Infarct Artery Patency Predicts Outcome of Serial Electropharmacological Studies in Patients With Malignant Ventricular Tachyarrhythmias

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Background. **Surviving myocardial cells near the infarct border zone form the arrhythmogenic substrate for sustained ventricular tachycardia (VT) in humans. Infarct-related artery (IRA) patency may modulate the electrophysiological function of this arrhythmogenic substrate and its response to antiarrythmic drug therapy. We postulated that effective antiarrhythmic drug therapy selected during serial electrophysiological studies in patients with VT after a myocardial infarction would be identified more frequently when the IRA is patent than when chronically occluded.**

Methods and Results. **Consecutive patients ($n=64$) with documented coronary artery disease and remote myocardial infarction presenting with spontaneous sustained VT or ventricular fibrillation (VF) were studied. These patients underwent 4±2 electropharmacological studies identifying effective antiarrhythmic drug therapy in 16 (25%) patients. Drug responders did not differ significantly from nonresponders in demographic, electrocardiographic, angiographic, or hemodynamic measurements. A patent IRA was associated with antiarrhythmic drug response significantly more frequently than was an occluded IRA (45% versus 9%, $p=0.001$). Patency of the IRA was the only independent predictor of response to antiarrhythmic drug therapy in this study population. The sensitivity and specificity of using a patent IRA to predict successful drug testing were 81% and 67%, respectively.**

Conclusions. **The outcome of electropharmacological studies was predicted by the patency of the IRA. A patent IRA was associated with a greater probability of finding effective drug therapy. (*Circulation* 1993;87:764–772)**

KEY WORDS • **artery, infarct-related** • **tachycardia, ventricular** • **drugs, antiarrhythmic** • **electropharmacological studies**

Patients with sustained ventricular tachycardia (VT) and ventricular fibrillation (VF) without reversible causes are at high risk of subsequent sudden cardiac death.[1,2] After 1 and 2 years of follow-up, 25% and 39% of these patients, respectively, would experience recurrences of VT/VF in the absence of effective therapy.[3] Several therapeutic options are currently available for the management of such patients: These include antiarrhythmic drugs, implantable devices, and transcatheter or surgical ablative procedures.

For many patients, the initial therapeutic approach is an attempt to identify effective antiarrhythmic drug therapy. Therapy with an antiarrhythmic drug that renders VT/VF noninducible is associated with a more favorable outcome than drug therapy during which VT/VF remains inducible.[3–5] This invasive approach selects therapy that prevents sustained VT/VF better than does the noninvasive approach of suppression of spontaneous ventricular arrhythmia.[6,7] However, the invasive approach does have certain limitations. The probability of finding effective drug therapy during serial electropharmacological trials is low: 23%, 9%, and 8% at the first, second, and third drug trials, respectively.[8] Effective antiarrhythmic drugs can be identified for no more than 40–50% of these patients.[9–11] Furthermore, multiple electropharmacological studies can be time consuming and have inherent risks.[12] Thus, before undertaking a series of electropharmacological trials, it would be useful to know which patients are likely or unlikely to respond.

Previous studies have indicated that certain patient and electrophysiological characteristics are associated with a higher probability of successful outcome.[13–16] However, the effect of infarct-related artery (IRA) patency on the outcome of serial electropharmacological studies has not been studied previously. It is possible that antiarrhythmic drug delivery would be greater to the

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arrhythmogenic substrate in the peri-infarct zone with a patent IRA than with an occluded IRA. We hypothesized that the probability of finding effective drug therapy would be greater in patients with a patent IRA than in those with an occluded IRA. Accordingly, the purpose of the present study was to assess whether the outcome of serial electropharmacological studies in a patient with sustained VT/VF is related to the patency of the IRA.

Methods

Patients

Patients with sustained VT/VF that was not due to reversible causes were considered potential candidates for this study. Patients were eligible when they met all of the following inclusion criteria: 1) coronary artery disease and history of remote myocardial infarction, 2) spontaneous and inducible sustained VT/VF at a baseline antiarrhythmic drug-free electrophysiological study, 3) serial electropharmacological studies were performed, and 4) cardiac catheterization and coronary angiography were performed.

Hemodynamic and Angiographic Assessment

Cardiac catheterization and coronary angiography were performed before electrophysiological study. Angiographic assessment of coronary anatomy was performed in multiple views. Left ventriculography was performed in both right and left anterior oblique projections. Cardiac volumes were determined using the single-plane area–length method,[17] and cardiac output was calculated as the product of stroke volume and heart rate. Patients requiring coronary artery bypass surgery or percutaneous transluminal coronary angioplasty had the procedure performed before electrophysiological study. The patency of the IRA and the presence or absence of collateral vessels were assessed by a single experienced angiographer (M.T.) who was blinded to the outcome of the serial electropharmacological studies. Left ventricular ejection fraction (LVEF) was determined by radionuclide ventriculography in an antiarrhythmic drug-free state.

Electrophysiological Studies

Baseline electrophysiological studies were performed using standard techniques.[6–8] Cardiac stimulation was performed at twice diastolic threshold using stimuli 2 msec in duration. Our ventricular stimulation protocol consisted of introduction of one, two, and three premature ventricular extrastimuli after eight-beat drive trains at pacing cycle lengths of 600, 500, and 400 msec. Burst pacing consisted of six and 12 beats of rapid pacing starting at 300 msec. The cycle length of burst pacing was decreased by 10 msec until loss of 1:1 ventricular capture. The protocol was first applied at the right ventricular apex and when necessary was repeated at the right ventricular outflow tract. The end point of the study was completion of the stimulation protocol or reproducible induction of sustained VT/VF.

Electropharmacological studies were performed after initiation of antiarrhythmic drug therapy for at least five drug half-lives. At each subsequent electropharmacological study, electrode catheters were reinserted. The stimulation protocol that was used during the baseline study was applied only at the site where sustained VT/VF was induced during the baseline study.[18] Antiarrhythmic drugs were tested until an effective therapy was identified or until at least three drug trials had been evaluated.[8] Drug trials included at least a class IA agent (usually quinidine), a combination of class IA and class IB agents (usually quinidine/mexilitine), and a class III agent (usually sotalol). Propafenone and other investigational drugs were less frequently used. When an effective drug therapy was not identified, patients were treated with empiric amiodarone therapy, surgical therapy, or implantation of an automatic cardioverter-defibrillator.

Angiographic Definitions

The degree of myocardial perfusion from the IRA was graded using the classification of the Thrombolysis In Myocardial Infarction (TIMI) Trial[19]: grade 0, no perfusion with no anterograde flow beyond the site of obstruction; grade 1, contrast fails to opacify coronary bed distal to the obstruction; grade 2, contrast opacifies the distal coronary bed although contrast filling or clearance is delayed; and grade 3, normal pattern of contrast filling. The IRA was considered patent when there was TIMI grade 2 or 3 anterograde flow. Collateral vessels were considered to be present when the artery distal to the occlusion was moderately or completely opacified. For this study, the IRA was also considered patent if the vessel had been revascularized by successful coronary artery bypass surgery or percutaneous transluminal coronary angioplasty. In a few patients with two infarction sites, VT was assumed to arise as a consequence of the more recent infarction, and the appropriate coronary artery was considered to be the IRA.

A coronary vessel was considered significantly diseased when its luminal diameter was narrowed by $\geq$60%. A myocardial infarction was localized to the site of a wall motion abnormality. A left ventricular aneurysm was considered present when the infarcted segment showed dyskinetic movement during systole.[20,21]

Electrophysiological Definitions

VT was defined as five or more consecutive ventricular beats with a cycle length <500 msec. VT lasting >30 seconds or requiring cardioversion because of hemodynamic collapse was considered sustained. Drug therapy was considered effective when it prevented the induction of four or more repetitive ventricular responses. Ventricular effective and functional refractory periods were determined using the extrastimulus technique and standard definitions.[22] Differences in ventricular refractory periods were compared in responders on their effective antiarrhythmic drug with nonresponders on their first ineffective antiarrhythmic drug.

Data Analysis

Continuous data are presented as mean±1 SD. Unpaired data were compared by two-tailed t test for continuous variables and by χ^2 analysis or Fisher's exact test for comparison of proportions. Variables tested as univariate predictors of response to oral antiarrhythmic drug therapy were age, sex, presence of left ventricular aneurysm, location of myocardial infarction, presence of Q waves on the surface ECG, history of cardiac arrest, number of diseased coronary arteries, patent IRA, collaterals to IRA, LVEF, VT cycle length, ven-

TABLE 1. Clinical, Angiographic, and Hemodynamic Characteristics of the Study Group

Number	64
Age (years)	61±10
Male (%)	60 (94%)
LVEF	0.32±0.14
VT cycle length (msec)	264±54
Number of drug trials	4±2
Presenting arrhythmia	
Sustained VT	47 (73%)
VF	17 (29)
Number of diseased vessels	
1	25 (31%)
2	22 (38%)
3	17 (31%)
Mean	2±1
Infarct location	
Anterior	27 (42%)
Inferior	28 (44%)
Two sites	9 (14%)
LV aneurysm	10 (16%)
IRA patent	29 (45%)
IRA occluded	35 (55%)
Collateral vessels to IRA	
Present	38 (59%)
Absent	26 (41%)
LVEDP (mm Hg)	17±8
Cardiac output (L/min)	5.2±1.9
End-diastolic volume (mL)	218±79
End-systolic volume (mL)	143±71
Stroke volume (mL)	76±30
EDV index (mL/m^2)	110±37
ESV index (mL/m^2)	72±36
Stroke volume index (mL/m^2)	40±20

Data are mean±1 SD. LVEF, left ventricular ejection fraction; VT, ventricular tachycardia; VF, ventricular fibrillation; LV, left ventricle; IRA, infarct-related artery; LVEDP, left ventricular end-diastolic pressure; EDV, end-diastolic volume; ESV, end-systolic volume.

tricular effective and functional refractory periods, and cardiac hemodynamic parameters. Univariate predictors of outcome having a value of $p<0.10$ were identified, and multivariate stepwise logistic regression analysis was applied.[23] A two-tailed value of $p<0.05$ was regarded as statistically significant.

Results

Patient Characteristics

We identified 64 consecutive patients who fulfilled all the four inclusion criteria as listed in "Methods." This study group is characterized in Table 1. These patients were generally men with low LVEF. Most of the patients had at least two-vessel coronary artery disease. All patients had a history of remote myocardial infarction. Only nine patients (14%) had suffered two previous myocardial infarctions. The remaining 55 patients had a single previous myocardial infarction.

Responders and Nonresponders to Drug Therapy

Effective antiarrhythmic drug therapy could be identified for 16 patients (25%). The clinical characteristics of responders and nonresponders are shown in Table 2. There were no significant differences in patient demographics between responders and nonresponders. As expected, nonresponders had undergone a greater number of electropharmacological studies compared with responders (4±2 versus 2±1, $p=0.005$). None of the electrocardiographic or angiographic measures were significantly different between responders and nonresponders. However, no effective drug therapy could be identified for all 10 patients with left ventricular aneurysm ($p<0.06$). The VT cycle length was similar in responders (273±75 msec) and nonresponders (261±45 msec). However, the VT cycle length was shorter in patients presenting with VF (231±33 msec) compared with those presenting with VT (276±55 msec, $p<0.05$).

Hemodynamic Data

Table 3 shows the hemodynamic data for responders and nonresponders. No significant differences were found in the hemodynamic measurements between responders and nonresponders.

Electrophysiological Data

Electrophysiological measurements obtained at baseline and during serial electropharmacological studies for responders and nonresponders are presented in Table 4. At baseline, responders and nonresponders did not differ significantly in their ventricular effective refractory periods at any of the three pacing cycle lengths. Responders had longer ventricular functional refractory periods than nonresponders, although these differences were only statistically significant at a pacing cycle length of 500 msec ($p=0.02$). During serial electropharmacological studies, responders tended to have longer ventricular effective and functional refractory periods than nonresponders, but these differences were only significant at pacing cycle length of 500 msec (Table 4). Antiarrhythmic drug–induced changes in ventricular effective and functional refractory periods were not statistically significant between the two groups.

Effect of IRA Patency Status on Outcome of Electropharmacological Studies

The IRA was patent in a total of 29 patients (45%) and remained occluded in the remaining 35 patients. Among the 29 patent IRAs, five were revascularized by coronary artery bypass surgery and one by coronary angioplasty. Thirteen of the 29 patients with a patent IRA (45%) were drug responders. In contrast, only three of 35 patients (9%) who had an occluded IRA were responders (Figure 1). This difference was highly statistically significant ($p=0.001$). Effective drug therapy could be identified for five of the six patients whose IRAs were revascularized. To assess this relation in a more homogeneous patient group, the data were analyzed separately for the 52 patients who had only one previous myocardial infarction and sustained monoform VT induced at the baseline electrophysiological study. Three patients with inducible VF and nine patients with two infarction sites were excluded from this analysis. Ten of 23 patients (44%) with a patent IRA were

TABLE 2. Clinical, ECG, and Angiographic Characteristics of Responders and Nonresponders According to Presenting Arrhythmia

	VF		VT	
	Responders	Nonresponders	Responders	Nonresponders
Number	5	12	11	36
Age (years)	56±7	61±10	60±10	61±10
Male	5	11	11	33
LVEF	0.34±0.06	0.30±0.15	0.35±12	0.31±0.14
VT cycle length (msec)	215±27	238±34	299±75	269±46
Number of drug trials	2±2	3±2	2±1	4±2
ECG				
Q wave present	5	10	5	22
Q wave absent	0	2	6	14
Induced VT morphology				
Right bundle branch block	0	5	4	16
Left bundle branch block	1	6	5	14
IVCD	3	0	2	5
Infarct location				
Anterior	2	6	4	15
Inferior	2	4	6	16
Two sites	1	2	1	5
No. diseased vessels				
1	1	3	4	17
2	3	6	3	10
3	1	3	4	9
Mean	2±1	2±1	2±1	2±1
Left ventricular aneurysm	0	2	0	8
Collateral vessels to IRA				
Present	3	7	4	24
Absent	2	5	7	12

Data are mean±1 SD. VF, ventricular fibrillation; VT, ventricular tachycardia; LVEF, left ventricular ejection fraction; IVCD, intraventricular conduction delay; IRA, infarct-related artery.

responders compared with only three of the 29 patients (10%) with an occluded IRA ($p=0.009$) (Figure 1). Collateral vessels supplying the IRA were present in two of three drug responders and 25 of 32 drug nonresponders having an occluded IRA (p=NS).

The effect of IRA patency on the outcome of electropharmacological studies was also assessed when the induction of ≤15 complexes of repetitive ventricular responses was accepted as an indication of antiarrhythmic drug efficacy.[24] Using this criterion, an additional six patients were classified as drug responders. Antiarrhythmic drug response was significantly higher in patients with a patent IRA compared with an occluded IRA. Seventeen of 29 patients with a patent IRA (59%) were classified as drug responders compared with only five of 35 patients (14%) who had an occluded IRA ($p<0.001$).

Effect of Left Ventricular Systolic Function

The significant relation between the IRA patency status and the outcome of drug testing depended on the patient's LVEF. Effective antiarrhythmic drug therapy was found in a significantly greater proportion of patients with a patent IRA (64%) than in those with an

TABLE 3. Hemodynamic Data in Responders and Nonresponders

	Responders ($n=16$)	Nonresponders ($n=48$)
Systolic BP (mm Hg)	111±40	102±21
LVEDP (mm Hg)	17±7	18±8
Cardiac output (L/min)	5.6±2.3	5.1±1.8
EDV (mL)	215±84	219±78
ESV (mL)	132±73	147±71
Stroke volume (mL)	83±29	74±30
EDV index (mL/m^2)	102±35	112±38
ESV index (mL/m^2)	63±35	75±36
Stroke volume index (mL/m^2)	39±11	40±22

BP, blood pressure; LVEDP, left ventricular end-diastolic pressure; EDV, end-diastolic volume; ESV, end-systolic volume.

TABLE 4. Electrophysiological Data in Responders and Nonresponders

	Responders (n=16)	Nonresponders (n=48)
Drug-free		
PCL600-ERP (msec)	268±26	269±24
PCL500-ERP (msec)	260±28	253±25
PCL400-ERP (msec)	248±22	240±25
PCL600-FRP (msec)	301±19	289±27
PCL500-FRP (msec)	289±24	273±23*
PCL400-FRP (msec)	274±17	264±24
Antiarrhythmic drugs		
PCL600-ERP (msec)	309±25	298±37
PCL500-ERP (msec)	297±26	283±34
PCL400-ERP (msec)	286±31	275±41
PCL600-FRP (msec)	338±25	327±34
PCL500-FRP (msec)	331±26	312±34*
PCL400-FRP (msec)	315±23	298±40†
Drug-induced changes		
PCL600-ERP (msec)	41±33	26±25
PCL500-ERP (msec)	39±32	29±29
PCL400-ERP (msec)	40±40	32±33
PCL600-FRP (msec)	38±37	38±32
PCL500-FRP (msec)	43±34	37±30
PCL400-FRP (msec)	42±32	30±31

Data are mean±1 SD; PCL, pacing cycle length; ERP, effective refractory period; FRP, functional refractory period. *p<0.05, †p<0.07.

occluded IRA (7%, p=0.003) when LVEF was ≥0.35 (Figure 2). However, this effect was not statistically significant in patients with and without a patent IRA (33% versus 10%, p=NS) when the LVEF was <0.35 (Figure 2).

Similarly, in patients with one previous myocardial infarction and sustained monoform VT, effective anti-

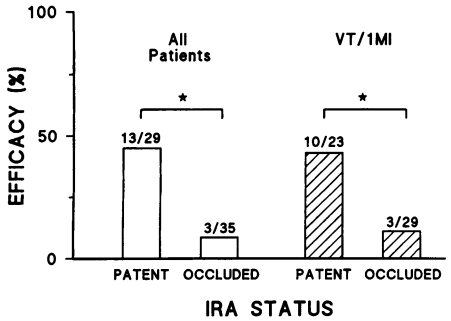

FIGURE 1. *Bar graph showing the effect of infarct-related artery (IRA) patency on outcome of drug testing in patients with inducible ventricular tachycardia (VT) and ventricular fibrillation as well as in patients with only inducible monoform VT and one infarction site (1MI).* ★p<*0.01.*

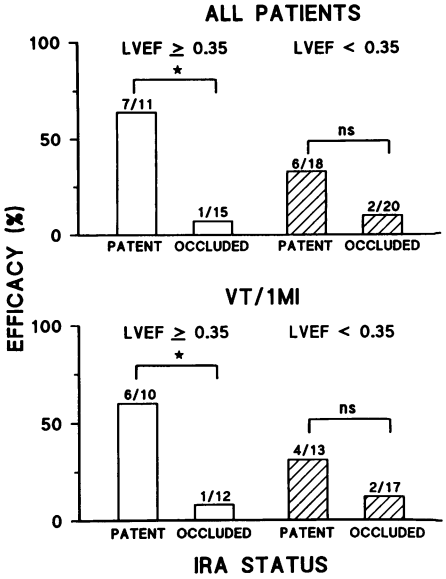

FIGURE 2. *Bar graphs showing the effect of infarct-related artery (IRA) patency on antiarrhythmic efficacy according to whether left ventricular ejection fraction (LVEF) was ≥0.35 or <0.35. The significant effect of IRA patency was only observed in patients with LVEF ≥0.35 as shown for all patients* (top panel) *as well as for patients with only inducible monoform ventricular tachycardia (VT) and one infarction site (1MI)* (bottom panel). ★p<*0.05.*

arrhythmic drug therapy was found in a significantly greater proportion of patients with a patent IRA than in those with an occluded IRA (60% versus 8%, p=0.02) when LVEF was ≥0.35 (Figure 2). However, no significant difference in drug response was noted between patients with and without a patent IRA (31% versus 12%, p=NS) when the LVEF was <0.35.

Patients With Patent and Occluded IRAs

There were no significant differences in hemodynamic measurements between patients with patent and occluded IRAs (Table 5). The ventricular effective and functional refractory periods were similar at baseline in

TABLE 5. Hemodynamic Data in Patients With Patent and Occluded Infarct-Related Arteries

	Patent IRA (n=16)	Occluded IRA (n=48)
Systolic BP (mm Hg)	102±31	105±23
LVEF	0.33±0.15	0.32±0.13
LVEDP (mm Hg)	18±8	17±8
Cardiac output (L/min)	5.2±2.0	5.2±2.0
EDV (mL)	215±91	221±70
ESV (mL)	142±88	143±55
Stroke volume (mL)	74±23	78±35
EDV index (mL/m^2)	109±42	111±34
ESV index (mL/m^2)	72±44	72±28
Stroke volume index (mL/m^2)	37±10	43±25

Data are mean±1 SD. IRA, infarct-related artery; BP, blood pressure; LVEF, left ventricular ejection fraction; LVEDP, left ventricular end-diastolic pressure; EDV, end-diastolic volume; ESV, end-systolic volume.

TABLE 6. Electrophysiological Data in Patients With Patent and Occluded Infarct-Related Arteries

	Patent IRA (n=29)	Occluded IRA (n=35)
Drug-free		
PCL600-ERP (msec)	267±25	270±24
PCL500-ERP (msec)	255±20	255±30
PCL400-ERP (msec)	244±23	241±25
PCL600-FRP (msec)	294±31	292±23
PCL500-FRP (msec)	282±22	274±27
PCL400-FRP (msec)	271±25	264±20
Antiarrhythmic drugs		
PCL600-ERP (msec)	305±30	298±38
PCL500-ERP (msec)	289±27	286±38
PCL400-ERP (msec)	280±28	278±48
PCL600-FRP (msec)	332±27	327±35
PCL500-FRP (msec)	331±27	315±38
PCL400-FRP (msec)	305±25	302±47
Drug-induced changes		
PCL600-ERP (msec)	46±25	23±25*
PCL500-ERP (msec)	35±25	29±35
PCL400-ERP (msec)	37±31	33±39
PCL600-FRP (msec)	44±33	35±33
PCL500-FRP (msec)	36±26	39±35
PCL400-FRP (msec)	34±25	34±38

Data are mean±1 SD; IRA, infarct-related artery; PCL, pacing cycle length; ERP, effective refractory period; FRP, functional refractory period. *p<0.01.

patients with patent and occluded IRAs (Table 6). Similarly, the ventricular refractory periods measured during antiarrhythmic therapy were similar in patients with patent and occluded IRAs. Antiarrhythmic drug-induced changes in the ventricular effective refractory period tended to be higher in patients with a patent IRA, but this difference was only statistically significant at a pacing cycle length of 600 msec (p<0.005).

Predictive Value of IRA Patency Status

Stepwise logistic regression analysis was applied to univariate predictors of antiarrhythmic drug response. Patency of the IRA was the only independent predictor of successful suppression of VT/VF induction during electrophysiological studies (p=0.004). The predictive value of a patent IRA in the study population is shown in Table 7. In the whole study group, a patent IRA had a sensitivity of 81% and specificity of 67% for the prediction of successful electropharmacological studies. The overall positive and negative predictive values of a patent IRA were 45% and 91%, respectively. The sensitivity and specificity of a patent IRA were 77% and 67%, respectively, when only patients with sustained VT and one infarction site were considered. In this latter group of patients, the positive and negative predictive values of a patent IRA were 44% and 90%, respectively.

TABLE 7. Predictive Value of Patent Infarct-Related Artery

	Responders	Nonresponders	Total
Patent IRA	13	16	29
Occluded IRA	3	32	35
Total	16	48	64

IRA, infarct-related artery. Sensitivity, 81%; specificity, 67%; positive predictive value, 45%; negative predictive value, 91%.

Discussion

Importance of Infarct Artery Patency

Sustained VT in the setting of remote myocardial infarction usually is due to reentry. This reentry usually involves surviving tissue in the peri-infarct zone. Survival of this tissue is dependent on adequate coronary perfusion. A patent IRA can have an arrhythmogenic role by continuing to nourish the region of the myocardium that is critical to reentry.[25-35] In the case of an occluded IRA, the critical region to tachycardia maintenance can be nourished by collateral blood vessels. Using the technique of subselective coronary catheterization and cold saline mapping, it is possible to identify such a tachycardia-related blood vessel.[32-35] The concept of destroying the arrhythmogenic substrate by interrupting its blood supply has led to the development of a transcoronary technique to ablate VT in humans. The early experience that was reported using this new technique in very selected patients has been promising.[34,35] Alternatively, during treatment, a patent IRA allows delivery of an antiarrhythmic drug to the myocardium critical to reentry.

Major Findings of This Study

The present study assessed the relation of IRA patency to the outcome of electropharmacological studies in patients with remote myocardial infarction and VT/VF. We postulated that when the IRA was patent, there would be a greater drug effect on the arrhythmogenic substrate. Our study shows that a patent IRA was associated with a significantly higher probability of finding effective antiarrhythmic drug therapy. This positive effect of IRA patency on the outcome of electropharmacological studies may be modulated by the severity of the underlying left ventricular dysfunction. A patent IRA was associated with significantly greater antiarrhythmic response when the patient's LVEF was ≥0.35. A similar trend was seen in patients with more marked reduction in left ventricular function. Antiarrhythmic drug–induced changes in the ventricular effective refractory period tended to be slightly higher in patients with a patent IRA compared with those with an occluded IRA.

Clinical and Electrophysiological Predictors of Antiarrhythmic Efficacy

Previous studies have identified certain clinical and baseline electrophysiological predictors of successful electropharmacological studies. Clinical predictors of successful drug response include young age, female sex, absence of structural heart disease, and preserved left ventricular function.[13-15] The electrophysiological pre-

dictors include a short corrected QT interval and a short electrogram coupling initiating VT.[16] In the present study, we did not find any significant differences in age, sex, or LVEF between responders and nonresponders. Importantly, the present study differs from previous studies in the type of patients assessed. Previous studies have included a heterogenous group of patients with different etiologies of heart disease. The nature of our hypothesis dictated that we studied a more homogeneous group of patients with coronary artery disease and remote myocardial infarction. The mean age of our patients and their male preponderance reflect the selection process. Accordingly, neither age nor sex would be expected to discriminate between responders and nonresponders in our group of patients. Nevertheless, the observation that none of the patients with a left ventricular aneurysm had a successful outcome from electropharmacological studies is consistent with previous reports.[14] No other clinical or hemodynamic factors distinguished drug responders from nonresponders in the present study.

Clinical Significance of IRA Patency

Previous studies have identified coronary artery disease and remote myocardial infarction as independent predictors of failure to respond to antiarrhythmic drugs selected by the electropharmacological approach.[13–16] The likelihood of finding effective drug therapy in the present population is 25–30%.[13,14] A major clinically relevant finding of the present study is that we have identified a subgroup of such patients with a high likelihood of response (45%). For clinical purposes, the presence of an occluded IRA may be quite useful. The presence of an occluded IRA has a negative predictive value of 91%.

Potential Mechanisms

The mechanisms by which IRA patency increases the probability of successful electropharmacological studies are not clear. It is possible that in the presence of a patent IRA, there would be greater delivery of antiarrhythmic drug to the region of the myocardium containing the arrhythmogenic substrate. Furthermore, the local tissue concentrations of antiarrhythmic drugs may be significantly lower at the arrhythmogenic focus in the presence of an occluded IRA.[36] The importance of local drug concentrations for determining beneficial antiarrhythmic effects was highlighted in a study reported by Friedman et al.[35] In one of their patients with inducible VT, intracoronary infusion of lidocaine at 0.6 mg/min prevented VT induction despite an undetectable plasma lidocaine concentration. Furthermore, VT remained inducible in the presence of a therapeutic plasma lidocaine concentration after its intravenous administration in the same patient. Similarly, after permanent coronary artery occlusion in dogs, high local concentrations of procainamide in the infarct area from coronary sinus retroinfusion were more effective than intravenous infusion in suppression of VT.[36] These observations emphasize the importance of attaining sufficient local myocardial drug concentrations for optimal antiarrhythmic effects.

Nevertheless, pharmacodynamic factors must also be considered. The electrophysiological substrate in the infarct zone with a patent artery may differ from that associated with an occluded artery. Indeed, VT is less frequently induced after a myocardial infarction in patients who have received thrombolytic therapy compared with patients who did not receive this therapy.[37,38] Furthermore, the failure to induce VT in these patients correlated with IRA patency.[38] In addition, late potentials are significantly less frequent in patients after successful thrombolytic therapy for acute myocardial infarction compared with those patients who do not experience successful thrombolytic therapy.[39–41] Because the electrophysiological effects of antiarrhythmic drugs are dependent on resting membrane potential and cellular coupling and because these characteristics may be a function of IRA patency, IRA patency could thus influence the magnitude of antiarrhythmic drug effects.[42]

Limitations

Ventricular stimulation during electropharmacological studies was performed only at the site where sustained VT/VF was induced during the baseline study.[18] Morady et al[43] have reported that performing programmed stimulation at more than one ventricular site increases the sensitivity of detecting VT during electropharmacological studies. These investigators have suggested that about 50% of drug trials may have false-negative results when ventricular stimulation is performed only at the right ventricular apex. It is possible that our patient responders included a number of false-negative responses. However, the number of false-negative responses is unlikely to be as high as 50%. The proportion of patient responders observed in the present study was similar to that reported by Rae et al,[9] who assessed antiarrhythmic drug efficacy in a similar patient population using a protocol that included stimulation at two right ventricular sites. We used a rigid definition of antiarrhythmic drug response (five or fewer induced ventricular repetitive responses), and ventricular stimulation was performed at the right ventricular outflow tract in some patients if this was the site at which VT/VT was induced during the baseline study. Moreover, we have no data to suggest that a higher false-negative response rate should be expected in patients with a patent IRA compared with a closed IRA.

Conclusions

This study assessed the effect of IRA patency on the outcome of electropharmacological studies in patients with VT/VF in the setting of remote myocardial infarction. Our findings demonstrate that successful electropharmacological studies are more likely in patients with a patent IRA. An occluded IRA is associated with a very low probability of finding effective drug therapy. This information can be used to stratify patients as potential drug responders or nonresponders at an early stage. Furthermore, the results of this study suggest that coronary artery revascularization should be considered in patients with an occluded coronary artery presenting with VT/VF before embarking on electropharmacological testing. Future studies will be needed to address this hypothesis.

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