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# Association of Arterial Pulse Pressure With Long-Term Clinical Outcomes in Patients With Heart Failure

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## ABSTRACT

**OBJECTIVES** This study assessed the association between pulse pressure (PP) and adverse outcomes at 1 year in patients hospitalized for heart failure (HF).

**BACKGROUND** PP has been shown to be predictive of the development of HF. The value and utility of PP assessment in patients with prevalent HF is less clear.

**METHODS** We conducted a retrospective cohort study from clinical registry data linked to Medicare claims for 40,421 HF patients entered in the Get With the Guidelines-HF program. Cox proportional hazards models were used to estimate the association between discharge PP and all-cause mortality and the composite outcome of all-cause mortality/readmission by 1 year.

**RESULTS** A nonlinear association between PP and mortality (expressed as hazard ratio [HR] per 10-mm Hg increase in PP) was observed in patients with HF and reduced (<0.40) ejection fraction (EF). Risk decreased as PP increased up to 50 mm Hg (adjusted HR: 0.946; 95% confidence interval [CI]: 0.900 to 0.995; $p = 0.03$). When PP was ≥50 mm Hg, risk increased as PP increased (adjusted HR: 1.091; 95% CI: 1.050 to 1.135; $p < 0.001$). In patients with HF and preserved EF (≥0.40), there was a significant association between PP and mortality with risk increasing as PP increased, although the magnitude of the risk was significantly impacted by systolic blood pressure (SBP). Qualitatively similar observations were obtained for the composite outcome and use of EF ≥0.50 to define HF with preserved EF.

**CONCLUSIONS** The association between PP at hospital discharge and 1-year outcomes is a function of HF phenotype, SBP, and absolute PP. (J Am Coll Cardiol HF 2016;4:42-9) © 2016 by the American College of Cardiology Foundation.

Arterial pulse pressure (PP) has been shown to be associated with all-cause (1) as well as cardiovascular mortality in cardiovascular disease-free (2) and older hypertensive (3) populations. PP has also been shown to be a strong determinant of incident coronary heart disease (4,5), atrial fibrillation (6), and recurrent events after myocardial infarction (7,8).

Prospective cohort studies in patients without heart failure (HF) at baseline have demonstrated that PP is strongly and positively associated with subsequent development of HF (9,10). However, an inverse

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association between PP and adverse cardiovascular outcomes has been described in other HF patient populations (11–16). There is also a growing awareness of the impact of left ventricular (LV) ejection fraction (EF) on this association (16).

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The purpose of the present study was to assess the association between arterial PP at hospital discharge and clinical outcomes by 1 year in a broad spectrum of HF patients receiving contemporary, guideline-based therapy.

## METHODS

**DATA SOURCES.** The Get With The Guidelines-Heart Failure (GWTG-HF) program is among the largest quality improvement initiatives focusing on patients hospitalized with HF and has been previously described (17–20). Patients hospitalized with new or worsening HF as primary diagnosis or patients who developed significant HF symptoms such that HF was the primary discharge diagnosis were included in the registry starting January 1, 2005. Patients were enrolled in the program regardless of EF. Hospitals from all regions of the United States are represented, and a variety of institutions participated, from community hospitals to large tertiary medical centers.

Data collected for each patient included demographics, medical/surgical history, admission medications, admission and discharge vital signs, physical examination findings, rhythm on admission, serum laboratory tests, pharmacological and nonpharmacological interventions, in-hospital outcomes, and discharge status information. Trained personnel (e.g., dedicated research coordinators and/or quality improvement/assurance personnel) entered chart-abstracted data, using standardized definitions. All participating hospitals were required to submit GWTG-HF protocol to their institutional review board for approval. Because data collected were used for hospital quality improvement, sites were granted a waiver of informed consent under the common rule. Quintiles are the data collection coordination center for the American Heart Association/American Stroke Association Get With The Guidelines programs. The Duke Clinical Research Institute served as the data analysis center and had an agreement to analyze de-identified data for research purposes.

We obtained clinical data from the GWTG-HF registry and Medicare claims data from the Centers for Medicare and Medicaid Services (CMS). Medicare data included inpatient claims and corresponding denominator files from January 1, 2005, through December 30, 2010. We linked data from the GWTG-HF registry to the research identifiable inpatient claims data with the use of indirect identifiers admission date, discharge date, sex, and age or date of birth (21). Combinations of these identifiers are almost always unique, enabling identification of registry hospitalizations in Medicare claims data. For patients with multiple linked hospitalizations in the registry, we selected the first hospitalization for analysis.

**STUDY POPULATION.** From January 1, 2005, to December 30, 2010, there were 53,484 CMS-matched patients discharged alive from 265 fully participating hospitals. From these patients, we excluded: 1) 2,144 patients who did not have eligible fee-for-service Medicare at the time of index HF hospitalization discharge; 2) 1,811 patients who died in-hospital; 3) 4,719 patients (8.8%) missing discharge blood pressure information; 4) 8 patients who were using LV-assist devices; 5) 1,891 patients who left against medical advice or were discharged to short-term hospital or hospice service; and 6) 2,490 patients whose EF status was missing. The final sample size for analysis was 40,421 patients from 258 sites.

**PP determination.** Pulse pressure is defined as the difference between the brachial arterial systolic and diastolic pressures obtained, in conformance with the local standard of care for assessment of vital signs. In this study we used the PP on the basis of the systolic

**ABBREVIATIONS AND ACRONYMS**

**CMS** = Centers for Medicare and Medicaid Services
**EF** = ejection fraction
**GWTG** = Get With The Guidelines
**HF** = heart failure
**LV** = left ventricle
**PP** = pulse pressure
**SBP** = systolic blood pressure

Publications as Editor in Chief, *Harvard Heart Letter*, and from Duke Clinical Research Institute, serving on clinical trial steering committees, Harvard Clinical Research Institute clinical trial steering committee, HMP Communications as Editor in Chief, *Journal of Invasive Cardiology*, *Journal of the American College of Cardiology* as Associate Editor and as Section Editor, Pharmacology, Population Health Research Institute clinical trial steering committee, Slack Publications as Chief Medical Editor, *Cardiology Today's Intervention*, WebMD CME steering committees, and Deputy Editor of *Clinical Cardiology*; has received research funding from Amarin, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Forest Laboratories, Ischemix, Medtronic, Pfizer, Roche, Sanofi, The Medicines Company; and support from FlowCo, PLx Pharma, and Takeda. Dr. Fonarow has received research support from Agency for Healthcare Research and Quality, and U.S. National Institutes of Health; and is a consultant for Amgen, Bayer, Gambro, Janssen, Novartis, and Medtronic. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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