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EDITORIAL COMMENT

# Evidence Mounts That Severity of Disease Impacts the Prognosis for Patients With Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy*

Hugh Calkins, MD

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is an important cause of sudden death in young adults (1,2). Since ARVD/C was first described in 1982 by Marcus et al. (4), remarkable progress has been made in understanding all aspects of this disease. This progress includes an improved understanding of: 1) the optimal approach to diagnosis; 2) the natural history of ARVD/C; 3) the genetic basis of this condition; 4) the fundamental pathophysiological mechanisms of ARVD/C; 5) the link between ARVD/C and exercise; and 6) the prevention of sudden death.

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In this issue of *JACC: Clinical Electrophysiology*, Kikuchi et al. (3) report on the relationship between the long-term outcomes of patients with ARVD/C and extent of disease. The authors chose to assess the severity of disease by determining the number of "points" accumulated by applying 2010 diagnostic criteria to these patients' conditions (4). The study population consisted of 90 patients with ARVD/C diagnosed between 1974 and 2012 at the Tokyo Womens' Medical University Hospital. Duration of follow-up was 10.2 ± 7.1 years. Sixteen patients were lost to follow-up. Patients were divided into 3 groups based on whether they had 4 to 6 diagnostic points, 7 to 9 diagnostic points, or 10 or more diagnostic points. During follow-up, 19 patients died from cardiac causes, 28 were hospitalized with worsening heart failure, and 47 patients experienced sustained ventricular tachycardia and ventricular fibrillation. Patients in the 2 groups with more severe disease, as assessed by the number of diagnostic points, were at increased risk of developing 1 of these 3 major adverse cardiovascular events.

Before interpreting the results of this study in the context of our own experience with ARVD/C and published studies, we would like to call the reader's attention to some of the limitations of this study as well as some of the unique features of the patient population reported in this study. A review of the clinical characteristics of the patients in this study, as presented in the article's Table 1 (3), makes it immediately clear that this was a cohort of patients with severe ARVD/C. The mean age of diagnosis of ARVD/C was 44 ± 15 years old; and 76% were male patients. This contrasts with our experience, where the mean age of presentation of ARVD/C is in the early 30s, and men represent slightly more than 50% of subjects (2,5). It is also striking that 74% of patient had sustained ventricular tachycardia or an aborted cardiac arrest prior to diagnosis of ARVD/C and that the mean right ventricular ejection fraction was severely depressed at 30 ± 12%. Despite this very high risk profile, implantable cardioverter-defibrillators (ICDs) were implanted in only 18% of patients, beta-blockers were prescribed in only 24% of patients, and angiotensin-converting enzymes and angiotensin receptor blockers were used in less than one-third of

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From the Division of Cardiology, Department of Medicine, Johns Hopkins Hospital, Baltimore, Maryland. Dr. Calkins is a consultant for and has received research support from Medtronic, St. Jude Medical, and Boston Scientific. The Johns Hopkins Arrhythmogenic Right Ventricular Dysplasia program receives research support from St. Jude Medical.

patients. This approach to management of patients with ARVD/C is not consistent with current recommendations (6). It should also be noted that the exercise history of the patients in this study, both prior to diagnosis and during follow-up, is not reported. ICD implantation and exercise restriction are 2 of the most important components in the management of ARVD/C patents today (6). I suspect both the severity of disease in this highly selected patient population and the outdated management approach reflect the very high rate of major adverse cardiac events reported in this study.

Despite these limitations, I consider this report a welcome addition to the studies of ARVD/C and particularly to the research concerning identification of patients with worse long-term outcomes. I find the results of this study to be reassuring and also consistent with our experience in managing patients with ARVD/C. Although it is theoretically possible to develop malignant arrhythmia during the very early "electrical phase" of the disease, this is extremely uncommon. The results of our registry, consistent with the results of this study, tell a different story. The more severe the extent of disease in ARVD/C, the worse the outcomes (5,7). For this study, the authors used the number of points accumulated by applying 2010 diagnostic criteria as a way to assess severity of disease (3). Previous studies, including those from our center, have assessed severity of disease using different metrics but have arrived at the same conclusions (2,5). Patients with more severe disease do worse. The severity of disease can be assessed in many different ways including premature ventricular complex frequency, extent of T-wave inversion, extent of myocardial dysfunction, and presence of prior sustained ventricular tachycardia or sudden death (2,5).

At the end of the day, we congratulate Kikuchi et al. (3) for the considerable effort which was spent obtaining these unique data and interpreting their findings through a new lens. This article is an important contribution to the rapidly growing research of ARVD/C.

**REPRINT REQUESTS AND CORRESPONDENCE:** Dr. Hugh Calkins, Johns Hopkins Hospital, Sheikh Zayed Tower 7125R, 1800 Orleans Street, Baltimore, Maryland 21287-6568. E-mail: hcalkins@jhmi.edu.

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