

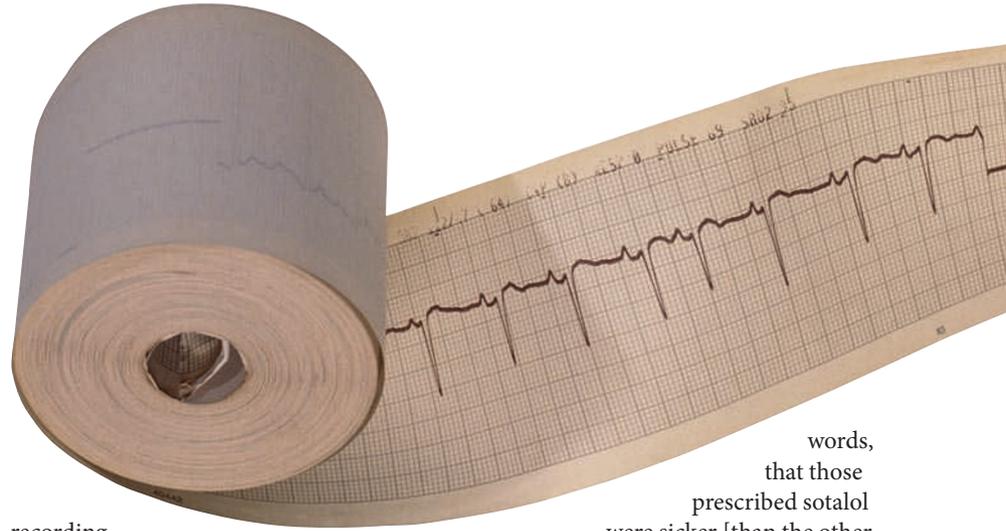
ARRHYTHMIAS

Antiarrhythmic drugs in the treatment of ARVC

The first-line therapy for arrhythmogenic right ventricular cardiomyopathy (ARVC) is considered to be β -blockers, which are generally well tolerated. However, findings from the Multidisciplinary Study of Right Ventricular Dysplasia now show this approach to be ineffective. The study investigators report that β -blockers neither improve nor worsen incident ventricular arrhythmias. Sotalol, a related drug, was also ineffective and possibly harmful. These results raise questions, therefore, about the value of these drugs as protective agents in the treatment of patients with ARVC.

ARVC is an inherited disorder characterized by formation of scar tissue and fat deposition in damaged areas of the myocardium, and patients with ARVC are at risk of sudden death. They also experience ventricular arrhythmias that are not life-threatening but reduce their quality of life. Implantable cardioverter-defibrillators are often prescribed for patients with ARVC, but these devices are not widely available and they neither improve quality of life nor reduce the risk of sudden death. "In fact," says study investigator Gregory Marcus, "quality of life may be reduced with a defibrillator if a patient experiences painful shocks." For most patients, pharmacological intervention (usually a β -blocker or sotalol) is required to reduce the symptoms caused by arrhythmias. However, the efficacy of antiarrhythmic agents has not been rigorously evaluated in patients with ARVC, and limited data are available to support such use of these drugs. The Multidisciplinary Study of Right Ventricular Dysplasia assessed the efficacy of antiarrhythmic drugs in patients who, on the basis of extensive testing, had been diagnosed with ARVC and were enrolled in the North American ARVC Registry, an initiative established by the study investigators.

A total of 95 patients with implantable cardioverter-defibrillators were included in the study. The devices were capable of



recording and storing data and the patients were followed up every 3–6 months over an average period of more than 1 year. No deaths occurred during the study, which confirms that defibrillation therapy is beneficial for patients with ARVC. During the course of the study, patients had been treated with a β -blocker ($n = 58$), sotalol ($n = 38$) or amiodarone ($n = 10$) at doses prescribed by their physicians. Treatment with β -blockers or sotalol did not significantly affect the incidence of ventricular arrhythmias—patients on these drugs experienced a similar number of these episodes in comparison with those not treated with antiarrhythmic agents. By contrast, amiodarone treatment was associated with a significant reduction in arrhythmias. These results oppose the findings of a frequently cited European study of 81 patients, which found that sotalol, but not amiodarone, was an effective treatment for ARVC. An important feature of the North American study is that drug doses were chosen by the individual treating physicians and not by the study investigators. Marcus explains, "there are at least two very important caveats to our sotalol findings: first, as this was an observational study, we could not absolutely exclude the possibility of 'confounding by indication' (in other

words, that those prescribed sotalol were sicker [than the other patients]). Second, the doses used in our study, reflecting a North American population, were substantially lower than those used in the previous European study that reported success with sotalol." Marcus also notes that the results for amiodarone cannot be explained by confounding by indication, which, he adds, "if anything, would have made amiodarone look less effective than it actually was."

The findings have raised several questions that should be addressed in future, prospective studies. First, a randomized study would be needed to clarify whether the results for sotalol are dose-related or attributable to confounding by indication. Second, despite its effectiveness, amiodarone has long-term adverse effects and its use is therefore generally avoided in young, otherwise healthy patients. Analogs of amiodarone, such as dronedarone, are currently in development—whether these agents will prove to be more suitable than the currently available treatments for ARVC remains to be established.

Sharmini Rajanayagam

Original article Marcus, G. M. *et al.* Efficacy of antiarrhythmic drugs in arrhythmogenic right ventricular cardiomyopathy. A report from the North American ARVC Registry. *J. Am. Coll. Cardiol.* 54, 609–615 (2009).