Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an uncommon inherited cardiomyopathy characterized by defective desmosomes, fibrofatty replacement of the right ventricular (RV) myocardium (and sometimes that of the left ventricle), abnormal depolarization and repolarization, ventricular tachyarrhythmia, and premature death. Since the first comprehensive description of the clinical manifestations of ARVC by Marcus et al. (1) in 1982, our knowledge of its genetic causes, pathophysiology, epidemiology, clinical manifestations, and natural history has greatly improved (2,3). Despite these strides, no single test is conclusively diagnostic in the disease’s early stages. Instead, ARVC diagnosis continues to be based on major and minor criteria derived from imaging studies, electrophysiology tests, family history, and histopathology.

Published in 1994, the Task Force Criteria (TFC) included major and minor abnormalities of RV morphology (localized aneurysms), size, and global and regional function (4). These abnormalities, however, were described using qualitative terms with no objective criteria to distinguish between normal, mild, and severe anomalies. Notably, fatty infiltration and thinning of the RV free wall, which were thought to be key cardiac magnetic resonance (CMR) features of ARVC since the early 1990s (5), were not included in the 1994 TFC. This exclusion was prescient, as subsequent studies demonstrated low specificity and inconsistent interpretation of fat distribution in ARVC (6).

The original TFC were revised in 2010 (7). On the basis of a comparison of 108 probands in the North American ARVC/D Registry and normal control subjects (8), the revised Task Force Criteria (rTFC) included the same 6 categories (imaging, arrhythmia, depolarization abnormalities, repolarization abnormalities, family history/genetics, and histopathology). However, several quantitative criteria replaced qualitative features, and threshold values were derived to distinguish between minor and major criteria to maximize specificity. In the imaging domain, a finding of regional RV akinesis, dyskinesis, or dyssynchronous contraction remained a requisite subjective criterion; however, objective threshold values for RV dilation and dysfunction were specified.

Nearly all published information on ARVC is in adult patients, which is hardly surprising given that the disease’s phenotypic expressions usually begin to manifest in early adulthood. Nonetheless, given the importance of early detection and the common practice of screening family members of probands by imaging, detailed knowledge of the diagnostic performance of noninvasive imaging tests in pediatric patients referred for evaluation of possible ARVC is valuable. In this issue of the Journal, Etoom et al. (9) describe their institutional experience with echocardiography and CMR in pediatric patients referred for assessment of possible ARVC. The authors analyzed clinical, echocardiographic, CMR, electrocardiographic (ECG), signal average ECG, 24-h Holter monitor, endomyocardial biopsy, and, when
available, genetic test results in 142 patients whose mean age at imaging was 13.8 ± 3.2 years. Among the 23 patients with definite disease based on the rTFC, major CMR criteria were necessary for establishing the diagnosis in 11 (48%). Notably, only 2 patients met major echocardiographic criteria and none met minor criteria.

The findings of Etoom et al. (9) are a welcome addition to our knowledge about noninvasive imaging in young patients with possible ARVC. The results suggest that there is an important role for CMR, but not echocardiography, in assessing RV size, function, and regional wall motion abnormalities (RWMAs) (9). Interestingly, unlike studies in adults, in whom a large proportion of patients are diagnosed based on arrhythmia and ECG criteria, RV abnormalities detected by imaging were responsible for the diagnosis in most patients in the study by Etoom et al. (9). This observation contrasts with findings of te Riele et al. (10) who followed 69 gene-positive individuals (mean age 27 years) over a mean period of 5.8 years, during which electrical abnormalities often preceded imaging-based anomalies. Whether these discrepant findings can be explained by referral bias or by actual age-dependent differences in disease expression requires further study.

The study by Etoom et al. (9) highlights certain drawbacks when applying the rTFC imaging criteria to pediatric patients. First, RWMAs of the RV are required to satisfy major and minor rTFC imaging criteria (7). However, diagnosis of RWMAs is subjective. In light of the RV’s complex geometry and contraction pattern and lack of diagnostic standardization, it is not surprising that the intra- and inter-rater reproducibility of diagnosing RWMAs in the study by Etoom et al. (9) was low (intraobserver κ = 0.57; inter-rater κ = 0.40). Moreover, the diagnosis of positive RWMAs in 16% of subjects categorized as “no” ARVC and in 22% categorized as “possible” ARVC suggests modest specificity of this criterion. In contrast, several studies have shown that the reproducibility of RV volumes and ejection fraction measurements, the other elements of the rTFC imaging criteria, is good (11). Second, it is worth noting that the normative RV data used to determine the rTFC threshold values were derived from a study of 462 individuals whose mean age was 60 ± 10 years (range 45 to 84 years) (12). Despite adjusting RV volumes to body surface area, the substantial age discrepancy between the rTFC normal control subjects and the patients in the study by Etoom et al. (9) can potentially affect CMR test characteristics in young individuals. Third, the normal RV volumes were obtained using a fast gradient recall echo cine CMR technique, which yields significantly lower values than the currently-used cine steady-state free-precession technique (13). This limitation likely affects the utility of the rTFC RV volume criteria in both children and adults.

The aforementioned drawbacks of the rTFC imaging criteria can be overcome with refinements based on newer CMR technology. First, the current subjective assessment of RV RWMAs should be replaced with quantitative measures, which will likely reduce this key criterion’s diagnostic variability. This, for example, can be accomplished by feature-tracking CMR, which can be applied to existing standard cine CMR images, allowing for semiautomatic measurements of RV (and left ventricular) wall displacement, strain, and strain rate (14). Second, the rTFC threshold values of RV volumes and ejection fractions should be re-evaluated based on comparison between a large cohort of ARVC probands with a large group of age-matched normal control subjects studied by steady-state free-precession cine CMR. Third, refining the CMR examination protocol may improve efficiency and allow imagers to focus on the scan’s clinically important aspects. Specifically, the utility of spin-echo imaging deserves critical reassessment given that evaluation of myocardial fat is not a diagnostic criterion for ARVC. In contrast, the role of imaging fibrosis by late gadolinium enhancement deserves further study.

Improving the diagnostic utility of noninvasive imaging in detecting early ARVC manifestations is an important goal. Although the findings of Etoom et al. (9) and others demonstrate a critical role for CMR, it is imperative to replace criteria based on old imaging techniques with measures derived from contemporary methods and to substitute less reproducible qualitative measures with reliable quantitative parameters. Finally, exploration of advanced imaging techniques, such as T1 mapping and diffusion tensor imaging by CMR and 3-dimensional myocardial deformation imaging by echocardiography, may identify more sensitive and specific markers of phenotypic expression in gene carriers and family members of ARVC probands.

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