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EDITORIAL COMMENT

The "Accordion Sign," a New Tune in Arrhythmogenic Right Ventricular Dysplasia/ Cardiomyopathy Magnetic Resonance Imaging?*

Maarten Groenink, MD, PhD,
Arthur A. M. Wilde, MD, PhD
Amsterdam, the Netherlands

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is an important cause of sudden cardiac death at a young age, which is often the first clinical manifestation of the disease (1). Other clinical signs, such as nonfatal ventricular tachycardia and electrocardiographic and cardiac morphological abnormalities, may develop slowly during adolescence and adulthood. A system of major and minor criteria, developed by the Task Force for Inherited Cardiomyopathies, is now widely used to confirm diagnosis in patients suspected of ARVD/C (2). In the past decade, ARVD/C has progressively been associated with mutations in genes encoding proteins involved in the desmosome apparatus of cardiomyocytes (3–9). In theory, "wear and tear" of the inappropriate connection system of myocytes may result in inflammatory reactions, causing wall motion abnormalities and nonspecific degenerative features such as fibrofatty replacement, and focal aneurysms in particular, in certain predilection areas of the right ventricle (RV), called "triangle of dysplasia." These degenerative features are believed to underlie the life-threatening arrhythmias and heart failure in early and advanced stages of the disease.

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Morphological features have always been difficult to detect, even by means of biopsy. Recent advances in magnetic resonance (MR) technology have increased the potential to detect structural changes in the thin-walled RV in vivo (10). It was recently shown that degenerative features could also be detected in the left ventricular (LV) myocardium of many ARVD/C patients by cardiac magnetic resonance imaging (CMR) (10). Several other studies have shown the value of CMR in detection of the myocardial morphological alterations and functional abnormalities, thought to be caused by the disease process (11,12). In summary, CMR seems to be an important diagnostic tool to detect relatively early manifestations of ARVD/C. Moreover, the lack of radiation exposure or ionizing contrast media facilitates screening in asymptomatic family members.

In this issue of the *Journal*, Dalal et al. (13) showed that several degenerative features could be detected by CMR in a small group of family members of ARVD/C patients with desmosome mutations in either the plakophilin 2, desmoplakin, or desmoglein 2 genes. LV involvement was scarcely shown. RV wall motion abnormality, however, was frequently encountered in mutation carriers. The authors suggest that the "accordion sign," an extended area of focal bulging of the RV wall, might be an early sign of ARVD/C in asymptomatic patients, reflecting an early stage of the disease, whereas LV involvement is a relatively late feature. The accordion sign was present in the majority of mutation carriers and in none of the individuals without a desmosome mutation. The discriminatory power of Task Force criteria increased clearly from 0.68 to 0.79 when the accordion sign was included as a minor criterion, even when family history was not accounted for (from 0.71 to 0.84).

Although these ongoing studies have elucidated many aspects of ARVD/C pathophysiology, worrisome aspects about the detection of patients remain. The burden of the diagnosis "ARVD/C" is not trivial for patients/families, often implying placement of an implantable cardioverter-defibrillator (ICD), and worries about offspring and other family members. The role of specific desmosome mutations in the disease process seems undisputed, although their exact contribution is uncertain. Does every single variant in either desmosomal gene lead to a phenotype, or is compound heterozygosity more rule than exception as part of the explanation for the phenotypical heterogeneity (9)? The fact remains that they are still not incorporated in Task Force criteria, in contrast, for instance, to Marfan Syndrome Task Force criteria (14). As Dalal et al. (13) state in their article, prediction models were used to detect a desmosome mutation and not ARVD/C.

It is still difficult to get the bigger picture. Clear manifestation of left-sided disease seems to be present in ARVD/C patients. However, clinical presentation of ARVD/C patients mostly, or at least primarily, suggest affection of the RV, by origin of ventricular tachycardia or RV failure.

MR techniques used to detect areas of "delayed hyperenhancement" (fibrosis), high T2 signal intensity (inflammation), or high T1 signal intensity (fat) are dependent on a regular heart rhythm, which is often not present in patients suspected of ARVD/C. The results are often difficult to

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From the Department of Cardiology, Academic Medical Centre, Amsterdam, the Netherlands.

interpret due to motion artefacts, wrong timing of inversion times, and other technical issues. However, these MR techniques seem reasonably reproducible in experienced centers (15). Bright blood steady-state free-precession MR techniques may be a more robust technique, more widely applicable, and easier to interpret. As cardiologists, we may feel more comfortable looking at moving images, which remind us of echocardiography. Regional dyskinesia and focal bulging of the RV wall have been associated with ARVD/C before (10–12). However, careful evaluation of RV motion patterns in normal controls or in patients with left-sided pathology may show the same features, particularly in the area of the moderator band. This feature may also be the reason for the relatively high proportion of false positives in CMR screening for ARVD/C (15). The question is, of course, to what extent we will accept "normal" variation in RV motion patterns, and this is also relevant for asymptomatic carriers of a desmosomal gene mutation. This issue calls for new studies to quantify regional motion patterns by MR tagging or strain encoding MR methods (16) in both normal and ARVD/C patients.

Reprint requests and correspondence: Dr. Arthur A. M. Wilde, Academic Medical Center, University of Amsterdam, Department of Cardiology, B2.239, Meibergdreef 9, P.O. Box 22700, Amsterdam 1100DE, the Netherlands. E-mail: a.a.wilde@AMC.UVA.NL.

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