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EDITORIAL COMMENT

Gaps in Adherence to Guideline-Directed Medical Therapy Before Defibrillator Implantation*

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Drugs don't work in patients who don't take them.
—C. Everett Koop, M.D. (1)

Guideline-directed medical therapy (GDMT) is the mainstay of initial and chronic management of heart failure with reduced ejection fraction (HFrEF). The term GDMT refers to the drug treatments that benefit patients with HFrEF, and it evokes the body of evidence-based literature and the endorsement of several professional societies. The cornerstone of therapy is the initiation of heart failure (HF)-approved beta-blockers and renin-angiotensin inhibitors (RAIs) shown to improve symptoms, cardiac function, and mortality (**Figure 1**) (2). A patient newly diagnosed with HFrEF requires close follow-up and careful titration of multiple medications as hemodynamics, electrolytes, and symptoms permit. Although the known benefits of GDMT have solidified, a persistent observable gap remains in the provision and receipt of GDMT for both ambulatory and hospitalized patients with HFrEF (3).

In this issue of the *Journal*, Roth et al. (4) use the National Cardiovascular Data Registry (NCDR) ICD Registry to identify receipt of GDMT before placement of an implantable cardioverter-defibrillator (ICD) for the primary prevention of sudden cardiac death. The study selected NCDR registry patients with Medicare and Medicare Plan D prescription benefits who had received a primary prevention ICD between 2007 and 2011. The NCDR database was linked to Medicare Part D

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prescription data to assess adherence to a HF-approved beta-blocker and RAI for the 90 days before ICD implantation. Astonishingly, only 61.1% of patients received a beta-blocker and RAI before ICD implantation and only 28.3% received an adequate supply (defined as ≥80% coverage for the 90 days before ICD implantation). The findings are consistent and expand on a previous study that provided a snapshot of beta-blocker and RAI use at time of ICD placement, in which one-quarter of eligible patients were not on GDMT (5). The new analysis suggests that an even larger portion of patients are not adhering to GDMT before undergoing implantation of a primary prevention ICD, which is recommended by current HFrEF guidelines.

Failure to adequately treat with GDMT before a primary prevention ICD implantation suggests that at least some patients who may have responded to medical therapy with improvements in left ventricular ejection fraction (LVEF) above the range at which they would derive sufficient benefit from the ICD are needlessly receiving a costly and invasive device therapy. The Intervention in Myocarditis and Acute Cardiomyopathy-2 cohort study of patients with nonischemic HFrEF reported >90% beta-blocker and RAI use and noted a ≥10% LVEF improvement for 70% of patients and ≥20% LVEF improvement for

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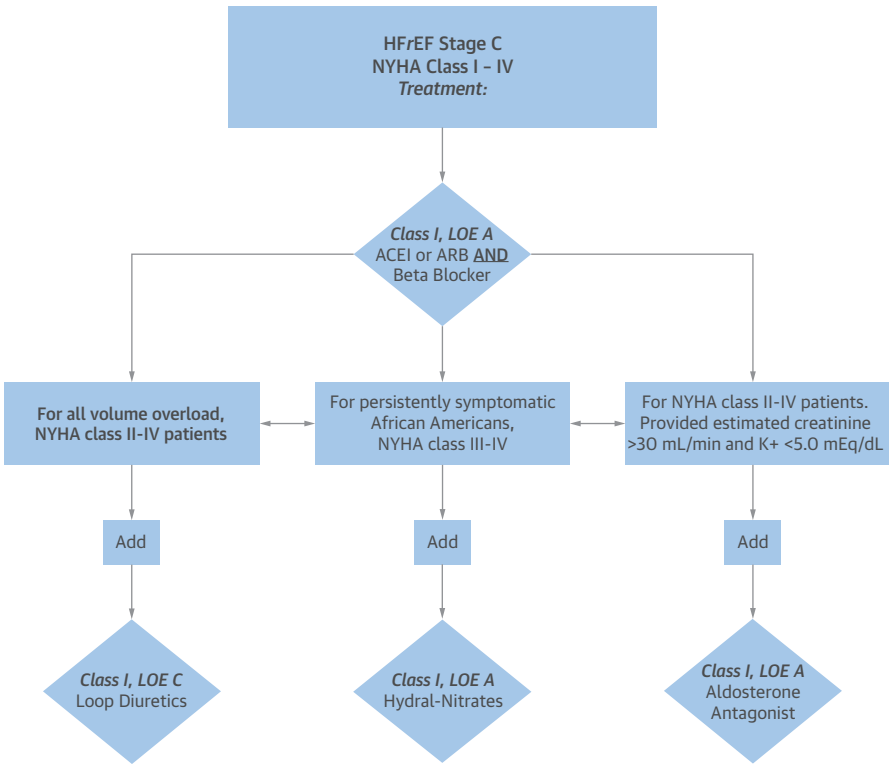
FIGURE 1 Guideline-Directed Medical Therapy in Stage C Heart Failure With Reduced Ejection Fraction Patients



Guideline-directed medical therapy for stage C heart failure with reduced ejection fraction (HFrEF). Reproduced with permission from Yancy et al. (2). ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; K+ = potassium; LOE = Level of Evidence; NYHA = New York Heart Association.

39% of patients by 6 months (6). A single-center Italian study also reported that 67% of patients with nonischemic cardiomyopathy treated with GDMT (87% beta-blocker and 95% RAI usage rates) no longer met criteria for a primary prevention ICD (7).

In the paper by Roth et al. (4), one caveat to the society guideline recommendations during much of the study period between 2007 and 2011 is that they were vague regarding the duration of "optimal medical therapy" before a primary prevention ICD implantation for patients with nonischemic HFrEF, as the evidence was uncertain (8,9). It was not until 2010 that the Heart Failure Society of America guidelines discussed the duration of optimal medical therapy as 3 to 6 months before ICD placement (10). The American College of Cardiology Foundation and the American Heart Association followed with similar recommendations in 2013 (2).

There are important limitations to the study by Roth et al. (4) that deserve further consideration before accepting that GDMT is substantially underused before primary prevention defibrillator placement. One difficulty with administrative data is knowing the true rate of contraindications and intolerance to GDMT. Roth et al. included patients with chronic renal disease, who likely have higher rates of intolerance to RAI, and the comorbidity was associated with an 11% lower relative risk of receiving GDMT before ICD implantation. In the IMPROVE HF (Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting) study, detailed chart review revealed 6% to 8% of patients had contraindications or were intolerant to beta-blockers or RAIs (11). Another limitation of the data is that studies have shown that some patients do not use prescription benefits when purchasing inexpensive generic drugs, and medication use and adherence may not be captured for this group of patients (12). However, medication intolerance and incomplete prescription data are likely only a partial explanation for the large, observed gap in treatment.

Of greater concern is that medical providers may not be prescribing GDMT and titrating doses appropriately in eligible patients with HFrEF. Despite the promotion in professional society guidelines of