Improved Prediction of Sudden Cardiac Death Risk
Staying Within the Echocardiogram but Extending Beyond the Ejection Fraction

Sumeet S. Chugh, MD; Audrey Uy-Evanado, MD

Risk stratification of patients to identify those who will benefit most from the primary prevention implantable cardioverter-defibrillator (ICD) remains a challenge. For the last decade, measurement of the left ventricular ejection fraction (LVEF) as a clinical risk predictor is recognized to be inadequate. In fact, contemporary real-world data indicate that of the patients identified using this methodology, the proportion of patients who benefit from the ICD at the end of a year may be as low as 1.1%. It is also accepted, however, that novel noninvasive imaging techniques will make major strides toward this goal in the near future. In this context, the low-hanging fruit is the potential role of risk markers measured from the same echocardiogram that would provide the LVEF. In this issue of Circulation: Cardiovascular Imaging, Konety et al report their results regarding the association between multiple echocardiographic predictors and risk of sudden cardiac death (SCD) in a meta-analysis performed from the ARIC (Atherosclerosis Risk in Communities) and CHS (Cardiovascular Health Study) cohorts. It is worth deliberating on their findings in the setting of existing knowledge, as well as the specific methodology used in their analysis.

See Article by Konety et al

Perhaps their most significant finding is a stark reminder of the poor utility of the LVEF as a sole predictor of SCD risk. In this relatively small analysis of 319 SCD patients, only 16.3% of ARIC SCD cases (total n=44) and 24.4% of CHS cases (total n=275) were found to have reduced LVEF (defined as LVEF <50% in ARIC and <55% in CHS) at the time of their baseline echocardiogram. We are not provided with any other subcategory of LVEF values. However, based on available community-based data, even if we estimate a generous 30% as having severely reduced LVEF (<35% as stipulated by current guidelines), only a combined 13.5% of all who suffered SCD (5.4% of ARIC and 8.1% of CHS cases) would have qualified for an ICD.

Although findings were not consistent between the 2 cohorts, in their meta-analysis of the combined population, Konety et al identified additional echocardiographic measures as potential SCD risk markers. Presence of mitral annular calcification was associated with a 2-fold increased risk of SCD and left ventricular (LV) diastolic function (assessed as mitral E/A >1.5 or <0.7) with a one-and-a-half-fold increased risk. Increased LV mass and left atrial diameter were also associated with elevated SCD risk. Although these markers are of interest, there are some caveats that arise from important gaps in their analysis. The statistical models were constructed using their definition of reduced LVEF (<50% to 55% depending on cohort), which unfortunately does not coincide with the clinically used cutoff (LVEF <35%) based on the ICD randomized clinical trials. Therefore, the new markers they describe were not adjusted for the guideline-indicated and most commonly used LVEF threshold, and we cannot be sure about the clinical relevance of these markers for the subjects included in this particular meta-analysis.

It turns out, however, that there is a growing literature in support of increased LV mass calculated from the echocardiogram as a significant predictor of increased SCD risk. In the Oregon Sudden Unexpected Death Study, the risk conferred by LV mass was independent of and equivalent to LVEF <55%. The combined use of the 2 risk markers had an additive effect on SCD risk, leading to calls for prospective clinical evaluation and utilization of these findings. Subsequently, the role of LV mass as a predictor of SCD risk was independently validated in the Kuopio longitudinal cohort study. In 2 separate studies, one performed in the community and the other in a cohort of primary prevention ICD patients, increased LV diameter measured on the echocardiogram was reported as a significant and independent predictor of increased SCD risk. Most recently, eccentric LV hypertrophy as defined by measurement of relative LV wall thickness on the echocardiogram was identified as a significant predictor from the MADIT-RIT (Multicenter Automatic Defibrillator Implantation Trial-Reduce Inappropriate Therapy) trial, a primary prevention, combined cardiac synchronization-implantable defibrillator population. A subsequent, community-based study showed that any form of abnormal LV geometry (eccentric or concentric) in combination with LVH predicts increased SCD risk in patients with LVEF >35%. In fact, even abnormal concentric LV geometry in the absence of increased LV mass was independently predictive of increased SCD risk.

The findings of Konety et al tantalize us with the possibility of novel SCD risk markers identifiable on the echocardiogram, but more work is needed in larger numbers of patients before mitral annular calcification and left atrial diameter can

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From the The Heart Institute, Cedars-Sinai, Los Angeles, CA. Address correspondence to Sumeet S. Chugh, MD, Cedars-Sinai Medical Center, Advanced Health Sciences Pavilion, Suite A3100, 127 S. Vicente Blvd, Los Angeles, CA 90048. E-mail: sumeet.chugh@cshs.org (Circ Cardiovasc Imaging, 2016;9:e005133.
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be added to the current repertoire of risk markers. In the meantime, the published literature has offered up several promising markers, including increased LV mass and abnormal LV geometry, that are ripe for further testing and clinical adoption. With the echocardiogram rapidly evolving as a hand-held, widely available point-of-care diagnostic tool,\(^7,18\) the potential enhancement of SCD risk stratification by simultaneous evaluation of multiple risk markers, including the LVEF, holds significant promise.

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References


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