128.4 ± 29.8</td>
<td>53–195</td>
<td>130.1 ± 24.7</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>82.6 ± 12.8</td>
<td>42–120</td>
<td>67.4 ± 15.0</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>10.3 ± 1.9</td>
<td>7–15</td>
<td>11.6 ± 2.0</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>113 ± 62</td>
<td>49–380</td>
<td>121 ± 71</td>
</tr>
<tr>
<td>Creatinine clearance (ml/min)</td>
<td>32 ± 15</td>
<td>15–96</td>
<td>50 ± 19</td>
</tr>
<tr>
<td>Cholesterol* (mg/dl)</td>
<td>164 ± 85</td>
<td>67–501</td>
<td>183 ± 50</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>119 ± 65</td>
<td>49–336</td>
<td>126 ± 56</td>
</tr>
<tr>
<td>Thyroid-stimulating hormone (n=55)</td>
<td>6.8 ± 10.4</td>
<td>0.3–44.7</td>
<td>6.4 ± 10.9</td>
</tr>
<tr>
<td>Iron (n=34)</td>
<td>35 ± 16</td>
<td>12–74</td>
<td>52 ± 16</td>
</tr>
<tr>
<td>Vitamin B12 (n=48)</td>
<td>545 ± 394</td>
<td>38–1648</td>
<td>603 ± 321</td>
</tr>
</tbody>
</table>

* Independent t-test
** Mann-Whitney test
n = number of patients

BMI = body mass index
AF = atrial fibrillation
Heart failure in elderly patients is the frequent outcome of most cardiovascular diseases, such as hypertension, valvular disease, chronic ischemic heart disease, and following an acute myocardial ischemic event [19-21]. Additionally, aging is associated with reduced aortic and left ventricular compliance, with increased aortic impedance and abnormal LV diastolic function. These conditions lower the threshold for the development of heart failure when the heart is exposed to precipitating factors such as hypertension and/or atrial fibrillation [19,21].

The very old hospitalized heart failure patients in this study were more frequently female, usually with several comorbid conditions, such as renal failure, anemia, hypertension, diabetes mellitus, or status post-stroke or transient ischemic attack. Almost all patients suffered from moderate to severe mental deterioration, and the majority of them were frail or fully dependent. These characteristics are similar to those described among patients hospitalized in long-term acute care in other studies [1,12,13,21]. It should be emphasized that the clinical and outcome data of this very old patient population is less frequently reported, especially with regard to their long-term follow-up and outcome [12,13]. Recently Komajda et al. [21] described the clinical profile, outcomes and treatment of 741 octogenarians (median age 84 years), compared with those of 2836 younger patients (median age 68 years) hospitalized for heart failure who were enrolled in the Euro Heart Failure Survey II. The results of our study are in accordance with EHFS II. Octogenarians were more likely to be women and had a greater prevalence of hypertension, AF, and non-cardiac comorbidities, including stroke, anemia, and kidney dysfunction. Octogenarians in EHFS II were less likely to undergo investigations during hospitalization, with coronary angiography performed in only 17% of the elderly patients vs. 41% of the younger ones. The etiology of heart failure among our oldest-old patients was mainly coronary artery disease. Attending physicians in the present study also preferred to manage the patients conservatively, without additional evaluation of ischemia, whether non-invasively or by cardiac catheterization, unless performed in the previous general hospital. This conservative approach can be attributed to the low functional status of the study patients, and to the presence of comorbidities and multi-organ age-related physiologic alterations.

Similar to therapy administered to the elderly patients in EHFS II, underuse and underdosage of recommended heart failure medications were observed in our patient cohort [21]. Furosemide was frequently used in our patients to alleviate signs and symptoms of heart failure and to maintain their stable state (Killip class I). Angiotensin-converting enzyme inhibitors and aldosterone antagonists were used, but more cautiously. Angiotensin receptor blockers were not used at all. The use of beta-blockers was also less frequent, probably due to the high rates of or concern for conduction abnormalities or sick sinus syndrome, as well as hypotension which is frequently observed in very aged patients. Anticoagulants were used less often, although 51% had AF. As indicated in the recent AF guidelines [11], and despite the high rate of CHADS (Cardiac failure, Hypertension, Age, Diabetes, and Stroke [Doubled]) criteria, we frequently avoided using anticoagulation due to the high risk of bleeding complications and falls as well as the inability to safely sustain adjusted chronic anticoagulation, especially after discharge. The use of statins was low, despite the recommendation for their use without any age limit. However, evidence to support this recommendation is sparse since very old patients were either excluded or only a few of them were included in the large lipid-modifying studies [3,12,13].

There are limited data regarding optimal drug therapy for heart failure in old patients over age 80. Heart failure medications are of special concern, as polypharmacy may pose certain hazards such as hypotension, aggravating already disturbed renal function and precipitating falls and fractures. However, small studies and subgroup analysis in large clinical trials have demonstrated the safety and efficacy of standard therapy in oldest-old heart failure patients [1,3]. Many of the drugs used to treat heart failure show altered pharmacokinetics (i.e., digoxin) and pharmacodynamics (i.e., beta-blockers) in octogenarians, because of age-related changes in renal function.

In view of these potential adverse effects and the absence of clinical trials enrolling sufficient numbers of elderly patients, drugs like beta-blockers and ACEIs should usually be up-titrated slowly to a maximally tolerated dose, which is often lower than the "clinical trial target dose."

One year mortality among study patients hospitalized in a long-term acute care facility was very high (57%), despite the fact that the majority were stable and in Killip class I. Although 1 year mortality in EHFS II patients hospitalized in a general hospital was increased in octogenarians in comparison to younger patients (39% versus 24%, P < 0.001) [21], it was substantially lower than the rate observed among LTAC patients. It seems that this disparity in mortality rate is due to differences in the patients’ functional status of dependency. Functional status is a strong independent predictor of mortality, especially in the very old hospitalized population, and it seems to be associated with high mortality, probably irrespective of the severity of the heart failure or its existence at
all [14]. Other predictors of mortality were impaired kidney function and lower BMI, similar to other heart failure series among the elderly [3, 21, 22].

Cognitive impairment in heart failure is multifactorial, as both conditions have common risk factors, such as atherosclerosis, hypertension and diabetes mellitus [15]. Hemodynamic abnormalities, such as low cardiac output and hypotension, are associated with cognitive impairment in hospitalized patients. Dehydration and electrolyte disturbances, which often arise from excessive diuresis, can predispose to delirium. The impact of frailty and cognitive impairment in elderly patients with heart failure is important. Such patients are more likely to present with atypical symptoms, such as confusion, delirium, functional decline, falls, immobility, nocturia, and nocturnal incontinence [16-20].

There are insufficient echocardiographic data to assess the diastolic and systolic function in study patients. From EHFS II and the recent published Israeli survey we can predict that diastolic heart failure was common in about half or more of our patients [21-23].

Can the use of echocardiographic evaluation in oldest-old patients during their follow-up be of clinical benefit? We believe that echocardiographic evaluation of cardiac function, valve deterioration and intracardiac thrombi to rule out endocarditis is feasible and likely to be cost-effective in this very old population.

Another therapeutic dilemma is whether we should try to prolong the life expectancy of our patients or concentrate our efforts on improving their quality of life. As described above, most of our patients were stable, almost without heart failure symptoms and in Killip class I most of the time. Adding new drugs or increasing the dosage of medications to that recommended by the guidelines to prolong life may not necessarily alleviate their symptoms and could potentially induce a higher rate of adverse effects.

Although the average age of hospitalized heart failure patients is 72–74 years in national and international large surveys, special reference to the octogenarian population is lacking [21, 22, 24]. Repeat surveys are needed in this oldest-old population, better adherence to guidelines with cautious implementation and gradual titration of therapy, as well as additional surveys seem warranted.

**STUDY LIMITATION**

This is a retrospective observational survey; although all the patients hospitalized during the study period were included, the study cohort was relatively small.

**CONCLUSIONS**

The oldest-old hospitalized heart failure patients were usually women, fully dependent or frail, and had a high rate of comorbidities. Adherence to guidelines and recommended heart failure medications was poor. Low usage rates of ACEIs, angiotensin receptor blockers and beta-blockers, as well as anticoagulants in patients with AF and statins in patients with coronary artery disease, may partially explain the exceptionally high mortality. In order to improve the therapeutic approach in the oldest-old population, better adherence to guidelines with cautions and gradual titration of therapy, as well as additional surveys seems warranted.

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**Capsule**

**An innovative strategy to interfere with S. aureus growth learned from S. epidermidis**

The emergence of drug-resistant Staphylococcus aureus has spurred researchers to search for a new way to fight this bacterium, and it seems that the commensal bacterium Staphylococcus epidermidis has already got it figured out. Iwase et al. examined bacterial species in the nasal cavities of 88 volunteers and found that the absence of S. aureus correlated with the presence of an ‘inhibitory’ type of S. epidermidis. In cell culture experiments, the inhibitory S. epidermidis blocked biofilm formation by S. aureus. The commensal bacterium secretes an inhibitory factor, a serine protease called Esp, necessary for biofilm destruction *in vitro*. The findings suggest an innovative strategy to interfere with *S. aureus* growth. Notably, *S. aureus* grown in culture with Esp for one year did not develop resistance to the protein.

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Eitan Israeli

**Capsule**

**Candidate host immune genes relevant for vertical transmission and pathogenesis of Toxoplasma**

Ortiz-Alegría and co-authors reviewed the evidence for association of host immune genes and vertical transmission of Toxoplasma. *Toxoplasma gondii* infects a variety of vertebrate hosts, including humans. Transplacental passage of the parasite leads to congenital toxoplasmosis. A primary infection during the first weeks of gestation causes vertical transmission at low rate, although it causes major damage to the embryo. Transmission frequency increases to almost 80% by the end of pregnancy, but the proportion of ill newborns is low. For transmission and pathogenesis, the parasite genetics is certainly important. Several host innate and adaptive immune response genes are induced during infection in adults, which control the rapidly replicating tachyzoite. The T helper 1 (Th1) response is protective, although it has to be modulated to avoid inflammatory damage. Paradoxical observations on this response pattern in congenital toxoplasmosis have been reported, as it may be protective or deleterious, inducing sterile abortion or favoring parasite transplacental passage. Regarding pregnancy, an early Th1 microenvironment is important for control of infectious diseases and successful implantation, although it has to be regulated to support trophoblast survival. Polymorphism of genes involved in these parallel phenomena, such as Toll-like receptors, adhesins, cytokines, chemokines or their receptors, immunoglobulins or Fc receptors, might be important in susceptibility for *T. gondii* vertical transmission, abortion or fetal pathology.

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Eitan Israeli

“The souls of emperors and cobbleres are cast in the same mold. The same reason that makes us wrangle with a neighbor creates a war betwixt princes”

Michel de Montaigne (1533-1592), French essayist