# Letters

## TO THE EDITOR

# Size Matters?

Seeking High-Risk Populations Among "Normal" Individuals

We read with great interest the paper by Tsao et al. (1) and the accompanying editorial by Fonarow and Hsu (2) in a recent issue of JACC: Heart Failure. Tsao et al. (1) reported that asymptomatic adults, even with borderline reduction of left ventricular ejection fraction (LVEF) (between 50% and 55%), were more likely to develop heart failure (HF) or die when compared with those with LVEF >55%. As Fonarow and Hsu state, to improve the outcome of HF, it is of utmost clinical importance to detect and intervene in the subjects at a higher risk. However, it is noteworthy that this borderline LVEF group was only 3.5% of the total cohort, and the observed HF events in this group accounted for only 6.8% of all events. Emphasis should also be placed on detecting high-risk individuals within the group of normal LVEF patients, who account for 85.1% of HF events. We would like to add some points to this discussion.

The size of the left ventricle (LV) (e.g., left ventricular end-diastolic dimension [LVEDD]), along with functional parameters, is a predictor of adverse cardiac events. From our own registry of patients with HF with preserved ejection fraction, we noted that patients with enlarged LVEDD had worse outcomes. Within a multicenter registry of acute HF patients (West-Tokyo Heart Failure registry: 1,996 patients registered between 2006 and 2015), 294 patients had a "normal" LVEF  $\geq$ 55%. When these patients with "normal" LVEF were further divided in accordance with the reference normal value of echocardiographic data in Japanese subjects (3), those with below normal left ventricular diastolic diameter (small LV group, n = 145) had a significantly lower rate of adverse events, including all-cause death and HF rehospitalization (Cox proportional regression analysis, hazard ratio: 0.64; 95% confidence interval: 0.42 to 0.96; p = 0.03; median follow up of 366 days), when compared with patients with larger LVEDD (large LV group, n = 149). Mean LVEF was similar

between these 2 groups (61.8% and 61.5% for the small and large LV groups, respectively).

We support the authors' conclusion that patients with borderline LVEF have a worse prognosis than those with LVEF >55% and should be carefully monitored. In addition to this, we would also like to add that the size of the LV could also be considered to further risk-stratify the subjects with apparently normal LVEF. In their paper, Tsao et al. (1) stated that enlargement of LVEDD was indeed associated with development of HF in their cohort, but detailed subclassification by referencing normal LVEDD may aid in better understanding of the role of LVEF in the prediction of future adverse events.

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**1.** Tsao CW, Lyass A, Larson MG, et al. Prognosis of adults with borderline left ventricular ejection fraction. J Am Coll Cardiol HF 2016;4:502-10.

**2.** Fonarow GC, Hsu JJ. Left ventricular ejection fraction: what is "normal?". J Am Coll Cardiol HF 2016;4:511-3.

**3.** Daimon M, Watanabe H, Abe Y, et al. Normal values of echocardiographic parameters in relation to age in a healthy Japanese population: the JAMP study. Circ J 2008;72:1859-66.

### **REPLY:** Size Matters?



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We thank Dr. Takei and colleagues for their interest in our study (1). Management of individuals at greater risk for morbidity and mortality is wellestablished among those with heart failure (HF) with reduced left ventricular ejection fraction (LVEF), but discrimination of risk among individuals with borderline or heart failure with preserved

