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PERSPECTIVE

Impact of Current Versus Previous Cardiac Resynchronization Therapy Guidelines on the Proportion of Patients With Heart Failure Eligible for Therapy

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ABSTRACT

OBJECTIVES This study sought to ascertain the impact of heart failure (HF) guideline change on the number of patients eligible to undergo cardiac resynchronization therapy (CRT).

BACKGROUND The 2013 HF guideline of the American College of Cardiology Foundation and American Heart Association (ACCF/AHA) narrowed the recommendations for CRT. The impact of this guideline change on the number of eligible patients for CRT has not been described.

METHODS Using data from Get With The Guidelines–Heart Failure between 2012 and 2015, this study evaluated the proportion of hospitalized patients with HF who were eligible for CRT on the basis of historical and current guideline recommendations. The authors identified 25,102 hospitalizations for HF that included patients with a left ventricular ejection fraction (LVEF) ≤35% from 283 hospitals. Patients with a medical, system-related, or patient-related reason for not undergoing CRT were excluded.

RESULTS Overall, 49.1% (n = 12,336) of patients with HF, an LVEF ≤35%, and no documented contraindication were eligible for CRT on the basis of historical guidelines, and 33.1% (n = 8,299) of patients were eligible for CRT on the basis of current guidelines, a 16.1% absolute reduction in eligibility ($p < 0.0001$). Patients eligible for CRT on the basis of current guidelines were more likely to have CRT with an implantable cardioverter-defibrillator or CRT with pacing only placed or prescribed at discharge (57.8% vs. 54.9%; $p < 0.0001$) compared with patients eligible for CRT on the basis of historical guidelines.

CONCLUSIONS In this population of patients with HF, an LVEF ≤35%, and no documented contraindication for CRT, the current ACCF/AHA HF guidelines reduce the proportion of patients eligible for CRT by approximately 15%. (J Am Coll Cardiol HF 2017;5:388–92) © 2017 by the American College of Cardiology Foundation.

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The 2009 American College of Cardiology Foundation and American Heart Association (ACCF/AHA) heart failure (HF) guidelines recommended cardiac resynchronization therapy (CRT) in patients with a left ventricular ejection fraction (LVEF) ≤35%, New York Heart Association (NYHA) functional class III or IV symptoms, and a QRS duration of ≥120 ms (1). However, evidence since that time has demonstrated CRT to be effective in patients in NYHA functional class II (2), and it has revealed that the benefit of CRT is most evident in those patients with a QRS duration ≥150 ms (3), as well as patients with a left bundle branch block (LBBB) pattern (4). On the basis of these data, the current (2013) ACCF/AHA HF guidelines expanded the eligibility criteria for CRT to include patients in NYHA functional class II but limited the criteria to recommend CRT only in patients with an LVEF ≤35%, sinus rhythm, and LBBB or non-LBBB and a QRS duration ≥150 ms (5). Using the AHA's Get With The Guidelines-Heart Failure (GWTG-HF) registry, we describe the difference in the proportion of patients eligible for CRT on the basis of current and historical guidelines.

METHODS

We used patients from the GWTG-HF registry from October 1, 2012 to September 30, 2015 who had at least 75% complete data on medical history (n = 192,254). Patients' baseline and discharge characteristics, diagnostic test and laboratory values, medical history, medications, outcomes at discharge, and device-related measures are submitted by trained health care workers into the Internet-based GWTG-HF Patient Management Tool (Quintiles Real-World and Late Phase Research, QuintilesIMS, Durham, North Carolina). Information on cardiac rhythm was not collected, and patients without sinus rhythm could not be excluded. For the present study, we excluded patients with the following: quantitative LVEF, QRS duration or QRS morphology information missing (n = 24,620); LVEF >35% (n = 106,570); new onset HF (n = 12,642); death in hospital (n = 1,519); transfer to another acute care facility or hospice (n = 3,295); left against medical advice or discharge information missing (n = 715); and discharge to a skilled nursing facility or rehabilitation center (n = 6,327). We further excluded 11,464 patients with a documented contraindication to CRT. "Not being NYHA functional class III or IV" was also listed as a contraindication for CRT within the GWTG-HF, but these patients were not excluded from this study.

We defined patients to be guideline eligible for CRT according to historical guidelines if they met the following criteria: QRS duration ≥120 ms and NYHA functional class III or IV (i.e., patients documented as "not being NYHA functional class III or IV" were not eligible for CRT on the basis of historical guidelines). We defined patients to be guideline eligible for CRT on the basis of current guidelines if they met the following criteria: LBBB with a QRS duration ≥120 ms or non-LBBB (right bundle branch block or interventricular conduction delay) with a QRS duration ≥150 ms and NYHA functional class III or IV (i.e., patients who were documented as "not being NYHA functional class III or IV" with non-LBBB were not eligible for CRT on the basis of current guidelines). For patients with LBBB, NYHA functional class was not included in our eligibility assessment. However, only 2% of our final study cohort was documented as not being in NYHA functional class III or IV, and we believe that most patients hospitalized for HF are at least in NYHA functional class II.

Baseline characteristics are presented as medians with 25th and 75th percentiles for continuous variables and percentages for categorical variables. Patients' baseline characteristics were compared between patients eligible for CRT on the basis of historical versus current guideline recommendations by using standardized differences. Device-related measures before and during hospitalization and device- and medication-related measures at discharge are presented as percentages and are compared by patients eligible for CRT on the basis of historical versus current guidelines with the use of 2 sample Student *t* tests. CRT eligibility on the basis of historical versus current guideline recommendations was also examined for QRS morphology and QRS duration subgroups. All p values are 2-sided, with $p < 0.05$ considered statistically significant. All analyses were completed using SAS version 9.4 software

ABBREVIATIONS AND ACRONYMS

ACCF/AHA = American College of Cardiology Foundation and American Heart Association

CRT = cardiac resynchronization therapy

CRT-D = cardiac resynchronization therapy with an implantable cardioverter-defibrillator

CRT-P = cardiac resynchronization therapy with pacing only

GWTG-HF = Get With The Guidelines-Heart Failure

HF = heart failure

ICD = implantable cardioverter-defibrillator

LBBB = left bundle branch block

LVEF = left ventricular ejection fraction

NYHA = New York Heart Association

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TABLE 1 Baseline Characteristics

	Overall (N = 25,102)	Eligible According to Current Guideline Recommendation (n = 8,299)	Eligible According to Historical Guideline Recommendation (n = 12,336)	Absolute Standardized Difference (%)
Age, yrs	67 (56–78)	73 (63–81)	72 (62–81)	6.48
Female	8,144 (32.5)	2,505 (30.2)	3,769 (30.6)	0.79
Race				4.70
White	14,281 (57.0)	5,832 (70.3)	8,412 (68.3)	
Black	7,589 (30.3)	1,509 (18.2)	2,426 (19.7)	
Hispanic	2,070 (8.3)	622 (7.5)	984 (8.0)	
Asian/Pacific Islander	492 (2.0)	145 (1.8)	210 (1.7)	
Other	646 (2.6)	183 (2.2)	291 (2.4)	
Insurance				3.42
No insurance/not documented	1,290 (6.0)	194 (2.8)	301 (2.9)	
Medicaid	3,970 (18.6)	770 (11.0)	1,257 (12.1)	
Medicare	10,942 (51.2)	4,186 (60.0)	6,185 (59.4)	
Other	5,168 (24.2)	1,825 (26.2)	2,662 (25.6)	
Medical history				
Atrial fibrillation or flutter	9,093 (36.2)	3,645 (43.9)	5,356 (43.4)	1.01
CVA or TIA	3,894 (15.5)	1,274 (15.4)	1,971 (16.0)	1.72
Diabetes	11,523 (45.9)	3,779 (45.5)	5,692 (46.1)	1.22
Hypertension	20,152 (80.3)	6,488 (78.2)	9,694 (78.6)	0.98
Ischemic origin	16,038 (63.9)	5,808 (70.0)	8,697 (70.5)	1.13
LVEF (%)	24 (19–30)	23 (18–30)	23 (19–30)	1.96

Values are median (interquartile range) or n (%).
CVA = cerebrovascular accident; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack.

(SAS Institute, Inc., Cary, North Carolina). Institutions included in the GWTG-HF program had their participation approved by their respective institutional review boards, and a waiver for informed consent was granted because GWTG-HF is a quality improvement initiative. Quintiles (QuintilesIMS) acts as the coordinating data center, and all data were de-identified with analysis performed at the Duke Clinical Research Institute (Durham, North Carolina).

RESULTS

Our final study population included 25,102 patients from 283 hospitals; 12,336 (49.1%) patients were eligible for CRT on the basis of historical guidelines, and 8,299 (33.1%) patients were eligible for CRT on the basis of current guidelines ($p < 0.0001$). Apart from QRS duration and morphology, there were no significant differences in the baseline characteristics between the 2 groups (Table 1). Essentially all patients with a QRS duration of 120 to 149 ms (n = 5,303) were eligible for CRT on the basis of historical criteria, but only 1,129 (21.3%) of patients with a QRS duration of 120 to 149 ms were eligible for CRT on the basis of current criteria. Essentially all patients with a QRS duration ≥150 ms were eligible for CRT on the basis of historical and current guidelines (Figure 1A). Of the 12,588 patients with a QRS duration ≥120 ms, 2,651 (21.1%) had LBBB, and 9,937 (78.9%) had non-LBBB. Of those patients with non-LBBB, 4,174 (42.0%) had a QRS duration of 120 to 149 ms, and 5,763 (58.0%) had a QRS duration ≥150 ms. Essentially all patients with LBBB were eligible for CRT according to historical and current guidelines. Alternatively, essentially all patients with non-LBBB were eligible for CRT according to historical guidelines, but only 56.8% were eligible for CRT on the basis of current guidelines (Figure 1B).

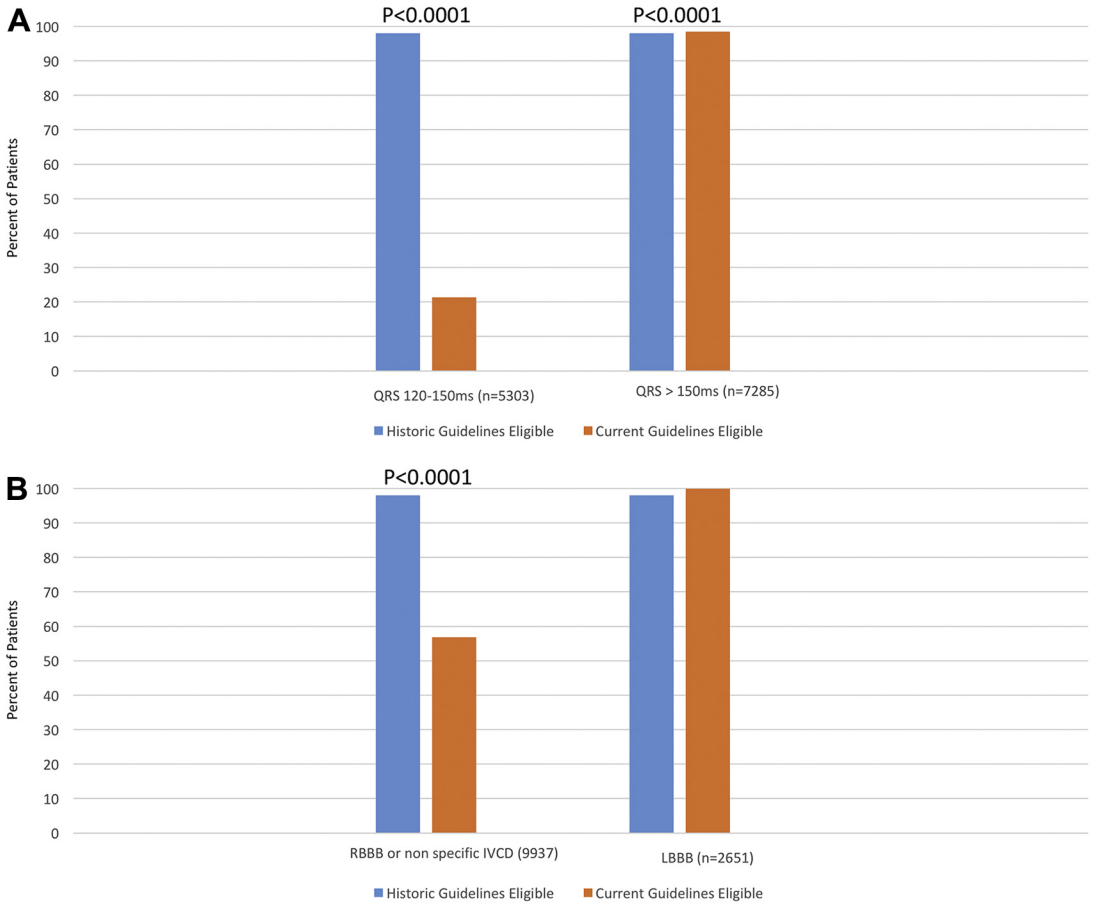
Table 2 provides device-related characteristics and medications at discharge. Patients eligible for CRT on the basis of current guidelines were more likely to have CRT with implantable cardioverter-defibrillator (CRT-D) or CRT with pacing only (CRT-P) present at admission (39.4% vs. 38.6%; $p = 0.01$), were more likely to have CRT-D or CRT-P placed during admission (13.2% vs. 11.3%; $p < 0.0001$), and were more likely to have CRT-D or CRT-P placed or prescribed at discharge (57.8% vs. 54.9%; $p < 0.0001$).

DISCUSSION

Using a large database of patients hospitalized with HF, we found that compared with historical guidelines, current guidelines reduced the proportion of patients eligible for CRT from 49.1% to 33.1% (absolute difference, 16.1%; relative difference, 32.7%). In keeping with the change in guidelines, only ~20% of patients with a QRS duration of 120 to 149 ms and ~60% of patients with non-LBBB were eligible for CRT according to current guidelines, whereas almost all such patients were eligible for CRT according to historical guidelines.

Prescribing adherence to guideline-directed medical therapy was high in this population; however, documented prescribing adherence to device therapy in eligible patients was less ideal. Approximately 65% of patients in our total population had an implantable cardioverter defibrillator (ICD) therapy placed or prescribed at discharge. However, we did not examine ICD eligibility within this study, so the number of patients eligible for ICD in our cohort is not known. Conversely, only 55% of patients eligible for CRT on the basis of historical guidelines and 58% of patients eligible for CRT on the basis of current guidelines had CRT-D or CRT-P placed or prescribed at discharge. This is important because patients eligible for CRT according to historical guidelines included those individuals

FIGURE 1 CRT Eligibility



(A) Eligibility for cardiac resynchronization therapy (CRT) stratified by QRS duration. **(B)** Eligibility stratified by bundle branch block type. IVCD = interventricular conduction delay; LBBB = left bundle branch block; RBBB = right bundle branch block.

with the weakest evidence for the benefit of CRT, specifically patients with non-LBBB and a QRS duration of 120 to 150 ms (3–5). Given that the most recent ACCF/AHA HF guidelines were released almost a full year after our patient enrollment began, the rates of CRT therapy implementation may have been even higher in those patients who were eligible according to current guidelines compared with historical guidelines if the data were taken from a population of patients enrolled after the current guidelines had been released for some time.

STUDY LIMITATIONS. First, these findings may not be generalizable to all hospitalized patients with an LVEF ≤35% or to an outpatient population, and unmeasured confounding may exist. Second, the GWTG-HF registry does not explicitly capture NYHA functional class information. However, "not being NYHA functional class III or IV" was listed as a contraindication for CRT in the GWTG-HF program at the time our population was enrolled, and we could identify such patients as not being eligible for CRT where appropriate. Third, although we excluded all patients with a documented contraindication to CRT, some patients may have had an undocumented contraindication. Finally, although we had complete data on LVEF, QRS duration, and QRS morphology, data on some other collected variables were missing.

TABLE 2 Device-Related Characteristics and Medications at Discharge

	Overall (N = 25,102)	Eligible According to Current Guideline Recommendation (n = 8,299)	Eligible According to Historical Guideline Recommendation (n = 12,336)	p Value*
Pre-admission device-related characteristics				
ICD or CRT-D present	11,452 (45.6)	4,839 (58.3)	7,243 (58.7)	0.20
CRT-D or CRT-P present	5,872 (23.4)	3,268 (39.4)	4,763 (38.6)	0.01
CRT-P present	297 (1.2)	173 (2.1)	253 (2.1)	0.70
Device-related procedures performed during admission				
ICD placement	331 (2.4)	57 (1.3)	81 (1.2)	0.48
CRT-D or CRT-P	877 (6.3)	582 (13.2)	746 (11.3)	<0.0001
Device-related performance measures at discharge				
ICD placed or prescribed at discharge	13,779 (64.5)	5,821 (73.8)	8,545 (73.0)	0.004
CRT-D or CRT-P placed or prescribed at discharge	6,656 (54.9)	4,708 (57.8)	6,656 (54.9)	<0.0001
Medications at discharge				
ACEI or ARB at discharge	16,963 (95.2)	5,201 (94.3)	7,852 (94.3)	0.92
Beta blocker at discharge	22,477 (98.4)	7,318 (98.1)	10,971 (98.2)	0.14
Aldosterone antagonist at discharge	9,299 (47.3)	3,109 (48.1)	4,628 (47.9)	0.54

Values are n (%). *The p value represents significance for *z*-value and accounts for the overlap of patients eligible for CRT on the basis of historical and current guidelines.

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CRT-D = cardiac resynchronization therapy with an implantable cardioverter-defibrillator; CRT-P = cardiac resynchronization therapy with pacing; ICD = implantable cardioverter defibrillator.

CONCLUSIONS

Among patients with HF, an LVEF ≤35%, and no documented reason for not prescribing CRT, the proportion of patients eligible for CRT on the basis of historical versus current ACCF/AHA guidelines dropped from 49.1% to 33.1%. This drop in the proportion of patients eligible for CRT may lead to a reduction in the cost of HF care in the hospitalized population, but given that only ~55% of patients eligible for CRT had the therapy placed or prescribed at discharge, improvements still need to be made in the prescribing adherence of device therapy in patients with HF.

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