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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 ≥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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REPLY: Size Matters?

Seeking High-Risk Populations Among "Normal" Individuals

We thank Dr. Takei and colleagues for their interest in our study (1). Management of individuals at greater risk for morbidity and mortality is well-established 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 ejection fraction (HFPEF) is not well understood. Dr. Takei and colleagues describe that among a group of patients with HFPEF, those with a greater left ventricular (LV) end-diastolic dimension had a greater risk of adverse outcomes (HF rehospitalization, all-cause mortality) than those with diastolic diameter below the normal reference value, despite normal LVEF. These results are interesting and highlight the importance of LV cavity dimension in prognosis. These findings also imply that some of those with greater risk actually have normal LV dimensions, another area of subclinical disease for investigation.

Previously, the Framingham Heart Study has similarly shown the importance of LV cavity size in asymptomatic individuals free of HF, whereby greater LV cavity dimension was associated with higher risk for incident HF (2). Notably, nearly all participants had normal LVEF. Thus, we examined the relations of LV end-diastolic dimension (LVEDD) in our study. In multivariable models not including LVEF, LVEDD was associated with both outcomes of interest, HF/all-cause mortality and HF alone. Inclusion of LVEDD in models including the LVEF group only modestly attenuated the association of LVEF with the outcomes. Our collective results, including those of Dr. Takei and colleagues, suggest that both LVEF and LVEDD are important contributors to risk of HF and mortality. Additionally, beyond linear LV dimensions, LV volumes and integrative measures of LV geometry have been associated with cardiovascular disease in population studies (3,4). The ultimate relative contributions of these measures in prognosis of the asymptomatic adult with borderline LV systolic function remain to be determined.

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EMS, HEMS, ECMO Center, ICU Team: Are You Ready for Hypothermic Patients?

Extracorporeal Membrane Oxygenation in Severe Accidental Hypothermia

It was with great interest that we read the article by Aubin et al. (1) published in *JACC: Heart Failure*. Transport destination for patients (core body temperature <28°C) with unstable circulation or who are in cardiac arrest is a hospital with extracorporeal rewarming (extracorporeal membrane oxygenation [ECMO], cardiopulmonary bypass) capacity (2,3). In southern Poland, we have arranged the severe hypothermia treatment system based on 3 pillars: education, coordination, and equipment (4). The E-learning platform is free and adjusted to different levels of the rescue system: basic life support (fireguards, police, mountain rescuers), advanced life support (ambulance and helicopter emergency medical service [HEMS] staff), and hospital emergency department staff. To date, 25,000 people have successfully completed that learning activity.

Early qualification for extracorporeal rewarming of hypothermic patients with cardiac arrest/hemodynamic instability is necessary to prepare operating room and staff or to haul the equipment. Coordination of transport, treatment, and approval of extracorporeal life support therapy are the tasks of the ECMO coordinator. Dispatch rescue centers have continuous contact with the ECMO coordinator, which allows early notification about victims having suspected or confirmed severe hypothermia. Notepads used in ambulances to enter data in medical records are scanned online for predefined key words describing the cooled patient. Mountain rescuers also inform the ECMO coordinator at the start of their search and rescue missions. Cardiac arrest in severe hypothermia usually requires prolonged chest compression during transport. We use an interactive map of available mechanical chest compression devices, which allows delivery of devices to the rescue team from the nearest location.

All cardiac surgery centers are equipped with ECMO and can admit deeply hypothermic patients with cardiac arrest or hemodynamic instability. We hope to