

Mortality associated with the quality of care of patients hospitalized with congestive heart failure

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Abstract

Objective. This study examined the association between use of angiotensin converting enzyme inhibitors (ACEIs) and risk of death in elderly patients hospitalized with left ventricular systolic dysfunction (LVSD).

Design. Retrospective cohort study.

Setting. Despite evidence showing the benefit of treating LVSD with ACEI, elderly patients with LVSD are often not treated with an ACEI. Concern that the risk of ACEI treatment might exceed the benefits in elderly patients is a possible reason.

Study participants. We abstracted records from 2943 Medicare beneficiaries hospitalized for congestive heart failure in 69 hospitals in five states. The presence of LVSD was determined from recorded ejection fractions or a narrative description of ventricular function. Discharge medications and dosages were abstracted.

Main outcome measures. Mortality was tracked for one year using Health Care Finance Administration MEDPRO files.

Results. There were 621 patients aged 65 years or older with LVSD. The mean age (SD) was 77.4 years (7.0). At discharge 79% were prescribed an ACEI and, of these, 47% were discharged at the dose recommended by clinical practice guidelines. There were 195 deaths (31.4%) during the year of follow-up. Compared with patients discharged at a recommended ACEI dose, patients not prescribed an ACEI at discharge had an adjusted hazard ratio for death (95% CI) of 1.63 (1.02, 2.60) and patients prescribed an ACEI at a less than recommended dose had a hazard ratio of 1.30 (0.86, 1.97).

Conclusions. Our results show that ACEI use at discharge in elderly patients with LVSD is associated with decreased risk of death.

Keywords: angiotensin-converting enzyme inhibitors, congestive heart failure, left ventricular systolic dysfunction, mortality, outcome assessment, process assessment, quality of health care

In 1995 heart failure caused over 600 000 hospital discharges, 530 000 emergency room visits, and 44 000 deaths among Medicare beneficiaries aged 65 years and older [1,2]. Recent clinical trials have demonstrated that treatment with angiotensin converting enzyme inhibitors (ACEIs) is effective

in reducing the risk of death among patients with heart failure due to left ventricular systolic dysfunction (LVSD) [3–6]. This evidence has been incorporated into clinical practice guidelines, which recommend that ACEIs be used to treat patients with LVSD and that the prescribed dose be com-

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parable to that used in the clinical trials [7,8]. Despite these improvements in treatment, rates for hospitalization and, until 1988, deaths due to heart failure have been increasing in the United States [2,9,10]. Since LVSD accounts for approximately half of the hospitalized cases of heart failure in the elderly, appropriate use of these drugs could result in reduced mortality in older patients. However, while considerable evidence suggests that this is the case, many patients with LVSD do not receive recommended doses of ACEIs [11–14]. For example, a study of over 1600 randomly selected Medicare beneficiaries hospitalized with heart failure in 1994 found that only 14% of the patients with LVSD were treated with the recommended dose of ACEIs at discharge [14].

Although the reasons for the under-treatment of LVSD with ACEIs are not known, factors may include a concern over adverse drug side effects and the lack of efficacy of ACEIs in the elderly. However, these concerns may not be warranted. For example, Havranek *et al.* [15] showed that Medicare patients with LVSD treated with an ACEI at hospital discharge were less likely to die during the follow-up period. However, Havranek *et al.* did not examine the possibility that recommended doses of ACEIs might have adverse consequences in older patients. The purpose of this study is to add to the evidence regarding treatment with ACEIs by examining the association between the prescribed dose of an ACEI and subsequent risk of death among heart failure patients with LVSD.

Methods

Study design

This was a retrospective cohort study of 621 Medicare beneficiaries hospitalized for congestive heart failure (CHF) due to LVSD. Sixty-four hospitals in Colorado, Connecticut, Georgia, Oklahoma, and Virginia participated in the study. Thirty-two hospitals out of 64 participated voluntarily in a quality improvement trial.

Study population

We randomly selected the medical records of 50 Medicare beneficiaries who had been hospitalized with a principal diagnosis of CHF [*International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) codes 428 inclusive] from each of the study hospitals. If fewer than 50 eligible patients had been discharged during the enrollment period, we evaluated all admissions for CHF. One state used DRG code 127 to identify patients for inclusion in the study. Admissions were identified using the Health Care Financing Administration's (HCFA) MEDPRO file for each state.

Patients were included in the study if they were hospitalized between the dates of June 30, 1995 and September 30, 1996, and were discharged alive from the hospital. Patients were excluded from the cohort if their hospitalization had been terminated against medical advice or if they were transferred to another hospital. Patients with a diagnosis of valvular heart disease, acute myocardial infarction, cor pulmonale, chronic

obstructive lung disease treated with oxygen, thiamine deficiency, amyloidosis, and thyrotoxicosis were excluded from the cohort.

Data

Medical record personnel at each hospital copied and transmitted each chart for data abstraction by trained nurses and/or medical record specialists. We assessed inter-rater reliability by re-abstraction of a random replicate sample of 35 charts. The kappa estimates of inter-rater reliability for the outcome measures were 0.81 for the treatment with ACEIs for patients with LVSD to 0.89 for patients who received the target dose of an ACEI.

We abstracted data regarding age, sex, race, length of stay, a recorded history of previous myocardial infarction, chronic obstructive pulmonary disease, bronchitis, emphysema, hypertension, and diabetes. To analyze the effects of treatment on patients of advancing age, we divided the cohort into four equal age groups: 65–72 years, 73–77 years, 78–82 years, and 83 years and older. We abstracted clinical information on patients' history of paroxysmal nocturnal dyspnea (PND), dyspnea on exertion (DOE), and orthopnea. Physical findings abstracted included pedal edema, pulmonary rales, an S₃ gallop, and evidence of elevated jugular vein pressure. Laboratory information abstracted from the medical record included highest serum creatinine and serum potassium levels, the admission chest radiograph, and the presence of atrial fibrillation on admission.

We identified patients with LVSD by looking in the medical record for a measure of left ventricular ejection fraction (LVEF) that was obtained during either a previous or the current hospitalization. We also recorded any narrative description of left ventricular function that included any of the following phrases: systolic dysfunction; dilated cardiomyopathy; congestive cardiomyopathy; diffuse or global hypokinesia; and description of the ejection fraction (EF) including normal, increased, mildly, moderately, or severely reduced. For previous hospitalization the abstractor looked for a note from a physician mentioning that the patient had a determination of an EF in the past.

We defined LVSD as any measured EF equal to or less than 40%. If no information was obtained regarding the EF from the chart, we classified patients as having LVSD if the narrative description of the left ventricular function included the descriptive phrases 'systolic dysfunction', 'dilated cardiomyopathy', 'congestive cardiomyopathy', or 'diffuse or global hypokinesia', or if the EF was described as reduced in the narrative description. Patients with a description of the EF who were not classified as having LVSD were considered as patients suffering from a diastolic dysfunction.

We abstracted information regarding medication prescription and dosage from the physician discharge summary, nurse discharge summary, and last progress note. The following ACEIs by generic and trade names were identified and abstracted: benazepril, captopril, enalapril, fosinopril, lisinopril, quinapril, and ramipril. We defined target doses for individual ACEIs according to those identified in a

randomized, controlled clinical trial designed to reduce risk of death in patients with LVSD. The target doses are as follows: captopril, 50 mg tid; enalapril, 10 mg bid; lisinopril, 20 mg qd; ramipril, 5 mg bid [16]. To define target doses for ACEIs not examined in clinical trials, we used the following estimates of appropriate dosage based on the manufacturer's stated average doses: benazepril 20 mg qd, fosinopril 40 mg qd, and quinapril 10 bid [17].

We used ACEI dose to define three groups of patients with respect to their ACEI therapy: (1) not treated; (2) treated but not at target ACEI dose at discharge; and (3) discharged on target ACEI dose. Thirty-eight patients (6%) were treated with an ACEI at a greater dose than the target dose. We recorded any mention in the chart of a contraindication to ACEIs and excluded those patients. We computed a severity of illness index for each patient using the Deyo modification of the Charlson co-morbidity index [18]. The Charlson index is a weighted sum of selected co-morbidities that were defined by the discharge conditions for the index admission.

Follow-up

Follow-up began on the date of discharge for the index hospitalization and continued for one year following discharge. We used the HCFA MEDPRO files to identify subsequent hospitalizations and dates of death.

Statistical analysis

Differences in the proportions of patients within ACEI treatment groups were assessed for statistical significance with a chi-square test [19]. Differences in means across the three groups were tested for significance with ANOVA [20]. We used Kaplan–Meier plots to assess the association between treatment group and mortality [21]. Then, we examined the bivariate association between ACEI dose and mortality stratified by patient characteristics with a chi-square test for trends across groups [19]. We used a Cox proportional hazards model to examine the association between mortality and ACEI dose, controlling for the other patient characteristics [21]. We entered interaction terms between treatment and all other variables into these models, including age (as continuous and ordinal variables) to assess the effect of treatment by age. None of these interaction terms was significant at a 5% level with the likelihood ratio test and these interaction terms were dropped from the model. Then we implemented a backward elimination in examining whether the withdrawal of the least significant covariate would change the hazard ratio. If this change were 10% or less, this covariate was not considered as a confounding factor and was removed from the model. These criteria were used until we defined the best model. We found no co-linearity between variables and no violation of the proportional hazard assumption in our model. Finally, to account for possible clustering within hospitals, we conducted a second set of analyses with generalized estimating equation (GEE) procedures using SAS Proc Genmod. To explore this difference between survival analysis and GEE procedures, we conducted logistic regression and obtained exactly the same results as we did for the GEE

Table 1 Patients with congestive heart failure ($n=2943$): exclusion criteria

Exclusions	<i>n</i>	%
Incomplete chart	267	11.5
Transferred to another hospital	7	0.3
Died during hospitalization	2	0.1
Age less than 65 years	121	5.2
Secondary heart failure	599 ¹	25.8
VF not determined	584	25.2
LVDD	659	28.4
Contraindication to ACEI	83	3.6
Total	2322	100

ACEI, angiotensin converting enzyme inhibitor; LVDD, left ventricular diastolic dysfunction; VF, ventricular function.

¹ Patients may have more than one condition: cor pulmonale or chronic obstructive pulmonary disease requiring home oxygen ($n=283$), aortic stenosis ($n=202$), mitral stenosis ($n=49$), end-stage renal disease ($n=38$), acute MI ($n=41$), heart failure attributed to thyrotoxicosis ($n=3$).

procedures. When using these two techniques, we used one-year mortality as a binary variable. However, the survival analysis allowed us to take into account the time until censoring and our results were unchanged. All analyses were implemented with the SAS software (SAS Institute Inc., Cary, NC, USA).

Results

Between June 30, 1995 and September 30, 1996, we identified 2943 eligible patients who were discharged from the participating hospitals with a principal diagnosis of heart failure. We excluded 2322 (78.9%) of these patients from the analysis for the following reasons (see Table 1): 267 (11.5%) were ineligible after chart review; 599 (25.8%) had secondary causes of heart failure; 584 (25.2%) did not have documented ventricular function; and 659 (28.4%) had left ventricular diastolic dysfunction. Additionally, we excluded patients if they (1) were younger than 65, (2) died during hospitalization, (3) were transferred to another hospital, (4) had an incomplete chart, and (5) had a stated contraindication to ACEIs noted in their medical chart (20.7%).

We included 621 patients with LVSD in the analysis. The determination of LVSD in patients depended on the documentation of a previous or current EF for 519 (84%). For the 102 other (16%) patients we relied on a narrative summary. Among those patients with LVSD and an EF determination, the median of the lowest estimate recorded in the chart was 25% with a 25th–75th intraquartile range from 20 to 33%.

The mean (SD) age of patients with LVSD was 77.4 (7.0) years. Forty-three percent of the patients were female and

81% were white. Seventy-seven percent had a history of heart failure, while 67% were hypertensive (prior history of hypertension or hypertension at admission), and 50% had a previous myocardial infarction. A history of orthopnea was recorded in the medical record for 42% of the patients with LVSD, DOE for 40%, and PND for 36%. Clinical examination recorded rales in 85% of patients with LVSD, edema in 66%, jugular venous distension (JVD) in 50%, and an S₃ gallop in 30%. We found an admission CXR confirming heart failure for 85%. Atrial fibrillation was described in the reports for 25% of the 597 patients who had electrocardiograms performed on admission. The median Charlson co-morbidity index was two.

Treatment of patients with LVSD

Among the 621 patients with LVSD, 490 (79%) were prescribed an ACEI at discharge, and ACEIs were prescribed

at target dose for 116 (19%) of the patients. The ACEIs prescribed included captopril (34%), enalapril (29%), lisinopril (25%), quinapril (4%), benazepril (4%), fosinopril (3%), and ramipril (1%). The percentage of patients at an ACEI target dose was 11% (95% CI 6–17%) for captopril, 29% (95% CI 22–37%) for enalapril, 28% (95% CI 20–36%) for lisinopril, 50% (95% CI 27–73%) for quinapril, 45% (95% CI 23–68%) for benazepril, 10% (95% CI 3–45%) for fosinopril, and 0% (95% CI 0–0%) for ramipril. The mean (SD) ACEI dose as a proportion of the recommended dose among treated patients was 47% (50%). Table 2 illustrates the association between patient characteristics and ACEI dosing. With the exception of patients with a previous history of hypertension, symptoms of PND, physical findings of S₃ gallop and atrial fibrillation on admission, no patient characteristics were associated with ACEI dosing (see Table 2).

We found no differences in the proportions of patients treated with an ACEI or those treated with the recommended

Table 2 Demographic characteristics, symptoms, and findings at admission of patients with left ventricular systolic dysfunction (LVSD) and no contraindication to ACEI, *n* = 621

Characteristics	ACEI dosage			
	<i>n</i>	Target 19%	Less than target 60%	Not prescribed 21%
Mean age (SD)	77.4 (7.0)	76.4 (6.7)	77.4 (6.9)	78.3 (7.4)
Age				
Q1: 65–72 years	155	38 (25%)	91 (59%)	26 (17%)
Q2: 73–77 years	155	27 (17%)	92 (59%)	36 (23%)
Q3: 78–82 years	156	23 (15%)	100 (64%)	33 (21%)
Q4: > 83 years	155	28 (18%)	91 (59%)	36 (23%)
Sex				
Male	353	60 (17%)	223 (63%)	70 (19%)
Female	268	56 (21%)	151 (56%)	61 (23%)
Race (<i>n</i> = 619)				
White	502	90 (18%)	301 (60%)	111 (22%)
Not white	117	26 (22%)	72 (62%)	19 (16%)
Previous history HF	478	88 (18%)	286 (60%)	104 (22%)
Prior MI	311	54 (17%)	193 (62%)	64 (21%)
COPD, bronchitis, emphysema	225	37 (16%)	142 (63%)	46 (20%)
Hypertension	417	88 (21%)	249 (60%)	80 (19%) ¹
Diabetes	254	52 (20%)	151 (59%)	51 (20%)
Current smoker	68	15 (22%)	39 (57%)	14 (21%)
Symptoms and findings				
PND	221	50 (23%)	135 (61%)	36 (16%) ¹
DOE	248	47 (19%)	154 (62%)	47 (19%)
Orthopnea	260	59 (23%)	152 (58%)	49 (19%)
Leg edema	412	86 (21%)	240 (58%)	86 (21%)
Pulmonary rales	530	103 (19%)	313 (59%)	114 (22%)
S ₃ gallop	186	44 (24%)	113 (61%)	29 (16%) ¹
JVD	308	66 (21%)	183 (59%)	59 (19%)
Atrial fibrillation (<i>n</i> = 597)	148	24 (16%)	82 (55%)	42 (28%) ¹

¹*P* value < 0.05.

ACEI, angiotensin converting enzyme inhibitor; COPD, chronic obstructive pulmonary disease; DOE, dyspnea on exertion; HF, heart failure; JVD, jugular venous distension; MI, myocardial infarction; PND, paroxysmal nocturnal dyspnea.

Table 3 Admission characteristics of patients with left ventricular systolic dysfunction (LVSD) and no contraindication to ACEI, $n = 621$

Characteristics	ACEI dosage			
	<i>n</i>	Target 19%	Less than target 60%	Not prescribed 21%
CXR confirms CHF ($n = 596$)	508	98 (19%)	306 (60%)	104 (20%)
Mean (SD) potassium	617	4.2 (0.5)	4.2 (0.5)	4.2 (0.6)
Mean (SD) creatinine	616	1.4 (0.6)	1.4 (0.6)	1.6 (0.7) ¹
Minimum EF ($n = 519$)				
$\leq 20\%$	163	33 (20%)	108 (66%)	22 (14%)
21–30%	203	45 (22%)	117 (58%)	41 (20%)
31–40%	153	29 (19%)	89 (58%)	35 (23%)
Charlson index				
Mean (SD)	621	2.1 (1.2)	2.5 (4.0)	2.9 (5.3)
1	191	36 (19%)	121 (63%)	34 (18%)
2	261	58 (22%)	151 (58%)	52 (20%)
≥ 3	169	22 (13%)	102 (60%)	45 (27%)

¹ P value < 0.05 .

ACEI, angiotensin converting enzyme inhibitor; CHF, congestive heart failure; CXR, chest X-ray.

ACEI dose with respect to minimum EF, Charlson comorbidity index, chest radiographic confirmation of CHF, or mean serum potassium (Table 3). In contrast, the mean (SD) serum creatinine among patients not prescribed an ACEI was 1.6 mg% (0.7) compared with 1.4 mg% (0.6) for patients prescribed an ACEI ($P = 0.040$) (Table 3).

Patients not prescribed an ACEI at discharge were more likely to be discharged on calcium channel blockers ($P = 0.001$) and hydralazine ($P = 0.001$). Otherwise, the use of anticoagulants, beta-blockers, digoxin, diuretics, and nitrates was comparable among patients discharged on an ACEI and those not (Table 4). Finally, there was no difference noted between those discharged on an ACEI and those not with respect to the prescription at discharge of a low sodium diet, instructions to weigh daily, the dissemination of smoking cessation recommendations, and the scheduling of a physician office visit within 14 days of discharge.

Survival of patients with LVSD

Patients diagnosed with LVSD were at high risk of death after discharge. There were 195 deaths during the one-year follow-up period, which comprised 31.4% of the cohort.

Bivariate analysis

Among patients not prescribed an ACEI at discharge, 50 died (38%); for patients discharged on an ACEI at less than target dose, 117 died (31%); and among patients discharged at target dose, 28 died (24%). Among patients not prescribed an ACEI at discharge, the crude estimated one-year risk ratio (RR) of death (95% CI) was 1.58 (1.07–2.33); for patients discharged on an ACEI at less than target dose, the risk ratio of death was 1.30 (0.91–1.85); and for those discharged at a recommended ACEI dose, the risk ratio of death was 1.0

(reference). Patients in both ACEI treatment categories were more likely to survive than those not prescribed an ACEI, and those discharged at recommended doses were more likely to survive than the other patients (Figure 1). Risk factors statistically associated (RR) (95% CI) with one-year mortality included: age (continuous) (older patients are of higher risk) ($P = 0.008$), gender (increased risk for male) [1.30 (1.02–1.65)], race (increased risk for white) [1.51 (1.05–2.16)], history of heart failure [2.94 (1.88–4.60)], diabetes [1.32 (1.05–1.66)], symptoms of PND [0.68 (0.52–0.88)], creatinine (continuous) ($P < 0.001$), length of stay (continuous) ($P = 0.001$), and the use of hydralazine [1.59 (1.10–2.31)] and nitrate at discharge [1.33 (1.05–1.69)].

We also analyzed the role of patients having received an ACEI on admission. Among the 621 patients with LVSD, 300 (48%) were on an ACEI when admitted to the hospital. Among these patients, 12% received the target dose of the ACEI prescribed. Among patients who were receiving an ACEI on admission, at discharge the same dose was prescribed for 45%, an increased dose for 34%, a lower dose for 16%, and the ACEI was omitted for 5%. The impact of ACEI dose at discharge on subsequent survival is shown in Figure 2. There was a strong, graded increase in risk of death as discharge dose decreased from target to no ACEI prescribed at discharge among patients who were receiving the drug on admission. In contrast, no significant trends were noted for those patients who were started on an ACEI during their stay.

Multivariate analysis

The results of the Cox proportional hazard model are presented in Table 5. After controlling for age and other confounding factors, the risk of death increased as ACEI

Table 4 Discharge characteristics of patients with left ventricular systolic dysfunction (LVSD) and no contraindication to ACEI, *n* = 621

Characteristics	ACEI dosage			
	<i>n</i>	Target 19%	Less than target 60%	Not prescribed 21%
Low sodium diet	412	76 (18%)	255 (62%)	81 (20%)
Daily weights	53	9 (17%)	33 (62%)	11 (21%)
Smoking cessation (<i>n</i> = 68)	13	3 (23%)	7 (54%)	3 (23%)
14 day follow-up	435	84 (19%)	264 (61%)	87 (20%)
ACEI on admission	300	91 (30%)	195 (65%)	14 (5%) ¹
Discharge medications				
Anticoagulants	198	43 (22%)	113 (57%)	42 (21%)
Anticoagulants for AF (<i>n</i> = 148)	84	18 (21%)	46 (55%)	20 (24%)
Beta blocker	62	12 (19%)	36 (58%)	14 (23%)
Calcium blocker	68	11 (16%)	30 (44%)	27 (40%) ¹
Digoxin	451	92 (20%)	273 (61%)	86 (19%)
Diuretics	583	108 (19%)	356 (61%)	119 (20%)
Hydralazine	33	6 (18%)	11 (33%)	16 (48%) ¹
Nitrates	339	68 (20%)	197 (58%)	74 (22%)
Mean (SD) length of stay (days)	621	5.7 (3.9)	6.2 (4.2)	6.3 (4.1)

¹*P* value < 0.05.

ACEI, angiotensin converting enzyme inhibitor; AF, atrial fibrillation.

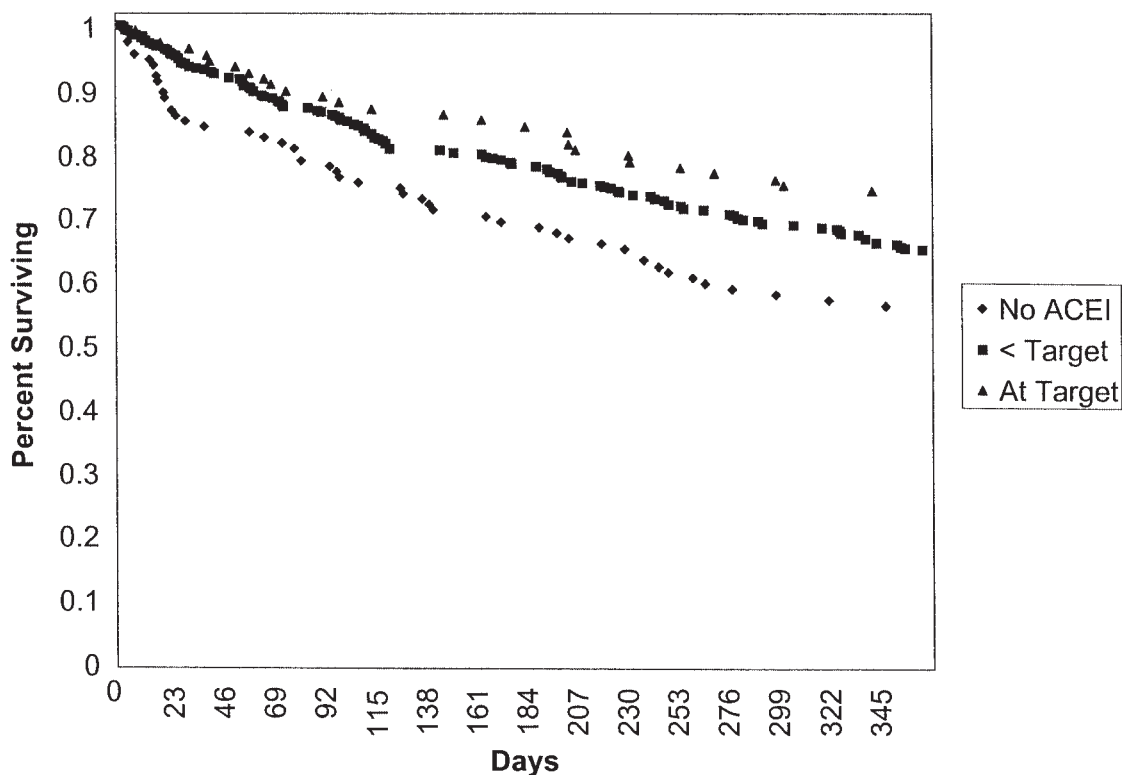


Figure 1 Survival of patients with congestive heart failure due to left ventricular systolic dysfunction by discharge ACEI dosing, *n* = 621.

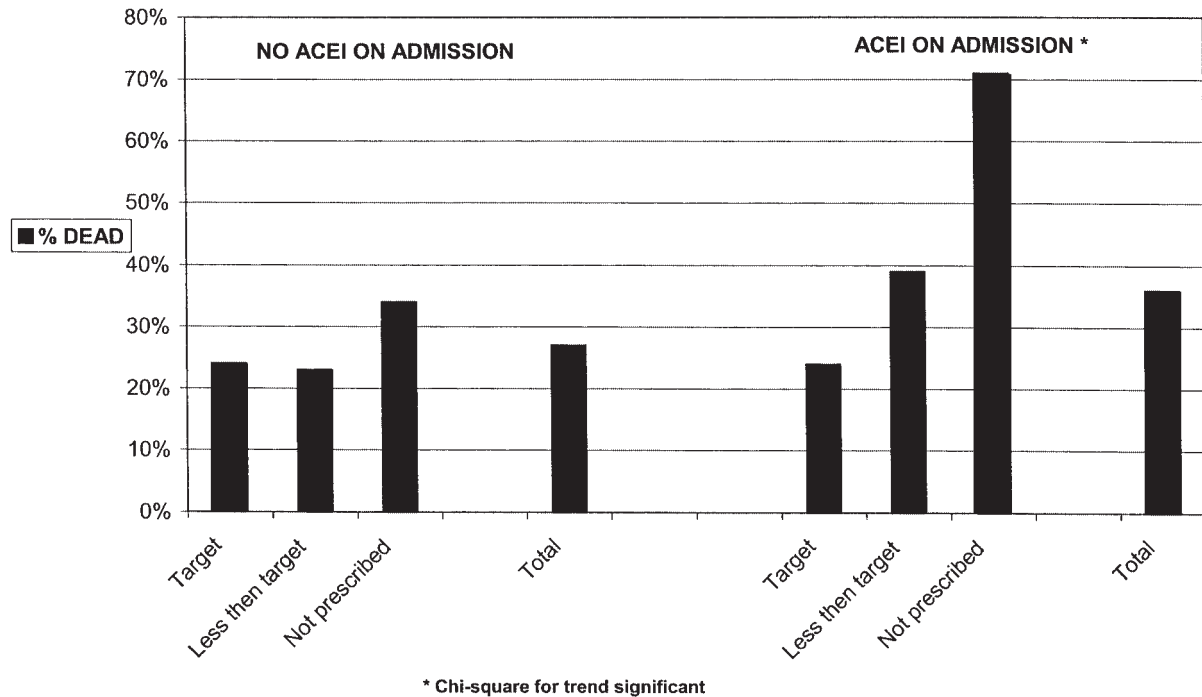


Figure 2 Risk of death among patients with left ventricular systolic dysfunction with or without ACEI on admission, $n=621$.

Table 5 Mortality in relation to ACEI dose of patients with LVSD and no contraindications to ACEI, Cox proportional model, $n=621$

	Adjusted hazard ratio	Lower 95% CI	Upper 95% CI	<i>P</i> value
Target	Reference	Reference	Reference	Reference
Less than target	1.30	0.86	1.97	0.213
ACEI not prescribed	1.63	1.02	2.60	0.042
Age (continuous)	1.02	1.00	1.04	0.033
History of heart failure	3.11	1.91	5.08	<0.001
PND	0.71	0.51	0.98	0.037
Charlson co-morbidity index (continuous)	1.04	1.00	1.07	0.017
Creatinine (continuous)	1.32	1.11	1.57	0.002
Length of stay (continuous)	1.04	1.01	1.07	0.005

ACEI, angiotensin converting enzyme inhibitor; PND, paroxystal nocturnal dyspnea.

treatment regressed from target to subtarget levels [hazard ratio (95% CI): 1.30 (0.86–1.97)] and to not prescribed [hazard ratio (95% CI): 1.63 (1.02–2.60)] (Table 6). Age, history of heart failure, PND, creatinine, Charlson co-morbidity index, and length of stay were statistically associated with increased risk of mortality (Table 5).

Finally, the results of the secondary analysis with GEE procedures demonstrated that the association between target dose and one-year mortality is not statistically significant: when target dose is the reference group, the odds ratio (95% CI) for subtarget is 1.30 (0.85–2.00) ($P=0.221$), and

the odds ratio for ACEI not prescribed is 1.56 (0.85–2.88) ($P=0.152$).

Discussion

Our findings that elderly patients with LVSD who did not receive an ACEI have higher mortality rates are consistent with earlier studies that led to the development of national guidelines. The guidelines we used were those available at the time we carried out the study [7,8]. Recently, new guide-

Table 6 Mortality in relation to ACEI dose of patients with LVSD and no contraindications to ACEI, $n=621$

ACEI dose % suggested target	n	Estimated Kaplan–Meier one year mortality n (%)	Estimated Kaplan–Meier crude RR ¹ (95% CI)	Adjusted hazard ratio (95% CI) ²
Target	116 (19%)	28 (26%)	1.00	1.00
Less than target	374 (60%)	117 (35%)	1.36 (0.95–1.92)	1.30 (0.86–1.97) $P=0.213$
Not prescribed	131 (21%)	50 (44%)	1.69 (1.16–2.47) $P=0.016^3$	1.63 (1.02–2.60) $P=0.042$

ACEI, angiotensin converting enzyme inhibitor; LVSD, left ventricular systolic dysfunction; PND, paroxysmal nocturnal dyspnea.

¹RR = relative risk, calculated from Kaplan–Meier results.

²Adjusted for age, history of heart failure, PND, Charlson co-morbidity index, creatinine, and length of stay.

³Log rank test.

lines related to CHF management and treatment have been published with the same conclusions about ACEI use [22, 23], even if some ACEIs have not been proven effective and safe [24]. In the last decade, clinical trials [7,8,25] have demonstrated that appropriate treatment of patients with CHF is associated with significant improvements in CHF symptoms and results in longer survival. A recent meta-analysis including 32 randomized, placebo-controlled trials of ACEI use in 7105 patients with symptomatic CHF convincingly showed that treatment with ACEIs reduces the risk of death OR, 0.77: 95% CI, 0.67–0.88. The reduction of total mortality was observed for several different ACEIs and was similar for various subgroups examined (age, sex, etiology, and New York Heart Association Class). However, patients with the lowest EF appeared to have the greatest benefit [5]. A recent study has demonstrated that the use of high dose versus low dose of lisinopril for patients with heart failure reduces risk of death by 8% and hospitalization by 24% [26]. Another recent study showed that among very old patients the adjusted rate of all-cause mortality was 10% less in ACEI recipients compared with patients receiving digoxin (RR, 0.89: 95% CI, 0.83–0.95) [27]. Based on these trials, recommendations about quality measures for CHF have been published from a conference consensus [28].

Our study demonstrates that elderly patients prescribed doses of an ACEI at discharge that are lower than those used in randomized, controlled clinical trials (which form the basis of the clinical guidelines) are at increased risk of death. We also found increased mortality among patients who were not prescribed an ACEI at discharge when compared with those discharged at subtarget doses of an ACEI. These results are consistent with the treatment results that CHF clinical practice guidelines indicate would occur. Thus, our results provide additional support for the importance of utilizing evidence-based therapy for elderly patients with CHF.

Limitations

One concern regarding our data is that care was observed over a short time period (i.e. during the course of a hospitalization for heart failure). It is possible that adjustments

in an ACEI dose would be continued following discharge. If this were true, then the increased correlation between ACEI dose and death might reflect other unmeasured patient factors rather than characteristics of physician care. We examined this possibility by: (1) limiting the analysis to those patients on an ACEI at admission; (2) analyzing changes in ACEI dose over course of hospital care; and (3) controlling for multiple co-morbidities.

There were other limitations in our study. Firstly, because hospital participation was voluntary, it is possible that selection bias occurred. Therefore, the hospitals included in the study may not be representative of all hospitals in the United States. In the study hospitals, patients' demographic and socio-economic characteristics could vary systematically or randomly across hospitals. The prescribing patterns could also differ considerably between these hospitals and other hospitals. Additionally, it is possible that the study hospitals may have been more active in developing continuous quality improvement interventions than non-study hospitals. This selection bias threatens the external validity and generalizability of the study.

Because we did not know if all of the patients were eligible for target doses of an ACEI, we cannot determine why the patients were not prescribed target levels. It may be that some patients who cannot tolerate target doses are more likely to have worse outcomes than those who can tolerate target doses. Additionally, for patients with a terminal illness or those discharged to hospice, the goals of therapy may not be long-term survival. Because this study is not a clinical trial, the reasons for using a specific medication are not randomly distributed.

We used an intention-to-treat analysis and assumed that all patients remained in the same type and dose of treatment as prescribed at index discharge. Our analysis does not include measures of patient compliance. However, in clinical practice not every patient is discharged from the hospital at target doses because of the necessary period of dose titration to establish target dose. Therefore, our intention-to-treat analysis could have introduced a misclassification bias to the study because patients who ultimately receive target levels of an ACEI would

remain in the subtarget group in the analysis. Thirdly, it is possible that subtarget doses of an ACEI might be appropriate for patients with an elevated creatinine value. We must interpret the data for this subgroup with caution. Fourthly, because our study included patients who were hospitalized during a period of 16 months, it is possible that we missed changes in patterns of care that occurred during this time period. Finally, one state utilized a different sampling procedure for selecting patients with CHF (i.e. it used DRG codes instead of ICD-9 codes). However, because the diagnosis of CHF was confirmed for all patients by clinical indicators, it eliminated the possibility of incorrect selection due to different codes. Indeed, we observed no significant differences between patients from the state using DRG codes and the states using ICD-9 codes regarding the values for the key quality indicators.

Conclusion

We found a substantial, clinically important, gradient (dose–response) decreased risk of death among elderly CHF patients with LVSD who were treated with a target dose of an ACEI compared with patients receiving subtarget doses of ACEIs and patients who were not treated with ACEIs. Our findings suggest that compliance with the ACEIs prescribing recommendations listed in clinical practice guidelines for elderly patients with CHF due to LVSD confers benefit and clinicians should consider using ACEI doses consistent with these recommendations when managing these patients.

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