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EDITORIAL COMMENT

Seeing beneath the surface: Are current risk scores enough in hypertrophic cardiomyopathy?

Vendo para além da superfície: as pontuações de risco atuais são suficientes na miocardiopatia hipertrófica?

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''The most solid advice I can give is this: always try to see beneath the surface.''
Ernest Hemingway

Risk stratification for sudden cardiac death (SCD) in hypertrophic cardiomyopathy (HCM) has always been an exercise in approximation. Over the years, more sophisticated algorithms have sought to convert clinical heterogeneity into numerical risk estimates, giving clinicians a sense of precision and objectivity. Yet, despite successive updates to European and American guidelines, the essential question remains controversial but unavoidable: are we truly identifying the patients who will experience malignant ventricular arrhythmias, or merely those who fit our models?

Current risk scores mainly depend on easily measurable factors – wall thickness, gradients, arrhythmic surrogates (like left ventricular ejection fraction), and clinical history. While these variables certainly reflect aspects of disease severity, they do not directly evaluate the arrhythmic substrate itself. The ongoing gap between predicted risks and actual events, along with only moderate agreement between current European Society of Cardiology (ESC) and American College of Cardiology/American Heart Association (ACC/AHA) guidelines, highlights the inherent limitations of score-based methods. In HCM, the problem may not be that risk scores are poorly designed, but that they ask the wrong questions. These existing risk stratification scores are fundamentally limited because they cannot assess the arrhythmogenic substrate directly. HCM is not just a disease of hypertrophy; it involves electrical heterogeneity, myocardial disarray, coronary microvascular dysfunction,[1] and fibrosis.[2] It is therefore notable that, until recently, risk stratification mainly relied on macroscopic and functional markers, while the microscopic architecture responsible for re-entrant arrhythmias largely remained unseen. It is important to note that, in the early stages of HCM, before overt structural remodeling, arrhythmogenesis is often driven by primary electrical instability rather than macroscopic substrate. Ion channel dysfunction, impaired calcium cycling, and increased myofilament calcium sensitivity promote triggered activity through both early and delayed afterdepolarizations.[3] These cellular and molecu-

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lar abnormalities may trigger ventricular arrhythmias even in the absence of significant fibrosis or myocyte disarray. Nonetheless, cardiac magnetic resonance imaging with late gadolinium enhancement (LGE) has transformed the landscape by enabling the visualization and quantification of myocardial fibrosis – arguably the most relevant substrate for malignant ventricular arrhythmias.

Late gadolinium enhancement quantification, especially when extensive, is linked to a significantly higher risk of SCD and appropriate ICD therapy, regardless of established risk models.[4–6] Despite the widely used >15% LGE threshold proposed by Chan et al.,[7] evidence shows an increased arrhythmic risk even at lower extents of LGE. LGE $\geq$5% of left ventricular mass is associated with a sevenfold increase in SCD risk after multivariable adjustment.[4] Recently, LGE $\geq$10% has become the preferred cutoff for re-stratifying intermediate-risk patients and has been recognized as an independent predictor of arrhythmic events in these individuals.[5,6]

The study by Amador et al.[8] offers timely and compelling evidence supporting this paradigm shift. By analyzing multiple generations of ESC and ACC guidelines within a large, multicentre cohort, the authors show that although guideline performance has improved over time, their discriminative ability remains modest and agreement between societies is far from ideal. In this context, myocardial fibrosis measured by LGE is not merely a minor modifier but a significant and independent predictor of arrhythmic events.

Perhaps the most provocative finding is not that increasing LGE burden confers higher risk – a concept now well supported – but that the complete absence of LGE consistently identifies a subgroup with remarkably low arrhythmic risk, even among patients who would otherwise meet criteria for ICD consideration. This observation directly challenges a rigid, score-driven approach to decision-making and exposes a paradox of contemporary practice: we are increasingly comfortable implanting devices in patients with borderline calculated risk, yet often reluctant to withhold therapy when the arrhythmic substrate itself appears absent.

Furthermore, this study revisits the issue of the ''optimal cutoff''. The authors identified a significantly lower LGE extent (8%) as a predictor, contrary to current international recommendations. Equally important is the study's contribution to the ongoing debate about LGE thresholds. The arbitrary nature of fixed cut-offs, such as the >15% threshold endorsed by recent ESC guidelines, is evident from the trade-off between sensitivity and specificity observed in this cohort. Lower thresholds increase sensitivity but risk overtreatment; higher thresholds improve specificity but may overlook vulnerable patients. These findings suggest that searching for a universal LGE cutoff may be misguided. Fibrosis should not be categorized, but treated as a continuous, contextual biomarker, whose extent and progression better reflect disease severity and arrhythmic risk.[9]

Although the recognized value of LGE for risk stratification is acknowledged, the technique has inherent limitations that affect its predictive accuracy. Various LGE quantification methods exist and produce inconsistent results,[5] and no consensus has been reached on the best approach. A signal threshold method using 6 standard deviations above the reference myocardium has been shown to offer better reproducibility in HCM.[5,9] Beyond total LGE burden, the spatial pattern and texture of fibrosis are important for arrhythmic risk: heterogeneous, irregularly shaped fibrosis may be more arrhythmogenic than confluent, homogeneous scars. Advanced texture analysis techniques, such as LGE dispersion mapping, can characterize fibrosis heterogeneity and dispersion, potentially improving arrhythmic risk assessment.[10]

These data highlight the need to reconsider how risk stratification in hypertrophic cardiomyopathy is performed. While continued refinement of risk scores remains essential, greater emphasis should be placed on identifying the underlying arrhythmogenic substrate itself and understanding its interaction with clinical variables. Although LGE extent can improve HCM risk stratification, it is unlikely to function as a standalone tool, and LGE does not replace clinical judgment or established risk markers.

In this context, seeing beneath the surface is not just a metaphor – it is a clinical necessity. As imaging technologies advance, the challenge is clear: risk stratification in HCM must go beyond surrogate markers and evolve into an integrated model that captures myocardial substrate, genetic complexity, and disease biology. Until then, myocardial fibrosis remains, quite simply, tough to beat.

Conflicts of interest

The authors have no conflicts of interest to declare.

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