JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2024 PUBLISHED BY ELSEVIER ON BEHALF OF THE
AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION

VOL. 83, NO. 6, 2024

Implantable Hemodynamic Monitors Improve Survival in Patients With Heart Failure and Reduced Ejection Fraction

JoAnn Lindenfeld, MD,[a] Maria Rosa Costanzo, MD,[b] Michael R. Zile, MD,[c] Anique Ducharme, MD,[d] Richard Troughton, MD,[e] Alan Maisel, MD,[f] Mandeep R. Mehra, MD, MSc,[g] Sara Paul, DNP,[h] Samuel F. Sears, PhD,[i] Frank Smart, MD,[j] Nessa Johnson, PhD,[k] John Henderson, MS,[k] Philip B. Adamson, MD,[k] Akshay S. Desai, MD,[g] William T. Abraham, MD,[l] on behalf of the GUIDE-HF, CHAMPION, and LAPTOP-HF Investigators

ABSTRACT

BACKGROUND Trials evaluating implantable hemodynamic monitors to manage patients with heart failure (HF) have shown reductions in HF hospitalizations but not mortality. Prior meta-analyses assessing mortality have been limited in construct because of an absence of patient-level data, short-term follow-up duration, and evaluation across the combined spectrum of ejection fractions.

OBJECTIVES The purpose of this meta-analysis was to determine whether management with implantable hemodynamic monitors reduces mortality in patients with heart failure and reduced ejection fraction (HFrEF) and to confirm the effect of hemodynamic-monitoring guided management on HF hospitalization reduction reported in previous studies.

METHODS The patient-level pooled meta-analysis used 3 randomized studies (GUIDE-HF [Hemodynamic-Guided Management of Heart Failure], CHAMPION [CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients], and LAPTOP-HF [Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy]) of implantable hemodynamic monitors (2 measuring pulmonary artery pressures and 1 measuring left atrial pressure) to assess the effect on all-cause mortality and HF hospitalizations.

RESULTS A total of 1,350 patients with HFrEF were included. Hemodynamic-monitoring guided management significantly reduced overall mortality with an HR of 0.75 (95% CI: 0.57-0.99); $P = 0.043$. HF hospitalizations were significantly reduced with an HR of 0.64 (95% CI: 0.55-0.76); $P < 0.0001$.

CONCLUSIONS Management of patients with HFrEF using an implantable hemodynamic monitor significantly reduces both mortality and HF hospitalizations. The reduction in HF hospitalizations is seen early in the first year of monitoring and mortality benefits occur after the first year. (J Am Coll Cardiol 2024;83:682-694) © 2024 Published by Elsevier on behalf of the American College of Cardiology Foundation.

Listen to this manuscript's audio summary by Editor-in-Chief Dr Valentin Fuster on www.jacc.org/journal/jacc.

From the [a]Vanderbilt Heart and Vascular Institute, Vanderbilt University Medical Center, Nashville, Tennessee, USA; [b]Midwest Cardiovascular Institute, Naperville, Illinois, USA; [c]Medical University of South Carolina, Ralph H. Johnson Department of Veterans Affairs Medical Center, Charleston, South Caroline, USA; [d]Montreal Heart Institute, Université de Montréal, Montreal, Quebec, Canada; [e]Christchurch Heart Institute, University of Otago, Christchurch, New Zealand; [f]University of California San Diego, La Jolla, California, USA; [g]Center for Advanced Heart Disease, Brigham and Women's Hospital, Boston, Massachusetts, USA; [h]Catawba Valley Health System, Conover, North Carolina, USA; [i]East Carolina University, Greenville, North Carolina, USA; [j]Louisiana State University School of Medicine, New Orleans, Louisiana, USA; [k]Abbott, Abbott Park, Illinois, USA; and the [l]Ohio State University, Wexner Medical Center, Columbus, Ohio, USA.

Marat Fudim, MD, MHS, served as Guest Associate Editor for this paper. Javed Butler, MD, MPH, MBA, served as Guest Editor-in-Chief for this paper.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received September 28, 2023; revised manuscript received November 17, 2023, accepted November 20, 2023.

ISSN 0735-1097/$36.00

https://doi.org/10.1016/j.jacc.2023.11.030

Elevated intracardiac and pulmonary artery pressures (PAPs) are common in all types of cardiovascular disease and are associated with increased mortality.[1-4] Even mild elevations in PAP predict excess mortality whether measured using right heart catheterization or Doppler echocardiography.[5] Implantable hemodynamic monitoring (IHM) devices have shown that pulmonary hypertension is common in patients with both heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF).[6] Baseline elevated PAP, either measured directly by an implanted sensor or indirectly by thoracic impedance, predicts higher heart failure hospitalization (HFH) rates and higher mortality in patients with heart failure (HF) across ejection fractions.[7-11] Additionally, mortality and HFH increase when PAP increases further and decrease with reductions in PAP.[7,10] IHM devices that directly measure PAP have been shown to reduce HFH in individual trials and in several meta-analyses.[12-20] Therapies that reduce HFH generally reduce mortality; thus, one might expect to see a reduction in mortality using IHM devices designed to lower PAP or left atrial pressure (LAP) in patients with HF, although previous meta-analyses based on aggregate data have shown only a small and nonsignificant reduction in mortality.[17-19] However, these studies evaluated mortality in a combined HF population including both HFrEF and HFpEF, had a short mean follow-up, and did not include individual patient-level data. Unlike other meta-analyses to date, we had unique access to patient-level data in 3 similarly conducted randomized trials of IHM devices—2 using an implantable PAP sensor and 1 using an implantable LAP sensor.[13-16] The individual trials were powered for their primary endpoints, recurrent HFH with or without cardiovascular mortality, but not for overall mortality alone. Based on prior trials and meta-analyses, we hypothesized that a patient-level pooled analysis would demonstrate reduced mortality by utilizing IHM particularly in the HFrEF population specifically, in which the majority of death is cardiovascular in cause.

SEE PAGE 695

METHODS

Patient-level data with long-term follow-up was included for 3 randomized clinical trials (**Table 1**): the GUIDE-HF (Hemodynamic-Guided Management of Heart Failure; NCT03387813), the CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients; NCT00531661), and the LAPTOP-HF (Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy; NCT01121107).[21-23] The design and results of the GUIDE-HF, CHAMPION and LAPTOP-HF trials have all been published, with the exception of LAPTOP-HF results, which were presented at the Heart Failure Society of America Conference in 2016.[13-15,21-23]

All trials enrolled HF patients with a prior HFH or elevated natriuretic peptides and used an implantable hemodynamic monitor for HF management. The CHAMPION and GUIDE-HF trials utilized the CardioMEMS PA Sensor (Abbott) implanted in the distal pulmonary artery via a right heart catheterization, whereas the LAPTOP-HF trial utilized the HeartPOD LAP sensor (Abbott, formerly St Jude Medical) implanted in the interatrial septum via a transseptal catheterization. **Table 1** outlines the specifics of each trial, including the primary endpoint, major inclusion criteria, follow-up duration, sample size, and safety outcomes. All patients were required to be on stable and optimally titrated guideline-directed medical therapy (GDMT) for HF at enrollment. In each trial, patients were randomized to a treatment group receiving IHM via an implanted device or a control group receiving standard-of-care. All patients provided written informed consent prior to study participation, and the protocols were approved by the Institutional Review Board of each site. Additional detail regarding trial designs and randomization is included in the Supplemental Appendix, Section 1. This patient-level meta-analysis was performed utilizing follow-up through 24 months for CHAMPION and LAPTOP-HF and follow-up before COVID-19 for GUIDE-HF.[24] The patient cohort for this pooled analysis included all HFrEF subjects for whom therapy was initiated following successful implantation of the IHM device. A supplementary analysis was performed, in which follow-up during COVID-19 was included for GUIDE-HF, and 24 additional patients randomized but not implanted in LAPTOP-HF were included. HFrEF was defined as an LVEF ≤40%, because it was the criteria in all 3 trials and is recognized as the threshold of classification for HFrEF patients in the current American Heart Association/American College of Cardiology/Heart Failure Society of America heart failure guidelines.[25] The follow-up period was truncated at 2 years, because the number of subjects was limited after 2 years, and both trials with continued follow-up (CHAMPION and LAPTOP-HF) had adequate representation with at least 100 subjects at risk at 24 months. HFH was defined

ABBREVIATIONS AND ACRONYMS

GDMT = guideline-directed medical therapy

HF = heart failure

HFH = heart failure hospitalization

HFpEF = heart failure with preserved ejection fraction

HFrEF = heart failure with reduced ejection fraction

IHM = implantable hemodynamic monitoring

LAP = left atrial pressure

PAP = pulmonary artery pressure

similarly across all 3 trials as unplanned hospital admissions determined to be caused by acute decompensated HF and requiring intravenous diuretic agents. HFH was included in the pooled meta-analysis according to the adjudication by the Clinical Events Committee of each trial.

STATISTICAL ANALYSIS. Analyses of the pooled data set was not pre-specified in the Statistical Analysis Plan for each trial. Poolability of the data sets was evaluated by testing between-trial heterogeneity for both HFH and mortality separately. Interaction testing for HFH at 12 months was completed using the Andersen-Gill model with an interaction term to identify each trial. No significant evidence of heterogeneity was found between the trials (interaction $P = 0.30$). Interaction testing for mortality was completed using the Cox proportional hazards model with an added interaction term. For mortality, the interaction at 24 months was significant (interaction $P = 0.03$) indicating evidence of heterogeneity between trial data sets. However, when only CHAMPION and LAPTOP-HF were included, the interaction for mortality at 24 months was nonsignificant (interaction $P = 0.6$), suggesting that the evidence of heterogeneity is likely caused by the overall shorter follow-up in GUIDE-HF compared with the other 2 trials. The GUIDE-HF trial data was included in mortality analyses despite the shorter follow-up duration for completeness of patient-level data. Baseline demographics were analyzed using mean ± SD for continuous variables or percentages for categorical variables. Recurrent HFH were evaluated using the Andersen-Gill model with robust sandwich variance estimates including covariates for the randomized group and an indicator for trial. The pooled data set was truncated to 12 months of follow-up for recurrent HFH analyses and at 24 months of follow-up for survival analyses. Patient follow-up was only censored for death or withdrawal. Survival analyses were conducted using both Kaplan-Meier estimates of freedom from all-cause mortality and the Cox proportional hazards model with model-based variance and P value testing using a log-rank test. Statistical tests were 2-tailed at the 5% significance level and not adjusted for multiplicity. PA pressures were analyzed using a general linear model at 12 months using an area under the pressure-time curve. Statistical analyses were performed using SAS version 9.4 or higher.

RESULTS

A total of 1,350 patients with HFrEF (LVEF ≤40%) were included. The median follow-up period was 12.2 months (Q1, Q3: 7.8, 21.8 months). Safety outcomes for GUIDE-HF and CHAMPION are included in **Table 1**, with device or system related complications occurring in 0.8% and 1.4% of patients, respectively. Complications of the implant procedure for LAPTOP-HF are included in Supplemental Table 1. In total, 25% were women and 25% were Black (**Table 2**, Supplemental Table 2). The majority of patients in all trials had NYHA functional class III HF. Approximately one-half of the patients had an ischemic etiology of HF, and the mean ejection fraction was similar across studies at 25%. Baseline PAP pressures were similar in CHAMPION and GUIDE-HF, with PAP diastolic similar at baseline to the baseline LAP in LAPTOP-HF. Approximately 78% of patients were taking an angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, or angiotensin receptor-neprilysin inhibitor; 95% were taking a beta-blocker; and just over 52% of patients were taking a mineralocorticoid receptor antagonist.

Figure 1 shows the reduction in HFH at 12 months in each of the 3 studies. Each study demonstrated an early and significant decrease in HFH in the IHM group compared with the control group. The observed treatment effect was similar in each study, with a 29% reduction in GUIDE-HF (HR: 0.71; 95% CI: 0.53-0.96; $P = 0.027$), 31% reduction in CHAMPION (HR: 0.69; 95% CI: 0.53-0.89; $P = 0.004$), and 48% reduction in LAPTOP-HF (HR: 0.52; 95% CI: 0.38-0.71; $P < 0.0001$).

The overall pooled meta-analysis for HFH demonstrates a significant 36% reduction in HFH (**Figure 2**) (HR: 0.64; 95% CI: 0.55-0.76; $P < 0.0001$). A supplemental analysis using GUIDE-HF complete follow-up and the LAPTOP-HF as a randomized cohort shows a similar significant reduction in HFH (Supplemental Figure 1) (HR: 0.69; 95% CI: 0.59-0.80; $P < 0.0001$).

Survival at 2 years is shown in each of the 3 studies in **Figure 3**. The GUIDE-HF trial did not show a significant difference in mortality across the limited follow-up, whereas both the CHAMPION and LAPTOP-HF trials demonstrated similar mortality curves with increased separation between treatment and control groups after approximately 12 months of follow-up through 2 years. The CHAMPION trial trend of reduced mortality approached significance (HR: 0.67; 95% CI: 0.44-1.00; $P = 0.050$), and the LAPTOP-HF demonstrated a 44% reduction in mortality independently (HR: 0.56; 95% CI: 0.34-0.93; $P = 0.023$). **Figure 4** demonstrates the mortality pooled meta-analysis with a significant 25% reduction in mortality (HR: 0.75; 95% CI: 0.57-0.99; $P = 0.043$). A supplemental analysis with the addition of GUIDE-HF follow-up during COVID-19 and the LAPTOP-HF subjects who were randomized but not implanted shows a similar and significant reduction in mortality

TABLE 1 Summary of Studies

	GUIDE-HF Randomized Arm[16,21]	CHAMPION[13,14,23]	LAPTOP-HF[15,22]
Design	Prospective, multicenter, randomized, controlled, single-blinded evaluation of the CardioMEMS HF System	Prospective, multicenter, randomized, controlled, single-blinded evaluation of the CardioMEMS HF System	Prospective, multicenter, randomized, controlled evaluation of the LAP Monitoring System (HeartPOD and PAM)
Pressure sensor	Hemodynamic management using PAP via implanted sensor	Hemodynamic management using PAP via implanted sensor	Hemodynamic management using LAP via a transseptal lead
Patient engagement	• Blinded to treatment group; implanted control group • Daily PAP measurements • Interventions communicated by phone through blinded caller, minimum contact frequency for both groups	• Blinded to treatment group; implanted control group • Daily PAP measurements • Interventions communicated by phone, matched contact frequency between groups	• Unblinded to treatment group; unimplanted control group • Twice daily recording of symptoms, weights, and blood pressure; continuous measurement of LAP • Interventions communicated through handheld PAM
Trial dates	March 2018 to January 2021	September 2007 to December 2014	June 2010 to April 2015
Duration of follow-up—HFrEF, mo	12 mo Median 8.2 mo (Q1, Q3: 4.6, 11.4 mo) (pre-COVID-19)	Continued until last subject reached 6 mo Median 17.0 mo (Q1, Q3: 11.5, 23.0 mo)	Continued until last subject reached 12 months Median 22.8 mo (Q1, Q3: 14.6, 34.8 mo)
Primary endpoint	Composite of HF hospitalizations, urgent HF visits, and all-cause mortality at 12 mo	HF hospitalizations at 6 mo	HF major acute cardiovascular and neurological events at overall follow-up
Major inclusion	NYHA functional class II/III/IV with prior HF hospitalization or elevated BNP/NT-proBNP	NYHA functional class III with prior HF hospitalization	NYHA functional class III with prior HF hospitalization or persistently elevated BNP
Sample size (HFrEF)	Baseline: 531 12 mo: 63 24 mo: not applicable	Baseline: 456 12 mo: 332 24 mo: 104	Baseline: 363 12 mo: 305 24 mo: 169
Safety outcomes	DSRCs: 0.8% (8/1,022)	DSRCs: 1.4% (8/575) Sensor Failure: 0% (0.575)	Not reported previously (see Supplemental Table 1)
Notes	Study affected by COVID-19 pandemic; pre-COVID-19 follow-up utilized (before March 13, 2020).		Study stopped because of implant-related complications; follow-up continued in therapy-initiated patients.

BNP = brain natriuretic peptide; DSRC = device or system-related complication; HFrEF = heart failure with reduced ejection fraction; LAP = left atrial pressure; NT-proBNP = N-terminal pro-brain natriuretic peptide; PAM = Patient Advisory Module; PAP = pulmonary artery pressure.

(Supplemental Figure 2) (HR: 0.76; 95% CI: 0.58-1.00; $P = 0.042$). An additional supplemental analysis including only the trials with follow-up beyond 12 months (CHAMPION and LAPTOP-HF) also shows a significant reduction in mortality (Supplemental Figure 3) (HR: 0.62; 95% CI: 0.45-0.86; $P = 0.0031$).

A Forest plot summarizing the effects of IHM on HFH and mortality for the pooled population and each trial independently is included in Supplemental Table 3, demonstrating consistency in the treatment effect across trials for HFH. For mortality, consistency is observed for CHAMPION and LAPTOP-HF, but GUIDE-HF differs qualitatively largely caused by the limited follow-up time (median 7.9 months).

Changes in hemodynamics are shown in Supplemental Table 4, demonstrating a reduction in PAP diastolic or LAP in the pooled population and each trial, as evaluated using AUC analysis and paired change from baseline. The differences in pressure were significant within the treatment group and between groups for the pooled analysis and for GUIDE-HF, but not for CHAMPION or LAPTOP-HF.

Analysis of HFH and mortality according to subgroups of baseline GDMT demonstrated generally greater treatment effect for both HFH and mortality in patient groups on 3 GDMT groups compared with those on fewer (Supplemental Tables 5 and 6).

DISCUSSION

This patient-level meta-analysis demonstrates that management of HFrEF patients using IHM reduces mortality over longer follow-up and confirms the previously reported reduction in HFH. These data are consistent with studies demonstrating a correlation between HFH and mortality. Gheorghiade et al[26] showed that HFHs are one of the strongest predictors for mortality, and multiple studies have demonstrated that mortality increases as the number of HFHs increases.[27-30] In addition, increasing PAP or LAP correlate closely with increasing mortality, and small decreases in PAP correlate with decreased mortality.[7] This meta-analysis represents an important confirmation that in addition to reducing early HFH, hemodynamic-guided therapy also results in

JACC VOL. 83, NO. 6, 2024
FEBRUARY 13, 2024:682-694

TABLE 2 Baseline Demographics in Pooled Population and by Study

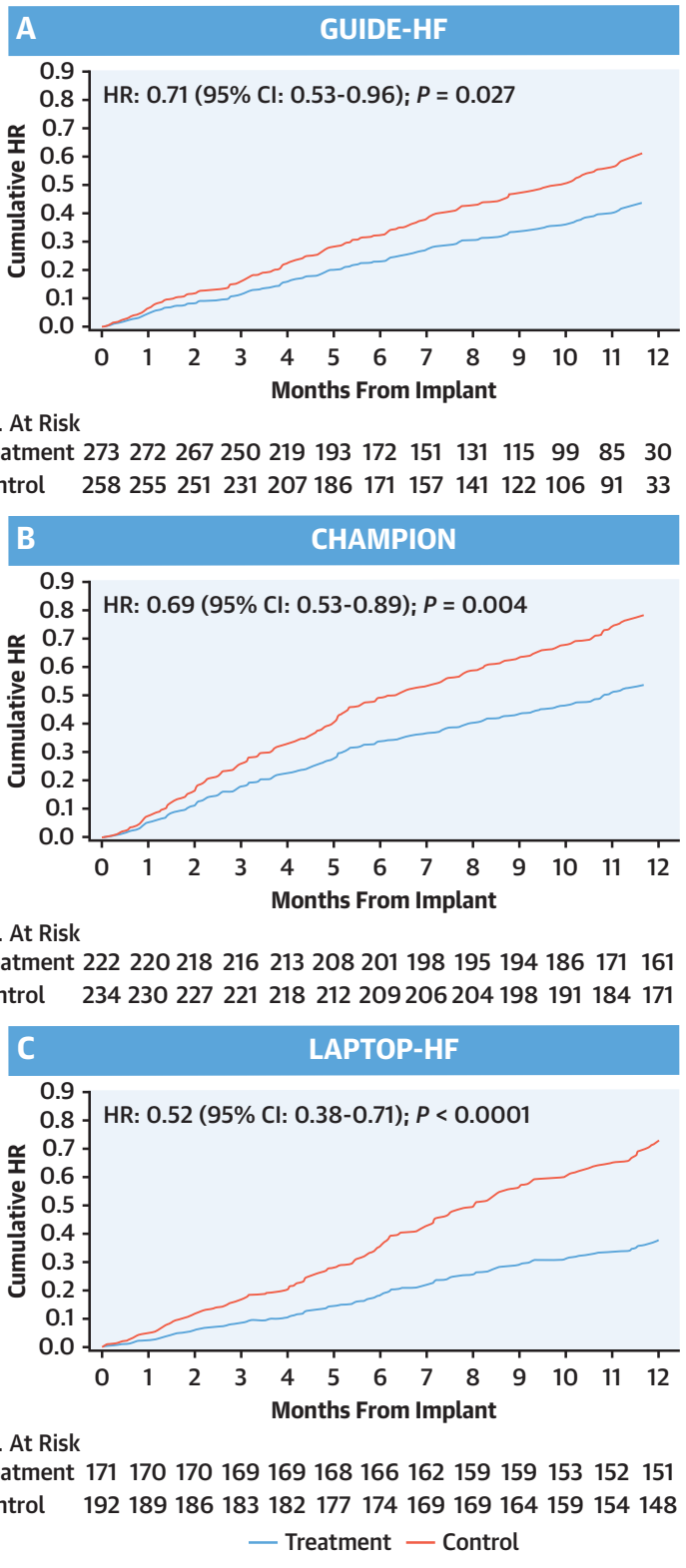
	All Subjects (N = 1,350)	GUIDE-HF (n = 531)	CHAMPION (n = 456)	LAPTOP-HF (n = 363)
Age, y	63.5 ± 12.6	67.2 ± 11.4	60.7 ± 12.8	61.7 ± 12.7
Female	25.3 (342)	29.2 (155)	24.3 (111)	20.9 (76)
Race				
White	71.1 (960)	73.6 (391)	71.3 (325)	67.2 (244)
Black	24.7 (334)	24.9 (132)	25.7 (117)	23.4 (85)
Other	4.1 (56)	1.5 (8)	3.1 (14)	9.4 (34)
NYHA functional class				
II	13.6 (183)	31.6 (168)	0.0 (0)	4.1 (15)
III	84.1 (1,136)	62.5 (332)	100.0 (456)	95.9 (348)
IV	2.3 (31)	5.8 (31)	0.0 (0)	0.0 (0)
Medical history				
Ischemic etiology	54.5 (736)	50.5 (268)	62.9 (287)	49.9 (181)
Previous myocardial infarction	45.5 (449)	39.9 (212)	52.0 (237)	NA
Diabetes	48.9 (660)	49.0 (260)	47.8 (218)	50.1 (182)
Atrial flutter or fibrillation	50.7 (500)	55.6 (295)	45.0 (205)	NA
Baseline characteristics				
BMI, kg/m^2	31.1 ± 7.0	31.4 ± 7.4	30.1 ± 6.3	32.0 ± 7.1
Heart rate, beats/min	74.7 ± 12.8	74.8 ± 12.6	73.4 ± 12.6	76.2 ± 13.2
Systolic blood pressure, mm Hg	116.8 ± 18.9	116.9 ± 17.9	120.6 ± 21.2	111.8 ± 15.8
Diastolic blood pressure, mm Hg	70.0 ± 11.6	69.3 ± 11.0	72.6 ± 12.9	67.8 ± 10.1
LVEF, %	24.9 ± 8.1	25.9 ± 8.3	24.3 ± 8.0	24.3 ± 7.7
PA systolic pressure, mm Hg	45.3 ± 15.2	45.1 ± 15.4	45.5 ± 14.9	NA
PA diastolic pressure, mm Hg	19.4 ± 8.7	19.3 ± 8.9	19.4 ± 8.4	NA
PA mean pressure, mm Hg	29.7 ± 10.5	29.5 ± 10.9	29.9 ± 10.2	NA
PCWP, mm Hg	18.3 ± 8.7	17.8 ± 9.0	18.8 ± 8.3	NA
Left atrial pressure, mm Hg	19.7 ± 10.1	NA	NA	19.7 ± 10.1
Cardiac output, L/min	4.48 ± 2.05	4.52 ± 2.46	4.44 ± 1.43	NA
Cardiac index, L/min/m^2	2.13 ± 0.88	2.15 ± 1.05	2.12 ± 0.61	NA
Laboratory analyses				
Serum creatinine, mg/dL	1.5 ± 0.5	1.5 ± 0.6	1.4 ± 0.5	NA
Estimated GFR, mL/min/1.73 m^2	57.8 ± 23.2	54.4 ± 22.8	61.7 ± 23.1	NA
BNP, pg/mL	412.0 (192.0, 918.0)	412.0 (192.0, 918.0)	NA	NA
NT-proBNP, pg/mL	1,811.0 (1,020.0, 3,487.0)	1,811.0 (1,020.0, 3,487.0)	NA	NA
Treatment history				
Previous CRT	38.8 (524)	40.5 (215)	37.9 (173)	37.5 (136)
Previous defibrillator	56.7 (765)	68.0 (361)	77.0 (351)	14.6 (53)
Guideline-directed medical therapy				
ACEi or ARB or ARNi	77.6 (1,048)	75.1 (399)	78.1 (356)	80.7 (293)
ARNi	25.5 (252)	47.5 (252)	0.0 (0)	NA
Beta-blocker	94.7 (1,278)	95.1 (505)	93.4 (426)	95.6 (347)
MRA	52.3 (706)	51.0 (271)	45.2 (206)	63.3 (229)
Diuretic	95.1 (1,284)	94.2 (500)	93.0 (424)	99.2 (360)
Hydralazine	14.5 (143)	15.3 (81)	13.6 (62)	NA
Nitrate	22.6 (223)	24.1 (128)	20.8 (95)	NA

Values are mean ± SD, % (n), or median (Q1, Q3).

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker, ARNi = angiotensin neprilysin inhibitor; BMI = body mass index; BNP = brain natriuretic peptide; CRT = cardiac resynchronization therapy; GFR = glomerular filtration rate; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NT-proBNP = N-terminal pro-brain natriuretic peptide; PA = pulmonary artery; PCWP = pulmonary capillary wedge pressure.

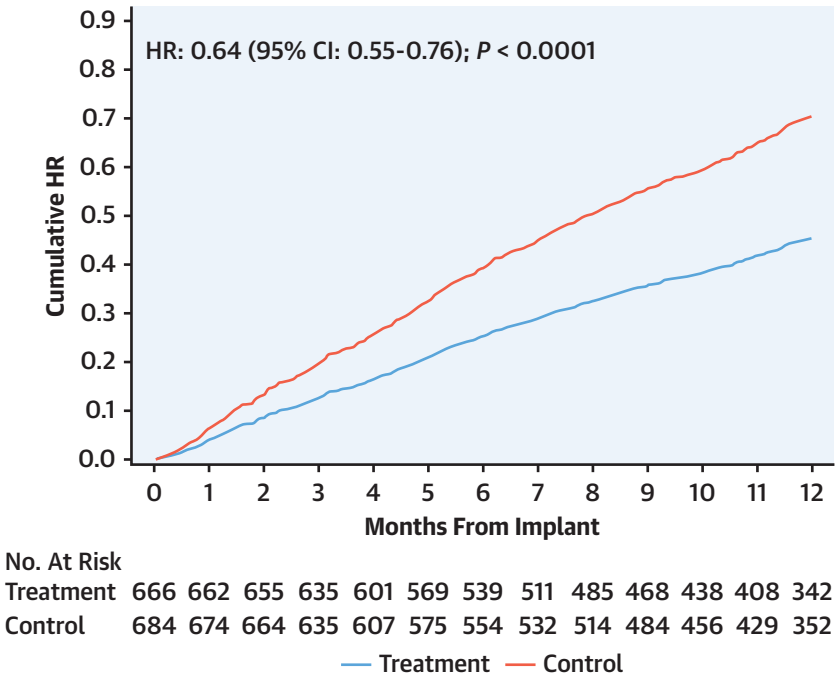
decreased mortality in patients with HFrEF. In the CHAMPION trial, increasing PAP was managed in large part with diuretic agents.[31] The results of a meta-analysis suggests that diuretic agents reduce both HFH and mortality in HF patients, although only 221 of the 928 patients had mortality data available.[32] Although safety concerns have been raised with diuretic agents, studies with IHM in which most changes in therapy consisted of adjustments in diuretic agents have not yielded adverse safety

FIGURE 1 Heart Failure Hospitalizations for Implantable Hemodynamic Monitoring and Medical Therapy by Study



Heart failure hospitalizations through 12 months for (A) GUIDE-HF, (B) CHAMPION, (C) LAPTOP-HF, with implantable hemodynamic monitoring (treatment) in blue and medical therapy (control) in red. A significant and consistent reduction in heart failure hospitalizations was observed at 12 months in each study. HR, 95% CI, and *P* values estimated using Andersen-Gill model. CHAMPION = CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients; GUIDE-HF = Hemodynamic-Guided Management of Heart Failure; LAPTOP-HF = Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy.

FIGURE 2 Heart Failure Hospitalizations for Implantable Hemodynamic Monitoring and Medical Therapy in Pooled Population

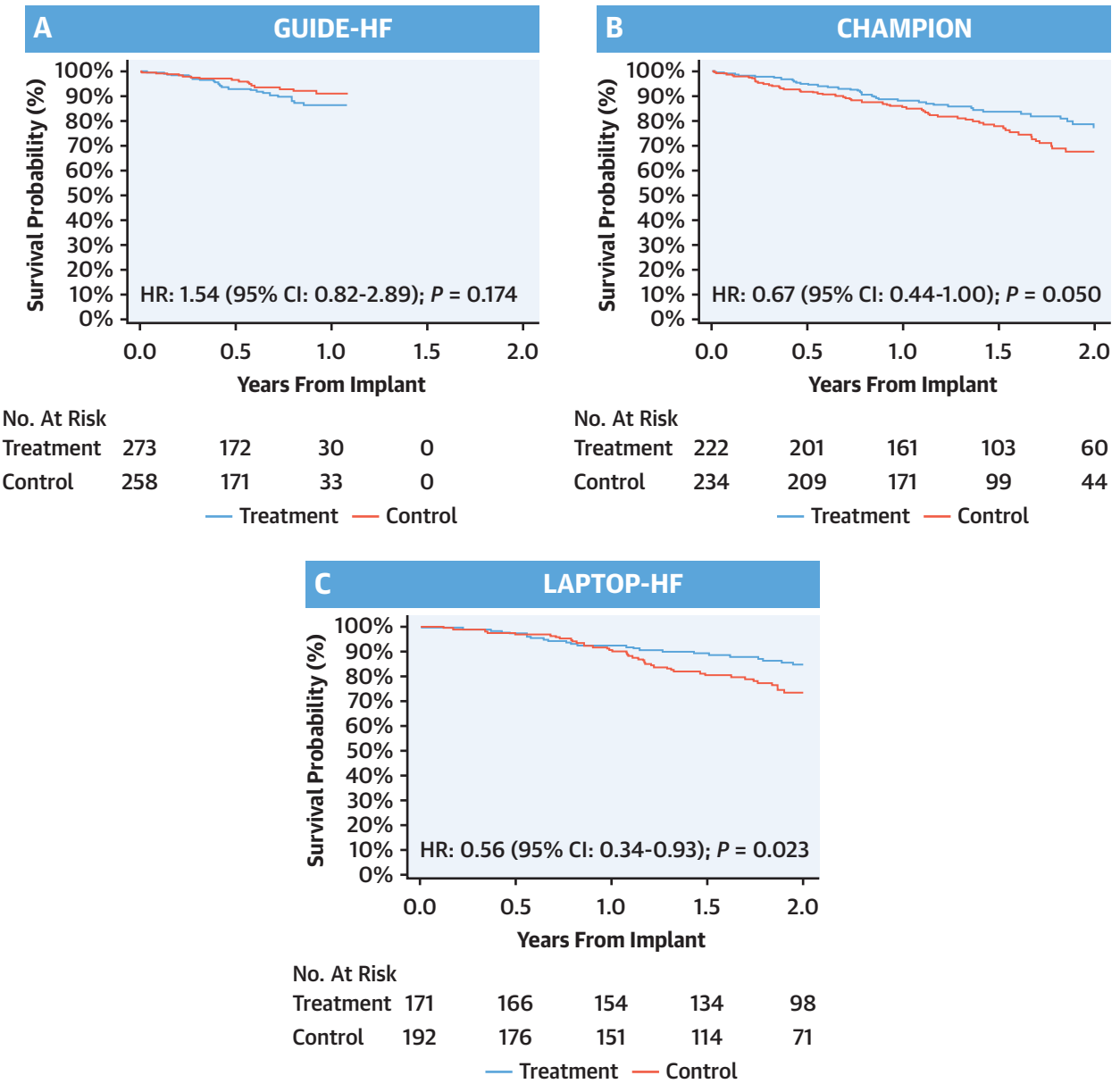


Heart failure hospitalizations through 12 months for implantable hemodynamic monitoring (treatment) in blue and medical therapy (control) in red. A significant 36% reduction in heart failure hospitalizations was observed at 12 months in the pooled population. HR, 95% CI, and *P* values estimated using Andersen-Gill model.

signals.[13,16,33,34] This finding may be related to the fact that hemodynamics guided by IHM dictate both increases and decreases in diuretic doses over time. A benefit of IHM on mortality is not surprising because it is known that left ventricular filling pressures often increase for days or weeks before an HF exacerbation[11] and that patients are often discharged with inadequate decongestion.[35-37] Elevations in PA or LA pressures or distension of these structures have been associated with sympathetic activation,[38,39] increased heart rate,[40] increased myocardial wall stress,[41] decreased renal function,[42] and arrhythmias,[43,44] all of which are detrimental in HF. It is therefore possible that reductions in PAP and LA pressure might improve mortality by improving one or several of these adverse effects. Management of HF with IHM devices leads to timely decongestion, thus reversing many of these adverse effects and contributing to improved mortality (**Central Illustration**). The mortality benefit of management with IHM devices was also shown in a propensity-matched study of Medicare patients.[45]

Previous meta-analyses of IHM devices using different studies have demonstrated a consistent and highly significant reduction in HFH virtually identical to that observed in our analysis. However, in contrast to our findings, previous analyses were unable to demonstrate a significant reduction in mortality.[17-19] Several important differences may explain these different mortality results. We excluded 3 trials used in other meta-analyses—COMPASS-HF (Chronicle Offers Management to Patients with Advanced Signs and Symptoms of Heart Failure), REDUCE-HF (Results of the Reducing Decompensation Events Utilizing Intracardiac Pressures in Patients With Chronic Heart Failure), and MONITOR-HF (Remote Haemodynamic Monitoring of Pulmonary Artery Pressures in Patients With Chronic Heart Failure) for several reasons.[12,20,46] First, and most practically important, is that patient-level data was not available for the trials. Second, there were issues with both COMPASS-HF and REDUCE-HF that reduced their applicability. COMPASS-HF was the first randomized trial of IHM, and the primary endpoint of mortality and HFH was not statistically significantly reduced caused by the lower-than-expected event rates in the control group and the inclusion of NYHA functional class IV subjects.[47] In addition, the investigators lacked guidance

FIGURE 3 Survival for Implantable Hemodynamic Monitoring and Medical Therapy by Study

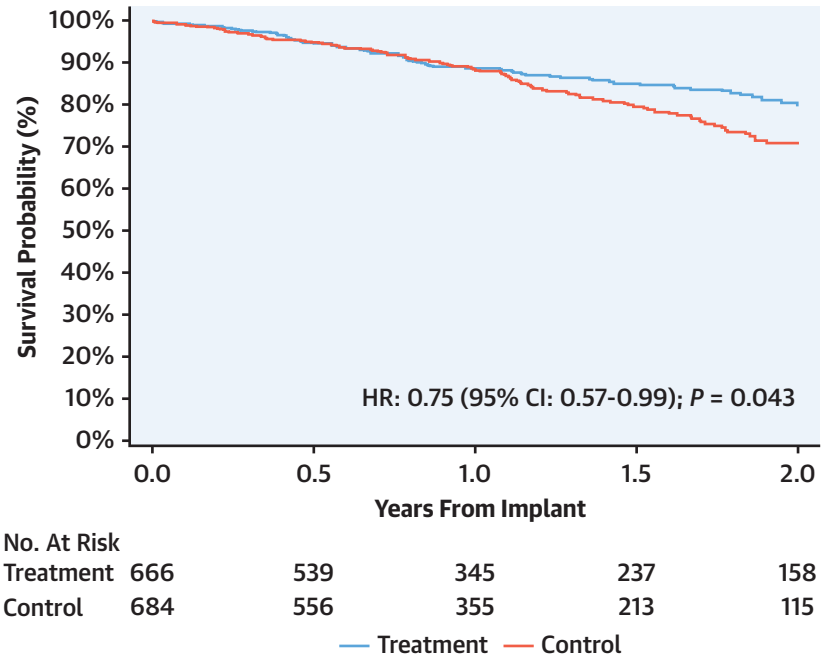


Survival through 24 months for (A) GUIDE-HF, (B) CHAMPION, and (C) LAPTOP-HF, with implantable hemodynamic monitoring (treatment) in blue and medical therapy (control) in red. Outcomes varied by study, with no reduction in mortality in GUIDE-HF (A), a trend toward reduced mortality in CHAMPION (B), and a significant 44% reduction in mortality in LAPTOP-HF (C) at 24 months. Survival estimated using Kaplan-Meier estimates; HR, 95% CI, and *P* values estimated using Cox Proportional Hazards model. Abbreviations as in Figure 1.

on how to manage changes in device-derived pressures, and medication changes in response to elevated pressures often did not occur because of lack of symptoms. Although REDUCE-HF was designed to enroll 1,300 patients, the study was terminated after randomization of 400 patients because of IHM lead failures. Therefore, the study was unable to test clinical efficacy endpoints adequately.[46]

Although the LAPTOP-HF study was included in only one previous meta-analysis, patient-level mortality data were not available for that analysis but were available for this analysis.[17] In the most recent

FIGURE 4 Survival for Implantable Hemodynamic Monitoring and Medical Therapy in Pooled Population



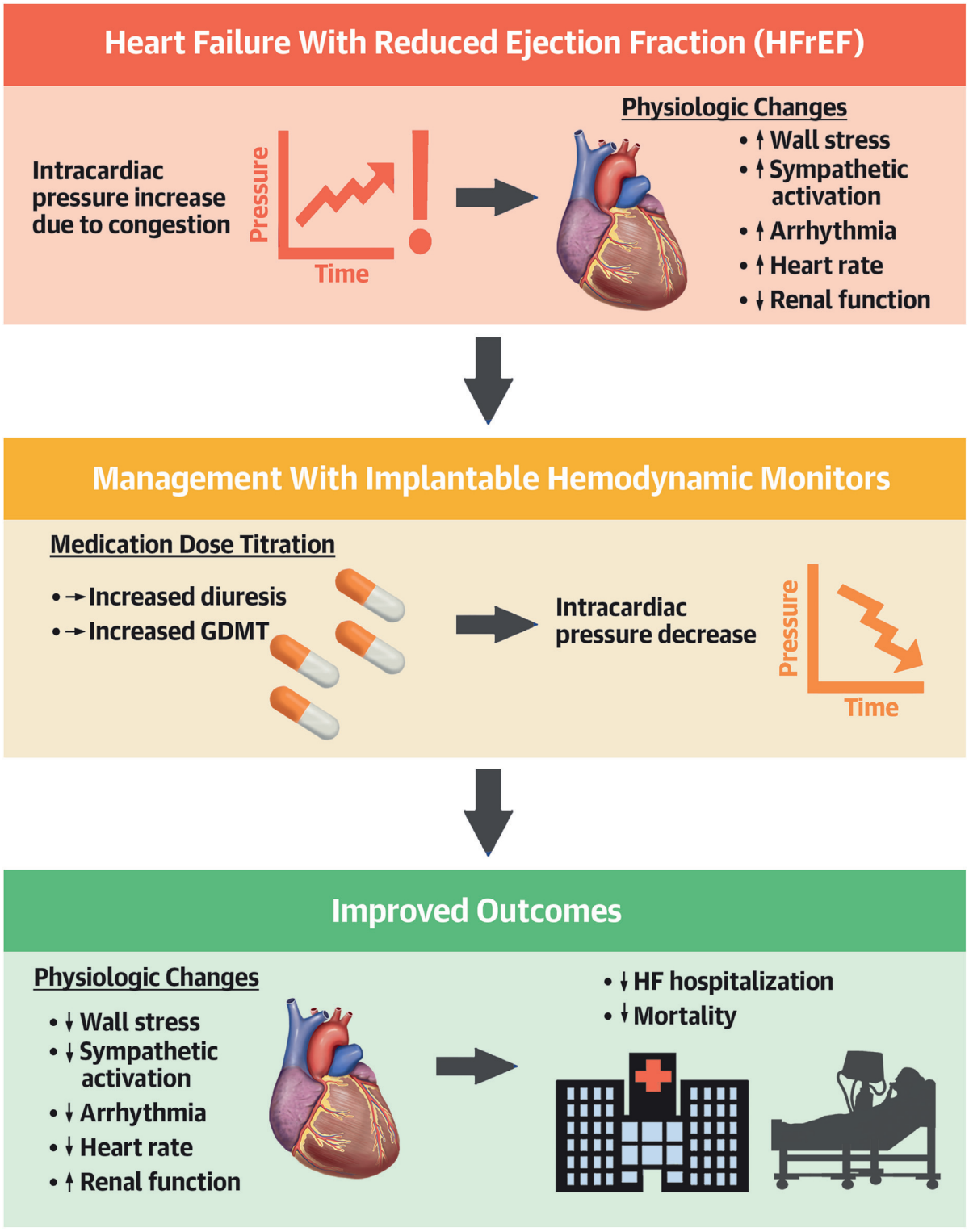
Survival through 24 months, with implantable hemodynamic monitoring (treatment) in blue and medical therapy (control) in red. A significant 25% reduction in mortality was observed at 24 months in the pooled population. Survival estimated using Kaplan-Meier estimates; HR, 95% CI, and *P* values estimated using Cox Proportional Hazards model.

meta-analysis on the effects of IHM, there were only 231 deaths in the 4 trials and both HFpEF and HFrEF were included.[17] Furthermore, we had access to extended follow-up at the patient level that was not available in other meta-analyses. Finally, we evaluated only patients with HFrEF because the sample size of HFrEF patients was large enough to provide a meaningful long-term analysis. The number of patients with HFpEF was inadequate to evaluate mortality beyond 1 year of follow-up. Because patients with HFrEF have higher PAP than those with HFpEF, modest increases in PAP are more likely to lead to an HF exacerbation.[10,11] In addition, cardiovascular mortality represents a higher percentage of mortality in HFrEF than in HFpEF patents, thus requiring larger numbers of patients with HFpEF to demonstrate a reduction in all-cause mortality by reducing cardiovascular mortality.[48,49]

Despite differences in device, blinding, and follow-up duration, all 3 of the individual studies included in this meta-analysis show a consistent reduction in HFH within 1 year, suggesting that the inclusion of all 3 studies in the mortality analysis would reflect the most accurate result including the totality of evidence available. A key finding of our meta-analysis is that mortality differences between patients treated according to IHM values and those receiving standard-of-care did not occur until after 1 year. Although the explanation for the delayed effect on mortality is uncertain, it is likely that the effect of IHM on mortality may be delayed because it takes time to see the benefits of reversing elevated cardiac filling pressures on ventricular remodeling.

The patients in the 3 trials included in this meta-analysis had symptomatic HF and required either a previous HFH (CHAMPION) or a previous HFH or elevated natriuretic peptides (GUIDE-HF and LAPTOP-HF). The GDMT in each trial had high utilization of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, and mineralocorticoid receptor antagonists. All trials were conducted before there were guideline recommendations for sodium-glucose cotransporter-2 inhibitors. The angiotensin receptor-neprilysin inhibitor sacubitril/valsartan was not available for CHAMPION and LAPTOP-HF but was available for GUIDE-HF, with 48% of subjects taking an angiotensin receptor-neprilysin inhibitor at baseline. Components of GDMT have been shown to lower PAP.[50-52] However, even with broad application of

CENTRAL ILLUSTRATION **Impact of Implantable Hemodynamic Monitoring in Heart Failure Patients With Reduced Ejection Fraction**



Lindenfeld J, et al. J Am Coll Cardiol. 2024;83(6):682-694.

Pressure-based management in HF with reduced ejection fraction is based on data that congestion leads to elevated intracardiac pressures, which can induce physiologic changes. Implantable hemodynamic monitors can detect elevations in intracardiac pressures and justify titrations of diuretic agents and GDMT that lower intracardiac pressures. When used over a period of time, management of intracardiac pressures is not only hypothesized to lead to positive physiologic changes, but also has been demonstrated to reduce both HF hospitalizations and mortality. GDMT = guideline-directed medical therapy; HF = heart failure.

angiotensin receptor-neprilysin inhibitors and sodium-glucose cotransporter-2 inhibitors, there is a high residual risk of mortality and HFH especially in patients with HFrEF who could still benefit from IHM devices, because many of these patients likely have an increase in PAP preceding their HFH.[48,53] Importantly, supplemental analyses demonstrated that the impact of IHM does not decrease with greater adoption of GDMT but actually demonstrates a greater treatment effect relative to patients on lower GDMT.

STUDY LIMITATIONS. Patient numbers in device trials are much smaller than in pharmacotherapy trials. GUIDE-HF had a notably shorter follow-up compared with the other 2 studies, but was included for completeness despite affecting the pooled mortality analysis. Certainly, GDMT has been shown to improve PAP and mortality. The patients in these trials were on excellent medical therapy given the guideline recommendations at the time the studies were conducted, but only 1 trial utilized angiotensin receptor-neprilysin inhibitors, and none had significant numbers of patients using sodium-glucose cotransporter-2 inhibitors. However even with the most up-to-date medical therapy using sodium-glucose cotransporter-2 inhibitors, both HFpEF and HFrEF sodium-glucose cotransporter-2 inhibitor trials showed the persistence of a high dual risk of both hospitalization for HF and mortality.[48,53] The included trials utilized different hemodynamic measures (PAP or LAP), and GUIDE-HF and CHAMPION were single-blinded whereas LAPTOP-HF was unblinded with patient visibility of LAP. Together with the early termination of the LAPTOP-HF trial and impact of COVID-19 on GUIDE-HF, these differences could affect their generalizability.

CONCLUSIONS

This patient-level pooled meta-analysis with long-term follow-up confirms that using IHM devices to manage patients with HFrEF results in fewer HFHs and, for the first time, demonstrates a reduction in mortality. This suggests that the consistent reduction in HFHs may correlate to improved mortality over a longer follow-up period.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Abbott (Abbott Park, Illinois) funded the CHAMPION, LAPTOP-HF, and GUIDE-HF studies. Dr Lindenfeld has received consulting fees from Abbott, Alleviant, AstraZeneca, Axon, Biotronik, Boston Scientific, CVRx, Edwards Lifesciences, Medtronic, Merck, Vascular Dynamics, Vectorious, and VWave; and has received grants from AstraZeneca. Dr Costanzo is a consultant for Abbott. Dr Zile has received research funding from Novartis; and has been a consultant for Novartis, Abbott, Boston Scientific, CVRx, EBR, Endotronix, Ironwood, Merck, Medtronic, and Myokardia V Wave. Dr Ducharme has received consulting fees from Abbott, Akcea, Alnylam, AstraZeneca, Bayer, Boehringer Ingelheim, Novartis, Pfizer, and Sanofi; and has received grants from AstraZeneca, Bayer, Corvia, Eidos, Novartis, Novo Nordisk, Pfizer, and Servier. Dr Troughton has received research grants from Health Research Council of New Zealand; has received consulting fees from Merck, Bayer, American Regent, and Roche Diagnostics; and has received honoraria payments from Roche Diagnostics. Drs Maisel and Paul are consultants for Abbott. Dr Mehra is a consultant for Natera, Paragonix, Moderna, Janssen, Broadview Ventures, Mesoblast, and Baim Institute for Clinical Research; is a consultant for Abbott; has served on the Clinical Events Committee for GUIDE-HF through the Baim Institute for Clinical Research; and has stock in NuPulseCV, Leviticus, Transmedics, and FineHeart. Dr Sears has received research grants from Medtronic and Zoll; is a consultant for Abbott, Medtronic, and Milestone Pharmaceutical; and has received personal fees from Medtronic and Zoll. Dr Smart has received research grants from Amgen; and is a consultant for Abbott. Dr Johnson, Mr Henderson, and Dr Adamson are full-time employees and shareholders for Abbott. Dr Desai has received institutional research grants from Abbott, Alnylam, AstraZeneca, Bayer, and Novartis; and is a consultant for Abbott, Alnylam, AstraZeneca, Axon Therapeutics, Avidity, Biofourmis, Boston Scientific, Cytokinetics, GlaxoSmithKline, Medpace, Merck, Novartis, Parexel, Regeneron, Roche, and Verily. Dr Abraham has received personal fees from Zoll Respicardia, Cardionomic, WhiteSwell, AquaPass, Cordio, Vectorious, Impulse Dynamics, and Edwards Lifesciences; and has personal equity in V-Wave Medica. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr JoAnn Lindenfeld, Vanderbilt Heart and Vascular Institute, Vanderbilt University Medical Center, 1215 21st Avenue South, Suite 5037, Nashville, Tennessee 37232, USA. E-mail: Joann.lindenfeld@vumc.org. @LindenfeldJoann.

PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: IHMs that detect increases in pulmonary artery or left atrial pressure reduce HFHs and mortality in patients with reduced left ventricular ejection fraction.

TRANSLATIONAL OUTLOOK: Further studies are needed to identify additional patient populations who might benefit from IHM.

REFERENCES

1. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022;43(38):3618–3731.

2. Magne J, Pibarot P, Sengupta PP, Donal E, Rosenhek R, Lancellotti P. Pulmonary hypertension in valvular disease: a comprehensive review on pathophysiology to therapy from the HAVEC Group. *J Am Coll Cardiol Img*. 2015;8(1):83–99.

3. Guazzi M, Borlaug BA. Pulmonary hypertension due to left heart disease. *Circulation*. 2012;126(8):975–990.

4. Guazzi M, Naeije R. Pulmonary hypertension in heart failure: pathophysiology, pathobiology, and emerging clinical perspectives. *J Am Coll Cardiol*. 2017;69(13):1718–1734.

5. Kolte D, Lakshmanan S, Jankowich MD, Brittain EL, Maron BA, Choudhary G. Mild pulmonary hypertension is associated with increased mortality: a systematic review and meta-analysis. *J Am Heart Assoc*. 2018;7(18):e009729. https://doi.org/10.1161/JAHA.118.009729

6. Rao SD, Adusumalli S, Mazurek JA. Pulmonary hypertension in heart failure patients. *Card Fail Rev*. 2020;6:e05. https://doi.org/10.15420/cfr.2019.09

7. Zile MR, Bennett TD, El Hajj S, et al. Intracardiac pressures measured using an implantable hemodynamic monitor: relationship to mortality in patients with chronic heart failure. *Circ Heart Fail*. 2017;10(1):e003594. https://doi.org/10.1161/CIRCHEARTFAILURE.116.003594

8. Zile MR, Sharma V, Johnson JW, Warman EN, Baicu CF, Bennett TD. Prediction of all-cause mortality based on the direct measurement of intrathoracic impedance. *Circ Heart Fail*. 2016;9(1):e002543. https://doi.org/10.1161/CIRCHEARTFAILURE.115.002543

9. Brown JR, Alonso A, Warman EN, Bilchick KC. Long-term impact of intrathoracic impedance findings on survival and heart failure hospitalizations after cardiac resynchronization therapy in ICD Registry patients. *Europace*. 2018;20(7):1138–1145.

10. Stevenson LW, Zile M, Bennett TD, et al. Chronic ambulatory intracardiac pressures and future heart failure events. *Circ Heart Fail*. 2010;3(5):580–587.

11. Zile MR, Bennett TD, St John Sutton M, et al. Transition from chronic compensated to acute decompensated heart failure: pathophysiological insights obtained from continuous monitoring of intracardiac pressures. *Circulation*. 2008;118(14):1433–1441.

12. Bourge RC, Abraham WT, Adamson PB, et al. Randomized controlled trial of an implantable continuous hemodynamic monitor in patients with advanced heart failure: the COMPASS-HF study. *J Am Coll Cardiol*. 2008;51(11):1073–1079.

13. Abraham WT, Adamson PB, Bourge RC, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. *Lancet*. 2011;377(9766):658–666.

14. Abraham WT, Stevenson LW, Bourge RC, et al. Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: complete follow-up results from the CHAMPION randomised trial. *Lancet*. 2016;387(10017):453–461.

15. Abraham WT, Adamson PB, Costanzo MR, et al. Hemodynamic monitoring in advanced heart failure: results from the LAPTOP-HF trial. *J Card Failure*. 2016;22:940.

16. Lindenfeld J, Zile MR, Desai AS, et al. Haemodynamic-guided management of heart failure (GUIDE-HF): a randomised controlled trial. *Lancet*. 2021;398(10304):991–1001.

17. Curtain JP, Lee MMY, McMurray JJ, Gardner RS, Petrie MC, Jhund PS. Efficacy of implantable haemodynamic monitoring in heart failure across ranges of ejection fraction: a systematic review and meta-analysis. *Heart*. 2023;109(11):823–831. https://doi.org/10.1136/heartjnl-2022-321885

18. Hajduczok AG, Muallem SN, Nudy MS, DeWaters AL, Boehmer JP. Remote monitoring for heart failure using implantable devices: a systematic review, meta-analysis, and meta-regression of randomized controlled trials. *Heart Fail Rev*. 2022;27(4):1281–1300.

19. Clephas PRD, Radhoe SP, Boersma E, et al. Efficacy of pulmonary artery pressure monitoring in patients with chronic heart failure: a meta-analysis of three randomized controlled trials. *Eur Heart J*. 2023;44(37):3658–3668. https://doi.org/10.1093/eurheartj/ehad346

20. Brugts JJ, Radhoe SP, Clephas PRD, et al. Remote haemodynamic monitoring of pulmonary artery pressures in patients with chronic heart failure (MONITOR-HF): a randomised clinical trial. *Lancet*. 2023;401(10394):2113–2123. https://doi.org/10.1016/S0140-6736(23)00923-6

21. Lindenfeld J, Abraham WT, Maisel A, et al. Hemodynamic-GUIDEd management of Heart Failure (GUIDE-HF). *Am Heart J*. 2019;214:18–27.

22. Maurer MS, Adamson PB, Costanzo MR, et al. Rationale and design of the Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy Study (LAPTOP-HF). *J Card Fail*. 2015;21(6):479–488.

23. Adamson PB, Abraham WT, Aaron M, et al. CHAMPION trial rationale and design: the long-term safety and clinical efficacy of a wireless pulmonary artery pressure monitoring system. *J Card Fail*. 2011;17(1):3–10.

24. Zile MR, Desai AS, Costanzo MR, et al. The GUIDE-HF trial of pulmonary artery pressure monitoring in heart failure: impact of the COVID-19 pandemic. *Eur Heart J*. 2022;43(27):2603–2618.

25. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2022;79(17):e263–e421. https://doi.org/10.1016/j.jacc.2021.12.012

26. Gheorghiade M, Vaduganathan M, Fonarow GC, Bonow RO. Rehospitalization for heart failure: problems and perspectives. *J Am Coll Cardiol*. 2013;61(4):391–403.

27. Setoguchi S, Stevenson LW, Schneeweiss S. Repeated hospitalizations predict mortality in the community population with heart failure. *Am Heart J*. 2007;154(2):260–266.

28. Lee DS, Austin PC, Stukel TA, et al. "Dose-dependent" impact of recurrent cardiac events on mortality in patients with heart failure. *Am J Med*. 2009;122(2):162–169.

29. Lindmark K, Boman K, Stålhammar J, et al. Recurrent heart failure hospitalizations increase the risk of cardiovascular and all-cause mortality in patients with heart failure in Sweden: a real-world study. *ESC Heart Fail*. 2021;8(3):2144–2153.

30. Okumura N, Jhund PS, Gong J, et al. Importance of clinical worsening of heart failure treated in the outpatient setting: evidence from the Prospective Comparison of ARNI With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial (PARADIGM-HF). *Circulation*. 2016;133(23):2254–2262.

31. Costanzo MR, Stevenson LW, Adamson PB, et al. Interventions linked to decreased heart failure hospitalizations during ambulatory pulmonary artery pressure monitoring. *J Am Coll Cardiol HF*. 2016;4(5):333–344.

32. Faris R, Flather M, Purcell H, Henein M, Poole-Wilson P, Coats A. Current evidence supporting the role of diuretics in heart failure: a meta analysis of randomised controlled trials. *Int J Cardiol*. 2002;82(2):149–158.

33. Angermann CE, Assmus B, Anker SD, et al, for the MEMS-HF Investigators. Pulmonary artery pressure-guided therapy in ambulatory patients with symptomatic heart failure: the CardioMEMS European Monitoring Study for Heart Failure (MEMS-HF). *Eur J Heart Fail*. 2020;22(10):1891–1901.

34. Heywood JT, Zalawadiya S, Bourge RC, et al. Sustained reduction in pulmonary artery pressures and hospitalizations during 2 years of ambulatory monitoring. *J Card Fail*. 2023;29(1):56–66.

35. Lala A, McNulty SE, Mentz RJ, et al. Relief and recurrence of congestion during and after hospitalization for acute heart failure: insights from Diuretic Optimization Strategy Evaluation in Acute Decompensated Heart Failure (DOSE-AHF) and Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARESS-HF). *Circ Heart Fail*. 2015;8:741–748.

36. Kociol RD, McNulty SE, Hernandez AF, et al. Markers of decongestion, dyspnea relief, and clinical outcomes among patients hospitalized with acute heart failure. *Circ Heart Fail*. 2013;6(2):240–245.

37. Gheorghiade M, Pang PS, Ambrosy AP, et al. A comprehensive, longitudinal description of the in-hospital and post-discharge clinical, laboratory, and neurohormonal course of patients with heart

failure who die or are re-hospitalized within 90 days: analysis from the EVEREST trial. *Heart Fail Rev*. 2012;17:485–509.

38. Kaye DM, Lambert GW, et al. Neurochemical evidence of cardiac sympathetic activation and increased central nervous system norepinephrine turnover in severe congestive heart failure. *J Am Coll Cardiol*. 1994;23(3):570–578.

39. Kurz MA, Wead WB, Roberts AM. Reflex inotropic responses to distension of left atrium or pulmonary veins. *Am J Physiol*. 1990;258(1 Pt 2):H121–H126.

40. Furnival CM, Linden RJ, Snow HM. Reflex effects on the heart of stimulating left atrial receptors. *J Physiol*. 1971;218(2):447–463.

41. Cuspidi C, Sala C, Negri F, et al. Prevalence of left-ventricular hypertrophy in hypertension: an updated review of echocardiographic studies. *J Hum Hypertens*. 2012;26(6):343–349.

42. Mullens W, Abrahams Z, Francis GS, et al. Importance of venous congestion for worsening of renal function in advanced decompensated heart failure. *J Am Coll Cardiol*. 2009;53(7):589–596.

43. Kanmanthareddy A, Reddy YM, Boolani H, et al. Incidence, predictors, and clinical course of atrial tachyarrhythmias in patients with pulmonary hypertension. *J Interv Card Electrophysiol*. 2014;41(1):9–14.

44. Reiter MJ, Stromberg KD, Whitman TA, et al. Influence of intracardiac pressure on spontaneous ventricular arrhythmias in patients with systolic heart failure: insights from the REDUCEhf trial. *Circ Arrhythm Electrophysiol*. 2013;6(2):272–278.

45. Abraham J, Bharmi R, Jonsson O, et al. Association of ambulatory hemodynamic monitoring of heart failure with clinical outcomes in a concurrent matched cohort analysis. *JAMA Cardiol*. 2019;4(6):556–563.

46. Adamson PB, Gold MR, Bennett T, et al. Continuous hemodynamic monitoring in patients with mild to moderate heart failure: results of The Reducing Decompensation Events Utilizing Intracardiac Pressures in Patients With Chronic Heart Failure (REDUCEhf) trial. *Congest Heart Fail*. 2011;17(5):248–254.

47. Abraham WT, Perl L. Implantable hemodynamic monitoring for heart failure patients. *J Am Coll Cardiol*. 2017;70(3):389–398.

48. McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med*. 2019;381(21):1995–2008.

49. Solomon SD, McMurray JJV, Claggett B, et al. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. *N Engl J Med*. 2022;387(12):1089–1098.

50. Mamazhakypov A, Hein L, Lother A. Mineralocorticoid receptors in pulmonary hypertension and right heart failure: From molecular biology to therapeutic targeting. *Pharmacol Ther*. 2022;231:107987. https://doi.org/10.1016/j.pharmthera.2021.107987

51. Tran JS, Havakuk O, McLeod JM, et al. Acute pulmonary pressure change after transition to sacubitril/valsartan in patients with heart failure reduced ejection fraction. *ESC Heart Fail*. 2021;8(2):1706–1710.

52. Mullens W, Martens P, Forouzan O, et al. Effects of dapagliflozin on congestion assessed by remote pulmonary artery pressure monitoring. *ESC Heart Fail*. 2020;7(5):2071–2073.

53. Packer M, Anker SD, Butler J, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med*. 2020;383(15):1413–1424.

KEY WORDS heart failure hospitalizations, heart failure with reduced ejection fraction, implantable hemodynamic monitoring, implantable hemodynamic monitors, mortality

APPENDIX For an expanded Methods section as well as supplemental figures and tables, please see the online version of this paper.