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Temporal Trends of Digoxin Use in Patients Hospitalized With Heart Failure

Analysis From the American Heart Association Get With The Guidelines-Heart Failure Registry

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ABSTRACT

OBJECTIVES The aim of this study was to assess temporal trends and factors associated with digoxin use at discharge among patients admitted with heart failure (HF).

BACKGROUND Digoxin has class IIa recommendations for treating HF with reduced ejection fraction (HFrEF) in the United States. Digoxin use, temporal trends, and clinical characteristics of HF patients in current clinical practice in the United States have not been well studied.

METHODS An observational analysis of 255,901 patients hospitalized with HF (117,761 with HFrEF and 138,140 with preserved EF [HFpEF]) from 398 hospitals participating in the Get With The Guidelines-HF registry between January 2005 and June 2014 was conducted to assess the temporal trends and factors associated with digoxin use.

RESULTS Among 117,761 HFrEF patients, only 19.7% received digoxin at discharge. Digoxin prescriptions decreased from 33.1% in 2005 to 10.7% in 2014 ($p_{trend} < 0.0001$). Factors associated with digoxin use in HFrEF included atrial fibrillation (AF) (odds ratio [OR]: 2.14; 95% confidence intervals [CI]: 2.02 to 2.28), history of implantable cardioverter defibrillator use (OR: 1.39; 95% CI: 1.32 to 1.46), chronic obstructive pulmonary disease (OR: 1.13, 95% CI: 1.08 to 1.18), diabetes mellitus (OR: 1.10, 95% CI: 1.06 to 1.14), younger age (OR: 0.96, 95% CI: 0.95 to 0.97), lower blood pressure (OR: 0.96, 95% CI: 0.96 to 0.97), and having no history of renal insufficiency (OR: 0.91, 95% CI: 0.85 to 0.97). Use of digoxin in patients with HFpEF ($n = 138,140$) without AF was 9.8% in 2005, which decreased to 2.2% in 2014 ($p_{trend} < 0.0001$).

CONCLUSIONS One in 5 HFrEF patients received digoxin at discharge, with a significant downward temporal trend in use over the study period. Use of digoxin in HFpEF patients without AF was very low and decreased over the study period. (J Am Coll Cardiol HF 2016;4:348–56) © 2016 by the American College of Cardiology Foundation.

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Heart failure (HF) accounts for approximately 1 million admissions as a primary diagnosis each year in the United States (1). Moreover, the readmission rate approaches almost 30% at 90 days (2). Therefore, currently, there is a major focus on reducing HF hospital readmission. The Digitalis Investigator Group (DIG), a large randomized, placebo-controlled trial in patients with HF, showed that digoxin significantly reduced hospitalizations for HF, but it also had no impact on all-cause or cardiovascular mortality (3). Moreover, the DIG pre-specified high-risk subgroup analysis demonstrated that at a 2-year follow up, there was a reduction in all-cause mortality or hospitalization and HF-related mortality for patients with New York Heart Association functional class III/IV symptoms, with left ventricular ejection fractions <25%, and with a cardiothoracic ratio >55% on chest x-rays (4). However, observational studies and post hoc analysis of other subgroups of the DIG trial have reported adverse effects of digoxin on mortality in patients with atrial fibrillation (AF) and those with HF (5–9). Currently, the American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Failure Society of America recommend the use of digoxin, which could be beneficial in patients with current or previous symptoms of HF and reduced left ventricular ejection fraction (HFrEF) to decrease hospitalization for HF (Class IIa; Level of Evidence: B) (10), whereas the European Society of Cardiology (ESC) gives class IIb recommendation for use of digoxin in HFrEF to decrease HF hospitalizations (11).

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Despite the reported beneficial effects of digoxin on HF hospitalizations in the prospective placebo-controlled randomized DIG trial and worsening of symptoms after digoxin withdrawal, some studies have reported that digoxin use has progressively declined (5,12). It is now unclear how the current literature, guidelines, and modern medical therapy have affected the current use of digoxin in patients with HF. Therefore, the goal of this study is to characterize the use of digoxin over the past 10 years among patients hospitalized with HF in the United States. The study also aimed to evaluate the association between different characteristics of patients hospitalized with HFrEF and discharged on digoxin. Changes in the use of digoxin over the past 10 years among patients with HFrEF and in patients with HFpEF were also analyzed, with further comparison of those patients with and without AF.

ABBREVIATIONS AND ACRONYMS

ACC = American College of Cardiology

AF = atrial fibrillation

AHA = American Heart Association

COPD = chronic obstructive pulmonary disease

ESC = European Society of Cardiology

GWTG = Get With The Guideline

HF = heart failure

HFpEF = heart failure with preserved ejection fraction

HFrEF = heart failure with reduced ejection fraction

ICD = implantable cardioverter defibrillator

METHODS

DATA SOURCE. The American Heart Association's Get With The Guidelines (GWTG) program is a hospital-based continuous quality improvement program that collects data from participating centers that evaluate the adherence guidelines on stroke, coronary artery disease, and HF. The GWTG-HF registry has been prospectively collecting data from participating centers since 2005. The program enrolls patients who are either admitted with new or decompensated HF or those with new heart HF symptoms during hospitalization, in whom HF is the primary discharge diagnosis. Participating centers submit data on consecutive eligible patients. In participating centers, health care workers are trained to input variables using standardized definitions. Health care information on baseline characteristics, discharge characteristics, medications, medical history, laboratory values, and outcomes at discharge are input into the database. Race/ethnicity is self-reported by the individual patients at registration and not determined by health care personnel.

All of this information is submitted using the GWTG-HF Patient Management Tool (Outcomes Sciences Inc., Cambridge, Massachusetts), which is an internet-based patient management tool. This

(clinical trial steering committee), HMP Communications (Editor in Chief, *Journal of Invasive Cardiology*), *Journal of the American College of Cardiology* (Guest Editor; Associate Editor), Population Health Research Institute (clinical trial steering committee), Slack Publications (Chief Medical Editor, *Cardiology Today's Intervention*), and WebMD (CME steering committees); Other: *Clinical Cardiology* (Deputy Editor); has received research funding from Amarin, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Forest Laboratories, Ischemix, Medtronic, Pfizer, Roche, Sanofi Aventis, and The Medicines Company; has been a site co-investigator for Biotronik, St. Jude Medical; has been a trustee for American College of Cardiology; and has performed unfunded research for FlowCo, PLx Pharma, and Takeda; Dr. Butler has received honoraria from Travena Inc., and Takeda and research funding from the National Institute of Health; Dr. Yancy has received research funding from the Patient Centered Outcomes Research Institute; Dr. Fonarow has received honoraria from Amgen, Boston Scientific, Johnson & Johnson, The Medicines Company, Medtronic, Novartis, and Takeda; has received research funding from Gambro, Medtronic, the National Heart, Lung, and Blood Institute, and the National Institute of Health/ National Institute of Allergy and Infectious Diseases; and has been a consultant for Medtronic, Novartis, Amgen, and Janssen. The other authors have reported that they have no relationships relevant to the discussion of this paper to disclose.

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