CLINICAL APPLICATIONS OF INVASIVE ELECTROPHYSIOLOGIC STUDIES

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ABSTRACT

Although invasive electrophysiologic studies have contributed significantly to our understanding of the electrocardiographic manifestations of cardiac arrhythmias, intracardiac recording is often necessary when diagnosis is not possible from surface electrocardiograms (ECG). These studies provide information about the mechanisms of arrhythmias which form the basis for selecting effective modes of therapy. The efficacy of therapy and prognosis can be established from electrophysiologic data. Recent progress in the techniques is evolving these studies into direct therapeutic applications by delivering various forms of energies via the catheter for ablation of arrhythmogenic substrate. The risks from these invasive procedures are acceptably low.

AN invasive electrophysiological procedure involves introduction of multipolar electrode catheters via the venous and/or arterial system, positioning of the electrodes at various intracardiac sites for recording the local electrical activity, and electrically stimulating the atria and/or ventricles. Such studies are useful diagnostically by providing information about the nature of rhythm disturbance and determining its electrophysiological mechanism; therapeutically for selection of an effective therapy, and prognostically to identify patients at risk for sudden cardiac death. In this brief review, the clinical applications of invasive electrophysiological studies will be discussed. The technical details of the procedures are beyond the scope of this discussion.

Diagnostic Uses

The indication of electrophysiologic testing to diagnose cardiac arrhythmias and conduction disorders depends not only on the nature of the arrhythmias, but also on their clinical consequences. A patient with an asymptomatic arrhythmia may warrant either no therapy or an empiric trial of medication, rather than invasive evaluation. On the other hand, a person with recurrent syncope may benefit considerably from invasive investigation of possible arrhythmic etiology and initiation of electrophysiologically guided therapy. Supraventricular tachycardia in a young, otherwise, healthy individual may produce no significant symptoms. However, the same arrhythmia in a person with a significant underlying organic heart disease, e.g., coronary artery disease, cardiomyopathy, and valvular heart disease, may result in severe symptoms by causing hemodynamic deterioration. Some arrhythmias, although infrequent, are life threatening and their recurrence cannot be predicted by noninvasive methods. Invasive electrophysiologic studies should be performed without delay for the selection of an effective therapeutic approach to prevent the recurrence of these lethal arrhythmias.

Sinus Nodal Dysfunction

Sick sinus syndrome is the term generally used for the disorders of sinus node function that result in clinically significant bradyarrhythmias. These arrhythmias can manifest as (1) sinus bradycardia (less than 60 beats per minute), (2)
sinus arrest with junctional or ventricular escape rhythms, and (3) bradycardia-tachycardia syndrome. Ambulatory Holter monitoring should be the initial approach when these arrhythmias are suspected in symptomatic patients. The documentation of spontaneous occurrence of arrhythmia with its associated symptoms suggests a casual relationship, and no further diagnostic studies are needed.

The arrhythmias caused by sinus node dysfunction can be detected in most patients during prolonged (24 to 48 hours), continuous, ambulatory electrocardiographic recording. Ambulatory Holter monitoring should be the initial approach when these arrhythmias are suspected in symptomatic patients. The documentation of spontaneous occurrence of arrhythmia with its associated symptoms suggests a casual relationship, and no further diagnostic studies are needed.

Sinus node function is evaluated during invasive electrophysiologic studies by determining the sinus node recovery time (SNRT) and sinoatrial conduction time (SACT). SNRT is evaluated by pacing from the high right atrium at various cycle lengths (e.g., 600 to 300 msec at 50 msec decrements) for 30 to 60 seconds. The SNRT is the interval between the last paced atrial depolarization and the first spontaneous atrial depolarization, resulting from the sinus node impulse. The SNRT is corrected for the patient's spontaneous sinus cycle length by subtracting this interval from the SNRT. The upper normal limit for the corrected SNRT is approximately 550 msec. The clinical significance of a prolonged SNRT appears to be partly related to the degree of prolongation. Symptoms are most likely to be resolved with pacemaker implantation in patients with SNRT greater than 2 seconds. Furthermore, the replication of the patient's symptoms during a postpacing pause, may enhance the clinical significance of prolonged SNRT. The significance of a mild prolongation of SNRT in a patient with symptoms of presyncope or syncope and a negative Holter monitor recording is unclear. The decision to implant a permanent pacemaker in such patients is a matter of clinical judgement, based on the severity of symptoms and the findings of other clinical data.

The SACT is evaluated by the delivery of atrial extrastimuli during sinus rhythm or after a burst of atrial pacing at cycle length, slightly shorter than that of the sinus rhythm. Although the SACT is a sensitive indicator of sinus node dysfunction, the finding of an abnormal SACT alone has a limited value for making a decision to implant a permanent pacemaker.

**Conduction Disorders**

The major clinical uses of invasive electrophysiologic studies are localization of the site of the atrioventricular (A-V) block when this is not possible from electrocardiographic recording, and determination of the significance of various intraventricular conduction disturbances in estimating the risk of progression to high-grade block.

In patients with complete heart block, the electrocardiographic documentation is an indication for permanent pacemaker implantation. In some patients with the appropriate rate of the escape focus, usually A-V node or His bundle, electrophysiologic studies may provide information about the stability of the escape rhythm. The recovery time of junctional escape rhythm is measured, and a prolonged recovery time will indicate instability of the rhythm and the need for implantation of a permanent pacemaker on a prophylactic basis. Localization of the site of block is essential for determining the clinical significance of second-degree A-V block and the need for permanent pacemaker implantation. Patients with block in the His-Purkinje system are usually symptomatic and require permanent pacemaker implantation. Wenckebach (Type I) A-V block usually occurs in the A-V node and has a benign course, except occasionally in the elderly patients in whom it may have clinical implications similar to Type II A-V block. Wenckebach (Type I) A-V block can be predicted from the analysis of ECG in most cases. Type II second-degree A-V block associated with bundle branch block indicates conduction disturbance and block in the His-Purkinje system. When the site of A-V block cannot be determined from the analysis of ECG, an invasive electrophysiologic study is indicated. Such indications include (1) patients with Wenckebach (Type I) second-degree A-V block and bundle branch block, (2) persistent 2:1 A-V block associated with bundle branch block, (3) possible intra-His block (Type II A-V block with normal QRS complex), and (4) syncope when A-V block is suspected.
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For patients with an intraventricular conduction disturbance (right bundle branch block, left bundle branch block, left anterior fascicular block, left posterior fascicular block), electrophysiological study provides information on conduction delay in the His-Purkinje system (HV interval prolongation). A prolonged HV interval is considered to be a marker for progression into trifascicular block. The prognostic significance of HV prolongation will be discussed later. For a diagnostic purpose, electrophysiological study is indicated only in patients with symptoms suggestive of a bradyarrhythmia (syncope or presyncope) when no other cause can be identified. In many of these patients, ventricular tachyarrhythmias, rather than A V block, may cause the symptoms.

Tachyarrhythmias
The objectives of diagnostic electrophysiologic studies in patients with tachyarrhythmias are (1) determination of the electrophysiologic mechanism of tachycardia, (2) selection of an effective, electrophysiologically guided therapy, (3) localization of the site of origin of tachycardia, and (4) evaluation of the etiology of wide QRS complex tachycardias.

Supraventricular Tachycardia
Analysis of the surface electrocardiogram during supraventricular tachycardia is usually helpful in predicting the electrophysiologic mechanism of tachycardia. Empiric drug therapy may be initiated based on this information in patients with infrequent episodes and minimal symptoms. Invasive electrophysiologic studies, however, are indicated for (1) rapid diagnosis and selection of appropriate, effective drug therapy in patients with disabling or life threatening symptoms from the tachycardia, e.g., syncope, angina, and congestive heart failure, (2) selection of non-pharmacologic forms of therapy (pacemakers, electrical ablation, surgery) for recurrent supraventricular tachycardias refractory to anti arrhythmic drug therapy, and (3) localization of the site of tachycardia to determine if it is amenable to surgical excision.

Invasive electrophysiological studies provide clinically beneficial information in patients with ventricular pre-excitation. Although paroxysmal supraventricular tachycardia in these patients can be managed by noninvasive approaches, electrophyslogic studies identify patients at high risk from more serious arrhythmias in these patients. Atrial fibrillation occurs in 20% of patients with Wolff-Parkinson-White syndrome. If the antegrade refractory period of the accessory pathway is short, conduction via the anomalous connection will result in very rapid ventricular response. In addition to severe symptoms due to hemodynamic compromise, this arrhythmia can degenerate into ventricular fibrillation. Electrophysiological studies are necessary in such patients to guide medical or surgical therapy. Thus, electrophysiological studies are definitely indicated in patients with Wolff-Parkinson-White syndrome and atrial fibrillation, but may also be preferable in patients with supraventricular tachycardia.

In the latter group of patients, in spite of the absence of electrocardiographic documentation of atrial fibrillation, electrophysiologic studies can identify those at risk for degeneration of supraventricular tachycardia into atrial fibrillation. The role of invasive electrophysiological studies in asymptomatic patients with evidence of ventricular pre-excitation on the resting electrocardiogram is not settled and is controversial. Although most of these patients have a good prognosis, atrial fibrillation with rapid ventricular responses and ventricular fibrillation have been reported. The loss of pre-excitation in the resting electrocardiogram during exercise or after the administration of procainamide may identify accessory pathways with long ante grade refractory periods which carry low risk. Electrophysiologic studies may be indicated for a definitive identification of persons at high risk in certain job situations, e.g., airline pilots.

Wide QRS Complex Tachycardias
Differentiation between supraventricular tachycardia with aberrancy and ventricular tachycardia has important clinical implications. Some electrocardiographic criteria may be helpful, but in many cases the differentiation may be difficult. Electrophysiologic testing will identify the type of arrhythmia by determining the relationship between the atrial, His bundle, and ventricular depolarizations. Furthermore, the
mode of initiation of tachycardia and the response to atrial and ventricular stimuli provide additional electrophysiologic information.

**Ventricular Tachyarrhythmias**

Invasive electrophysiologic studies are being widely used in the diagnosis and selection of therapy for recurrent ventricular tachyarrhythmias occurring without identifiable, transient, and reversible factors, e.g., ischemia, electrolyte imbalance, and drug toxicity. The mechanism of such arrhythmias is presumed to be due to re-entrant circuits, resulting from the underlying heart disease (scar from infarction and cardiomyopathy) in most of the cases. Programmed ventricular stimulation is used to initiate and terminate these arrhythmias. However, the rate of inducibility, sensitivity, and specificity are dependent on the nature of the patient's spontaneously occurring arrhythmia, underlying heart disease, and the stimulation protocol.

An episode of ventricular tachycardia may be as short as three complexes or it may last longer, necessitating immediate intervention (intravenous drugs or electrical cardioversion) to terminate the arrhythmia. Various definitions were used for sustained tachycardia, for example, greater than 15 seconds or greater than one minute. These different criteria for the definition of sustained ventricular tachycardia caused problems when comparing the results of published data regarding the inducibility of clinical arrhythmias and the sensitivity and specificity of induced arrhythmias. Furthermore, different stimulation protocols (number of extrastimuli, sites of stimulation, strength of stimulus) added to this dilemma. However, sustained ventricular tachycardia is now defined as that lasting more than 30 seconds in most laboratories. In addition, the stimulation protocols have some similarities, although they are still not uniform. The inducibility of sustained monomorphic (same QRS morphology throughout the episode) ventricular tachycardia, in spite of some differences in the stimulation protocols, is approximately 90% with sensitivity and 85% with specificity. Recurrent sustained ventricular tachycardia usually occurs sporadically, therefore, empiric therapy using recurrence of tachycardia as an endpoint may cause significant delay in finding a successful therapy. Furthermore, any single drug is usually effective in only one-third of the patients. Thus, the chance of recurrence of tachycardia is very high and it may be life threatening. Invasive electrophysiologic studies can identify the failure or success of antiarrhythmic drugs in a much shorter time (1 to 2 weeks) and are preferred over empiric approaches in patients with sustained monomorphic ventricular tachycardia. The use of electrophysiologic studies in patients with monomorphic, as well as polymorphic, non-sustained ventricular tachycardia has no established clinical significance.

Patients surviving from out-of-hospital cardiac arrest have a very poor prognosis, with mortalities of 20% to 30% at 1 year and 30% to 40% at 2 years. Ventricular fibrillation is the presenting arrhythmia in most of the cases, although the earliest arrhythmia may be ventricular tachycardia which degenerates into ventricular fibrillation. Programmed ventricular stimulation can induce ventricular tachyarrhythmias in 30% to 75% of the survivors of out-of-hospital cardiac arrest. In spite of the lower inducibility, electrophysiologic studies are warranted in survivors of out-of-hospital cardiac arrest, due to the high risk of recurrence of ventricular fibrillation. Drug therapy, guided by the results of electrophysiologic testing, may be an effective means of preventing the recurrence of this lethal ventricular arrhythmia.

**Evaluation of Symptoms**

The etiology of transient neurologic and cardiac symptoms may not be identified by extensive neurologic and cardiac evaluation, including ambulatory Holter monitoring. Electrophysiologic testing may expose arrhythmias or conduction abnormalities which may explain the symptoms. The most common application is in patients with unexplained syncope. These prospective studies have demonstrated possible arrhythmic causes of syncope in 12% to 68% of such patients. The highest diagnostic yield is in patients with syncope and clinical evidence of organic heart disease. The need for identifying the cause of syncope is further emphasized by the fact that there is 24% incidence of sudden death in patients with a cardiovascular etiology, compared with 4% in patients with a non-cardiovascular cause. Furthermore, syncope rarely recurs after
the initiation of electrophysiologically guided therapy in patients with an identifiable etiology and also in those with a negative study. The evaluation of other possible arrhythmia-related symptoms, such as palpitations and dizziness by electrophysiologic testing, should be attempted only after extensive noninvasive investigation has failed and the symptoms are recurrent and disabling.

Therapeutic Uses

Invasive electrophysiologic studies have contributed significantly in selecting effective therapies because of the accurate information about the diagnosis, and more importantly, identifying electrophysiologic mechanisms of cardiac arrhythmias. Furthermore, the ability to induce and terminate the arrhythmia reproducibly provides an excellent opportunity to assess the efficacy of antiarrhythmic therapy.

Medical Therapy

The ability of a drug to prevent the induction of tachycardia which is inducible in the drug-free state is used as the endpoint for efficacy. The efficacy of antiarrhythmic drugs, determined by such electropharmacologic testing, has been shown to correlate with long-term efficacy in patients with recurrent sustained ventricular tachycardia.39,40 Electrophysiologically guided antiarrhythmic drug therapy in survivors of out-of-hospital cardiac arrest has been reported to be superior to other approaches in some studies.31,34 This issue is not completely settled and prospective, randomized, controlled studies are in progress. The efficacy of therapy, selected by electropharmacologic testing, has also been shown in patients with paroxysmal supraventricular tachycardia.41,42

Pacemaker Use

Electrophysiologic studies provide useful information in determining the need to implant permanent pacemaker for bradyarrhythmias, if such a decision is not possible from the results of noninvasive studies. In addition, hemodynamic assessment of different pacing modalities can be helpful for selection between single and dual chamber pacemakers.43 Recent technological advances have caused the development of antitachycardia pacemakers with the ability to automatically sense and terminate the tachycardia. Various pacing techniques are used in the electrophysiology laboratory,44 and these are also applied in the treatment of patients with permanent anti-tachycardia pacemakers.45,46 Extensive preimplant electrophysiologic testing, by repeated induction and termination of tachycardia, is used to select the most suitable pacing mode in patients who are candidates for this type of therapy. Another use of tachycardia termination, by electrical form of therapy, has been the development of the automatic, implantable, cardioverter defibrillator and its use in the survivors of out-of-hospital cardiac arrest has resulted in significant reduction in mortality.47 The function of the device must be tested electrophysiologically, by inducing the ventricular tachyarrhythmias at the time of implantation.

Surgical Therapy

The focus of a tachyarrhythmia can be localized by electrophysiologic testing. Surgical excision of a part of the re-entry circuit will terminate the arrhythmia and prevent the recurrence of tachycardia without drugs in most cases. Electrophysiologic studies identify the patients who fail other modes of therapy (drugs and pacemakers) and are suitable candidates for surgery. Surgical excision of accessory pathways, located by preoperative electrode catheter mapping in the electrophysiology laboratory and confirmed by intraoperative epicardial mapping, has become an established technique.48 Electrophysiologically guided surgical excision of the areas of the myocardium, essential for re-entry causing recurrent sustained ventricular tachycardia, is another promising new form of therapy. These areas are usually located in the endocardial border zone of the myocardial scar caused by a previous myocardial infarction and aneurysm formation. Simple resection of aneurysm results in only 50% reduction in the recurrence of tachycardia,49 compared to less than 30% by mapping guided endocardial resection.50 Preoperative endocardial catheter mapping is performed in the electrophysiology laboratory during an induced episode of ventricular tachycardia. Induction of tachycardia may sometimes be difficult during surgery, and the results of preoperative mapping compare favorably with direct intraoperative mapping.51
Catheter Ablation

The role of invasive electrophysiological studies is expanding, from diagnostic uses alone to interventional applications. Various forms of energy (electrical, radiofrequency, and laser) can be delivered via the electrode catheters and applied to the intracardiac structures. The objective of this procedure is non-surgical ablation of the tissue which forms anatomical and electrophysical substrate for arrhythmias, refractory to medical therapy. A wide experience has been gained with the use of synchronized direct current. The use of radiofrequency and laser is promising but still experimental. Successful ablation of the AV node-His Purkinje region has been reported with an efficacy of over 70% and associated with very low morbidity and mortality.52 A permanent pacemaker implantation is required after successful ablation which causes complete heart block. Ablation of the AV node-His bundle (AV junction) is indicated for (1) arrhythmias in which the AV junction is a part of the re-entry circuit (e.g., supraventricular tachycardias due to AV nodal re-entry and accessory pathways) and (2) supraventricular tachyarrhythmias with rapid anterograde atrioventricular conduction via the AV node and His bundle (e.g., atrial tachycardia, atrial flutter, and fibrillation). Ablation of atroventricular accessory pathways has not yet developed into a clinically acceptable procedure because of significant complications such as rupture of the coronary sinus causing pericardial tamponade. 53 The experience in the use of catheter ablation for ventricular tachycardia is quite limited and is associated with a much lower success rate and potential for serious complications.54

Prognosis

The data obtained during invasive electrophysiologic studies have been used to determine the prognostic significance of cardiac arrhythmias. The first such attempts were made to identify those at high risk for complete heart block from patients with conduction disorders. 15,55,56 This determination was based on the measurement of the HV interval (conduction time via the His Purkinje system) during sinus rhythm. The sensitivity of a prolonged HV interval was about 80%, 32% to 64% specificity, and a very low positive predictive value of 5% to 7%.
The prognostic value of electrophysiologic testing in survivors of sudden cardiac death has been reported in several studies.31-34,40 Noninducibility of ventricular tachyarrhythmias predicts a low rate of recurrence in one year, and continued inducibility after medical or surgical therapy is associated with a very high recurrence rate. Furthermore, the response to therapy determined by electrophysiologic testing has been shown to be an independent predictor of survival in patients with ventricular tachyarrhythmias.57

The inducibility of ventricular tachyarrhythmias during electrophysiologic testing has recently been used to identify groups at high risk for sudden cardiac death in patients surviving myocardial infarction. 58-60 However, the conflicting results of these studies have left the matter unresolved.

Complications

The risk of invasive electrophysiologic studies are small.61,62 Data gathered from six major institutions showed five deaths in 4,015 patients (0.12%) undergoing 8,545 studies (0.06%); other complications included cardiac perforation in 19, major hemorrhage in 4, arterial injury in 8, and venous thromboses in 20 patients.62 These complications and risks are similar to those in other diagnostic cardiac catheterization procedures. The addition of interventional procedure, e.g., ablation, will increase the incidence of complications.

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References