Arrhythmogenic right ventricular dysplasia cardiomyopathy (ARVD/C) is an important cause of sudden death in young adults. The past decade has witnessed remarkable progress in the understanding of all aspects of this disease. This progress includes an improved understanding of (1) the natural history of ARVD/C, (2) optimal approaches for diagnosis, (3) the genetic basis of this condition, (4) the fundamental pathophysiologic mechanisms of ARVD/C, (5) the link between ARVD/C and exercise, (6) sudden death prevention, and (7) the importance of left ventricular (LV) involvement in ARVD/C.

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In the present issue of Circulation: Arrhythmia and Electrophysiology, Berte et al report the results of their investigation of 32 patients with ARVD/C (47+14 years, 6 women). All patients underwent a comprehensive noninvasive evaluation. All patients underwent multidetector computerized tomography. Magnetic resonance imaging (MRI) was performed in 22 patients. The recently described Bordeaux high-dose isoproterenol infusion protocol was used in all patients (45 μg/min for 3 minutes). Genetic testing, although not part of the standardized evaluation, was performed in 20 patients, revealing mutations in PKP2 in 9 patients and ACTN2, TNNC1, DSC2, TMEM43 in 1 each. A subset of 14 patients who were referred for ventricular tachycardia (VT) ablation underwent endocardial and epicardial mapping.

There are several interesting findings of this study. Right ventricular (RV) fibrosis and wall motion abnormalities were present in 91% and 95% of the 22 patients who underwent cardiac magnetic resonance imaging. Fat was found on multidetector computerized tomography on the RV wall in all patients, with LV fat observed in two thirds. LV fibrosis and wall motion abnormalities were far less common, being observed in 64% and 91% of the 22 patients who underwent cardiac magnetic resonance imaging. When clinical and imaging characteristics of patients with (N=21) and without LV involvement (N=11) were compared, the only difference seen was that the LV ejection fraction was lower among patients with LV involvement (56±8% versus 63±8%). As suspected, right-sided premature ventricular contractions and nonsustained VT, whether observed spontaneously or with isoproterenol, were more commonly observed than left-sided premature ventricular contractions. Local abnormal ventricular activity was found within LV fat areas in all patients, and the density of local abnormal ventricular activity within the fatty substrate defined on computed tomography (CT) was similar between the LV and the RV. Following catheter ablation 13/14 patients are noninducible. VT recurred in 5/14 patients (36%) at a median follow-up of 19 months.

This article is a welcome addition to the literature on ARVD/C and particularly to the literature concerning the role of CT imaging in the evaluation of patients with ARVD/C, as well as the literature concerning LV involvement in ARVD/C. Before interpreting the results of this study in the context of our own experience with ARVD/C and the published literature, we would like to call the readers’ attention to an important limitation of this study. This limitation is our uncertainty as to whether the ARVD/C patients included in this article were accurately phenotyped. Our basis for concern rests on several factors. First, the demographics of this ARVD/C population are rather unusual, with a mean age of 47 years and >80% male. In our experience, the mean age of presentation of ARVD/C is in the early 30s, and men present slight >50% of subjects. Second, we are concerned that the 2010 Task Force Criteria may have not been applied correctly. Table 1 suggests that VT of unknown morphology was classified as a major criteria, whereas it is in fact a minor criteria. To further complicate matters, the diagnostic importance of VT or premature ventricular contractions observed only during a 45 μg/min infusion of isoproterenol is uncertain. The reported prevalence of epsilon waves in this article was 25%, which is nearly twice the prevalence of epsilon waves present in 815 ARVD/C patients included in several worldwide registries. Another issue of concern is that the incidence of T wave inversion in leads V4–V6, which is a minor criteria for ARVD/C especially relevant when left-sided involvement is considered, was not reported. We are also disappointed that so little attention was focused on performing, and accurately reporting, the results of genetic testing. The article does not list the specific mutations which were identified. Furthermore, no information is provided to inform us how a specific mutation was determined to be pathogenic or a variant of uncertain significance. TNNC1 and ACTN2 are not validated as genetic causes of ARVD/C. We are concerned that the authors are lumping actual genetic mutations with genetic variants. Whether these data were then used in the phenotyping process is also unclear. These concerns are reflected in the authors conclusion that genotype does not correlate with LV involvement. This conclusion stands in contrast to our experience, as well as that of others.
From our perspective, this article is an important contribution to the literature for 2 main reasons. The first concerns the diagnostic role of CT imaging in ARVD/C, and the second concerns the issue of left-sided involvement in ARVD/C. Let us start by considering the role of CT imaging in diagnosis. The 2 best established imaging tools for evaluation of ARVD/C are MRI and echocardiography. MRI has long been considered the optimal tool because it allows for evaluation of RV and LC size and function and the presence and location of fat and fibrosis. The major limitation of MRI is the inability to perform MRI in patients with an implanted device. The role of CT imaging for diagnosis of ARVD/C has not been well defined. We published an initial report on the role of CT imaging for diagnosis of ARVD/C in 2007. CT-detected variables associated with ARVD/C included intramyocardial fat, RV trabeculation, scalloping, and increased RV dimensions. Subsequent studies have added to this experience, reporting that RV fat, a bulging appearance, and increased RV dimensions point toward a diagnosis of ARVD/C. In this context, the present study is an important addition to the growing literature on the role of CT imaging for diagnosis of ARVD/C. However, the jury is still out. We think that a head-to-head comparison of MRI and CT imaging will be needed to ultimately define the diagnostic role of CT imaging in the evaluation of patients with suspected ARVD/C. We anticipate that within the next 5 years, clinical trials will be performed to specifically define the diagnostic role of CT imaging for diagnosis of ARVD/C. Let us shift briefly and think about LV involvement in ARVD/C. It has long been known that patients with advanced ARVD/C often have some evidence of LV involvement. Sen-Chowdhry and McKenna are credited with first recognizing that a subset of ARVD/C patients have left dominant disease. We have recently reported our experience. Among 38 patients with a pathogenic ARVD/C mutation (predominantly PKP2) and an abnormal MRI, 21 (55%) had LV abnormalities. Two of these 21 patients had LV-only involvement, and both had a non-PKP2 mutation (DSP and PLN). Subjects with RV-only involvement were more likely to be PKP2 mutation carriers. This relationship between LV involvement and genotype was also observed in our larger report involving 577 ARVD/C mutation carriers. We suspect the higher prevalence of left-sided involvement reported in the present study reflects the increased sensitivity of CT imaging for detecting fat and perhaps inaccurate phenotyping of the study subjects.

Disclosures

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References


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