

REPLY: Time to Diuretic in Acute Heart Failure



Dr. Wussler and colleagues made some important and legitimate remarks about our study results recently published in *JACC: Heart Failure* (1). We agree with their concerns that variables not following normal distribution should be presented as medians and interquartile ranges (IQRs) and that their differences should be tested with nonparametric tests. Using Mann-Whitney *U* test, we found there were no differences between B-type natriuretic peptide levels in the early group and those in the delayed group (1,025 pg/ml; interquartile range [IQR]: 596 to 1,871 pg/ml vs. 1,013 pg/ml; IQR: 571 to 1,836 pg/ml, respectively; $p = 0.729$). N-terminal pro-B-type natriuretic peptide levels (5,322 pg/ml; IQR: 2,532 to 12,346 pg/ml vs. 6,100 pg/ml; IQR: 2,927 to 14,218 pg/ml, respectively; $p = 0.078$), troponin I (0.05 ng/ml; IQR: 0.03 to 0.31 ng/ml vs. 0.06; IQR: 0.03 to 0.25 ng/ml, respectively; $p = 0.121$), and troponin T (0.03 ng/ml; IQR: 0.02 to 0.10 ng/ml vs. 0.03 ng/ml; IQR: 0.02 to 0.07 ng/ml, respectively; $p = 0.921$) did not differ between the groups either.

Regarding the predictors of delayed door-to-diuretics (D2D) time, we found there had been a mistake during coding of the categorical variables (i.e., ischemic heart disease, atrial fibrillation, and chronic obstructive pulmonary disease [COPD]) in the binary logistic regression analysis. To be more precise, the presence and absence of the comorbidities were erroneously switched. After correction, the presence of atrial fibrillation, COPD, and higher Get With the Guidelines score were independently associated with delayed D2D time, whereas the presence of ischemic heart disease, advanced New York Heart Association functional class, and higher heart rate were associated with early D2D time (Table 1). We offer our sincerest apology to the readers of *JACC: Heart Failure* for the inattentiveness. Nonetheless, the conclusion remains unaffected, and the D2D time was not associated with clinical outcomes in our study population.

Finally, we reported significant differences among clinical characteristics of patients with acute heart failure (AHF) in different registries (2), and we also coauthored the study of different post-discharge outcomes between patients with AHF from East Asia and those from Europe (3). As acknowledged in that report, our study results cannot be generalized to all patients with heart failure. Nonetheless, considering the subacute nature of AHF with heterogenous causes and pathophysiology, we are skeptical that D2D time

TABLE 1 Predictors of Delayed Door-to-Diuretics Time

	p Value	Odds Ratio	95% CI
Ischemic heart disease	0.004	0.74	0.60-0.91
Atrial fibrillation	0.017	1.31	1.05-1.64
COPD	0.033	1.43	1.03-1.98
NYHA	<0.001	0.76	0.65-0.88
Heart rate	<0.001	0.99	0.98-0.99
GWGT Score	0.030	1.01	1.00-1.03

Data are binary logistic regression with forward conditional modeling (delayed group as outcome variable). Variables included were age and sex and variables with p value < 0.1 in univariate analysis. Those variables were sex, age, ischemic heart disease, atrial fibrillation, previous VHD, COPD, current smoker, CRT implantation, NYHA functional class, systolic blood pressure (mm Hg), heart rate, lung congestion in X-ray, LVEF, GWGT score, and institution name.

COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; GWGT = Get With the Guidelines; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; VHD = valvular heart disease.

would be more critical in Caucasians than in Asians with AHF.

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Chronic Heart Failure Care and Costs



What Is the Efficiency of Investing in Quality?

We have read the recent study by Wadhwa et al. (1) with great interest. Rising direct health care costs associated with pandemic conditions such as chronic heart failure (CHF) are becoming major threats to the sustainability of health care systems in most Western countries. This concern has boosted the development

of a number of initiatives aimed at reducing hospitalizations and other key sources of health care costs associated with these patients.

Among the available cost-reduction approaches, recent research has shown that policies and interventions focused on cutting specific costs and using penalties may be associated with worsened health outcomes, which are the worst costs that patients and societies could face. A landmark example of this is the recent evaluation by Gupta et al. (2) in Medicare patients with CHF, in which a program implemented in 2010 that was aimed at reducing readmissions through financial penalties to hospitals was followed by concerning increases in 30-day mortality rates.

CHF is a complex, challenging condition, requiring multidimensional in-hospital, transitional, and long-term management approaches (3). In this context, population-based studies evaluating programs aimed at improving the holistic care of these patients have shown strong associations between program implementation and subsequent reductions in mortality and hospitalizations (4). Similarly, evidence from small randomized trials supports the benefits of comprehensive disease management programs in CHF in terms of hospitalization and death (5).

Current evidence, therefore, suggests that interventions with an emphasis on increasing quality of care rather than on reducing specific sources of health care costs may be the pathway to improving CHF health outcomes. Nevertheless, the implications, in terms of costs, of holistic management programs are currently less understood. Although improved quality is expected to reduce costs through, for example, minimizing preventable readmissions, paradoxically, longer survival would also be expected to yield higher long-term health care resource use and costs.

In this context, the study by Wadhera et al. (1) provides some valuable insights on the in-hospital or early post-discharge phase of the process. Optimal in-hospital CHF management involves a number of interventions, including a detailed etiological assessment, complete relief of congestive signs and symptoms, initiation of evidence-based pharmacotherapies, use of invasive procedures when appropriate, pre-discharge assessment by multidisciplinary teams, and careful design of the transitional and long-term care management plan of each patient. Because most of these are costly interventions, improving quality requires investments. Consistent with this, Wadhera et al. (1) observed that centers with higher odds of performing cardiac catheterizations, performing coronary revascularization procedures, more

frequently discharging patients to skilled nursing facilities, and more frequently providing home care on discharge had higher CHF inpatient costs.

Unfortunately, Wadhera et al. (1) could not quantify the potential long-term implications of improving in-hospital and post-discharge quality and outcomes, and further research is needed. Specifically, comprehensive, long-term health economics evaluations are mandatory, accounting simultaneously for clinical outcomes, costs, efficiency, and the value of money. Such evaluations would provide nuanced insights on the long-term implications of different CHF management programs, thereby aiding the design of the most effective, efficient interventions.

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