Published in final edited form as:

Am J Kidney Dis. 2008 April ; 51(4): 594–602.

Therapies for Acute Heart Failure in Patients With Reduced Kidney Function: A Community-Based Perspective

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Abstract

Background—Limited data exist describing the management of patients with reduced kidney function at the time of hospital presentation for acute heart failure (HF).

Study Design—Nonconcurrent prospective study.

Setting and Participants—Patients hospitalized with clinical findings of decompensated HF (n=4,350) at all 11 greater Worcester (MA) medical centers in 1995 and 2000 comprised the study sample. Patients were categorized into varying levels of kidney function based on their estimated glomerular filtration rate (eGFR).

Predictor—GFR estimates from serum creatinine levels measured at the time of hospital admission.

Outcomes—Hospital receipt of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, beta blockers, digoxin, and diuretics.

Measurements—Hospital charts were reviewed for the prescribing of disease modifying cardiac therapies as well as therapies designed to provide symptomatic relief from HF.

Results—The average eGFR level (ml/min per 1.73 m²) in our study sample was 64.4 (±33.1) and patients were further categorized into 3 eGFR levels of <30 (n=569), 30–59 (n=1,488), and ≥60 (n=2,293) for comparative purposes. Patients with higher eGFR levels (≥60) were more likely to be treated with angiotensin-converting enzyme inhibitors/angiotensin receptor blocker (56% vs 39%) and digoxin (51% vs 46%) during hospitalization for HF than patients with lower eGFR levels (<30) (p<.05). Patients with lower eGFRs (<30) were more likely to be prescribed beta blockers than patients with higher eGFR levels (≥60) (46% vs 39%) (p<.01). The use of ACE inhibitors/ARBs increased between 1995 and 2000 in 2 of the 3 eGFR groups examined: eGFR levels <30 (33% in 1995; 42% in 2000); eGFR levels ≥60 (51% in 1995; 59% in 2000). The use of beta blockers increased appreciably in all 3 eGFR groups (<30: 27% in 1995; 58% in 2000; ≥60: 25% in 1995; 49% in 2000). Less than one third of all patients, however, were treated with both disease modifying therapies in 2000.

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Financial Disclosure: None.

Limitations—We were unable to classify patients into those with systolic versus diastolic HF.

Conclusions—Our results suggest that the utilization of disease modifying therapies for patients hospitalized with clinical findings of acute HF and decreased kidney function remains less than desirable. Educational programs are needed to enhance the management of patients with decreased kidney function who develop HF.

Keywords

heart failure therapy; kidney dysfunction; population-based study

Introduction

Renal insufficiency is present in more than one-third of patients with congestive heart failure^{1,2}. Mild as well as moderate degrees of reduced kidney function have been associated with increased mortality in patients with this increasingly prevalent clinical syndrome^{1–3}. The effective treatment of heart failure in patients with kidney dysfunction is of considerable contemporary clinical and public health importance.

Despite the absence of data from large well-conducted randomized controlled trials specifically targeting patients with reduced kidney function, subgroup analyses of data from randomized trials and observational studies suggest that angiotensin converting enzyme (ACE) inhibitors and beta blockers are as effective in improving survival in patients with heart failure and renal insufficiency as in patients with normal kidney function^{1–6}. Several studies have shown, however, that patients with kidney disease and heart failure are less likely to receive effective cardiac medications than patients without renal dysfunction^{1, 2,7,8}.

The objectives of our community-wide study among residents of a large New England metropolitan area were to examine the use of evidence-based cardiac therapies in patients hospitalized with clinical findings of decompensated heart failure according to extent of kidney function at the time of hospital presentation. Data from the Worcester Heart Failure Study were utilized for purposes of this investigation^{9,10}.

Methods

Adult men and women of all ages from the Worcester (MA) metropolitan area hospitalized with clinical findings of possible heart failure (HF) at all 11 greater Worcester medical centers during 1995 and 2000 comprised the study population of this report^{9,10}. In brief, the medical records of patients with primary and/or secondary discharge diagnoses consistent with possible HF were reviewed at all area medical centers. The primary International Classification of Disease (ICD)-9 code reviewed for the identification of cases of acute HF was ICD-9 code 428. Additional diagnostic rubrics reviewed for the possible presence of HF included rheumatic heart failure, hypertensive heart disease, hypertensive heart and kidney disease, acute cor pulmonale, primary cardiomyopathies, pulmonary heart disease and congestion, acute lung edema, edema and dyspnea, and respiratory abnormalities^{9,10}. The vast majority (92%) of our case population came from ICD-9 diagnostic code 428. Patients included in this observational study were identified by passive cold pursuit surveillance as computerized printouts of these discharge diagnoses were obtained from all study hospitals and were reviewed by members of the study team; patients who resided outside of the Worcester metropolitan area were excluded from the study sample since this investigation is population-based. Each case of HF included in this study was independently validated, based on use of the Framingham criteria, which included the presence of 2 major criteria or 1 major and 2 minor criteria¹¹. Examples of the major criteria included paroxysmal nocturnal dyspnea and neck vein distention while examples of the minor criteria included bilateral ankle edema and nocturnal cough. Since the majority

(68%) of patients did not undergo echocardiography during the index hospitalization, we were unable to distinguish patients with systolic from those with diastolic dysfunction.

An incident (initial) case of acute HF was defined as the absence of a prior hospitalization for HF, a physician diagnosis of HF, or treatment for HF in the past based on the review of data contained in hospital and outpatient medical records. Patients who developed HF secondary to admission for another illness (e.g., acute myocardial infarction), or after an interventional procedure (e.g., coronary artery bypass surgery), were not included in the study sample. Kidney disease was classified into commonly accepted categories of estimated glomerular filtration rate (eGFR) (e.g., ≥ 60 , 30–59, and < 30 ml/min per 1.73m^2) (1.00, 0.50–0.99, < 0.50 mL/s/ 1.73m^2) based on the Modification of Diet in Renal Disease (MDRD) Study equation¹². Patient's initial serum creatinine value obtained during hospitalization for acute HF at each greater Worcester medical center was utilized for purposes of analysis. Patients who had previously undergone dialysis were excluded from this study population since concerns might be raised that the etiology, diagnosis, and management of HF in patients treated by dialysis might differ from those who were not managed by dialysis.

Data Collection

Information was collected by trained study physicians and nurses about patient's demographic and clinical characteristics through the review of information contained in hospital medical records. This included information about patient's age, sex, prior comorbidities (including HF), admission levels of blood pressure, and serum levels of sodium, potassium, creatinine, and blood urea nitrogen at the time of hospital admission. The presence of each of the comorbidities examined was determined based on the review of data contained in hospital charts with no independent validation of these prior conditions. Information was collected about the use of cardiac medications during hospitalization for HF, including the prescribing of ACE inhibitors, angiotensin receptor blockers (ARBs), beta blockers, digoxin, and diuretics. Patients who were treated with spironolactone were considered to have been treated with diuretics. For purposes of analysis, patients treated with ACE inhibitors/ARBs or beta blockers were considered to have received disease modifying therapies whereas patients treated with diuretics or digoxin were classified as having received therapies for the symptomatic relief of acute HF.

Data Analysis

Differences in the distribution of demographic, medical history, and clinical characteristics in patients with clinical findings of decompensated HF according to predefined eGFR cutpoints were examined through the use of chi-square tests and analysis of variance (ANOVA) for discrete and continuous variables, respectively. Differences in the utilization of various cardiac medications during hospitalization for acute HF according to serum levels of eGFR were examined through the use of chi square tests of statistical significance. Logistic regression modeling was used to examine the association between serum levels of eGFR and the prescribing of selected therapies while controlling for several potentially confounding demographic and clinical factors that might be associated with medication prescribing practices (see Table 3 footnote).

Results

The study sample consisted of 4,350 greater Worcester residents hospitalized with clinical findings of acute HF during 1995 and 2000. Of these, 2,293 patients (52.7 %) had an eGFR ≥ 60 ml/min per 1.73m^2 (≥ 1.0 ml/s/ 1.73m^2), 1,488 (34.2%) had an eGFR between 30–59 ml/min/ 1.73m^2 (0.50–0.98 ml/s/ 1.73m^2), and 569 (13.1%) patients had an eGFR < 30 ml/min/ 1.73m^2 (< 0.50 ml/s/ 1.73m^2). The mean age of the study sample was 76 years, 43% were men,

and 94% were white. The demographic characteristics of the study population were similar in greater Worcester residents hospitalized with acute HF in 1995 and in 2000.

Baseline Characteristics of the Study Sample

Patients with lower serum levels of eGFR were older, more likely to be male, were more likely to have a prior history of hypertension, coronary artery disease, HF, diabetes, peripheral vascular disease, and anemia, but were less likely to be a current smoker or to have had chronic obstructive pulmonary disease previously diagnosed, in comparison to patients with higher levels of eGFR (Table 1). Patients with reduced kidney function at the time of hospital presentation with acute HF were also more likely to have undergone coronary artery bypass surgery in the past in comparison to patients without kidney disease. Patients with a lower eGFR had a significantly lower heart rate at the time of hospital admission, and higher serum levels of potassium and blood urea nitrogen, in comparison to patients with higher eGFR's. The risk of dying during hospitalization for acute HF was significantly higher among patients with lower serum levels of eGFR (Table 1).

Utilization of Different Treatment Approaches According to Level of eGFR

In terms of prior prescribing practices, approximately 11% of patients with an eGFR <30 ml/min per 1.73m^2 (<0.50 ml/s/ 1.73m^2) had been prescribed ACE inhibitors/ARB's and beta blockers prior to hospitalization for acute HF based on the review of hospital medical records as compared to 16% of those with an eGFR 30–59 ml/min/ 1.73m^2 (0.50 – 0.98 ml/s/ 1.73m^2) and 13% of patients with an eGFR ≥ 60 ml/min per 1.73m^2 (≥ 1.0 ml/s/ 1.73m^2). Approximately 35% of patients with an eGFR <30 ml/min per 1.73m^2 (<0.50 ml/s/ 1.73m^2), 34% of those with an eGFR between 30–59 ml/min/ 1.73m^2 (0.50 – 0.98 ml/s/ 1.73m^2), and 28% of those with an eGFR ≥ 60 ml/min per 1.73m^2 (≥ 1.0 ml/s/ 1.73m^2) were prescribed both diuretics and digoxin prior to their index hospitalization.

Patients with lower serum eGFR levels were significantly less likely to be prescribed ACE inhibitors/ARBs than patients with higher eGFRs during hospitalization for acute HF (Table 2). On the other hand, patients with a lower eGFR were significantly more likely to be treated with beta blockers than patients with higher eGFRs. In terms of combination medical therapy (receipt of ACE inhibitors/ARBs and beta blockers), patients with the lowest serum eGFR levels were significantly less likely to have received both effective cardiac medications as compared to patients with more normal kidney function. The vast majority of study patients, irrespective of eGFR levels, were treated with diuretics. Patients with the lowest serum levels of eGFR were least likely to be treated with digoxin.

A significantly lower percentage of patients failed to be prescribed any of the disease modifying cardiac therapies (ACE inhibitors/ARBs and beta blockers) examined across all 3 eGFR groups between our 2 study years (Figure 1) ($p<.01$). Among patients with an eGFR <30 ml/min per 1.73m^2 (<0.50 ml/s/ 1.73m^2), 46.8% and 23.9% of patients were not prescribed any of these therapies in 1995 and 2000, respectively. These percentages were 30.3% and 22.7%, and 36.7% and 24.1%, respectively, in patients with an eGFR 30–59 ml/min/ 1.73m^2 (0.50 – 0.98 ml/s/ 1.73m^2) and ≥ 60 ml/min/ 1.73m^2 (≥ 1.0 ml/s/ 1.73m^2), respectively, in 1995 and in 2000. Despite these encouraging increases in the use of proven cardiac regimens between our 2 study years, less than one third of patients in each eGFR category were prescribed both classes of effective cardiac therapy in 2000. In terms of the utilization of therapies designed to provide acute symptomatic relief from HF, the prescribing of diuretic therapy during hospitalization for HF remained stable between 1995 and 2000 in each of the eGFR groups examined whereas the use of digoxin declined slightly over time (Figure 1).

After controlling for age, sex, and a variety of potentially confounding medical history and clinical factors (see footnote to Table 3), patients with the most severe renal dysfunction (eGFR < 30 ml/min per 1.73m² (<0.50 ml/s/1.73m²)) were significantly less likely to have received both ACE inhibitors/ARBs and beta blockers during hospitalization for HF. Similarly, patients with the poorest kidney function were significantly less likely to have been prescribed ACE inhibitors or ARBs during their acute hospitalization in comparison to patients with higher levels of kidney function. On the other hand, patients with an eGFR between 30–59 ml/min/1.73m² (0.50–0.98 ml/s/1.73m²), and those with an eGFR < 30 ml/min/1.73m² (<0.50 ml/s/1.73m²), were significantly more likely to have been treated with beta blockers than patients with normal kidney function (Table 3). When eGFR was expressed as a continuous variable, there was no statistically significant association between serum levels of eGFR and receipt of both ACE inhibitors/ARBs and beta blockers during hospitalization for acute HF. In contrast, for every unit increase in serum levels of eGFR, there was a 0.3% (95% CI 0.1–0.6%) increase in the likelihood of being prescribed beta blocker therapy but a 0.4% reduced likelihood (95% CI 0.2–0.7%) of being treated with ACE inhibitor/ARB therapy after previously described demographic, medical history, and clinical characteristics were controlled for.

With regards to changes in the prescribing of these cardiac medications between 1995 and 2000, after controlling for similar demographic and clinical covariates, patients who were hospitalized in 2000 were 5% more likely to have received ACE inhibitors/ARBs (95% CI 2% to 7%), 28% more likely (95% CI 25% to 32%) to have received beta blockers, and were 6% less likely to have received digoxin (95% CI 4% to 9%) in comparison to patients hospitalized with decompensated HF in 1995 at all greater Worcester medical centers. There was no significant association between time period of hospitalization and receipt of diuretic therapy.

Discussion

The results of this observational study among residents of a large New England metropolitan area suggest that although there have been modest improvements in the use of beneficial cardiac medications in patients with varying degrees of kidney dysfunction at the time of hospital presentation for acute HF, overall use of these effective therapies remains suboptimal.

To the best of our knowledge, this is the first population-based study that has examined the use of different treatment modalities in patients hospitalized with clinical findings of acute HF according to degree of renal dysfunction. Changing trends in the use of different therapies for patients hospitalized with HF have been examined previously without, however, a particular focus on these prescribing practices according to the presence of kidney disease^{13–15}.

Inhibition of the angiotensin-renin-aldosterone system is crucial to the management of patients with congestive HF and this therapeutic approach has been shown to improve survival in most subsets of patients with HF examined. However, since initiation of these agents can be associated with increased creatinine levels and/or hyperkalemia, patients with renal dysfunction have been largely excluded from randomized clinical trials that have evaluated this therapy in patients with HF. Fear of worsening kidney function is also commonly cited by physicians for failure to use these agents in patients with kidney dysfunction^{15,16}. Nevertheless, limited data suggest that these agents can be used safely and offer similar, if not greater, benefit in patients with renal dysfunction^{6,17–20}. In the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS), patients with HF assigned to enalapril therapy had a similar reduction in 1 year mortality (~30%) whether their serum creatinine findings were above or below the median levels of patients enrolled in this trial^{19,20}. In addition, although approximately one-third of patients treated with enalapril experienced significant increases in serum creatinine over the course of this trial, these levels normalized in the vast majority of patients without any change in treatment dose. In a review of clinical

trials of ACE inhibitors in patients with HF, these agents were well tolerated by most patients with varying degrees of renal insufficiency⁶.

Approximately 1 in 5 patients with HF may have poor tolerance to ACE inhibitors leaving angiotensin II antagonists as a treatment of choice²¹. Compared to ACE inhibitors, however, angiotensin II antagonists do not affect bradykinin accumulation and, therefore, it is believed that their administration may have fewer associated side effects²². The Evaluation of Losartan in the Elderly (ELITE) trial compared the use of Losartan to Captopril with regards to kidney dysfunction in elderly patients with symptomatic HF who were enrolled in a multicenter prospective study. Both early and subsequent (ELITE 2) studies found no differences in kidney function with the use of these agents although Losartan was associated with improved overall survival^{18,23}.

Despite these observations and findings from prior studies, more than half of metropolitan Worcester residents with clinical findings of decompensated HF did not receive these medications in either study year. Approximately one-third of patients were treated with ACE inhibitors in 1995 which is consistent with the findings observed among Medicare beneficiaries in the Cooperative Cardiovascular Project where only one third of patients with decreased left ventricular ejection fraction and kidney failure received this therapy in the mid-1990's⁷. In a study of more than 6,000 elderly patients from Alberta and British Columbia, those diagnosed with HF, coronary artery disease, and low eGFR levels were consistently less likely to have received ACE inhibitors/ARBs and beta blockers than patients with higher levels of GFR².

Numerous studies have convincingly demonstrated that initiation of beta blockade in patients with HF or left ventricular dysfunction is associated with a significant reduction in mortality. From a pathophysiologic standpoint, there is little reason to believe that these agents would be less advantageous in HF patients with renal dysfunction. Indeed, if carefully initiated and titrated, beta blockers may improve kidney function over the long term through an overall improvement in hemodynamic related parameters^{24,25}. Although a number of clinical trials evaluating beta blockers in patients with HF have excluded subjects with kidney failure, data from at least one large clinical trial suggests a similar survival benefit among patients with or without moderate renal insufficiency⁵.

Although the use of beta blockers in patients with renal dysfunction in our study was suboptimal, we observed significant improvements in the utilization of this therapy between 1995 and 2000. Changing trends in the prescription of beta blockers in patients with HF have also been previously documented in a study of elderly patients with HF admitted to Washington University Medical Center. Patients with HF with preserved left ventricular systolic function were more likely to have received beta blockers in 1995 (53%) in comparison to 1990 (34%)¹⁴.

Diuretics were utilized in the majority of patients with acute HF in our study, irrespective of the presence of kidney disease or study year. In the previous study of patients with a primary diagnosis of HF admitted to Washington University Medical Center, the use of diuretics among patients with HF and preserved left ventricular function increased from 66% in 1990 to 80% in 1995¹⁴.

A combination of furosemide and spironolactone was used successfully among patients with HF enrolled in the Randomized Aldactone Evaluation Study (RALES)²⁶. While the overall mortality from severe HF declined appreciably in this study, severe hyperkalemia developed in a few patients with high creatinine levels. Future studies should identify the safest combination of diuretics, such as furosemide and spironolactone, which may decrease the incidence of hyperkalemia in patients with HF and renal dysfunction.

Although digoxin has been shown to decrease the risk of HF related hospitalizations, it has never been shown to significantly impact mortality in patients with HF²⁷. Since the clearance of digoxin varies linearly with kidney function, and digoxin toxicity may be heralded by a variety of life threatening arrhythmias, one could argue that this agent should be used very cautiously in patients with kidney disease and only in patients who require it for control of their symptoms. Nevertheless, we found that the utilization of digoxin was as high or higher than that of ACE-inhibitors/ARBs or beta-blockers in patients with severe or moderate renal insufficiency in the present study.

Our data suggests that physicians may not always carefully weigh the perceived risks and potential benefits of HF therapies in patients with kidney disease. In their defense, most clinical trials evaluating the efficacy and safety of these drugs have excluded patients with renal dysfunction. Based on our observations, there is need for further study and educational efforts to enhance the treatment of patients with acute HF and kidney disease. Since less than one third of patients in each eGFR group were on both disease modifying cardiac therapies in 2000, there is considerable room for improvement in the use of these highly effective therapies so that patients long-term prognosis will be enhanced.

This study was based on the review of information contained in hospital medical charts. Information about treatment dosages and potential contraindications to the use of the treatment regimens examined was not collected. Differentiation of patients into those with systolic and diastolic dysfunction was not possible due to the large amount of missing data in hospital medical records about ejection fraction findings. Moreover, we utilized patients initial serum creatinine value to characterize their serum levels of eGFR and we did not assess serial changes in this laboratory parameter during the acute hospitalization. Inasmuch, there may have been some misclassification of the stage of chronic kidney disease in the study sample. We also did not examine the association between lack of use of disease modifying therapy and hospital death rates given the nonrandomized observational nature of this study. The strengths of this investigation include its population-based perspective among residents of a large and representative New England metropolitan area, inclusion of patients from different types of hospitals, and large number of patients with independently validated HF.

The results of our study provide insights into the use of different cardiac therapies in greater Worcester residents hospitalized with clinical findings of acute HF in relation to extent of kidney function. Similar to efforts that have been successfully used to enhance the treatment and outcomes of patients with acute myocardial infarction²⁸, approaches to improve drug prescribing practices and treatment adherence for patients with HF and reduced kidney function are warranted. Further studies are needed to define the more effective treatment for patients diagnosed with HF and kidney disease and encouragement for the use of proven treatment modalities, especially in those with symptoms associated with kidney insufficiency. Most clinical trials conducted to date have focused on patients with systolic heart failure and several large trials are currently investigating the role of ACE inhibitors, angiotensin receptor blockers, and beta blockers in patients with diastolic HF²⁹. The results of these trials should provide assistance to physicians in the management of this large group of patients with intact left ventricular systolic function. Additional analyses of these trials may also hopefully elucidate how the management of patients with kidney disease and diastolic heart failure might be enhanced.

Acknowledgements

This research was made possible by the cooperation of the medical records, administration, and cardiology departments of participating hospitals in the Worcester metropolitan area.

Support: This project was supported by funding from the National Institutes of Health (R37 HL69874).

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Figure 1.
Receipt of selected cardiac medications according to serum levels of estimated glomerular filtration rate (eGFR) and study year

Table 1
Patient characteristics according to serum levels of estimated glomerular filtration rate (eGFR)*

Characteristic	eGFR < 30 (n=569)	eGFR 30–59 (n=1,488)	eGFR ≥ 60 (n=2,293)	P value
<u>Demographics</u>				
Age (mean, yrs)	76.8	78.3	75.0	<0.001
Men (%)	55.4	51.7	34.3	<0.001
<u>Medical history (%)</u>				
Anemia**	77.0	60.3	44.8	<0.001
Angina	19.3	22.8	19.4	<0.05
Cancer	21.1	18.4	19.8	0.3
Coronary artery bypass grafting	26.5	23.1	14.5	<0.001
Chronic obstructive pulmonary disease	31.8	34.3	36.9	<0.001
Current cigarette smoker	6.7	6.7	12.3	<0.001
Diabetes mellitus	50.6	43.4	33.8	<0.001
Heart failure	85.6	79.6	68.1	<0.001
Hypertension	76.1	65.3	61.2	<0.001
Myocardial infarction	55.4	51.6	43.4	<0.001
Percutaneous coronary intervention	7.9	8.5	6.9	0.2
Peripheral vascular disease	29.0	21.8	12.7	<0.001
Stroke	16.5	16.3	13.5	<0.05
<u>Hospital admission findings (mean)</u>				
Heart rate (bpm)	84.8	88.7	93.5	<0.001
Systolic blood pressure (mmHg)	143.1	142.4	145.7	<0.05
Length of hospital stay (days)	7.0	6.8	6.2	0.1
Died during hospitalization (%)	9.7	8.0	5.3	<0.001
<u>Laboratory data on admission (mean, mg/dl)</u>				
Blood urea nitrogen	74.3	38.1	21.0	<0.001
Potassium	4.9	4.5	4.3	<0.001
Sodium	137.0	137.3	137.4	0.4

* ml/min per 1.73m²

** hematocrit <37 in women; <40 in men

Note: To convert eGFR in mL/min/1.73m² to mL/s/1.73m², multiply by 0.01667; blood urea nitrogen in mg/dL to mmol/L, multiply by 0.357. Potassium and sodium in mEq/L are equivalent to mmol/L.

Table 2

Use of different treatment practices according to serum levels of estimated glomerular filtration rate (eGFR)*

Therapy (%)	< 30 (n=569) %	30–59 (n=1,488) %	≥ 60 (n=2,293) %	P value
ACE inhibitors/ARBs	38.7	56.3	55.7	<0.001
Beta blockers	46.2	42.0	38.5	<0.01
Combination medical therapy ^o	17.6	24.3	23.8	<0.001
Diuretics	98.8	98.6	98.4	0.8
Digoxin	46.2	52.6	51.1	<0.001

* ml/min per 1.73m²^o receipt of ACE inhibitors/ARBs and beta blocker therapyNote: To convert eGFR in mL/min/1.73m² to mL/s/1.73m², multiply by 0.01667

Table 3

Association between serum levels of estimated glomerular filtration rate (eGFR) and receipt of effective cardiac therapies

Serum levels of eGFR (mL/min/1.73m ²)	ACE Inhibitors/ARBs and Beta Blockers			ACE Inhibitors/ARBs			Beta Blockers		
	Crude Odds Ratio (OR)	Age and Sex Adjusted OR	Multivariable Adjusted OR*	Crude OR	Age and Sex Adjusted OR	Multivariable Adjusted OR	Crude OR	Age and Sex Adjusted OR	Multivariable Adjusted OR
eGFR ≥60 [†]	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
eGFR 30–59	1.04	1.10	0.99	1.03	1.03	0.93	1.18	1.23	1.17
eGFR <30	(0.90,1.22)	(0.94,1.28)	(0.83,1.17)	(0.90,1.17)	(0.90,1.18)	(0.80,1.07)	(1.03,1.34)	(1.07,1.41)	(1.00,1.36)
	0.69	0.71	0.56	0.50	0.49	0.41	1.40	1.46	1.36
	(0.55,0.88)	(0.56,0.90)	(0.43,0.72)	(0.42,0.61)	(0.40,0.59)	(0.33,0.50)	(1.16,1.68)	(1.21,1.76)	(1.10,1.68)

* Controlling for age, sex, current smoking status, medical history of anemia, coronary heart disease, cancer, percutaneous coronary intervention/coronary bypass surgery, chronic obstructive pulmonary disease, diabetes, heart failure, peripheral vascular disease, stroke, admission heart rate and systolic blood pressure, length of hospital stay, and hospital survival status

[†] referent category

Note: To convert eGFR in mL/min/1.73m² to mL/s/1.73m², multiply by 0.01667