CARDIOMYOPATHIES

EAM-guided biopsy reveals cause of ventricular arrhythmias

The current diagnostic criteria for arrhythmogenic right ventricular cardiomyopathy (ARVC) are inadequate and frequently lead to an incorrect diagnosis, according to a study published in the *Journal of the American College of Cardiology*. The investigators used a novel biopsy technique to examine a group of patients who had been diagnosed with ARVC on the basis of noninvasive evaluation, and found that 50% of these individuals actually had myocarditis.

Although ARVC is a rare condition, with an incidence estimated at 1 in 2,500–5,000, it is a major cause of sudden cardiac death in young, apparently healthy individuals. The disease is characterized by substitution of myocardial tissue by fibrofatty infiltrates, which causes atrophy and thinning of the right ventricular wall, leading to electrophysiological abnormalities.

Research has shown that other myocardial disorders can mimic the clinical, morphological, histological, and electrocardiographic features of ARVC, which limits the diagnostic accuracy of these criteria. Although "endomyocardial biopsy remains the gold standard for the diagnosis of ARVC," says Dr Maurizio Pieroni, who was one of the investigators, "the extensive application of this technique has been limited by the low sensitivity of biopsies usually obtained from the interventricular septum, which is not frequently involved in the disease." In this context, the researchers developed a technique that uses three-dimensional electroanatomic voltage mapping (EAM) to identify electrically abnormal sections of the right ventricular wall and guide the selection of biopsy samples (Figure 1).

Pieroni and colleagues studied a group of 30 patients with a clinical diagnosis of ARVC. All patients underwent coronary angiography and programmed ventricular stimulation before EAM-guided biopsy. Histological and immunohistochemical examination of samples confirmed a diagnosis of ARVC in 15 patients, and myocarditis in the other 15 individuals.

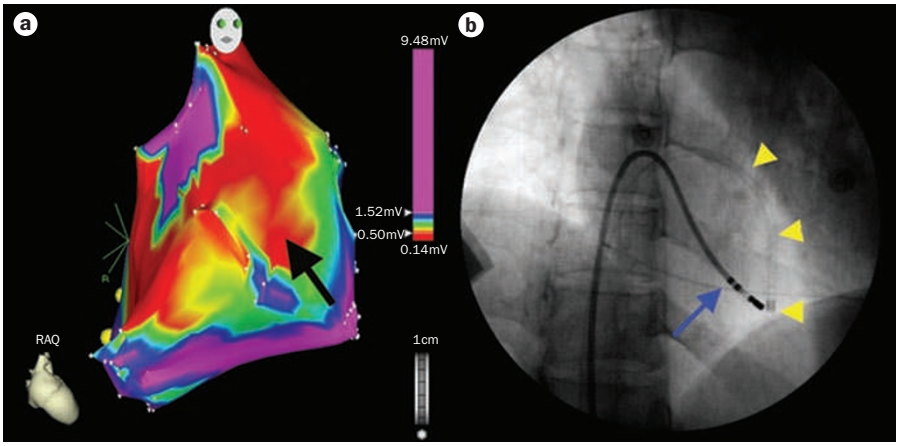

Figure 1 | Right anterior oblique view (30°) of electroanatomic map and EAM-guided endomyocardial biopsy in a patient with a noninvasive diagnosis of ARVC. **a** | Bipolar voltage map, showing an extensive low-voltage area (red area indicates voltage <0.5 mV) of the RV free wall. The black arrow shows the area from which biopsy samples were drawn. **b** | During the EAM-guided biopsy the mapping catheter (blue arrow) is kept in contact with a segment of the RV free wall with low voltages. The distal end of the sheath (yellow arrowheads) is positioned close to the catheter's tip, which allows multiple biopsy samples to be taken.

Furthermore, molecular analysis of the biopsy samples indicated viral etiology in five patients with myocarditis, which was not present in any of the patients with ARVC. The two diagnoses could not, however, be differentiated on the basis of echocardiographic, angiographic, or electrophysiological studies, or by the patients' clinical presentations. The EAM-guided biopsy technique was not associated with any major adverse effects.

Treatment of patients was determined by diagnosis; 13 individuals with ARVC received an implantable cardioverter-defibrillator (ICD) while those with myocarditis received medical therapy with β-blockers. One patient with myocarditis, who presented with syncope and inducible ventricular tachycardia, also received an ICD. During follow-up (mean 21 ± 8 months), appropriate ICD shocks for recurrent ventricular arrhythmias occurred in 47% of patients with ARVC. By contrast, all patients with myocarditis responded well to treatment and remained asymptomatic. "These findings support the notion that the identification of the underlying pathological substrate may influence both treatment and prognosis," explains Dr Pieroni. In the future, EAM-guided biopsy could be used to determine which patients are likely to benefit from ICD implantation, minimizing both the financial cost and detrimental effects on quality of life that are associated with inappropriate device therapy.

The researchers now plan to conduct a genetic analysis of the patients in their study, which they hope will shed new light on the complex relationship between gene mutations associated with ARVC, disease pathology, and arrhythmogenesis. In addition, they envisage that EAM-guided biopsy could be applied to the diagnosis of other cardiomyopathies and channelopathies. "The development of new mapping catheters and bioptomes, which will further improve this new approach, represents another challenge for the future," concludes Dr Pieroni.

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