Treatment and Risk in Heart Failure
Gaps in Evidence or Quality?

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Background—Although the absolute benefits of an intervention are proportional to patients' underlying risk, studies in heart failure have noted a paradoxical inverse relationship between treatment and risk. The extent to which this reflects higher rates of contraindications in patients with higher risk or larger gaps in care quality has not been explored.

Methods and Results—We studied 18 307 patients with left ventricular systolic dysfunction surviving hospitalization between January 2005 and June 2007 from 194 hospitals participating in Get With The Guidelines (GWTG)–Heart Failure. Patients were categorized according to their estimated risk for in-hospital mortality using a validated risk score. The proportions of patients with documented contraindications to angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and β-blockers as well as the use of these medications among patients without contraindications at hospital discharge was determined across levels of risk. For each therapy, the proportion of patients with contraindications was significantly higher with increasing patient risk ($P<0.001$ for each). Even after excluding those with contraindications, the use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and β-blockers was significantly lower with increasing risk ($P<0.001$ for each).

Conclusions—The use of evidence-based therapies is lower in patients with heart failure at higher risk of mortality both because of higher rates of contraindications to therapy and lower rates of use among eligible patients. Optimizing heart failure outcomes will require both the expansion of the evidence base for treating the highest-risk patients as well as the development of effective strategies to assure that eligible high-risk patients receive all appropriate therapies. **(*Circ Cardiovasc Qual Outcomes*. 2010;3:00-00.)**

Key Words: heart failure ■ pharmacotherapy ■ health policy and outcomes research

Several medications, including angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) and β-blockers, reduce mortality and morbidity in patients with heart failure (HF) and left ventricular systolic dysfunction (LVSD). Based on this evidence, clinical practice guidelines recommend these therapies for patients with LVSD and without contraindications to a given therapy.[1] These therapies are in some cases encouraged by national performance measures[2] and publicly reported as a means of evaluating the quality of HF care.[3] Further, national quality improvement efforts have focused on ensuring that patients hospitalized with HF are prescribed appropriate medications at discharge.[4]

The relative benefits of many therapies are typically consistent across the spectrum of risk,[5,6] thus conferring greater absolute benefits to higher-risk patients. However, studies have identified a "risk-treatment paradox" for common cardiovascular conditions, whereby higher-risk patients are less likely to receive recommended therapy.[7–10] This risk-treatment paradox may reflect 1 of 2 phenomena. First, higher-risk patients may have a higher prevalence of contraindications to therapy, rendering them ineligible for evidence-based therapy ("evidence gap"). Second, higher-risk patients may be less likely to receive therapy even when eligible for treatment ("treatment gap").

The extent to which the observed risk-treatment paradox in HF represents evidence gaps or treatment gaps is not well known. The objective of the present study was to clarify these contributors to risk-related differences in care by determining first the proportions of patients with HF and LVSD with physician-documented contraindications to recommended medical therapy and second the proportions of patients without contraindications who do not receive evidence based therapy as a function of estimated mortality risk.

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WHAT IS KNOWN

- A risk-treatment paradox has been identified for heart failure, whereby higher-risk patients are less likely to receive recommended therapy.
- This may reflect that higher-risk patients may have a higher prevalence of contraindications to therapy, rendering them ineligible for evidence-based therapy (evidence gap), or that higher-risk patients may be less likely to receive therapy even when eligible for treatment (treatment gap).

WHAT THE STUDY ADDS

- This study demonstrates that both an evidence gap (clinically documented contraindications were higher with increasing mortality risk) and a treatment gap (treatment rates among eligible patients were inversely associated with risk) exist.
- Thus, optimizing heart failure outcomes will require the development of effective strategies to assure that eligible high-risk patients receive all appropriate therapies and more broadly applicable evidence-based care strategies for patients who are not eligible for current guideline-recommended treatments.

Methods

Data Source

Data from the American Heart Association's (AHA) Get With The Guidelines-HF module (GWTG-HF) was used for this analysis. GWTG is a voluntary hospital-based national quality initiative. Participating hospitals are instructed to submit information on consecutive patients admitted to the hospital with new or worsening HF or patients who have significant HF symptoms during hospitalization to the program database using a Web-based interactive case report form and Patient Management Tool (PMT, Outcomes Sciences Inc, Cambridge, Mass). The diagnosis of HF is based on the treating clinicians' assessment. The GWTG-HF program and its component data elements have been described previously.[4,11]

All participating institutions were required to comply with local regulatory and privacy guidelines, and if required, submit the GWTG protocol for review and approval by their institutional review board. Because data were used primarily at the local site for quality improvement, sites were granted a waiver of informed consent under the common rule. Outcome Sciences served as the registry coordinating center. The Duke Clinical Research Institute served as the data analysis center and institutional review board approval was granted to analyze aggregate deidentified data for research purposes.

Study Population

Between January 2005 and June 2007, data were collected on 23 578 patients from 202 hospitals who had a diagnosis of HF, a left ventricular ejection fraction (LVEF) <40%, and were discharged alive. Patients were excluded if the admission date or time was invalid (n=1), data were missing for their discharge status (n=19) or left ventricular function (4156), or if they were transferred to a different acute care facility (n=544), left against medical advice (n=138), or were discharged to hospice (n=413). The final study cohort consisted of 18 307 patients with HF and LVSD surviving hospitalization from 194 hospitals.

Data Collection

The Patient Management Tool is used for point-of-care and/or chart-review data collection by personnel trained in case ascertainment, use of the patient management tool, standard coding instructions, and quality control. Data are collected from the medical record using standardized data elements and definitions for demographic and clinical characteristics, medical history, admission and discharge physical examination findings and laboratory values, in-hospital outcomes, discharge disposition, discharge medications, and contraindications to medications. Required fields are structured so that valid data must be entered before the data can be saved as a complete record and entered into the database. Range checks are used for inconsistent or out of range data and prompted the user to correct or review data entries that were outside a predefined range. Contraindications to medications are determined to be present if documented in the medical record by the treating clinicians. The contraindications collected for each medication are listed in Table 2. Contraindications are not explicitly defined (eg, hyperkalemia is not defined by a specific potassium value). For this analysis, the focus was on the prescription of and contraindications to ACE inhibitors or ARBs and β-blockers.

Risk Classification

Patients were categorized according to their estimated in-hospital mortality risk using the validated GWTG-HF risk prediction score.[12] The risk score uses age, heart rate, systolic blood pressure, serum sodium, serum BUN, race, and a history of chronic obstructive pulmonary disease to calculate an aggregate risk score. The performance characteristics of the risk prediction score have been previously reported and include a c-index of 0.75. For this study, patients were categorized into 6 groups based on their estimated risk of in-hospital mortality. The thresholds used were round percentages with estimated risks as follows: group 1: <1%, group 2: 1% to 2%, group 3: 2% to 3%, group 4: 3% to 4%, group 5: 4% to 5%, and group 6: ≥5%. This grouping corresponded with observed mean in-hospital mortality rates of 0.6%, 1.4%, 2.3%, 3.3%, 4.4%, and 8.8%, respectively.

Statistical Analysis

Patient characteristics were compared across risk categories using Cochran-Mantel-Haenszel tests for categorical variables and Cochran-Mantel-Haenszel nonzero correlation tests for continuous variables. In the analytic cohort, sex was missing in 1.7% and past medical history was missing in 2.5%. Therefore, missing sex and medical history were imputed to the dominant category (male and no/absent, respectively). The proportion of patients with documented contraindications to guideline recommended therapies and the proportion of eligible patients prescribed guideline recommended therapies were determined within each risk stratum and compared across risk strata using Cochran-Mantel-Haenszel tests. Reported contraindications were also compared across risk strata using Cochran-Mantel-Haenszel tests. For those with reported contraindications of worsening renal function and symptomatic hypotension, median discharge serum creatinine and mean discharge blood pressure measures were determined and compared across risk strata using Cochran-Mantel-Haenszel nonzero correlation statistics. Stratified analyses were performed for the Cochran-Mantel-Haenszel tests to compare the prescription of medications to ideal patients; the failure to prescribe medications to ideal patients; and the proportion of contraindications adjusting for hospital effects. All analyses were performed using SAS software (version 9.1, SAS Institute, Cary, NC). Drs Hernandez and Liang had full access to the data in the study and take full responsibility for the integrity of the data and the accuracy of the data analysis.

Results

Patient Characteristics

The characteristics of patients as a function of estimated mortality risk are shown in Table 1. Patients at higher risk were older and more likely to be Caucasian. They were more likely to have coexisting illnesses, including atrial fibrillation,

Table 1. Population Characteristics

Group (In-Hospital Mortality Risk)	1 (<1%) (n=4113)	2 (1.01%–2%) (n=5311)	3 (2.01%–3%) (n=3292)	4 (3.01%–4%) (n=2000)	5 (4.01%–5%) (n=1462)	6 (>5%) (n=2129)	*P* Value
Age, y, mean (SD)	56.7 (14.4)	68.0 (13.3)	73.6 (11.7)	75.4 (11.3)	77.7 (10.3)	79.0 (9.7)	*
Male	60.3	59.9	59.8	61.4	61.1	61.7	0.144
Race							*
White	40.3	64.4	76.3	81.1	84.0	85.7	
Black	49.6	22.6	12.6	8.5	7.1	5.3	
Hispanic	5.5	6.6	5.4	5.3	4.5	4.6	
Other	2.9	3.9	3.0	3.5	3.1	3.1	
Insurance							<0.001
Medicare	33.5	49.7	58.4	62.4	62.5	62.8	
Medicaid	12.9	6.9	4.3	3.3	3.4	1.8	
Other	34.0	32.9	30.0	28.7	29.4	30.8	
None	14.7	5.4	2.7	2.15	1.4	1.4	
Medical history							
CAD	37.3	52.2	56.2	56.0	58.7	60.5	<0.001
Prior MI	10.8	16.7	16.3	16.1	17.0	15.9	<0.001
Atrial fibrillation	12.6	23.7	29.4	32.0	34.3	41.3	<0.001
Peripheral vascular disease	7.3	11.05	12.6	13.3	12.8	16.4	<0.001
Stroke/TIA	9.9	12.9	14.3	15.8	14.9	13.7	<0.001
Hypertension	74.9	67.5	66.3	62.5	62.2	59.2	<0.001
Hyperlipidemia	32.3	38.2	38.9	40.4	38.0	37.4	0.005
Diabetes	39.3	41.6	39.6	39.7	38.2	39.9	0.069
Pulmonary disease*	17.1	22.4	25.2	31.4	32.6	34.9	*
Anemia	7.5	10.4	12.8	15.2	16.2	19.1	<0.001
Depression	7.1	9.2	8.5	10.1	9.5	8.6	0.026
ICD	11.6	16.3	17.4	19.7	19.4	19.8	<0.001
CRT	6.2	10.5	12.4	14.5	14.6	14.8	<0.001
Laboratory values at admission							
Sodium, mEq/L*	138 (136–140)	138 (135–140)	137 (135–140)	137 (135–140)	137 (134–139)	137 (134–140)	<0.001
Creatinine, mg/dL	1.3 (1.0–1.6)	1.3 (1.0–1.7)	1.4 (1.1–1.8)	1.4 (1.1–1.9)	1.5 (1.1–2.0)	1.6 (1.2–2.3)	<0.001
BUN*							*
Potassium, mEq/L	4.0 (3.7–4.3)	4.1 (3.8–4.4)	4.1 (3.8–4.4)	4.1 (3.8–4.5)	4.1 (3.8–4.5)	4.1 (3.8–4.5)	<0.001
In-hospital data							
Systolic blood pressure, mm Hg							*
Heart rate, bpm							*
Ejection fraction, %, mean (SD)	25.1 (7.9)	25.1 (7.7)	25.1 (7.7)	24.9 (7.7)	24.6 (7.8)	24.2 (7.6)	<0.001
ICD, %	9.6	11.9	10.0	7.6	5.9	4.5	<0.001
CRT, %	3.8	5.5	5.5	3.6	3.5	2.5	<0.001
Coronary angiography, %	14.0	11.6	9.0	8.0	6.4	3.9	<0.001
Length of stay, days	3 (2–5)	4 (2–6)	4 (2–6)	4 (3–7)	5 (3–7)	5 (3–8)	<0.001
Hospital characteristics							
Region							<0.001
Northeast	17.9	17.4	16.1	17.0	17.1	17.4	
Midwest	27.3	30.0	32.5	31.9	31.5	31.7	
South	40.8	35.4	34.1	34.9	33.0	32.9	
West	12.4	15.0	15.0	14.0	16.1	15.2	
Academic	57.0	59.7	57.3	56.7	54.9	55.1	<0.001
Bed size	338 (270–505)	338 (217–527)	342 (209–505)	353 (216–527)	375 (214–553)	353 (194–553)	<0.001

CAD indicates coronary artery disease; MI, myocardial infarction; TIA, transient ischemic attack; ICD, implantable cardioverter-defibrillator; and CRT, cardiac resynchronization therapy.

All continuous variables are displayed as medians (lower and upper quartiles) unless otherwise noted.

*Component variable in risk score; thus statistically significant differences among risk groups is expected.

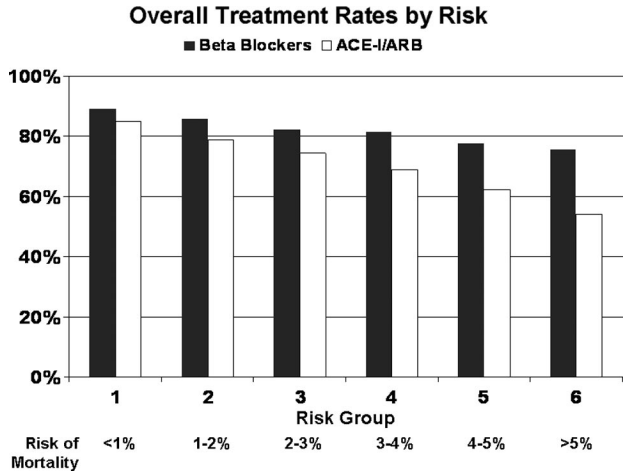

Figure 1. Treatment rates by level of risk among the entire cohort (*P* for trend <0.001 across levels of risk for both therapies).

peripheral vascular disease, prior stroke, pulmonary disease, anemia, and renal insufficiency.

Contraindications

Overall treatment rates declined with increasing risk (Figure 1). Of the overall cohort, 13% of the patients (n=2330) had a documented contraindication to ACE inhibitors and ARBs and 7% (n=1270) to β-blockers. For both ACE-inhibitors/ARBs and β-blockers, the proportion of patients with documented contraindications increased significantly with increasing risk (Figure 2 and Figure 3) The proportion of patients with a contraindication to one or both classes of medications was also greater with increasing risk (Figure 4). Stated conversely, the proportion of patients without any contraindication and therefore eligible for both therapies decreased with increasing mortality risk, although 67% of those in the highest-risk group were eligible for both therapies.

The frequencies of specific contraindications for each class of medication are shown in Table 2. Among those with documented contraindications to ACE-inhibitors, patients at higher risk were more likely to have worsening renal function ($P<0.001$) and symptomatic hypotension ($P<0.001$) and less likely to have allergy ($P<0.001$) or bilateral renal artery stenosis ($P=0.015$) documented as reasons for not prescribing an ACE inhibitor. Among those with documented contraindications to ARBs, higher-risk patients were more likely to have worsening renal function ($P=0.001$) and symptomatic hypotension ($P<0.001$) and less likely to have "other" reasons for not prescribing an ARB ($P<0.001$). Among those with documented contraindications to β-blockers, patients at higher risk were more likely to have symptomatic hypotension ($P<0.001$) and less likely to have bradycardia ($P<0.001$).

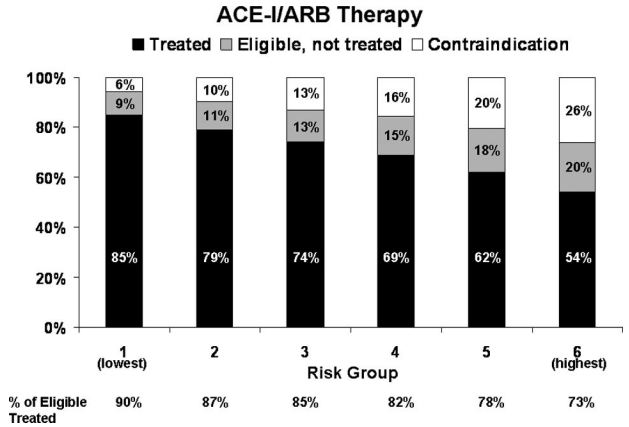

Figure 2. ACE-I/ARB eligibility and treatment rates by level of risk (*P* for trend <0.001 for all categories across levels of risk).

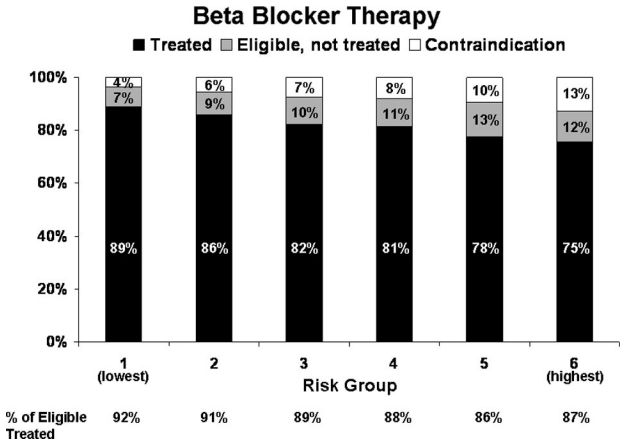

Figure 3. β-Blocker eligibility and treatment rates by level of risk (*P* for trend <0.001 for all categories across levels of risk).

Treatment Patterns by Level of Risk

The proportion of eligible patients (those without a documented contraindication) receiving a discharge prescription for ACE/ARBs and β-blockers were 84.9% and 89.7%, respectively. The proportions of patients eligible for therapy who were treated at discharge decreased with increasing mortality risk for both ACE/ARB ($P<0.001$) and β-blockers (<0.001) (Figures 2 and 3).

Discussion

In the present population of patients hospitalized with HF from all regions of the United States, rates of treatment with

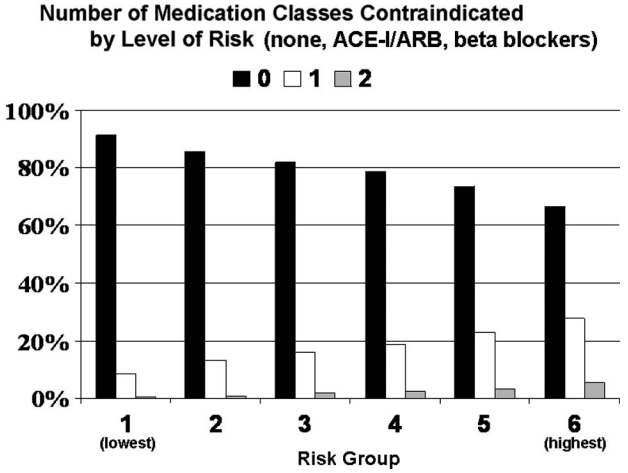

Figure 4. Proportion of patients with 0, 1, and 2 medications contraindicated by level of risk (*P* for trend <0.001 across levels of risk for each).

Table 2. Documented Contraindications by Medication Class

Contraindication	n	% of Those With a Documented Contraindication to Each Medication	% of Total Cohort
Any documented contraindication to ACE inhibitor	3580	100%	19.6%
Worsening renal function	1725	48.2%	9.4%
Symptomatic hypotension	488	13.6%	2.7%
Allergy (other than angioedema, rash, hives)	302	8.4%	1.7%
Hyperkalemia	159	4.5%	0.9%
Moderate-severe aortic stenosis	112	3.1%	0.6%
Bilateral renal artery stenosis	22	0.6%	0.1%
Angioedema, hives, severe rash	6	0.2%	<0.1%
Other	638	17.8%	3.5%
Unable to determine	116	3.2%	0.6%
Any documented contraindication to ARBs	2905	100%	15.9%
Worsening renal function	1429	49.2%	7.8%
Symptomatic hypotension	395	13.6%	2.2%
Hyperkalemia	119	4.1%	0.7%
Moderate-severe aortic stenosis	112	3.9%	0.6%
Allergy	85	2.9%	0.5%
Bilateral renal artery stenosis	21	0.7%	0.1%
Other	730	25.1%	4.0%
Any documented contraindication to β-blockers	1270	100%	6.9%
Asthma/severe reactive airway disease	358	28.2%	2.0%
Symptomatic hypotension	328	25.8%	1.8%
Bradycardia	176	13.9%	1.0%
Allergy to β-blocker	67	5.3%	0.4%
2nd- or 3rd-Degree heart block without pacer	20	1.6%	0.1%
Shock	1	<0.1%	<0.1%
Other	364	28.7%	2.0%

guideline-recommended medications decreased significantly across the spectrum of patient risk for 2 distinct reasons: significantly higher rates of clinician-documented contraindications to these therapies with higher risk as well as lower rates of treatment in eligible patients. Thus, lower treatment rates with increasing risk are driven both by gaps in the evidence as well as gaps in the quality of care. These findings suggest that improving care for the highest-risk patients with HF will require both the development of innovative therapies with greater applicability to patients with HF as well as efforts to improve the quality of care that target the highest-risk population.

To our knowledge, this is the only study to evaluate the proportion of patients with HF and LVSD who have clinically documented contraindications and are therefore ineligible for guideline recommended medical therapy across the spectrum of mortality risk. Of the highest-risk patients, 26% had contraindications to ACE inhibitor and ARB therapy and 13% to β-blockers, suggesting that the current evidence base for medical therapy of HF with LVSD becomes decreasingly applicable to patients with increasing risk. This underscores the importance of ongoing research to develop broadly applicable therapies for HF that can be incorporated into existing practice guidelines. Although the relative paucity of guideline recommendations with the strongest evidence support has been elucidated,[13] the findings of our study suggest that limitations in the evidence base disproportionately affect the highest-risk patients.

We also explored the nature of contraindications and found that worsening renal function was the most commonly documented contraindication overall and among high-risk patients. Indeed, the median creatinine level was 2.2 mg/dL among those with worsening renal function as a documented contraindication, which is greater than creatinine levels in most clinical trials of ACE inhibitors.[14–17] Although such trials typically excluded patients with higher creatinine levels, observational data suggest that patients with renal dysfunction treated with ACE inhibitors derive similar if not greater benefit than those with normal renal function.[18–21] Although the guidelines recommend that ACE inhibitors should be used with caution in those with markedly increased creatinine levels (>3 mg/dL or 265 μmol/L),[22] disproportionate concerns for complications attributable to worsening renal function may deprive many HF patients of the potential benefits of ACE inhibitor or ARB treatment. Clinicians should carefully consider the possible benefits of treatment against the risks rather than adopting a uniform practice of avoidance of ACE-inhibitors in all patients with relative contraindications.

Although other studies have characterized patterns of treatment among eligible patients across the spectrum of patient risk with the goal of defining the gap in quality of care, these studies have not been able to ascertain clinician-documented reasons for not providing therapy. Perhaps the largest study of this phenomenon in HF used relatively arbitrary definitions of contraindications (eg, systolic blood pressure of 120 mm Hg as a universal contraindication to prescribing ACE inhibitors).[7] The inability to assess clinically driven contraindications could result in misclassification of the population eligible for treatment with resultant implications on estimates of the size of the eligible population as well as treatment rates in this population. A unique strength of GWTG is the ability to clearly identify an ideal cohort for therapy (ie, those without clinical contraindications to therapy). Consistent with prior studies, we identified a risk-treatment paradox—rates of treatment among eligible patients decreased with increasing patient risk. Because the absolute benefits of a therapy with a given relative risk reduction are greatest in those with the greatest underlying risk,[23] this treatment gap deprives those with the greatest potential to benefit.

Approaches to addressing the risk-treatment paradox itself remain elusive. A recent study assessing physicians estimates of patient risk for acute coronary syndromes found that clinicians systematically underestimate risk, suggesting that the risk-treatment paradox, at least in part, arises from the lack of readily available approaches to understanding risk.[24] In the case of GWTG-HF, a validated risk model for inpatient

mortality using readily available clinical variables has been developed and will be provided at the point of care. If incorporated into clinical work flow, such risk models may be useful in helping clinicians better calibrate the intensity of treatment to risk.[23]

Another approach is to assess quality of care as a function of patient risk. Prescriptions of guideline-recommended medical therapies are process of care measures commonly used to evaluate and report quality of care for patients hospitalized with HF.[3,25] Current approaches to measuring and improving care for HF typically assume that therapies have similar safety, tolerability, and benefits across patient populations, raising the question of whether clinical quality should be reported as a function of risk.[26] Elucidating disproportionate omissions in care for the highest-risk patients may provide the necessary impetus for institutions and clinicians to develop specific approaches to ensuring that the highest-risk patients receive those therapies for which they are eligible.

Certain factors should be considered in the interpretation of this study. First, 3 of the 7 variables used in the risk model—specifically systolic blood pressure, heart rate, and BUN—are often related to decisions to provide evidence-based heart failure care. Indeed, the clustering of high-risk conditions may result in a clinician's judgment that the benefits of optimizing heart failure therapy may be outweighed by the risks of polypharmacy and adverse drug events. Although no specific levels of these variables are considered clear contraindications to therapy except perhaps at extremes, it is possible that patients in the highest-risk groups had higher rates of undocumented contraindications. This phenomenon could lead to an overestimate of the extent of underuse and underestimate the proportion of clinically meaningful contraindications. However, the hospitals that use GWTG are aware that a primary goal of the registry is to identify eligible patients for therapy and determine rates of care in these populations and thus are more likely to explicitly document contraindications for those who are not eligible for therapy. Second, risk groups were based on estimated risk of in-hospital mortality rather than after discharge mortality. However, risk categorization probably would not be different as risk of in-hospital mortality is closely associated with long-term mortality risk, and these same variables have been demonstrated to predict postdischarge mortality risk.[27,28] Third, the assessment of treatment was limited to the inpatient setting. Any significant changes in therapy after discharge may attenuate the variation identified in our study. However, it is known that the use of evidence-based therapies among eligible patients with heart failure are typically not added in the outpatient setting.[29] Finally, hospitals voluntarily participating in the GWTG program may have a higher likelihood of following guideline recommendations, probably making our results conservative estimates. However, this study includes a large sample of representative patients from numerous hospitals across the United States.

In summary, rates of use of guideline-based therapies in this hospitalized cohort of patients with HF and LVSD were significantly lower with increasing patient risk. This was because of higher rates of clinically documented contraindications, as well as a risk–treatment paradox, where treatment rates among eligible patients were inversely associated with risk of mortality. In identifying the contributors to lower rates of use of guideline-recommended therapies in patients with higher risk, our study provides insights into how this phenomenon could be minimized. Optimizing HF outcomes will require the development of effective strategies to ensure that eligible high-risk patients receive all appropriate therapies, more robust data on the risks and benefits of these therapies in patients with relative contraindications to identify larger groups of patients who can be safely treated with established therapies, and more broadly applicable evidence-based care strategies for patients who are not eligible for current guideline-recommended treatments.

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References

1. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, Jessup M, Konstam MA, Mancini DM, Michl K, Oates JA, Rahko PS, Silver MA, Stevenson LW, Yancy CW, Antman EM, Smith SC Jr, Adams CD, Anderson JL, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK, Nishimura R, Ornato JP, Page RL, Riegel B. ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult—Summary Article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society. *Circulation*. 2005;112:1825–1852.
2. Bonow RO, Bennett S, Casey DEJ, Ganiats TG, Hlatky MA, Konstam MA, Lambrew CT, Normand SL, Pina IL, Radford MJ, Smith AL, Stevenson LW, Bonow RO, Bennett SJ, Burke G, Eagle KA, Krumholz HM, Lambrew CT, Linderbaum J, Masoudi FA, Normand SL, Ritchie JL, Rumsfeld JS, Spertus JA. ACC/AHA Clinical Performance Measures for Adults With Chronic Heart Failure: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures (Writing Committee to Develop Heart Failure Clinical Performance Measures): endorsed by the Heart Failure Society of America. *Circulation*. 2005;112:1853–1887.
3. Hospital Compare Website. Available at: http://www.hospitalcompare.hhs.gov. Accessed September 24, 2009.
4. Hong Y, LaBresh KA. Overview of the American Heart Association "Get With The Guidelines" programs: coronary heart disease, stroke, and heart failure. *Crit Pathw Cardiol*. 2006;5:179–186.

5. Cohen-Solal A, McMurray JJ, Swedberg K, Pfeffer MA, Puu M, Solomon SD, Michelson EL, Yusuf S, Granger CB, CHARM I. Benefits and safety of candesartan treatment in heart failure are independent of age: insights from the Candesartan in Heart failure—Assessment of Reduction in Mortality and morbidity programme. *Eur Heart J*. 2008;29:3022–3028.
6. Meredith PA, Ostergren J, Anand I, Puu M, Solomon SD, Michelson EL, Olofsson B, Granger CB, Yusuf S, Swedberg K, Pfeffer MA, McMurray JJ. Clinical outcomes according to baseline blood pressure in patients with a low ejection fraction in the CHARM (Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity) Program. *J Am Coll Cardiol*. 2008;52:2000–2007.
7. Lee DS, Tu JV, Juurlink DN, Alter DA, Ko DT, Austin PC, Chong A, Stukel TA, Levy D, Laupacis A. Risk-treatment mismatch in the pharmacotherapy of heart failure. *JAMA*. 2005;294:1240–1247.
8. Ko DT, Mamdani M, Alter DA. Lipid-lowering therapy with statins in high-risk elderly patients: the treatment-risk paradox. *JAMA*. 2004;291:1864–1870.
9. Yan AT, Yan RT, Tan M, Fung A, Cohen EA, Fitchett DH, Langer A, Goodman SG, Canadian Acute CS. Management patterns in relation to risk stratification among patients with non-ST elevation acute coronary syndromes. *Arch Intern Med*. 2007;167:1009–1016.
10. McAlister FA, Oreopoulos A, Norris CM, Graham MM, Tsuyuki RT, Knudtson M, Ghali WA, Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) Investigators: exploring the treatment-risk paradox in coronary disease. *Arch Intern Med*. 2007;167:1019–1025.
11. Hernandez AF, Fonarow GC, Liang L, Al Khatib SM, Curtis LH, LaBresh KA, Yancy CW, Albert NM, Peterson ED. Sex and racial differences in the use of implantable cardioverter-defibrillators among patients hospitalized with heart failure. *JAMA*. 2007;298:1525–1532.
12. Peterson PN, Rumsfeld JS, Liang L, Albert NM, Hernandez AF, Peterson ED, Fonarow GC, Masoudi FA, on behalf of the American Heart Association Get With the Guidelines-Heart Failure Program. A validated risk score for in-hospital mortality in patients with heart failure from the American Heart Association Get With the Guidelines Program. *Circ Cardiovasc Qual Outcomes*. 2010;3:25–32.
13. Tricoci P, Allen JM, Kramer JM, Califf RM, Smith SC Jr. Scientific evidence underlying the ACC/AHA clinical practice guidelines. *JAMA*. 2009;301:831–841.
14. The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med*. 1991;325:293–302.
15. The SOLVD Investigators. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions [erratum appears in *N Engl J Med* 1992;327:1768]. *N Engl J Med*. 1992;327:685–691.
16. Pfeffer MA, Braunwald E, Moye LA, Basta L, Brown EJ Jr, Cuddy TE, Davis BR, Geltman EM, Goldman S, Flaker GC. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction: results of the survival and ventricular enlargement trial: the SAVE Investigators *N Engl J Med*. 1992;327:669–677.
17. The CONSENSUS Trial Study Group. Effects of enalapril on mortality in severe congestive heart failure: results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). *N Engl J Med*. 1987;316:1429–1435.
18. Masoudi FA, Rathore SS, Wang Y, Havranek EP, Curtis JP, Foody JM, Krumholz HM. National patterns of use and effectiveness of angiotensin converting enzyme inhibitors in older patients with heart failure and left ventricular systolic dysfunction. *Circulation*. 2004;110:724–731.
19. Ahmed A, Kiefe CI, Allman RM, Sims RV, DeLong JF. Survival benefits of angiotensin-converting enzyme inhibitors in older heart failure patients with perceived contraindications. *J Am Geriatr Soc*. 2002;50:1659–1666.
20. McAlister FA, Ezekowitz J, Tonelli M, Armstrong PW. Renal insufficiency and heart failure: prognostic and therapeutic implications from a prospective cohort study. *Circulation*. 2004;109:1004–1009.
21. Berger AK, Duval S, Manske C, Vazquez G, Barber C, Miller L, Luepker RV. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in patients with congestive heart failure and chronic kidney disease. *Am Heart J*. 2007;153:1064–1073.
22. Spertus JA, Furman MI. Translating evidence into practice: are we neglecting the neediest? *Arch Intern Med*. 2007;167:987–988.
23. Yan AT, Yan RT, Huynh T, Casanova A, Raimondo FE, Fitchett DH, Langer A, Goodman SG, Canadian Acute Coronary Syndrome Registry. Understanding physicians' risk stratification of acute coronary syndromes: insights from the Canadian ACS 2 Registry. *Arch Intern Med*. 2009;169:372–378.
24. Fonarow GC, Yancy CW, Albert NM, Curtis AB, Stough WG, Gheorghiade M, Heywood JT, Mehra M, O'Connor CM, Reynolds D, Walsh MN. Improving the use of evidence-based heart failure therapies in the outpatient setting: the IMPROVE HF performance improvement registry. *Am Heart J*. 2007;154:12–38.
25. Mehta RH, Liang L, Karve AM, Hernandez AF, Rumsfeld JS, Fonarow GC, Peterson ED. Association of patient case-mix adjustment: hospital process performance rankings, and eligibility for financial incentives. *JAMA*. 2008;300:1897–1903.
26. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. *JAMA*. 2003;290:2581–2587.
27. O'Connor CM, Abraham WT, Albert NM, Clare R, Gattis Stough W, Gheorghiade M, Greenberg BH, Yancy CW, Young JB, Fonarow GC. Predictors of mortality after discharge in patients hospitalized with heart failure: an analysis from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). *Am Heart J*. 2008;156:662–673.
28. Butler J, Arbogast PG, Daugherty J, Jain MK, Ray WA, Griffin MR. Outpatient utilization of angiotensin-converting enzyme inhibitors among heart failure patients after hospital discharge. *J Am Coll Cardiol*. 2004;43:2036–2043.

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