

Coronary Artery Revascularization in Patients With Sustained Ventricular Arrhythmias in the Chronic Phase of a Myocardial Infarction: Effects on the Electrophysiologic Substrate and Outcome

Josep Brugada, MD, Luis Aguinaga, MD, Lluís Mont, MD, Amadeu Betriu, MD, Jaume Mulet, MD, Ginés Sanz, MD

Barcelona, Spain

OBJECTIVES	The objective of this study was to analyze the influence of coronary artery revascularization in patients with ventricular arrhythmias.
BACKGROUND	Coronary artery revascularization is an effective treatment for myocardial ischemia; however, its effect on ventricular arrhythmias not related to an acute ischemic event has not been carefully studied.
METHODS	Sixty-four patients (58 men, mean age 65 ± 8 years old) with prior myocardial infarction, spontaneous ventricular arrhythmias not related to an acute ischemic event (55 ventricular tachycardia, 9 ventricular fibrillation) and coronary lesions requiring revascularization were studied prospectively. Electrophysiological study was performed before and after revascularization, and events during follow-up were analyzed.
RESULTS	At initial study 61 patients were inducible into sustained ventricular arrhythmias. After revascularization, in 62 survivors, 52 out of 59 patients previously inducible were still inducible (group A), and 10 patients were noninducible (group B). No differences were found in clinical, hemodynamic, therapeutic and electrophysiological characteristics between both groups. During 32 ± 26 months follow-up, 28/52 patients in group A (54%) and 4/10 patients in group B (40%) had arrhythmic events ($p = 0.46$). An ejection fraction $<30\%$ predicted recurrent arrhythmic events ($p = 0.02$), but not the presence of demonstrable ischemia before revascularization ($p = 0.42$), amiodarone ($p = 0.69$) or beta-adrenergic blocking agent therapy ($p = 0.53$). Total mortality was 10% in both groups.
CONCLUSIONS	In patients with ventricular arrhythmias in the chronic phase of myocardial infarction, probability of recurrence is high despite coronary artery revascularization, but mortality is low if combined with appropriate antiarrhythmic therapy. Recurrences are related to the presence of a low ejection fraction but not to demonstrable ischemia before revascularization, amiodarone or beta-blocker therapy nor are they the results of electrophysiological testing after revascularization. (J Am Coll Cardiol 2001;37:529–33) © 2001 by the American College of Cardiology

The investigation of patients with sustained ventricular arrhythmias in the chronic phase of a myocardial infarction (MI) usually includes the study of coronary artery anatomy in order to detect those that might benefit from coronary artery revascularization. If indicated, coronary artery revascularization has proven to be an effective therapy for myocardial ischemia (1,2). However, limited information is available concerning the role of coronary artery revascularization in the modification of the electrophysiologic substrate and in the prevention of recurrences of ventricular arrhythmias in this group of patients (3–9). In this study, the effects of coronary artery revascularization on inducibility of ventricular arrhythmias and its influence on arrhythmia recurrence during follow-up were prospectively analyzed.

The role of ischemia in the occurrence of ventricular arrhythmias was also analyzed by comparing outcome after

successful revascularization in patients with and without demonstrable myocardial ischemia before revascularization.

METHODS

Patients. We conducted a prospective study in 64 consecutive patients presenting to our institution between February 1994 and December 1999 with sustained ventricular arrhythmias in the chronic phase of an MI and in whom coronary artery revascularization was indicated after clinical and angiographic evaluation. Patients, in whom clinical, electrocardiographic or enzymatic data suggested an acute ischemic event as a trigger of the arrhythmia, were excluded. **Coronary artery anatomy.** Coronary artery angiography was performed using standard techniques between one and eight days after the arrhythmic event.

Indication for coronary artery revascularization. Indication for revascularization was established either by the presence of significant coronary artery lesions and the suspicion of myocardial ischemia from clinical, electrocardiographic, stress testing or scintigraphic data or by the

From the Arrhythmia Section, Cardiovascular Institute, Hospital Clinic, University of Barcelona, Barcelona, Spain.

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Abbreviations and Acronyms

LVEF = left ventricular ejection fraction
 MI = myocardial infarction

severity of the lesions at the coronary angiogram (three-vessel disease or two-vessel disease including a proximal lesion in the left anterior descending coronary artery) but without evidence of myocardial ischemia.

Coronary artery revascularization. Coronary artery revascularization was performed between 3 and 10 days after coronary angiography. In patients with single- or uncomplicated double-vessel disease, percutaneous transluminal coronary angioplasty was performed. In patients with complicated double-vessel disease or triple-vessel disease, coronary artery bypass graft, using saphenous grafts and, whenever possible, internal mammary arteries, was performed.

Electrophysiological testing. Electrophysiological testing was simultaneously performed with the coronary angiography between one and eight days after the arrhythmic event, after informed written consent, in the fasting state and using mild sedation. All antiarrhythmic drugs were eliminated 5 half-life times before the procedure, except for amiodarone and beta-adrenergic blocking agents that were used at the same dose as before the study. Electrophysiological testing was performed using two quadripolar 6F catheters for recording and stimulation. The protocol for ventricular programmed stimulation used one to three premature beats during sinus rhythm and at three driven cycle lengths (600, 500 and 430 ms) at the right ventricular apex. The patient was considered inducible if a sustained ventricular tachycardia (>30 s) or a hemodynamically unstable arrhythmia requiring cardioversion was initiated. The patient was considered noninducible if no sustained arrhythmia was induced upon completion of the protocol.

Second electrophysiological testing. A second electrophysiological study was performed between 3 and 15 days after

coronary artery revascularization using the same protocol as the previous one. No new antiarrhythmic drugs were used between the first and the second study, and those patients on amiodarone or beta-blockers continued at the same dose regimen.

Antiarrhythmic treatment. The antiarrhythmic treatment was decided after completion of the second electrophysiological study, mainly on the basis of the clinical arrhythmia and the results of the programmed ventricular stimulation.

Follow-up. Patients were followed at three-month intervals in the outpatient clinic. A patient was considered to be suffering from a recurrent arrhythmic event if a sustained ventricular arrhythmia was documented either on a 12-lead electrocardiogram or on a defibrillator electrogram or if sudden death occurred. A patient was considered to be suffering from recurrent myocardial ischemia if anginal complaints recurred after revascularization, in which case a noninvasive evaluation using a stress test and a second coronary angiography was performed to evaluate the results of revascularization.

Statistical analysis. Statistical calculations were performed using the SPSS package. The Fisher exact test or the chi-square test was used for categorical variables. One-way analysis of variance or the Student *t* test was used for comparison of continuous variables. Survival curves were plotted using the Kaplan-Meier method and analyzed by the log-rank test. A value of *p* < 0.05 was considered statistically significant.

RESULTS

Fifty-eight out of the 64 patients were men, and mean age was 65 ± 8 years old (range 38 to 77 years old). Previous MI was anterior in 60%, inferior in 30% and both in 10% of patients. Mean ejection fraction was 38 ± 9% (range 20% to 65%). None of the patients had had coronary artery revascularization before the clinical arrhythmic event. The spontaneous arrhythmic event was sustained monomorphic ventricular tachycardia in 55 patients and ventricular fibrillation in 9 patients (Fig. 1). The spontaneous arrhythmic event occurred between 1 and 95 months (mean 11 ± 35 months)

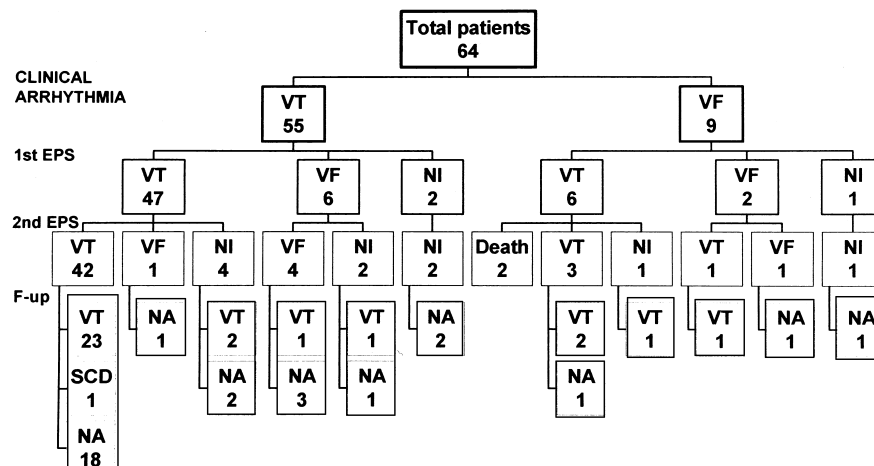


Figure 1. Flow-chart relating clinical arrhythmia, results of pre- and post-revascularization electrophysiological studies (1st EPS and 2nd EPS) and follow-up (F-up). Death = death during surgery; NA = no arrhythmia recurrence during follow-up; NI = noninducible; SCD = sudden cardiac death during follow-up; VF = ventricular fibrillation; VT = ventricular tachycardia. Numbers indicate patients in each category.

after the MI. At the moment of the clinical event, three patients were on amiodarone, and 21 were on beta-blocker therapy.

Eight patients had single-vessel disease (>70% narrowing of the artery); 12 patients had double-vessel disease, and 44 patients had triple-vessel disease. In 45 patients revascularization was indicated by angiographic and clinical data; in 19 patients the indication was established solely on the basis of coronary anatomy.

Percutaneous transluminal coronary angioplasty was successfully performed in 16 patients, and multiple coronary artery bypass graft was performed in 48 patients. Two of the patients with triple-vessel disease and evidence of ischemia died during surgery.

Initial electrophysiological study. An electrophysiological study was performed in all 64 patients. At the time of the study, 10 patients were receiving amiodarone (seven since the spontaneous arrhythmic event and three chronically because of other arrhythmias), and 21 were receiving beta-blockers. In 61 patients, programmed electrical stimulation induced a sustained ventricular arrhythmia. In 53 patients the induced arrhythmia was a monomorphic ventricular tachycardia (mean cycle length 270 ± 30 ms), and in eight patients ventricular fibrillation was the arrhythmia induced. In three patients no sustained ventricular arrhythmia could be induced (Fig. 1). No differences were observed in inducibility among patients with ventricular tachycardia or ventricular fibrillation as clinical arrhythmia and with or without amiodarone or beta-blocker treatment.

Electrophysiological study after coronary artery revascularization. In 52 patients, programmed electrical stimulation induced a sustained ventricular arrhythmia (group A). In 46 patients the induced arrhythmia was monomorphic ventricular tachycardia (mean cycle length 282 ± 50 ms) and in six patients a ventricular fibrillation. In 10 patients (eight with ventricular tachycardia and two with ventricular fibrillation as clinical arrhythmia) no sustained arrhythmia could be induced (group B). Comparing both studies, 5 out of the 53 patients with ventricular tachycardia at the initial study became noninducible, and in one patient ventricular fibrillation was now the arrhythmia induced. Two of the eight patients with ventricular fibrillation became noninducible, and in one patient ventricular tachycardia was now the arrhythmia induced, whereas the three noninducible patients in the first study remained noninducible in the second study (Fig. 1). No differences were observed among patients with inducible or noninducible arrhythmias concerning clinical data, number of vessels affected, indication for revascularization, ejection fraction, type of revascularization and presence of amiodarone or beta-blocker therapy (Table 1).

In 36 patients an automatic defibrillator was implanted (4 abdominal and 32 pectoral), and 14 of them had amiodarone as adjunctive therapy. The remaining 26 patients were treated with antiarrhythmic drugs (18 with amiodarone and 8 with sotalol). Twenty-one patients were on beta-blocker

Table 1. Clinical, Hemodynamic, Therapeutic and Follow-Up Data According to Inducibility of Ventricular Arrhythmias After Coronary Artery Revascularization

	Inducible After Revascularization	Noninducible After Revascularization	p Value
n	52	10	
Follow-up (months)	31 ± 26	35 ± 29	
Ejection fraction (%)	37 ± 9	39 ± 8	0.55
Ejection fraction < 30	12	1	0.35
Ejection fraction ≥ 30	40	9	
Bypass surgery	39	7	0.74
Coronary angioplasty	13	3	
Ischemia demonstrated	35	8	0.43
No ischemia demonstrated	17	2	
Amiodarone treatment	9	1	0.13
No amiodarone treatment	43	9	
Beta-blocker treatment	18	3	0.44
No beta-blocker treatment	34	7	
One-vessel disease	6	2	0.61
Two-vessel disease	11	1	
Three-vessel disease	35	7	
Clinical arrhythmia: VT	46	9	0.89
Clinical arrhythmia: VF	6	1	
Recurrent arrhythmic event	28 (54%)	4 (40%)	0.46
Total death	5 (10%)	1 (10%)	0.98

VF = ventricular fibrillation; VT = ventricular tachycardia.

therapy before the revascularization procedure and remained on that therapy.

Follow-up. Mean follow-up time was 32 ± 26 months (31 ± 26 for group A and 35 ± 29 for group B). During follow-up, 28 patients in group A (54%) and 4 patients in group B (40%) had recurrent arrhythmic events (log rank = 0.5, $p = 0.46$) (Fig. 1 and 2). All recurrent arrhythmic events were ventricular tachycardia, except for one patient in

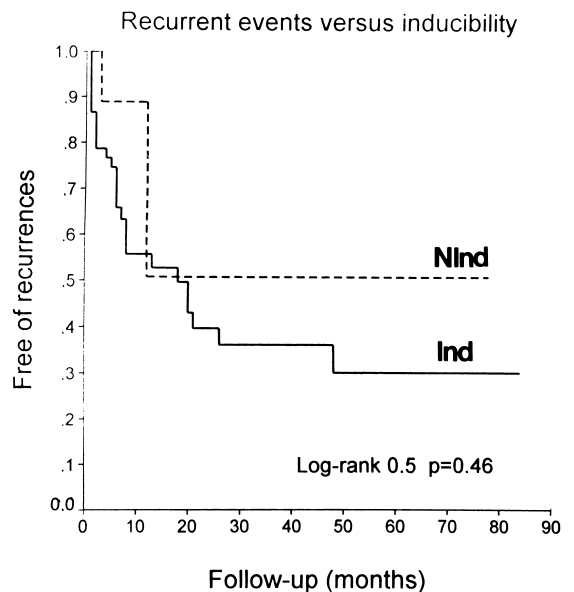


Figure 2. Kaplan-Meier analysis of freedom from recurrent arrhythmic events during follow-up according to the inducibility of ventricular arrhythmias after coronary artery revascularization. The difference between the groups was not significant ($p = 0.46$) by the log-rank test. Ind = the patient was inducible; NInd = the patient was not inducible.

Table 2. Clinical, Hemodynamic, Therapeutic and Follow-Up Data According to the Presence of Recurrent Arrhythmic Events During Follow-up

	Recurrent Arrhythmic Event	No Recurrent Arrhythmic Event	p Value
n	32	30	
Follow-up (months)	33 ± 24	34 ± 27	
Ejection fraction (%)	37 ± 9	38 ± 9	0.64
Ejection fraction < 30	9	4	0.02
Ejection fraction ≥ 30	23	26	
Bypass surgery	25	21	0.87
Coronary angioplasty	7	9	
Ischemia demonstrated	21	22	0.42
No ischemia demonstrated	11	8	
Amiodarone treatment	18	14	0.69
No amiodarone treatment	14	16	
Beta-blocker treatment	10	11	0.61
No beta-blocker treatment	22	19	
One-vessel disease	5	3	0.81
Two-vessel disease	6	6	
Three-vessel disease	21	21	
Inducible after revascularization	28	24	0.46
Noninducible after revascularization	4	6	
Clinical arrhythmia: VT	29	26	0.76
Clinical arrhythmia: VF	3	4	

VF = ventricular fibrillation; VT = ventricular tachycardia.

group A on amiodarone therapy that suffered sudden death. In patients with an automatic defibrillator implanted, successful radiofrequency ablation was performed in six patients due to recurrent slow ventricular tachycardia during follow-up, and five received amiodarone due to recurrent ventricular tachycardia not amenable to radiofrequency ablation. In the three survivors with recurrent arrhythmic events in group B, an automatic defibrillator was implanted.

Five patients died in group A (one sudden death, one fatal stroke and one pulmonary, one tracheal and one cerebral malignancy). One patient died of cardiac insufficiency in group B. Total mortality was 10% in both groups.

One single patient in group A that underwent percutaneous transluminal coronary angioplasty of a single lesion and had no arrhythmic recurrences during follow-up presented with recurrent myocardial ischemia demonstrated by a positive stress test. Coronary angiography demonstrated restenosis of the left anterior descending coronary artery, and a second successful angioplasty and stent placement was performed.

Incidence of events according to the presence of myocardial ischemia before the revascularization procedure. During follow-up, 21 of 43 patients (49%) with evidence of ischemia before revascularization had arrhythmic events, compared with 11 of 19 patients (58%) with no evidence of ischemia before revascularization (log rank = 0.66, p = 0.42) (Table 2).

Incidence of events according to the left ventricular ejection fraction (LVEF). In 9 of 13 patients (69%) with an LVEF <30%, arrhythmic events occurred during follow-

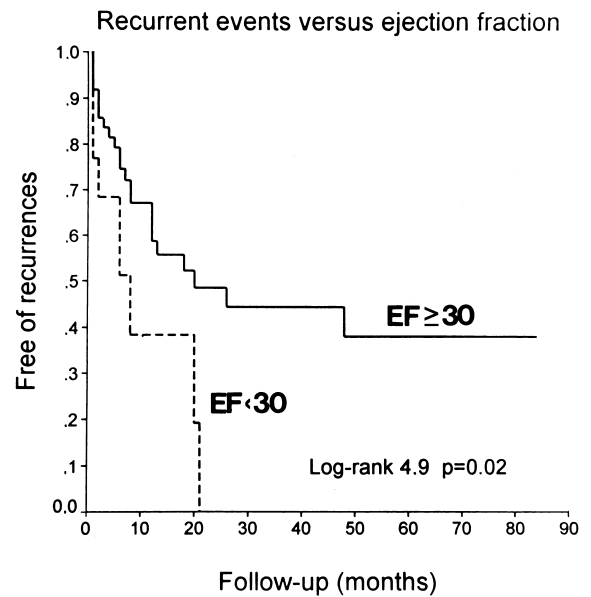


Figure 3. Kaplan-Meier analysis of freedom from recurrent arrhythmic events during follow-up according to the left ventricular ejection fraction (EF) before surgery. The difference between the groups was significant (p = 0.02) by the log-rank test. EF < 30% = the patient had an ejection fraction < 30%; EF ≥ 30% = the patient had an ejection fraction ≥ 30%.

up, compared with 23 of 49 patients (47%) with an LVEF ≥30% (log rank = 4.9, p = 0.02) (Table 2; Fig. 3).

Incidence of events according to the presence of amiodarone as antiarrhythmic therapy. Fourteen of 30 patients (47%) without amiodarone therapy had arrhythmic events, compared with 18 of 32 patients (57%) on amiodarone therapy (log rank = 0.16, p = 0.69) (Table 2).

DISCUSSION

The influence of acute ischemic events in the genesis of sustained ventricular arrhythmias is one of the more controversial issues concerning patients in the chronic phase of an MI. The discussion is not only theoretical, but it has important practical aspects. If an acute ischemic event is responsible for the arrhythmia, prevention of ischemia should also prevent the occurrence of the arrhythmia. This has been clearly demonstrated in a highly selected group of patients with documented ischemia-related arrhythmias (mainly polymorphic ventricular tachycardia or ventricular fibrillation) in whom surgical revascularization alone effectively controlled the arrhythmias (7,8). However, in the majority of patients with an old MI, an ischemia-related mechanism as trigger for the arrhythmias cannot be demonstrated although neither can it be excluded. Correction of coronary artery lesions susceptible to revascularization, especially if some objective proof of reversible ischemia is present, should prevent arrhythmia occurrence if ischemia behaved as a trigger for the arrhythmia.

In this study, the influence of ischemia on the occurrence of ventricular arrhythmias was analyzed using two parameters: inducibility of arrhythmias before and after coronary

artery revascularization and arrhythmia recurrence during follow-up. Patients were divided into those with and those without reversible ischemia demonstrated before revascularization and those with and without inducible arrhythmias after revascularization.

Do coronary artery revascularizations modify the electrophysiological substrate? Our results clearly show that, despite effective coronary artery revascularization, the arrhythmia substrate is not modified in a significant proportion of patients. This is demonstrated by the high degree of inducibility after revascularization (only 9 of 61 patients became noninducible) but also by the high recurrence rate of ventricular arrhythmias during follow-up (32 of 61 patients). These results are similar to the ones of Geelen et al. (3) in a group of 18 patients with similar characteristics who presented with a 67% incidence of inducibility and a 66% incidence of appropriate shocks after revascularization and defibrillator implantation. Manolis et al. (5) found, however, in a similar group of 56 patients, that 33% of patients with inducible sustained arrhythmias became noninducible after revascularization, and only 30% of patients had major arrhythmic events during follow-up. Similar studies performed in survivors of cardiac arrest have shown that 47% of patients became noninducible after revascularization (especially those with ventricular fibrillation as induced arrhythmia). The incidence of arrhythmic events during follow-up was 10%, suggesting that ischemia did play a role in the occurrence of cardiac arrest in these patients (4). Ecker et al. (9) presented a clinical case some years ago that suggested that coronary artery revascularization could be an effective method of treatment in intractable ventricular tachycardia. A selected group of patients with coronary artery disease and ventricular arrhythmias induced during exercise was studied by Berntsen et al. (7). After revascularization, ventricular arrhythmias were abolished in all patients with ventricular fibrillation as clinical arrhythmia and in 90% of patients with ventricular tachycardia. In this group of patients with exercise-induced arrhythmias, ischemia should definitely play a role in such an occurrence, and revascularization seems the treatment of choice. In our series, the proportion of patients with still inducible arrhythmias or with arrhythmia recurrence is similar among those with and without demonstrable ischemia before revascularization. This suggests that the presence of demonstrable reversible ischemia is not a marker for an ischemia-related mechanism for arrhythmias and that demonstration of reversible isch-

emia represents a different subset of patients from those with exercise-induced arrhythmias in whom ischemia acts as the trigger for the arrhythmia.

How to approach a patient with an old MI, sustained ventricular arrhythmias and coronary artery lesions requiring revascularization. In all published series, survival after coronary artery revascularization in patients with ventricular arrhythmias is excellent (3-8). Cardiac mortality is low and between 5% and 10% at two to five years follow-up. In our own series, total mortality is 10%, and cardiac mortality is less than 3% at three-year follow-up. This suggests that the combination of coronary artery revascularization and antiarrhythmic therapy (drug therapy or defibrillator implantation) is an excellent combination and should be used systematically.

Reprint requests and correspondence: Dr. Josep Brugada, Arrhythmia Section, Cardiovascular Institute, Hospital Clinic, University of Barcelona, Villarroel 170, 08036, Barcelona, Spain. jbrugada@medicina.ub.es.

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