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#### **REPLY: Efficacy of Subcutaneous vs. Intravenous Administration of Furosemide in Patients With Worsening Heart Failure**



##### **The Devil Is in the Details**

We thank Drs. Rangaswami and McCullough for their interest in our work (1) and the use of subcutaneous furosemide in patients with heart failure. Decompensated heart failure is indeed more than simply an acute event, and we agree with the authors that an understanding of diuretic kinetics throughout the continuum of heart failure (from stable state to subtle congestion to overt decompensation) is important.

The pharmacokinetics of subcutaneous furosemide have been described in both normal healthy volunteers (2) and in patients with chronic New York Heart Association functional class II heart failure subjects (3). Although it would be of interest to further study the kinetics in overtly congested patients as Drs. Rangaswami and McCullough recommend, we find it compelling that the administration of 1 dose of subcutaneous furosemide resulted in significant diuresis in such congested patients in our clinic who carried a high risk of hospitalization. This experience alone justifies consideration of this novel method of diuresis to avoid the costs and inconvenience of intravenous therapy via infusion clinics or hospitals. The letter writers also suggest study of subcutaneously delivered torsemide. Although we agree to the appeal of advantages seen with torsemide when comparing oral formulations (4), we found that subcutaneous furosemide, with its more consistent drug delivery (over 5 h) and better bioavailability, already resulted in a prolonged hourly urine output rate compared with intravenous furosemide. It is possible that a subcutaneous formulation of torsemide would produce such an extended prolonged effect that it may be a hindrance to patient quality of life.

Further evaluation of subcutaneous furosemide is needed to assess its usefulness in the longer term (i.e., multiple consecutive doses) treatment of congestion. We find of interest the methods that the letter writers suggest, such as urinary furosemide measurements and correlation with noninvasive hemodynamic monitoring, and these may help in the future to guide dosing strategies. Last, we found a

high rate of 30-day hospitalization after diuretic therapy; however, we believe this finding to be due to selection bias of high-risk patients as well as only 1-time dosing of the subcutaneous diuretic. Further study of the ability to prevent hospitalizations for heart failure via a multiple dose strategy and the use of a correlate to congestion to guide dosing is warranted.

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## **Mechanisms of Discrepancy Between Pulmonary Artery Wedge Pressure and Left Ventricular End-Diastolic Pressure in Heart Failure With Preserved Ejection Fraction**



We read with great interest the article by Mascherbauer et al. (1), in which the relationship between mean pulmonary artery wedge pressure (PAWP) and left ventricular end-diastolic pressure (LVEDP) was