Editorial

Can the technicalities of electrophysiological testing for ventricular tachycardia be simplified?

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The increasing use of provocative electrophysiological techniques in the investigation of patients with documented spontaneous sustained uniform ventricular tachycardia¹ has led to widely divergent recommendations on the most efficient stimulation protocol—that is, the one most likely to induce the clinically documented tachycardia and least likely to induce a tachycardia from which the patient has not suffered or is unlikely to suffer in the future. The idea of the electrophysiological method is to induce a “clinical” arrhythmia by ventricular extrastimulation during sinus rhythm or ventricular pacing at various basic driving rates. Most of the information gained from provocative testing applies to patients who have had a myocardial infarction and who have presented with either documented or suspected tachycardias. The data are not, therefore, applicable to other forms of heart disease, for which information is lacking.

The best studied of all the ventricular tachycardias is sustained uniform tachycardia. Many controversial aspects of the methods of the clinical study have recently been ventilated. The optimal number of ventricular extrastimuli² is not known. Nevertheless, there is a substantial body of evidence suggesting that non-specific responses are much more commonly induced by three or more extrastimuli, and most investigators are agreed that the number of extrastimuli used should be limited to three or less. Similar arguments apply to the use of rapid bursts of pacing and many investigators no longer recommend this method.³ There is no consensus, however, and despite good clinical⁴ and experimental⁵ arguments for avoiding this type of stimulation, in many recently reported studies it is still used⁶ and indeed recommended.⁷

Stimulation sites

The number and location of sites of stimulation have been the subject of several papers in recent years. Again there is no widespread agreement. Most investigators advocate the use of triple extrastimuli at one or more right ventricular sites before resorting to left ventricular stimulation.⁷⁻⁹ Morady *et al*, however, preferred burst pacing to triple extrastimuli.¹⁰ Lin *et al* have recently shown that left ventricular stimulation added little to right ventricular stimulation at two sites.¹¹ Brugada and Wellens showed that addition of a third extrastimulus at a single right ventricular site and during sinus rhythm and three different ventricular drive cycles was more effective than changing the site of stimulation to the outflow tract.¹² This carefully designed twelve step protocol has been meticulously evaluated in various settings^{13,14} and is perhaps the most thoroughly studied protocol. This protocol correctly identified 90% of patients in terms of the presence or absence and duration of tachycardia after myocardial infarction.¹⁴ Other investigators, however, claim (but have not rigorously shown) equally good results using a protocol which includes burst pacing, outflow tract stimulation,^{6,7} and a high stimulation current.⁶ The value of isoprenaline as an adjunct is still being assessed.^{12,15} The reproducibility of the results⁷ and the use of indwelling electrode catheters for serial studies¹⁶ are other factors that confound the performance of these studies and their interpretation.

Estes *et al* have suggested that multiple (three or more) basic drive cycles with limitation of the number of extrastimuli to less than three increase the sensitivity of the test without diminishing specificity.⁹ If the optimal number of ventricular extrastimuli is unclear, so too is the range of coupling intervals over which they are to be delivered. Most uniform ventricular tachycardias associated with coronary artery disease require short coupling intervals

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Table Summary of formal investigations of high current stimulation

Author	No of patients	Patient type*	3VPS	Multiple drive cycle†	RV burst	2 RV sites	LV	High current and clinical value
Brugada and Wellens ¹²	(a) 24	Mixed	—	—	—	+	—	20 mA } not recommended
	(b) 24	Mixed	+	—	—	—	—	5 × threshold, recommended
Oseran <i>et al</i> ⁶	91	Mixed	+	—	+	+	—	10 mA, not recommended
Morady <i>et al</i> ²⁴	41	Mixed	+	—	—	+	—	10 mA, not recommended
Herre <i>et al</i> ²²	98	Mixed	+	—	+	+	—	10 mA, not recommended
Kennedy <i>et al</i> ²³	15	Asymptomatic	+	—	—	—	—	10 × threshold, not recommended
Mitchell <i>et al</i> ²¹	11	VTS	+	+	—	+	—	20 mA, not recommended
Weissberg <i>et al</i> ²⁵	70	Mixed	—	+	+	+	—	

*Type of clinical arrhythmias: VTS, sustained ventricular tachycardia; Mixed, mixed group with sustained tachycardia; ventricular fibrillation, and others.

†More than two basic drive rates.

+, part of study; —, not part of study.

RV, right ventricle; LV, left ventricle; VPS, ventricular premature stimuli.

just in excess of the myocardial refractoriness for their initiation.¹⁷ As the number of extrastimuli is increased refractoriness progressively shortens¹⁸ and very close intervals can be achieved. This often results in the initiation of non-specific responses that are of unknown clinical importance. According to Morady *et al* intervals of less than 180 ms for the second and third extrastimulus are associated with a considerable increase in the likelihood of induction of non-specific responses.¹⁹

Current

Shorter coupling intervals can also be achieved by increasing the current stimulation.²⁰ This aspect of ventricular stimulation protocols has been considered in several reports, again with widely differing conclusions. The table summarises those clinical studies that have studied the utility of high current stimulation as part of the investigation protocol. The patient groups studied are varied. A formal investigation of the value of high current in patients with documented tachycardia, undertaken by Brugada and Wellens, concluded that the additional yield of high current combined with a change in stimulation site (sensitivity 66%) was less than that obtained by increasing the basic drive rate and adding up to three extrastimuli (sensitivity 83%).¹² Similar findings were reported more recently by Mitchell *et al*.²¹ Herre *et al* documented an increase in sensitivity using four extrastimuli at multiple sites, but the specificity was reduced by induction of clinically undocumented arrhythmias in 45% of patients.²² This effect was even more exaggerated with burst pacing (46%) and high current (60%) with little gain in the inducibility of clinically documented tachycardias (73% with four stimuli and 79% with high current). In contrast, Oseran *et al* noted an increase in yield of 15% when high current was used.⁶ No information about non-clinical arrhyth-

mias is provided in this report.

Kennedy *et al* concluded that high current combined with triple extrastimuli induced ventricular fibrillation in 27% of patients free of spontaneous or induced sustained arrhythmias.²³ Ventricular fibrillation could be induced in six patients in whom no sustained arrhythmias were inducible at lower energies. Although two of these had had clinically documented fibrillation, electrophysiological testing cannot distinguish between "clinical" and "non-clinical" fibrillation and this response must be considered non-specific.

A paradoxical effect of high current was observed by Morady *et al*.²⁴ With a high current sustained arrhythmias could be induced in 62% of 26 patients in whom no arrhythmias were inducible at twice diastolic threshold. The coupling intervals of the initiating premature stimuli at the higher current were in excess of the ventricular refractory period at twice threshold. Paradoxically, tachycardia could not be induced by the higher current in three patients with inducible tachycardia at the lower current strength. Because of the design of the study it is not possible to designate these as "clinical" or "non-clinical" arrhythmias but it is noteworthy that most were non-sustained or multiform.

In this issue of the *British Heart Journal* Weissberg *et al* report the clinical usefulness of high current stimulation in 70 patients with documented or suspected ventricular arrhythmias.²⁵ Of the 34 patients in whom arrhythmias were induced, only three required a current of 5 mA and one a current of 10 mA to induce the tachycardia. The highest current level of 20 mA had no additional effect. Thus the report of Weissberg *et al* joins many others which failed to show any advantage of high current stimulation (see table). Unfortunately Weissberg *et al* provide no data about induction of non-clinical arrhythmias. As mentioned above, only Herre *et al* have specifically explored the problem of induction

of non-clinical responses by high current and have emphasised this important limitation of the technique.²²

The choice of protocol

There is no general agreement about the choice of an "optimum" protocol for clinical studies. This very lack of uniformity of study protocols makes it impossible meaningfully to compare the results of the different published studies. In addition, the patient groups vary considerably from one study to another. Thus in most studies measures of sensitivity and specificity are not obtainable. Although a scientific approach is essential in devising, evaluating, and reporting study protocols, the stimulation protocols must also be simple and practical, and should minimise discomfort (especially by reducing the study duration) to the patient. Attempts should be made, therefore, to remove redundant components of the protocol. The published evidence suggests that some methods of ventricular stimulation have a confounding effect and do not contribute useful information: (a) rapid burst pacing at any site; (b) stimulation of sites other than the right ventricular apex; (c) left ventricular stimulation; (d) use of four or more ventricular extrastimuli; (e) use of high current stimulation. These techniques should be limited to selected patients with particular problems and need not be employed for ventricular stimulation in routine clinical practice.

In an effort to improve the standard of clinical studies the North American Society of Pacing and Electrophysiology has published guidelines for investigation of patients with sustained uniform tachycardia.²⁶ It is hoped that these guidelines will also lead to a more standardised approach to investigation. The quest for standardisation should not be motivated by an obsessional pursuit of some ideal or "best" protocol because it is certain that there is no such thing. More importantly, as Mason *et al* have suggested,²⁷ there should be agreement between investigators that protocols contain certain elements and exclude others. A common protocol would be better still. Only then can different studies be meaningfully compared, the value of a given protocol in different clinical settings be compared, and the techniques further refined.

These considerations are especially important in the application of stimulation studies to the assessment of risk of developing a spontaneous tachycardia (for example after myocardial infarction) in patients who have not suffered spontaneous events—that is the unmasking of a predisposition to arrhythmias. The controversial study of Richards *et al* used a protocol incorporating a current of 20 mA to identify patients at risk of sudden death after myocardial

infarction.²⁸ No distinction, however, was made between induced sustained tachycardia, non-sustained tachycardia, and fibrillation and it is likely that many of these responses were "artefactual". The study reported that patients with electrical instability were at high risk of sudden death within the 12 month follow up period. The results of this study have not been duplicated by others.²⁹ Indeed Brugada *et al* have shown that a basis for sustained tachycardia is present in at least 42% of post-infarction patients.¹³ It is one thing to document the presence of a basis (by demonstrating inducibility) but it is another matter to show that this is capable of spontaneous activation in the future. In this sense, the concept of "clinical" versus "non-clinical" arrhythmias is especially relevant. It is upon this distinction that the definitions of specificity and sensitivity have been based. If these definitions are to be rigorously upheld, 12 lead electrocardiograms for all episodes of both clinical and induced arrhythmias must be available for comparison. For non-sustained or haemodynamically unstable tachycardias this is clearly impossible. If the arrhythmia is multiform ventricular tachycardia or ventricular fibrillation, no meaningful methods of comparison are available. For haemodynamically stable tachycardias a 12 lead electrocardiogram is a minimum requirement if the distinction is to be made. Even then it may be wrong (assuming perfect documentation) to designate an induced tachycardia as non-clinical merely because it had not been documented or had not actually occurred. It is now being recognised that a so-called non-clinical induced tachycardia may become manifest at some later date as a clinical problem in almost 50% of patients.³⁰ The oversimplified concept of clinical or non-clinical (documented or undocumented) arrhythmias may need to be revised and refined.

It is hoped that it will soon be possible to discover the characteristics of a potential substrate (for example the type of induced arrhythmia, mechanism of induction, etc) that identify it as being potentially important or clinically irrelevant and which may allow, prospectively, the distinction between spontaneously active and dormant substrates. Although we are some way towards achieving this in patients who have coronary artery disease there is no similar information about ventricular arrhythmias which commonly occur in other clinical settings such as dilated cardiomyopathy and hypertrophic cardiomyopathy, congenital structural defects after corrective surgery, and dysplastic conditions of the ventricles.

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