EDITORIAL
Intracardiac Extrastimulation Studies: How To? Where? By Whom?
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A CURIOUS ROLE REVERSAL has taken place among the invasive procedures in cardiovascular practice. The reputation of being the most demanding and protracted procedure in the cardiac catheterization laboratory has passed from the hemodynamic and angiographic to the electrophysiologic and electropharmacologic examination of patients with symptomatic tachycardias. Better equipment, microprocessors, and computers have streamlined diagnostic cardiac catheterization and coronary angiography, while the electrophysiologic studies have shifted from the simpler problems of conduction disturbances to the more demanding extrastimulation studies of life-threatening tachycardias. Such studies, particularly in patients with ventricular tachycardias, are difficult to standardize and contain within rigid time limits.

Despite their complexity and tedium, the demand for the extrastimulation studies is growing because of their diagnostic accuracy and therapeutic value in patients with symptomatic tachycardias. The introduction of single, double, triple or bursts of ventricular premature stimuli induces sustained ventricular tachycardia in the majority of patients in whom this arrhythmia occurs spontaneously.1 Not a single instance of sustained ventricular tachycardia could be induced by comparable extrastimulation techniques in more than 400 patients who had not had spontaneous ventricular tachycardia or ventricular fibrillation.2 Electropharmacologic testing has shown that the results of therapeutic trials in the laboratory correlated with subsequent suppression of ventricular tachycardia during chronic oral drug treatment.3 These observations indicate that the electrophysiologic and the electropharmacologic studies may contribute to a more rational therapy of sustained tachycardias, particularly when the treatment includes new drugs,4 drug combinations, new pacemaker design,5-7 and newly developed surgical techniques for ablation of arrhythmogenic foci.8-10

Most experts agree that the extrastimulation techniques are helpful in the management of patients with symptomatic tachycardias; but few agree about the value of these techniques in patients without arrhythmias. Greene et al. reported that the induction of repetitive ventricular responses (RVR) after a single premature stimulus applied during sinus rhythm or atrial pacing was a reliable marker of threatening ventricular tachycardia.11 However, subsequent studies have dampened the initial enthusiasm for the wide application of this procedure, because the induction of RVR after a single premature stimulus lacked sufficient diagnostic and prognostic sensitivity.12-14

Currently used procedures are difficult to simplify and shorten for several reasons. The examiner is responsible for the accurate diagnosis of the arrhythmia mechanism. The examination must often resolve whether the wide QRS premature complex or the wide QRS tachycardia represent ventricular arrhythmia, aberrant conduction within the bundle branches or ventricular myocardium, or one of the forms of preexcitation, e.g., conduction through the Kent bundle or the nodoventricular fibers.15 The examiner must be aware that a spontaneous impulse after premature stimulation may be due not only to intraventricular reentry, but also to spontaneous ventricular premature complexes, catheter-induced ventricular premature complexes, retrograde atrioventricular (AV) nodal reentry with aberrant conduction, and reentry within the His-Purkinje system.15, 16, 17 A stable and technically good His bundle ECG recording is an essential part of each extrastimulation procedure. Also, several atrial electrograms may be needed, even when the initial purpose of the study is the induction of ventricular tachycardia, because the examiner may encounter, in the course of the study, problems that require evaluation of the sinoatrial node function and determination of atrial, AV nodal, or His-Purkinje system refractoriness. In patients with documented or suspected AV bypass tract, the location and duration of the refractory periods of such tracts must be determined.18, 19

The design of the study is complex. Typical electrophysiologic investigation of ventricular tachycardia requires insertion of three to six intracardiac electrode catheters in order to record and/or stimulate from the following sites: right atrium, coronary sinus, AV junction at the His bundle site, and the apex, septum, inflow and outflow tracts of the right ventricle.20 When the left ventricle is entered, the recording and pacing electrodes are sequentially placed at the apex, septum, lateral wall and the base.20 Each study may include the following steps: (1) atrial pacing at incremental rates; (2) premature atrial stimulation during sinus rhythm and during atrial pacing; (3) ventricular pacing at incremental rates; (4) premature ventricular stimulation during sinus rhythm and during ventricular pacing; (5) introduction of a second premature stimulus; and (6) introduction of one or two additional premature stimuli or a burst of stimuli. Some of these procedures must be repeated at several basic stimulation rates and from various stimulation sites. Sometimes, drugs such as isoproterenol are used with pacing to aid in the induction of tachycardia.21 The studies

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become even more complex when endocardial electrode-catheter mapping is required. Pharmacologic studies are taxing to the endurance of both the examiner and the patient. In one laboratory, at least 4 days are needed to test the response to i.v. lidocaine, procainamide and phenytoin, and to oral quinidine and disopyramide. Even more time is required if the testing includes experimental, nonconventional drugs or drug combinations. Repeated studies may be needed, depending on the effectiveness of oral drug therapy. The determination of plasma drug concentrations is an essential part of each study.

The physician in charge of invasive cardiac electrophysiologic and electropharmacologic studies must be trained in clinical cardiology, clinical investigation and cardiac catheterization. The physician must have sound clinical judgment. A study of such magnitude and complexity requires an accurate definition of purpose, risk and potential short- and long-term benefits. Consideration must be given to the possible advantages or disadvantages of an alternate empirical treatment, not based on the results of extrastimulation studies. The study cannot be recommended without a thorough clinical evaluation and an understanding of the pathogenesis, natural history, and prognosis of the condition responsible for the arrhythmia under consideration.

Knowledge of theoretical and clinical cardiac electrophysiology is also required. Recording electrical activity from numerous intracardiac sites requires familiarity with the anatomy of the heart. To interpret the results competently, the study director is expected to have a grasp of the reentry mechanism, various forms of normal and abnormal automaticity, refractoriness, excitability, vulnerability and supernormality. Another prerequisite is experience in the analysis of complex arrhythmias. In interpreting the results of a tachycardia study, the operator must consider the method of its initiation, the rate and morphology of tachycardia, the width of tachycardia zone, implications of fragmented ventricular electrograms, and the relation between induced and spontaneous arrhythmia. The approach to the clinical electrophysiologic study must be flexible, based on a rapid assessment of the monitored phenomena. If necessary, the originally charted course must be altered to gain additional information or to alleviate the study-related discomfort of the patient.

The physician must have knowledge of pharmacologic properties and pharmacokinetics of the drugs used in the studies. He or she must also have technical skill. The operator must be skilled in arterial and venous catheterization, fluoroscopy, defibrillation, cardiopulmonary resuscitation, and in the operation of the diagnostic equipment. Additional training may be needed for setting up and utilizing endocardial catheter-mapping.

Cardiac electrophysiologic studies require a time commitment. In the laboratory of Dr. Wellens in Maastricht, Holland, the average time spent by the patient on the catheterization table during an electrophysiologic study of tachycardia was 2½ hours, and 5 more hours of examiner's time were needed for the analysis of the record. When the electrophysiologic studies culminate in surgery for the treatment of refractory arrhythmias, clinical electrophysiologists usually collaborate with the surgeons in the pre-, intra- and postoperative arrhythmia mapping and other aspects of management.

If the examination is incomplete or suboptimal, it can result in an incomplete understanding of the pathogenesis of the tachycardia. Since the results of electrophysiologic studies must be considered within the framework of the total clinical evaluation, all aspects pertinent to the patient's arrhythmogenesis must be investigated. In patients with ischemic heart disease, which is the most common cause of sustained symptomatic ventricular tachycardia, the management of arrhythmia frequently depends on the results of myocardial function tests and coronary arteriography. In other patients, a careful search for the etiology of ventricular tachycardia may necessitate diagnostic procedures, ranging from two-dimensional echocardiography for detection of mitral valve prolapse to right ventriculography for detection of an arrhythmogenic dysplasia of the right ventricle.

An incomplete or suboptimal electrophysiologic examination can also result in an inaccurate evaluation of the arrhythmias. Rigid protocols applicable to all patients under all conditions may not be feasible, because the electrophysiologic mechanisms of arrhythmias are diverse, and the potential sites of arrhythmogenic activity are practically limitless. Thus, the extrastimulation techniques vary among different laboratories, which may account for the reported differences in the incidence of induced ventricular tachycardia in apparently similar categories of patients. An inconclusive examination may result from technical limitations of the study. For instance, in some patients, ventricular tachycardia could be induced only by stimulating from the left ventricle and not from any of the sites within the right ventricle. In other patients, ventricular tachycardia could be induced only after isoproterenol.

An incomplete study may result in more serious consequences than merely an inconclusive result. For instance, in a patient considered for implantation of a radiofrequency-activated atrial pacemaker for treatment of refractory symptomatic supraventricular tachycardia, the pacemaker could induce dangerous ventricular arrhythmia if the examiner missed the presence of an AV bypass tract or failed to measure its refractory period.

A suboptimal examination may also result in an incomplete pharmacologic study. The process of drug testing is usually based on trial and error; yet the method of testing is crucial to the clinical decision. Kastor et al. estimated that effective drug control can be achieved in more than half of the patients evaluated for refractory ventricular tachycardia. Without any intention of underestimating these accomplishments, one must consider whether the therapeutic failure in...
the remaining patients was due to the differences in the clinical condition of the patients, mechanism of their arrhythmias, methods of study, or perhaps the choice or availability of proper antiarrhythmic drugs. Hence, comparing different results of therapy in different laboratories is like comparing the results of open heart surgery in different institutions.

Adequate diagnostic facilities are crucial. "Inadequacy" may range from the lack of facilities for performing left-heart catheterization, or for testing plasma drug concentrations, to a lack of facilities for intracardiac mapping, sophisticated pacemaker technology, or surgical therapy of arrhythmias.

The patient's safety depends on the prudence, experience, and technical skill of the operator. The conventional hazards of cardiac catheterization are magnified by the length of procedure, repeated procedures on successive days, prolonged insertion of indwelling catheters, use of cardiac depressing drugs, and application of electric stimuli during vulnerable period of excitability.

These studies are expensive. In Holland, the estimated cost of a single study is more than $800.22 This does not include the cost of hospitalization or treatment of complications arising from the study. No similar estimates are available for the study costs in this country.

Extrastimulation studies appear to be on the verge of ceasing to be purely experimental procedures and becoming legitimate diagnostic aids in the design of rational treatment of refractory sustained tachycardias. Yet most of our knowledge on the subject has come from studies conducted at university-affiliated hospitals by experienced clinical investigators working in properly equipped laboratories. The same laboratories have been the principal training sites of clinical electrophysiologists directing extrastimulation studies in patients with sustained, symptomatic tachycardias.

Anticipating greater demand for skilled study directors, consideration must be given to the need for qualified training centers and the design of the appropriate training programs. A typical 2-year cardiology training program is not expected to provide either sufficient instruction or experience to qualify its graduates for setting up an electrophysiology laboratory and performing extrastimulation studies in patients with tachycardias. From an informal poll in a small sample of active electrophysiology laboratory directors, the consensus is that acquiring the necessary competence requires 1–2 years of experience in a busy electrophysiology laboratory, preferably after the completion of routine training in clinical cardiology. Even if these demands are too rigorous, there is little doubt that mastering theoretical and practical clinical electrophysiology requires special training beyond the conventional training program in clinical cardiology. Competence in the practice of cardiac catheterization and angiography does not automatically assure similar competence in performing complex electrophysiologic and electropharmacologic studies.

While delegating to the experts the task of design-

ing the appropriate training programs for clinical electrophysiologists, the special problems of extrastimulation studies must be explained to the medical profession and the hospital administrators. These problems should be publicized before the hospitals start making financial and professional commitments to the laboratories. Acknowledging the need for special expertise and defining its scope can prevent discord within the ranks of our specialty. More important, we can contribute to a uniformly optimal service for a selected cohort of patients whose complex, life-threatening problems must be matched by the complexity of diagnostic and therapeutic procedures.

References
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