Extending the MADIT-ICD benefit score to heterogenous heart failure populations

Arwa Younis 📵 and Ilan Goldenberg 🕩 *

Clinical Cardiovascular Research Center, University of Rochester School of Medicine & Dentistry, 265 Crittenden Blvd CU, Rochester, NY 420653, USA

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This commentary refers to 'Predicted benefit of an implantable cardioverter-defibrillator: the MADIT-ICD benefit score' by A. Younis et al., https://doi.org/10.1093/ eurheartj/ehaa1057 and the discussion piece 'Prediction of sudden arrhythmic death in patients with heart failure: towards validation in a worldwide broader range of patients' by R. Fukuoka et al., https://doi.org/10.1093/eurheartj/ ehab159.

We agree with the comment made by Drs. Fukuoka, Kawamura, and Kohsaka that our MADIT-ICD benefit score¹ was developed and validated within the strict inclusion/exclusion criteria of landmark randomized clinical trials (RCTs), and therefore there is a need for further assessment and validation within more heterogenous realworld populations. Fukuoka et al.² mention three specific possible disparities (lack of inclusion of Asian populations, the applicability of the score to patients with multiple comorbidities, and to those without advanced left ventricular dysfunction) that we would like to address herein.

Patients enrolled in the multi-national Acute Decompensated Heart Failure Registry (ADHERE) International-Asia Pacific study of hospitalized heart failure (HF) were shown to be significantly younger compared with patients enrolled in the parallel US-based ADHERE registry (median age 67 vs. 75 years), but also displayed more advanced comorbidities and higher rates of complications and death.⁴ Lam et al.⁵ prospectively studied 5276 patients with stable HF and reduced left ventricular ejection fraction (LVEF ≤40%) from 11 Asian regions and showed significant heterogeneity among Asian patients with stable HF. The MADIT-ICD benefit score was developed in 4503 patients, of whom 1102 (24%) were enrolled in >40 non-US sites (mostly in Europe). Thus, the findings regarding major differences in the clinical characteristics and outcomes of HF patients enrolled in Asian-Pacific Registries stress the need for the assessment of the score in non-Western cohorts and especially among Asian HF patients. Nevertheless, it should be noted that our score comprises variables that address the different characteristics of patients enrolled in Asian-Pacific Registries, including age, aetiology of underlying cardiomyopathy. and associated comorbidities. We therefore expect a consistent performance of the score in Asian populations.

Fukuoka et al. also stress the importance of score validation in real-world setting among patients with more advanced comorbidities compared with those enrolled in RCTs. Although we fully agree with this point, it should be noted again that comorbidities are an important component of our Non-Arrhythmic Mortality Score. Thus, patients with advanced comorbidities who are usually excluded from RCTs are expected to derive a lower benefit from the ICD due to a higher non-arrhythmic vs. arrhythmic mortality based on the MADIT-ICD benefit score.

Lastly, we also agree on the importance of developing appropriate risk stratification algorithm for sudden cardiac death in patients without advanced LV dysfunction. However, we would like to stress that the primary aim of this study was to improve risk stratification for primary ICD implantation among patients with LVEF ≤35% who are indicated for the device based on current guidelines since the benefit of the ICD in this population is not uniform.

We would like to thank Fukuoka et al. for their support of implementation of our score in a broader range of populations. We believe that this would be an important step towards precision management that will facilitate appropriate selection for primary ICD implantation.

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CARDIOVASCULAR FLASHLIGHT

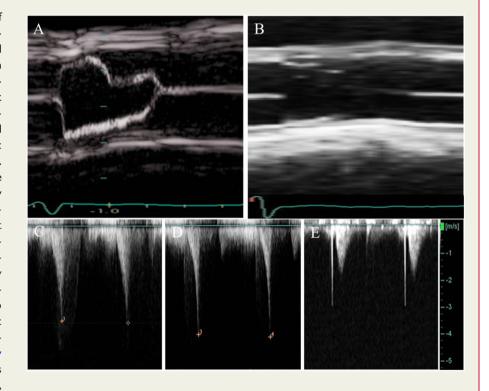
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'Heart within a heart': echocardiographic assessment of hypertrophic cardiomyopathy

Jonika M. Weerasekare (p) 1 and Jeffrey B. Geske (p) 2*

¹Mayo Clinic Alix School of Medicine, 200 1st SW, Rochester, MN, USA; and ²Department of Cardiovascular Diseases, Mayo Clinic, 200 1st SW, Rochester, MN, USA * Corresponding author. Tel: 507-284-3725, Email: Geske.jeffrey@mayo.edu

A 64-year-old woman with a history of hypertrophic obstructive cardiomyopathy, severe calcific mitral stenosis, and suprasystemic World Health Organ ization group 2 pulmonary hypertension presented with New York Heart Association class IV exertional dyspnoea, presyncope, chest tightness, and recurrent hospitalizations for diastolic heart failure in the past 8 months. Transthoracic echocardiography reve aled asymmetric septal hypertrophy and calcific mitral stenosis (Supplementary material online, Video S1). Left ventricular systolic function was hyperdynamic (left ventricular ejection fraction of 80%) with systolic mid-cavitary obliteration. Mitral valve systolic anterior motion was attenuated due to valvular calcification, with dynamic obstruction resulting from tubular outflow tract narrowing (Supplementary material online, Video S1). Continuous wave Doppler demonstrated narrow, late peaking gradients of 48 mmHg at



rest (*Panel C*) and 66 mmHg with Valsalva (*Panel D*), corresponding to combined mid-cavitary and outflow tract obstruction. M-mode of the aortic valve revealed premature systolic partial closure secondary to dynamic obstruction (*Panel A*).

Despite elevated operative risk in the setting of her comorbidities, she successfully underwent extended septal myectomy and mitral valve replacement. Echocardiography 8 days postoperatively demonstrated relief of obstruction (Supplementary material online, Video S2), with a more rounded Doppler envelope (gradient 16 mmHg, Panel E). Abolishment of aortic valve premature closure was demonstrated on reformatted M-mode imaging (Panel B).

The high temporal resolution of M-mode provides unique clinical information. In this patient with hypertrophic cardiomyopathy, premature systolic partial closure due to dynamic outflow obstruction presented as a 'heart within a heart' pattern, which resolved post-myectomy.

Supplementary material is available at European Heart Journal online.

Conflict of interest: The authors have submitted their declaration which can be found in the article Supplementary Material online.