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THERAPY OF VENTRICULAR TACHYCARDIA: ROLE OF ELECTROPHYSIOLOGY STUDIES 1987

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Abstract

Over the past ten years, electrophysiologic studies have improved our understanding of the basic mechanisms of a variety of arrhythmias. At present, the overwhelming weight of evidence suggests that sustained uniform ventricular tachycardia (VT), particularly that associated with coronary artery disease is due to reentry. In addition to establishing the mechanism of VT, the appropriate use of electrophysiologic studies, including both programmed stimulation and endocardial mapping, has allowed for the development of therapeutic modalities which can be based on objective endpoints. Therapeutic options available for the management of VT includes drugs, electrical devices and surgery or combinations of the above. One can consider VT the product of triggers which are usually ventricular premature complexes, and a substrate which is either functionally or anatomically determined, both of which can be modified by autonomic tone, heart rate, hemodynamics, ischemia, etc. Electrophysiologic testing is primarily directed at the substrate. It is the basic hypothesis that if the substrate can be rendered incapable of supporting sustained reentry, then no arrhythmia will result, regardless of the trigger or other factors involved.

Pharmacologic therapy of ventricular tachycardias has primarily been by empiric therapy or guided by noninvasive testing, particularly Holter monitoring. Empiric therapy has never been shown to be effective in treating VT

with at least a 50% recurrence rate in a year and a half. The use of Holter monitoring to guide pharmacologic therapy is limited by a) the absence of significant arrhythmias in 20 to 40% of patients, b) the spontaneous variability of these arrhythmias, c) failure to predict proarrhythmic effects of drugs on a single Holter, d) absence of arrhythmias may not predict success, and e) presence of arrhythmias may not predict failure. As a result, programmed stimulation has been employed to develop pharmacologic regimens to treat VT.

The basic assumptions of electrophysiologic testing of drugs are that 1) induced arrhythmia is the same as the patient's spontaneous arrhythmias, and 2) the laboratory responses to drugs predict response to chronic oral therapy. In patients with spontaneous VT comparing the induced rhythm (i.e. VT) to the clinical VT is easy. This is not the case with cardiac arrest where the initial rhythm is rarely documented. However, the use of an induced VT as a marker for the clinical arrhythmias in such patients is supported by the fact that in patients with cardiac arrest, the cardiac arrest is usually initiated by VT which may then degenerate to ventricular fibrillation. We believe that in using any method to guide therapy of these malignant arrhythmias it is better to err on the side of overpredicting failure than underpredicting success since failure may mean long hospitalizations and/or death. The ability to develop drug therapy depends on the ability to reproducibly initiate the tachycardia. In the vast majority of studies, over 90% of patients with sustained VT can have that rhythm replicated in the laboratory. The patients resuscitated from cardiac arrest have a slightly lower incidence, somewhere around 80% of tachycardia induction. It is to be stressed that the sensitivity and specificity of ventricular stimulation depends on the mode of stimulation. The more vigorous the stimulation, the more likely induction of nonspecific arrhythmias.

For the evaluation of drug therapy control studies are done to demonstrate reproducible initiation of the tachycardia. Then various drugs are administered on different days and the response to programmed stimulation tested. The criteria for drug efficacy, which we believe is most specific, is the prevention of induction of the clinical arrhythmia. Decreasing the tachycardia zone, rendering VT more difficult to initiate, decreasing the heart rate of VT, or prevention of any extra beats at all are appropriate

endpoints for arrhythmia occurrence. Some investigators use fifteen beats as a cut off for sustained arrhythmias but the data upon which this is based is somewhat empirical. We and others have found that successful therapy, i.e., prevention of induction of sustained tachycardias by one Type I agent usually predicts that another Type I agent or combination will work, and that failure to prevent induction predicts failure of Type I agents. This does not mean that one drug predicts another, but that one drug may predict a whole group of drugs. There is also no correlation between the spontaneous ectopy and the mode of induction or the efficacy of therapy.

Unfortunately, only 30 to 50% of patients will respond to antiarrhythmic therapy based on programmed stimulation using Type I drugs. Several studies have shown that the predictive accuracy of electrophysiologically guided therapy for these agents exceeds 80% for patients with sustained ventricular arrhythmias. Approximately 90% of patients in whom tachycardias are predicted to be successfully treated have no recurrence, while approximately 50 to 55% of patients in whom failure is predicted have a recurrence in the short term. There is a significantly higher recurrence rate in those predicted to be ineffective than in those predicted to be effective, and at least two studies have shown, using multivariate analysis, that persistent inducibility of tachycardias is an independent of subsequent sudden death in this group of patients. The other predictor is LV dysfunction.

In view of the limited response rate on standard drugs, amiodarone has been more widely employed in the United States. Controversy still exists, however, as to whether or not electrophysiologic studies are useful with this drug. It is our contention that electrophysiologic testing is of little value with amiodarone because of the low incidence of noninducibility, which approximates 13%. Thus, the vast majority of patients will remain inducible on amiodarone yet most will do well. However, approximately 30% of patients will have recurrence and there is no way to predict this recurrence. Programmed stimulation, however, may be useful in predicting the kind of result one will have. Thus, if one studies a patient taking amiodarone and the induced tachycardia is slow, recurrences are also likely to be slow.

Based on the available data, I believe that programmed stimulation is the most successful and reproducible method of replicating clinical ventricular

arrhythmias. In the selected populations that have been studied effective therapy on standard drugs is only achievable in <50% of patients. Response to conventional drugs (Type I) as assessed by programmed stimulation predicts clinical outcome, however, controversy still exists as to whether or not new antiarrhythmic agents, particularly amiodarone, can be assessed using programmed stimulation. The greater question is what is the real role of pharmacologic therapy? We have seen that there is no drug that is uniformly successful and that many can produce the lethal arrhythmias for which they are given to treat. The toxic to therapeutic ratios are narrow and patient compliance limits their utility. It is my belief that alternative methods of therapy will be developed through electrophysiologic tests over the next several years. These include electrical therapies and surgical therapies.

Of the electrical forms of therapies are antitachycardia pacemakers, low energy cardioverters and automatic implantable cardioverter-defibrillators (AICD). Electrophysiologic studies can be used to demonstrate that tachycardias can be terminated by programmed stimulation. The ability to initiate and terminate VT by programmed stimulation provides a means to judge whether or not cardioversion or pacemaker therapy is applicable. Electrophysiologic studies have demonstrated that tachycardia rate, size of the excitable gap, site of stimulation, and refractoriness and conduction velocity of the tissue between the pacing site and the reentrant circuit influence the ability to terminate tachycardias by pacing and therefore affect the utility of antitachycardia pacemakers. These studies have demonstrated that patients with coronary artery disease usually have multiple tachycardias and that tachycardias are more successfully treated by multiple extrastimuli than by single extrastimulus. However, the chance of acceleration of tachycardias is also greatest with rapid pacing which is the most effective form of therapy. Thus, for antitachycardia pacemakers to be useful the electrophysiologic test must show reproducible termination of the arrhythmia and absence of acceleration by the antitachycardia pacing modality. It appears that adaptive scanning burst capability will be the most important modality for treating these arrhythmias but new pacing algorithms are required to insure the fewest number of stimuli necessary to terminate the VT in order to limit the incidence of acceleration. Rapid VTs (greater than 200 beats per minute) require multiple extrastimuli

for termination and thus have the highest incidence of acceleration. Thus I believe that some form of defibrillator back-up is essential for any antitachycardia device. Low energy cardioversion was initially developed as a way to shock tachycardias with .5 to 2 joules of energy in order to terminate the tachycardia. This method has not been demonstrated to be more successful than rapid pacing alone and it is clearly more painful. Anything over one joule causes pain to the patient. The incidence of acceleration is also comparable (approximately 30%) to that of rapid pacing. Finally, cardioversion can produce atrial fibrillation which can then trigger the cardioverter. As a result, it is the general consensus that defibrillator back-up is generally required for all antitachycardia pacing and cardioversion devices.

The automatic implantable cardioverter defibrillator (AICD) has been available for patient implantation for seven years. This device which senses rate, with or without additional waveform characteristics, delivers up to four shocks to terminate a rapid VT or ventricular fibrillation (VF). The energy output of these shocks is 25 to 30 joules. In over 1500 implants to date, it is quite clear that this device saves lives. There is only a 5% incidence of sudden death in patients in whom the device has been implanted. The device is not perfect though. Approximately 5% of patients in whom the device is tested cannot have it implanted due to inadequate energy requirements. Furthermore, multiple epicardial patches are required to obtain adequate defibrillation thresholds and this may not be possible in patients who are having multiple bypass grafts implanted simultaneously. Finally, rapid tachycardias either sinus or nonsustained VT can trigger the device causing painful unnecessary discharges. Presently, AICD candidates include the following: 1) cardiac arrest in the setting of idiopathic dilated cardiomyopathy, 2) long QT syndrome refractory to beta blockade therapy, 3) patients with cardiac arrest and inducible VT/VF who have failed drugs and are not surgical candidates, 4) patients with cardiac arrest and no inducible arrhythmias, and probably 5) patients with persistently inducible rapid VT/VF while on amiodarone since such patients have a 25% incidence of sudden death in the following starting therapy. This is a device of the future. The role for electrical therapy will be enormous once we have a device which combines adaptive stimulation capabilities with low energy cardioversion and a defibrillator. It needs to be much smaller

than it currently is, it needs to be durable, and there needs to be a way in which the device can be implanted transvenously, since at the present time, it requires a thoracotomy.

The ultimate form of therapy for VT is removal or destruction of the pathophysiological substrate for the ventricular arrhythmia since this represents the only potential "cure" for these arrhythmias. In the past ten years, surgical forms of therapy have become directed by electrophysiologic information and have led to an increased success rate in the management of lethal ventricular arrhythmias refractory to other forms of therapy. This therapeutic option also enables one to address other factors such as ventricular dysfunction and ischemia at the same time the substrate is being directly attacked. To date, sustained uniform VT is the ventricular arrhythmia for which surgery has been most often employed. In approximately 80% of such patients the VT is related to coronary artery disease. While several concurrent coronary causes of VT are recognized, it is the surgical management of VT associated with coronary artery disease that is most well studied. The typical patient with sustained VT is one with prior large myocardial infarction and a left ventricular aneurysm with a depressed ejection fraction in the 25 to 30% range. Many have overt heart failure and the vast majority (approximately 80%) have residual significant coronary artery disease. The pathophysiologic substrate for VT associated with coronary artery disease appears to be the uncoupling of viable myocardial cells by connected tissue causing the conduction abnormalities requisite for reentry. In most instances, the tachycardias appear to be focal, i.e., arising in an area of 2 to 4 square centimeters. In a smaller number of patients, the circuit appears to be larger having macro-reentrant characteristics around the scar with a circumference of 6 to 12 centimeters. In many patients with coronary artery disease, multiple VTs with distinct morphologies are present spontaneously and/or following programmed stimulation. Because of the multiple morphologies, we believe that both pre-operative catheter mapping as well as intraoperative mapping should be performed. Catheter mapping allows the electrophysiologist more time to map multiple morphologies. Several investigations may be necessary to do this. Intraoperative mapping techniques have shown that these VTs appear to arise at or near the subendocardium, usually within 3 to 5 millimeters of the endocardial surface. The procedures currently used to treat VT include destruction or isolation of all subendocar-

dial scar, or selective subendocardial resection and/or destruction guided by activation mapping of the VTs. While the former techniques (subendocardial encircling ventriculotomy, encircling cryoablation, and total endocardectomy) do not require mapping, focal destructive procedures do. We prefer map guided surgery since : 1) approximately 10 to 15% of VTs arise outside the visible scar tissue, 2) removal of unnecessary scar tissue in the papillary muscles may result in unnecessary mitral valve replacement, and 3) VT in the periinfarction period frequently has no anatomic markings, therefore no landmarks are visible for the surgeon. Mapping techniques, however, are difficult to perform and fraught with pitfalls of interpretation. We believe that analysis of the response of electrograms to programmed stimulation during VT can provide important information relative to the timing of these electrograms and can help distinguish late from early sites. Despite the limitations of mapping, electrophysiologically guided surgery renders 75 to 90% of survivors free of clinical arrhythmias on or off drugs, with an acceptable mortality of 10 to 15%. The non-map guided surgery directed at visible scar or at abnormal electrograms in sinus rhythm is somewhat less successful, both in our hands and in others, but is occasionally necessitated by the inability to induce and / or map all clinical tachycardias. The surgical management of VT has moved ahead rapidly and at least three centers have demonstrated that surgically directed therapy provides superior long term results than medical therapy. This is especially true in patients who have recurrent ventricular tachycardia in the setting of recent infarction. These patients who have had an 80% one year mortality on medical therapy now have 80% survival with surgical forms of therapy.

Over the past ten years, great strides have been made in the diagnosis and treatment of VT as a result of the development of clinical electrophysiology. It is our hope that continued application of electrophysiologic studies will further improve and broaden our therapeutic options.