Hybrid Therapies for Ventricular Arrhythmias

PAOLO DELLA BELLA and STEFANIA RIVA

From the Arrhythmia Department, Institute of Cardiology, University of Milan, Centro Cardiologico Monzino, IRCCS, Milan, Italy

In recent years several trials demonstrated the efficacy of implantable cardioverter-defibrillation (ICD) therapy in reducing cardiac and total mortality in patients affected by rapid ventricular tachycardia (VT) and/or ventricular fibrillation. Nevertheless, ICD do not prevent arrhythmia recurrences, thus being a palliative and not a curative treatment modality. The tolerance to ICD therapy varies greatly, and within individuals, this leading to a nonuniform acceptance of this form of therapy. The very frequent occurrence of VT, defined as an arrhythmic storm, may be a life threatening condition. The majority of ICD patients is under antiarrhythmic drug therapy, to reduce episodes of VT or to make antitachycardia pacing more effective by slowing the tachycardia rate. Drug therapy, however, may cause additional problems, and does not represent the optimal solution. The prevention of VT and/or ventricular fibrillation episodes and excessive ICD therapy, remains a worthwhile goal. Radiofrequency catheter ablation (RFCA) is a curative approach, and can be expected to reduce the frequency of recurrent VT episodes in the majority of patients. The combination of these treatment modalities (ICD and RFCA) is often described as hybrid therapy, implying that the two treatments act providing some form of synergism. In experienced centers, RFCA is now performed, regardless of whether the VT rate is rapid and/or is hemodynamically unstable. Newer mapping and ablation techniques are now available, enhancing the acute success rate of the procedure. In this review the most recent application of VT catheter ablation and the use of advanced mapping and ablation techniques will be discussed. (PACE 2006; 29:S40–S47)

Until recently, antiarrhythmic drugs were the treatment of choice in the majority of patients with recurrent ventricular tachycardia (VT), whatever the underlying heart disease. However, within 2 years more than 40% of patients treated for sustained VT experience recurrences.1

Furthermore, the risk of sudden cardiac death remains high despite drug therapy, especially in patients with depressed left ventricular function and/or hemodynamically poorly tolerated VT.2 Serious side effects frequently limit the efficacy of antiarrhythmic drugs. The most effective drug, amiodarone, produces adverse effects within 5 years in almost 75% of patients, although not always serious enough to require withdrawal of the drug.

Alternative treatment options are surgical ablation, placement of an implantable cardioverter-defibrillator (ICD), and radiofrequency catheter ablation (RFCA). Antiarrhythmic surgery, e.g., endocardial resection, is highly effective in selected cases in limiting recurrences by removal of large segment of subendocardium (often more than 30 cm²). However, it is a major intervention associated with increased incidence of heart failure in the follow-up period.3–6

During the last decade, ICDs have proved superior to antiarrhythmic drug therapy for prolonging survival and preventing sudden cardiac death in survivors of sustained ventricular arrhythmias.7–9 Subsequently, ICDs were shown to be prognostically beneficial for primary prevention of ventricular arrhythmias in patients with coronary artery disease,10,11 and their rate of implantation is rapidly growing all over the world. Although ICDs prolong survival, they do not prevent VT recurrences, thus being a palliative and not a curative treatment. Within a year of implantation, 68% of patients experience arrhythmia recurrences7; sinus rhythm may be restored either by painless antitachycardia pacing or by an uncomfortable high voltage shock. Antitachycardia pacing is usually used for most monomorphic haemodynamically tolerated and slower VTs. In case of unstable VT or when pacing fails to restore sinus rhythm, a low energy cardioversion shock or defibrillation shock are required.

Individual tolerance of ICD shock varies, but frequent shocks are poorly tolerated virtually by all patients and significantly worsen the quality of life.12 In some cases, though, recurrent or incessant VT causes multiple appropriate ICD shocks during a short period of time. This condition is known as arrhythmic storm, i.e., three or more episode of VT separated by more than 5 minutes during 24 hours that result in proper shocks by the ICD.13 The incidence of this event ranges between 10 and 25%. It poses a significant threat on patient status and survival14–16 A recent study by Mitchell et al.,17 reports, indeed, that the mode of death in ICD patients is still sudden in 28% of cases, and that the most common mechanism is ventricular fibrillation or VT treated with appropriate shocks.
and followed by electromechanical dissociation. Many of these deaths may result from ICD shocks that are too frequent, too closely spaced, or too large in magnitude. This hypothesis is supported by reports of severe haemodynamic deterioration after internal DC shocks during ICD implantation, particularly in patients with poor left ventricular function.\textsuperscript{18}

Adequate adjustment of ICD programming and the use of antitachycardia pacing algorithms that reduce the number of shock to a tolerable level are important aspects of caring for this kind of patients. However, despite a multitude of programmable options, this is not an easy task. Many patients with episodes of VT terminated by antitachycardia pacing also receive shocks occasionally.\textsuperscript{19}

At least 50\% of patients with an ICD implanted receive concomitant antiarrhythmic drug therapy to reduce episodes of VT or to make antitachycardia pacing more effective by slowing the tachycardia rate.\textsuperscript{20} Drugs therapy, however, may cause additional problems, and sometimes render antitachycardia pacing less effective rather than more effective. It is well known that some drugs, notably amiodarone, may increase the energy required for defibrillation. Thus, repeat defibrillation testing is necessary when drug therapy is instituted, to be sure that the maximal ICD output provides an adequate safety margin for defibrillation.

The decreased incidence of VT induced by antiarrhythmic drugs may have adverse effects: the tachycardia rate may slow below the detection rate of the ICD, or fall into the range where sinus tachycardia can also occur, making diagnosis difficult. Furthermore, drugs may slow the sinus rhythm, causing the patient to be paced, producing adverse haemodynamic effects from right ventricular pacing; or induce proarrhythmic effects.\textsuperscript{21}

Thus, the development of treatment for the prevention of VT and/or ventricular fibrillation episodes and excessive ICD therapy, remains a worthwhile goal.

RFCA is a curative approach, and can be expected to reduce the frequency of recurrent VT in more than 70\% of patients.\textsuperscript{19,22–25} The procedure is indicated in the majority of cases in patients with an ICD previously implanted, in postinfarction cardiomyopathy as well as in idiopathic dilated cardiomyopathy. The long-term efficacy of the ablation procedure in this setting is well established since it reduces or abolishes ICD discharges.

In experienced centers, RFCA is now performed, regardless of whether the VT rate is rapid and/or is hemodynamically unstable. Newer mapping and ablation techniques are now available enhancing the acute success rate of the procedure.

Conventional Mapping and RFCA of VT

Catheter ablation performed by a single catheter approach and conventional mapping technique achieves a high rate of acute and long-term success in patients with tolerated postinfarction VT.\textsuperscript{24,26}

Optimal localization of the target area requires reproducible induction of the VT in the electrophyslogic laboratory and hemodynamic stability while endocardial mapping is undertaken to precisely localize the critical area(s) of re-entrant circuit. Targets for ablation are identified by the recording of isolated mid-diastolic potentials, earliest activation of the local electrograms, pace mapping in sinus rhythm, and/or the presence of concealed entrainment (Fig. 1).

The same mapping and ablation techniques, the same acute and long term success rate can be performed and obtained in patient with stable VT causing excessive ICD therapy.\textsuperscript{24,25}

Silva et al., recently reported that conventional RFCA is highly effective in controlling arrhythmic storm of tolerated VT in patients with previously implanted ICD.\textsuperscript{13} They performed 18 procedures in 15 patients, the success rate being 80\%, using conventional and/or cooled-tip catheters. In two patients, with a failed endocardial approach and in one patient with left ventricular apex aneurysm and a thrombus, RFCA was successfully performed with epicardial approach. The extensive involvement of the epicardium in the genesis of VT, particularly in idiopathic dilated cardiomyopathy, can be documented in almost 30\% of patients undergoing catheter ablation, as recently demonstrated by Soejima et al.\textsuperscript{27}

Electrical storms of monomorphic and tolerated arrhythmias are, however, unusual as the situation usually involves rapid and hemodynamically unstable VT. Silva et al., demonstrated that kind of electrical storms in only 3\% of patients with ICD. The majority of patients, particularly those with electric storms, presented with pleomorphic or untolerated forms of VT requiring three dimensional mapping systems or hemodynamic support that allows conventional point to point mapping techniques.

Conventional Catheter Ablation with the Aid of a Percutaneous Cardiopulmonary Support

Percutaneous cardiopulmonary support (pCPS) has proven to be a technique of value in high risk coronary patients undergoing percutaneous balloon angioplasty and in the management of cardiac emergencies characterized by acute lowering of cardiac output.\textsuperscript{28–30}

RFCA coupled with pCPS system has been attempted in one emergency setting (incessant sustained untolerated VT) in a series of 17 consecutive
Figure 1. Conventional catheter ablation of tolerated postinfarction ventricular tachycardia (VT). Panel A: 12-lead ECG showing the clinical arrhythmia presenting as iterative VT. Panel B: simultaneous recording of surface ECG and electrograms from the ablation site with low amplitude mid-diastolic potential indicated by arrow. Panel C: when the radiofrequency is delivered at the ablation site, termination of VT occurs in few seconds. RF = radiofrequency.
patients at our institution. In all cases the arrhythmia was related to coronary artery disease, idio-pathic dilated cardiomyopathy, or arrhythmogenic right ventricular dysplasia (mean left ejection fraction 35%). Fourteen of them experienced excessive ICD therapies (3–15 shocks/day), and three drug refractory VT associated with hemodynamic collapse. In the electrophysiologic laboratory we induced 58 episodes of sustained monomorphic VT (mean cycle length 317 ± 43 ms); 54/58 VTs were hemodynamically unstable requiring activation of pCPS to achieve and maintain a mean blood pressure of 79 ± 9 mmHg. Arterial and femoral sheats (15 and 17 Fr) were placed in the left femoral artery and vein, and connected to a pump coupled with an oxygenator and a heat exchanger; blood flow rates ranged from 1 to 6 L/min.

Termination and prevention of inducibility was obtained in 77% of VTs; acute clinical success was obtained in 59% of patients. We recorded few periprocedural complications: one patient experienced transient left ventricular stunning following pCPS interruption, one a periprocedural transient ischemic attack, and two a mild form of anemia.

At a mean follow up of 36 months (range 9–51) five patients (29%) remained free of recurrences of the ablated VTs; six experienced recurrences but with a significant reduction in the number of ICD therapies (1–5 shocks/month). No late adverse events related to the pCPS institution were observed.

In our experience pCPS has proved to be a safe and efficacy alternative strategy to map and ablate untolerated VT. It may not represent a procedural alternative to electroanatomic or noncontact mapping, but rather a possibility of performing catheter ablation, otherwise not feasible, in particular and emergency clinical setting like excessive ICD therapies or fast recurrent VT early after myocardial infarction or left ventricular surgery.

**Noncontact Mapping (Endocardial Solutions)**

Noncontact mapping allows an accurate reconstruction of the virtual three dimensional geometry of the left or right ventricle and the possibility to simultaneously map the entire endocardial surface, through the placement of a balloon mounted multielectrode array catheter. This system offers the possibility of an off-line analysis of
Figure 2. Linear ablation of postinfarction ventricular tachycardia (VT) guided by CARTO mapping. Panel A: Bipolar voltage map obtained during sinus rhythm. VTs exit points are indicated by arrows. Red circles represent the lesion sites encircling the edge of the scar area. Panel B: successful linear ablation demonstrated by lack of capture by pacing from scar.
each desired beat during either sinus rhythm or VT. Significant information can be obtained during VT on critical isthmus, and during sinus rhythm on the presence of areas of low voltage or scarring tissue by the analysis of activation pattern. Limitation of this mapping system relay on the need for two catheters in the left ventricle, and on the difficult encountered sometimes to attain a stable position of the balloon catheter. More over, the accuracy of the system decrease at increasing distance of the multi electrode array from the endocardium, as it may occur in dilated cardyomiopathy.

The use of noncontact system mapping allows RFCA of untolerated and nonsustained VT in different setting of underlying heart disease with high rate of acute an long-term success in patients with or without ICD previously implanted.33–35

Preliminary experience at our institution, reported in 2002, reported the use of noncontact mapping system to guide RFCA in 17 patients with poorly tolerated VT in prior myocardial infarction (11 patients), arrhythmogenic right ventricular dysplasia (3 patients), and idiopathic dilated cardiomyopathy (3 patients).36 Four patients underwent to RFCA for excessive ICD therapy discharge. Twenty seven episodes of VT were induced during the procedures, and a satisfactory mapping could obtained in all episodes. Identification of the exit point or the diastolic pathway guide the ablation procedure. The overall acute success rate was 64%, being significantly greater when targeting the diastolic pathway (78%) as compared to the exit point (16%) of the VT. Over the long term the recurrence rate was lower when prevention of all VT was achieved at the postablation electrophysiological study.

**Electro Anatomic Mapping System (CARTO)**

Catheter ablation of unstable VT can be performed during sinus rhythm with the guide of electroanatomic mapping system (CARTO).22,37,38 The system allows a three-dimensional reconstruction of the left ventricle coupled with both a voltage map (defining the scar area) and the activation map (localizing areas of latest activation during sinus rhythm) and displaying pattern of endocardial activation during VT22 whenever the arrhythmia is tolerated.

Sra et al., recently show that electro anatomic mapping is helpful in identifying sites for catheter ablation in 19 patients with prior myocardial infarction and refractory VT causing multiple ICD shocks (4–62 shocks during the 12 week preablation period).39 After the procedure, they observed that 66% of patients had no recurrence of VT during a mean follow up of 26 ± 8 weeks.

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<th>Table I. Baseline Population Characteristics of Patients Undergoing VT Catheter Ablation</th>
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Pts = patients; VT = ventricular tachycardia; MI = myocardial infarction; IDCM = idiopathic dilated cardiomyopathy; ARVD = arrhythmogenic right ventricular dysplasia.

**Catheter Ablation of VT at our Institution**

From January 2002 to March 2005 we performed RFCA in 139 patients with left VT (107 pts with prior myocardial infarction; 32 patients with idiopathic dilated cardiomyopathy) and in 40 patients with right VT (arrhythmogenic right ventricular dysplasia, ARVD). About 80% of them have an ICD previously implanted and were referred to our Institution for VT causing excessive discharge of therapy (including true arrhythmic storm 28% of the cases) (Table I). The characteristics of the ventricular arrhythmias, clinical and induced during EP study, are shown in Table II.

RFCA guided by electroanatomic mapping system CARTO was performed in 23% of patients with previously implanted ICD and recurrent postinfarction VT. However, the percentage reach 100% in the last year; this data supporting the fact that majority of this kind of patients need nonconventional mapping system cause of the presence of untolerated and/or pleomorphyc VT. An example of RFCA of postinfarction VT in an ICD patients is shown in Figure 2: linear ablation was performed to encircle the edge of the

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Abbreviations are as in Table I.
scar area during sinus rhythm; after effective ablation no capture can be obtained at the VT exit site.

Acute results of the procedures were shown in Table III. According to the results of the postprocedural electrophysiological study the acute outcome of the RFCA was defined as follows: Class A, interruption of the index VT and of all the induced VTs, and prevention of induction of any sustained ventricular arrhythmia; Class B, interruption of the index and/or other induced VTs, but persistent inducibility of other sustained VTs; Class C, failure at terminating the index VT.

Over the long term, prevention of any ICD therapy was obtained in 72% of patients with prior myocardial infarction, 64% of patients with idiopathic dilated cardiomyopathy, and 75% of patients with ARVD. In the remaining patients, however, a significant (more than 85%) reduction of the ICD discharge was obtained. Furthermore, when RFCA was guided by nonconventional mapping the acute success rate was still greater: 80% in patients with myocardial infarction and idiopathic dilated cardiomyopathy, and 72 in ARVD patients. Details are shown in Table IV.

**Conclusions**

The large diffusion of ICD has dramatically reduced sudden cardiac death from rapid VT and/or ventricular fibrillation. Furthermore, it is contributing to the growth of a novel population of patients with frequently recurrent VTs, and originating a broad clinical spectrum ranging from unpleasant frequent ICD shock interventions to life threatening arrhythmia storms. In this setting the hybrid therapy may be viewed as a synergistic form of treatment characterized by a combination of: (1) a potentially curative catheter ablation aimed at the modification of the arrhythmia substrate to eliminate or decrease the potential for arrhythmia recurrences, (2) a backup ICD, as a protection against the risk of sudden death due to unpredictable or untreatable sudden events.

### References

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