BRIEF REPORT

Utilization and Dosing of Angiotensin-Converting Enzyme Inhibitors for Heart Failure

Effect of Physician Specialty and Patient Characteristics

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To determine if physician specialty is associated with underutilization and underdosing of angiotensin-converting enzyme inhibitors among patients with heart failure, we reviewed the charts of 214 outpatients with decreased systolic function at an urban academic medical center. Regardless of whether patients were cared for by cardiologists, generalist physicians, or a combination of the two specialties, approximately 75% of the patients were taking an angiotensin-converting enzyme inhibitor. However, only approximately 60% of these patients were taking dosages proved to be efficacious in trials. Emphasis on adequate dosing is needed among all specialty groups.

KEY WORDS: angiotensin-converting enzyme (ACE) inhibitor; congestive heart failure; physician behavior; specialty; quality of care.

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Although randomized controlled trials have convincingly demonstrated that angiotensin-converting enzyme (ACE) inhibitors decrease mortality and hospitalization in patients with ejection fractions of 0.35 or less,¹⁻³ physicians often underutilize these medications.⁴⁻¹¹ Moreover, physicians may prescribe dosages that are less than those proved to be effective in large, multicenter trials.^{7,9,11}

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Little is known, however, about the factors associated with underutilization and underdosing.^{4,9} Some studies suggest that cardiologists are more likely than generalist physicians to prescribe ACE inhibitors in circumstances and dosages that accord with established guidelines.^{7,9,12,13} However, these latter studies are limited because they either were surveys of physicians' knowledge, or else did not limit their population to patients with decreased systolic function. Therefore, to determine if physician specialty and patient characteristics are associated with underutilization and underdosing of ACE inhibitors, we performed a cross-sectional study of outpatients with heart failure.

METHODS

Study Population

We retrospectively identified all patients seen at the University of Chicago's cardiology, general internal medicine, and geriatrics clinics between January 1, 1994, and June 30, 1996, who received an outpatient billing diagnosis of International Classification of Diseases code 428 (congestive heart failure) or 425.4 (cardiomyopathy).¹⁴ We reviewed the medical records of these patients, and then selected those patients with moderately or severely decreased systolic function (fractional shortening 18% to 24% and less than 18%, respectively), determined primarily through echocardiogram, and rarely through cardiac catheterization or nuclear scan. We divided the patients into three groups: (1) patients seen by a cardiologist, but not by a general internist or geriatrician, as determined through both the administrative computer system and review of the medical record; (2) patients seen by either a general internist or geriatrician, but not by a cardiologist; and (3) patients seen by a cardiologist and either a general internist or a geriatrician.

Data Collection

We obtained the history, comorbid conditions, and most recent vital signs, laboratory values, and medications from the medical record. We extracted demographic

and insurance data from the administrative billing system. We measured comorbid illnesses with the Charlson Comorbidity Index.¹⁵

Statistical Analysis

We compared patients from the different groups using the χ^2 test for categorical variables, and Student's *t* test or the Wilcoxon test for continuous variables. We defined an adequate ACE inhibitor dose as that proved to be efficacious in the large randomized, controlled trials of these medications (captopril, 50 mg tid; enalapril, 10 mg bid; lisinopril, 10 mg qd; ramipril, 5 mg bid).¹⁶ For the 20 patients (12%) on a different ACE inhibitor, we used the following criteria: benazepril, 20 mg qd; fosinopril, 20 mg qd; and quinapril, 10 mg bid, all taken orally. Dosage of ACE inhibitors was analyzed with both a binary variable of adequate or not, and a continuous variable calculated as the percentage of an adequate dose a patient received. For example, given that an oral dosage of captopril of 50 mg tid has been demonstrated to reduce mortality,³ a 25-mg dose on the same schedule was considered to be "not adequate" as it was only 50% of the adequate dose. Assuming that 85% of cardiologists would choose an ACE inhibitor for their patients with moderately or severely reduced systolic function, we have 80% power to detect an absolute difference of 25 percentage points in utilization of these medications by cardiologists and generalist physicians at a significance level of $p = .05$, two-tailed.

By chart review, three patients were unable to tolerate an ACE inhibitor. They were subsequently excluded from drug analyses except for when use of either an ACE inhibitor or the hydralazine/nitrate combination was the end point. We used multivariable logistic and linear regression to determine independent correlates of the utilization and dosing of ACE inhibitors (enter at $p \leq .10$, stay at $p \leq .05$, two-tailed). In the dosing analyses, we automatically adjusted for hypertension, coronary artery disease, and whether systolic blood pressure was less than 110 mm Hg. We also performed a subgroup analysis that excluded patients in whom the use of ACE inhibitors could be more complicated, namely, when creatinine level was above 3.0 mg/dL, potassium level was above 5.5 mmol/L, and systolic blood pressure was less than 100 mm Hg.^{12,13}

RESULTS

Study Sample and Patient Characteristics

We identified 647 outpatients with a diagnostic code of congestive heart failure or cardiomyopathy. For these, we retrieved 493 (76%) of the charts. Measurements of left ventricular function were available on 419 (85%) of these patients, and 214 (51%) had moderately or severely reduced systolic function. Patients of generalist physicians were older than those of cardiologists, and they were more

likely to be African American and to have a history of hypertension (Table 1).

Utilization and Dosing of Angiotensin-Converting Enzyme Inhibitors

Similar percentages of patients cared for by cardiologists, generalist physicians, and the combination of the two were prescribed ACE inhibitors (Table 2). Rates of use of ACE inhibitors were approximately 75%. However, among patients taking these medications, only 54% to 70% were on dosages proved to be efficacious in clinical trials. Of the three most commonly prescribed medications, dosage was adequate least frequently ($p \leq .05$) with captopril (46%) and enalapril (58%), than with lisinopril (82%).

Independent Correlates of Utilization and Dosing

Independent correlates of the use of ACE inhibitors were younger patient age (adjusted odds ratio [OR] 1.4 per 10 years; 95% confidence interval [CI] 1.1, 1.8) and no history of renal failure (OR 4.9; 95% CI 1.5, 15.8), model *c* statistic = 0.66. Adjusting for hypertension, coronary artery disease, and whether systolic blood pressure was less than 110 mm Hg, patients with no prior history of myocardial infarction were more likely (OR 2.8; 95% CI 1.2, 6.6) to be prescribed an adequate ACE inhibitor dose, model *c* statistic = 0.63. When the outcome was the percentage of an adequate dose that a patient received, younger patients ($\beta = 11\%$ per 10 years), patients without a prior history of myocardial infarction ($\beta = 35\%$), and patients of generalist physicians ($\beta = 58\%$) received higher doses of ACE inhibitors ($p \leq .05$). However, the latter model explained only 13% of the variance in dose. In subanalyses excluding patients with creatinine level above 3.0 mg/dL, potassium level above 5.5 mmol/L, and systolic blood pressure less than 100 mm Hg, the results were similar.

DISCUSSION

Regardless of physician specialty, most patients with decreased systolic function were prescribed an ACE inhibitor, but only about 60% were on dosages proved to be efficacious in controlled trials. No trends favoring specialist or combined specialist-generalist care were apparent; in fact, generalist physicians prescribed higher doses. We suspect that generalist physicians prescribed higher dosages than cardiologists because their patients were more likely to have hypertension, a factor that our regression analyses may have been unable to adjust for fully.

In comparison, a national survey using clinical vignettes found that generalist physicians were less likely than cardiologists to prescribe ACE inhibitors among asymptomatic patients with decreased systolic function, and they were also less likely to use dosage as an end point for titrating these medications.⁹ Studies of outpa-

Table 1. Patient Characteristics by Specialty*

Factor	Cardiologist (n = 82)	Generalist (n = 53)	Combination (n = 79)
Sociodemographic			
Female	50	58	57
Race			
African American	71	96 [†]	92 [‡]
White	26	2	8
Other	3	2	0
Age, years	58 ± 16	70 ± 17 [†]	70 ± 13 [‡]
Primary insurance	95	98	97
Secondary insurance	40	43	65 ^{‡§}
History			
Coronary artery disease	48	38	68 ^{‡§}
Myocardial infarction	27	30	33
Hypertension	56	83 [†]	80 [‡]
Atrial tachycardia	21	28	27
Diabetes mellitus	18	32	37 [‡]
Renal failure	6	6	8
Charlson Comorbidity Index score	2.1 ± 2.1	2.3 ± 1.9	2.5 ± 1.9 [‡]
Symptomatic	35	47	48
Physical examination			
Systolic blood pressure, mm Hg	122 ± 23	139 ± 28 [†]	132 ± 22 [‡]
Rales	20	23	26
Third heart sound	35	21	28
Peripheral edema	27	36	29
Laboratory values			
Serum sodium, mmol/L	139 ± 3.4	141 ± 3.3 [†]	138 ± 4.6 [§]
Serum potassium, mmol/L	4.2 ± 0.5	4.4 ± 0.6	4.4 ± 0.6
Serum creatinine, mg/dL	1.6 ± 1.6	1.7 ± 1.2	1.7 ± 1.1
Left ventricular function severely decreased [¶]	65	53	57

*For dichotomous variables, numbers reflect percentage of patients with the factor. For continuous variables, mean values and standard deviations are listed.

[†]p ≤ .05, patients of cardiologists compared with patients of generalist physicians.

[‡]p ≤ .05, patients of cardiologists compared with patients of combination physicians.

[§]p ≤ .05, patients of generalist physicians compared with patients of combination physicians.

^{||}Dyspnea, fatigue, paroxysmal nocturnal dyspnea, or orthopnea documented at most recent office visit.

[¶]Fractional shortening less than 18%.

Table 2. Utilization and Dosing of Angiotensin-Converting Enzyme Inhibitors by Specialty

Utilization and Dosage	Percentage of Patients Cardiologist (n = 82)	Percentage of Patients Generalist (n = 53)	Percentage of Patients Combination (n = 79)
ACE inhibitor use, % of patients (95% CI)			
ACE inhibitor	81 (71, 89)	77 (63, 87)	73 (62, 82)
Captopril	32 (22, 43)* [†]	6 (1, 16)	15 (8, 25)
Enalapril	25 (16, 36)	48 (34, 62)*	37 (26, 49)
Lisinopril	19 (11, 29) [†]	13 (6, 26)	8 (3, 16)
Other	6 (2, 14)	12 (4, 23)	13 (6, 22)
ACE inhibitor or hydralazine/nitrate combination	85 (76, 92)	83 (70, 92)	84 (74, 91)
Dosage among patients prescribed an ACE inhibitor			
Adequate [‡] , % of patients (95% CI)	56 (43, 69)	70 (53, 83)	54 (41, 68)
Percentage of adequate (mean ± SD) [§]	104 ± 87	146 ± 112*	93 ± 60

*p ≤ .05, patients of cardiologists compared with patients of generalist physicians.

[†]p ≤ .05, patients of cardiologists compared with patients of combination physicians.

[‡]Angiotensin-converting enzyme inhibitor dose at least equivalent to that proved to be efficacious in randomized controlled trials.¹⁶

[§]Percentage of the ACE inhibitor dose proved to be efficacious in randomized controlled trials.¹⁶

^{||}p ≤ .05, patients of generalist physicians compared with patients of combination physicians.

tients and inpatients with heart failure reported equal use of ACE inhibitors across specialties,^{7,17} but that cardiologists prescribed higher doses.⁷

Our study has limited power and generalizability because it was performed at one urban academic medical center. It is also possible that our results do not apply to asymptomatic patients. Furthermore, we may have underestimated the percentage of physicians who prescribed adequate dosages of ACE inhibitors, as they may have tried higher doses that their patients were unable to tolerate. However, our results were similar even after excluding patients with creatinine level above 3.0 mg/dL, potassium level above 5.5 mmol/L, and systolic blood pressure less than 100 mm Hg, and furthermore, we adjusted for blood pressure in the multivariable analyses.

Many physicians eventually adopt the basic findings from large randomized, controlled trials,¹⁸ but they may not prescribe the therapy actually tested in the studies. In particular, physicians may not follow medication dosage protocols. While studies in progress are testing the effect of different dosages of ACE inhibitors on outcomes,^{16,19,20} the Agency for Health Care Policy and Research, American Heart Association, and American College of Cardiology are currently recommending the dosages established in published trials.^{12,13,19} Emphasis on adequate dosing is still needed among all specialty groups.

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