Understanding ventricular tachycardia : towards individualized substrate-based therapy

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Chapter 9

Early Reperfusion Therapy Affects Inducibility, Cycle Length and Occurrence of Ventricular Tachycardia Late After Myocardial Infarction

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ABSTRACT

Background

This study aimed to evaluate the impact of early reperfusion during acute myocardial infarction (MI) on ventricular tachycardia (VT) inducibility, inducible VT cycle length (CL) and occurrence of spontaneous VT late after MI.

Methods and results

Five-hundred-six patients (440 male, 63±11yr) with prior MI who underwent electrophysiology study before implantation of an implantable cardioverter defibrillator for primary or secondary prevention were assessed. Patients were classified according to the reperfusion strategy {reperfusion (thrombolysis (n=44) or percutaneous coronary intervention (n=65)) vs. no reperfusion (n=397)} during acute MI. Monomorphic sustained VT was inducible in 351 (69%) patients. Inducibility in reperfused and non-reperfused patients was similar in primary prevention patients (56% vs.58%) but significantly higher for non-reperfused patients in secondary prevention patients (56% vs.79%, p=0.001). Induced VTCL was shorter (247±40 vs.287±63, p<0.001) and very fast VT (CL≤250 ms) was more often induced in reperfused patients (71% vs.47%, p=0.001). In primary prevention patients, non-reperfusion was associated with a doubled risk for first spontaneous VT during follow-up.

Conclusion

There are important differences in VT inducibility, induced VTCL and occurrence of spontaneous VT in the chronic infarct healing phase between patients with and without successful reperfusion during acute MI. These findings suggest differences in the chronic arrhythmogenic substrate.

INTRODUCTION

Survivors of acute myocardial infarction (MI) may be at risk for reentrant ventricular tachycardia (VT) originating from infarct scar.[1] In the past decades, early reperfusion therapies such as thrombolysis and primary percutaneous coronary intervention (PCI) have significantly improved outcome after acute MI.[2] Early reperfusion during MI results in myocardial salvage and improved ventricular function but also influences size, transmurality and geometry of myocardial fibrosis, which may function as a substrate for ventricular arrhythmias.[3-7] A fixed substrate may lead to reentrant tachycardias reproducible induced during electrophysiology study (EPS) and more than 90% of patients with sustained VT late after MI had the arrhythmia induced in the lab.[8] However, these data were derived before the widespread availability of reperfusion therapy and the role for EPS in patients late after reperfused MI is less clear. Mapping studies demonstrated that the 3-dimensional geometry of the infarcted area may determine VT reentry circuit characteristics.[9-12] In a small group of patients referred for treatment of VT late after MI, we previously demonstrated that early reperfusion affects the electroanatomical VT substrate.[13] In addition, cycle length (CL) of spontaneous and induced VTs was shorter in patients who underwent early reperfusion as compared to non-reperfused patients.

The aim of the present study was to evaluate the effect of early reperfusion during acute MI on VT inducibility, induced VTCL and the occurrence of spontaneous VT during follow-up in a larger population of patients with prior MI in one coronary territory who underwent EPS before implantable cardioverter defibrillator (ICD) treatment.

METHODS

Patients

Since 1996, information on all patients who received an ICD at the Leiden University Medical Center was prospectively collected in the departmental Cardiology Information System (EPD-Vision®, Leiden University Medical Center). Patient's history, baseline characteristics and results of studies before ICD-implantation were recorded. For the current study, all consecutive patients (1) with a prior MI in a single coronary territory and documented reperfusion strategy during the index MI; (2) without evidence of reversible ischemia assessed by coronary angiogram and nuclear imaging at the time of evaluation, and (3) who underwent EPS before ICD implantation were included. Patients with documented spontaneous monomorphic VT or ventricular fibrillation (VF) in the absence of a reversible cause were considered as secondary prevention ICD recipients and asymptomatic patients with left ventricular ejection fraction (LVEF) <40% without

prior documentation of a sustained ventricular arrhythmia primary prevention ICD recipients.[14-16]

All coronary angiograms performed in reperfused patients within 6 months before EPS were reviewed by an interventional cardiologist to evaluate the late patency of the infarct related artery. Patients with ≤ TIMI II flow of the infarct related artery were excluded from analysis. All patients were followed at our institute.

Myocardial infarction

The presence of prior MI was assessed using the definition for MI, as defined by the Task Force for the Redefinition of Myocardial Infarction.[17] Either acute MI had to be documented, or evidence of prior MI had to be present, based on any of the following criteria: 1) development of new pathological Q-waves with or without symptoms; 2) imaging evidence of a region of loss of viable myocardium that is thinned and fails to contract, in the absence of a non-ischemic cause; 3) pathological findings of a healed or healing MI.[17]

MI was considered to be present in more than one coronary artery region if the criteria for acute or prior MI were met for more than one of the regions provided by the three main coronary arteries.

The treatment of prior MI was assessed using the patients' medical charts. Patients were categorized as reperfused when TIMI flow grade 3 was achieved within 9 hours after onset of symptoms. Reperfused patients were subdivided into patients who had underwent primary PCI (defined as angioplasty and/or stenting without prior or concomitant fibrinolytic therapy)[18] and patients who had received thrombolytic therapy. All other patients were categorized as non-reperfused.

Electrophysiology study

Electrophysiological studies to test inducibility of VT were performed according to the current international guidelines.[19] Patients were studied in the post absorptive, non-sedated state. Antiarrhythmic drugs were discontinued for 5 half-lives, with the exception of amiodarone. EPS consisted of up to three basic drive cycle lengths (600, 500 and 400ms) with up to three ventricular extrastimuli and burst pacing from the right ventricular apex and right ventricular outflow tract. The positive endpoint of EPS was reproducible induction of a sustained monomorphic VT (SMVT).[19] Arrhythmias induced by anti-tachycardia pacing (ATP) to terminate the induced VT were not included in the analysis.

Ventricular arrhythmia during electrophysiology study

Ventricular arrhythmias were categorized according to the EHRA/HRS consensus document.[20] SMVT was defined as continuous VT with a similar QRS configuration from beat

to beat lasting for more than 30 seconds or requiring an intervention for termination. Separately scored arrhythmia not considered diagnostic for the presence of fixed reentry circuits and therefore non-specific were polymorphic VT, defined as VT with continuously changing QRS configuration from beat to beat and VF.[19]

For each patient, the mean CL of all induced SMVTs was calculated. Patients with missing data on one or more CLs were excluded from all analyses involving VTCL. Monomorphic VTs were categorized into the following four pre-defined subgroups according to CL: ≤250, 251-286, 287-320 and >320 ms (corresponding to a rate of ≥240, 240-210, 210-188 and <188bpm, respectively). A very fast VT was defined as a VT with CL ≤250 ms.

Implantable cardioverter defibrillator settings and follow-up

Defibrillators were programmed as follows: a ventricular arrhythmia monitor zone was programmed in all patients (150-188bpm). Ventricular arrhythmias faster than 188bpm were initially attempted to be terminated with two bursts of ATP followed by a defibrillator shock, if appropriate. In the case of a ventricular arrhythmia faster than 210bpm, device shocks were the initial therapy. Atrial arrhythmia detection was set to >170bpm with supraventricular tachycardia discriminators enabled. Settings were adapted, only when clinically indicated (i.e. hemodynamic well tolerated VT at high rate; VT in the monitor zone).

Patient follow-up was scheduled every three-six months. Device interrogation printouts were checked for appropriate and inappropriate ICD therapy (ATP or shocks). Therapies were classified as appropriate when they occurred in response to VT or VF and as inappropriate when triggered by sinus or supraventricular tachycardia, T-wave oversensing, or electrode dysfunction.

In both primary and secondary prevention ICD recipients, the correlation between treatment of acute MI and the occurrence of first spontaneous monomorphic VT during follow-up was assessed.

Statistical analysis

Dichotomous and categorical data are displayed as numbers and percentages. Continuous data are expressed as mean ± standard deviation or median and interquartile range where appropriate. Patients were grouped according to acute MI treatment. Different groups were compared for 1) inducibility of SMVT, 2) mean CL of induced SMVTs, 3) inducibility of very fast VT (CL ≤250ms), and 4) the occurrence of first spontaneous VT during follow-up in primary and secondary prevention ICD patients. Data were analyzed by means of the Chi-square test, the Student's t-test or the Mann-Whitney U-test as appropriate. For the Student's t-test, equal variances were assumed if Levene's test for equality of variances showed a p-value >0.05. Univariate relationships between baseline parameters and the mean CL of induced VTs were analyzed with linear regression analy-

sis. For each variable, the effect on the mean CL with a 95% confidence interval (95%-CI) was calculated. Variables with a p-value <0.10 were further evaluated in a multivariate model, using backward stepwise selection. At each step, the least significant variable was discarded from the model, until all variables in the model reached a p-value <0.25.

The cumulative incidence of first spontaneous VT during follow-up in primary and secondary prevention ICD patients was analyzed by method of Kaplan-Meier. The effect of acute MI treatment on the risk of spontaneous VT was assessed in a Cox regression model. As with linear regression analysis, first, univariate analyses were performed and variables with a p-value <0.10 were further evaluated in a multivariate model, using backward stepwise selection. At each step, the least significant variable was discarded from the model, until all variables in the model reached a p-value <0.25.

All analyses were performed with SPSS for Windows, version 17.0 (SPSS, Chicago, IL). P-values are all two-sided and for all tests, a p-value <0.05 was considered statistically significant.

RESULTS

Patients

Since 1996, 996 patients with prior MI in one coronary artery region received an ICD at the Leiden University Medical Center. Of these patients, 511 had a documented reperfusion strategy and underwent EPS before ICD implantation and after exclusion of reversible ischemia. Five patients (1%) were excluded due to lack of late patency of the infarct related artery. The remaining 506 patients (87% male, age 63 ± 11 years) comprised the studied sample. The presenting and documented arrhythmia was SMVT in 221 patients (44%) and VF in 113 (22%); 172 patients (34%) had no prior sustained arrhythmia. The majority of patients had a depressed left ventricular ejection fraction (36 ± 13%). Mean QRS duration was 115 ± 29 ms and mean creatinin clearance was 79 ± 39mL/min. Medication during EPS included amiodarone in 22% and ACE-inhibitors or ATII-antagonists in 75% of patients. Baseline characteristics are summarized in Table 1.

Myocardial infarction treatment

One-hundred-nine (22%) of 506 patients were treated with reperfusion therapy during the acute MI and 397 (78%) were not reperfused. Of the 109 reperfused patients, 65 (13%) underwent primary PCI and 44 (9%) received thrombolytic therapy. Before electrophysiological evaluation, the infarct-related artery was patent in 97 (89%), collaterally perfused in 11 (10%) and bypassed in one (1%) of the initially reperfused patients. In non-reperfused patients, the infarct-related artery was patent in 140 (35%), occluded in 116 (29%), collaterally perfused in 88 (22%) and bypassed in 53 (13%). Patients who were

reperfused were younger than non-reperfused patients (59 ±11 vs. 65 ±10, p<0.001), presented less often with SMVT (22% vs. 49%, p<0.001) and had a shorter interval between MI and electrophysiological evaluation (median 1.6, IQR 0.2 – 5.9 vs. median 10.5, IQR 2.1 – 17.5, p<0.001). In addition, reperfused patients had an anterior MI more frequently (72% vs. 52%, p<0.001), a shorter QRS-duration (median 100, IQR 90 – 120 vs. median 110, IQR 100 – 138, p=0.001), were less often treated with amiodarone (12% vs. 25%, p=0.001) but were more likely to receive beta-blockers (53% vs. 40%, p=0.014).

Table 1. Baseline Characteristics.

	All Patients (n=506)	Nonreperfused (n=397)	Reperfused (n=109)	*P* Value
Male sex	440 (87%)	341 (86%)	99 (91%)	0.176
Age, y	65 (57–71)	66 (58–73)	60 (51–68)	<0.001
Presenting arrhythmia				<0.001
Sustained VT	221 (44%)	197 (50%)	24 (22%)	
Ventricular fibrillation	113 (22%)	94 (24%)	19 (17%)	
No sustained arrhythmia	172 (34%)	106 (27%)	66 (61%)	
Location of MI				<0.001
Anterior	285 (56%)	206 (52%)	79 (72%)	
Nonanterior	221 (44%)	191 (48%)	30 (28%)	
Years from MI to EPS	7.5 (0.9–15.0)	10.5 (2.1–17.5)	1.6 (0.2–5.9)	<0.001
LVEF, %	36±13	35±13	37±13	0.180
NYHA classification				0.555
I	227 (45%)	172 (43%)	55 (50%)	
II	201 (40%)	164 (41%)	37 (34%)	
III	72 (14%)	56 (14%)	16 (15%)	
IV	6 (1%)	5 (1%)	1 (1%)	
QRS duration, ms	110 (94–130)	110 (100–138)	100 (90–120)	0.001
Renal clearance, mL/min*	79±39	77±41	85±27	0.066
Documented AF or atrial flutter	89 (18%)	69 (17%)	20 (18%)	0.823
Current smoking	126 (25%)	94 (24%)	32 (29%)	0.253
Amiodarone	111 (22%)	98 (25%)	13 (12%)	0.004
β-blocker	217 (43%)	159 (40%)	58 (53%)	0.014
ACE inhibitor or ARB	380 (75%)	291 (73%)	89 (82%)	0.070

ACE indicates angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin receptor blocker; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; EPS, electrophysiological study; and VT ventricular tachycardia.
Data are expressed as No. (percentages), mean±SD, or median (interquartile range).
* Renal clearance was determined with the formula of Cockroft-Gault.

Inducibility of ventricular arrhythmia

In 422 patients (83%), at least one ventricular arrhythmia was inducible: SMVT was induced in 351 (69%) patients, 45 of them were also inducible for polymorphic VT or VF. In 71 (14%) patients, only polymorphic VT or VF was induced. Inducibility of SMVT consisted of only one VT morphology in 222 (63%) and two or more different morphologies in 129 (37%) patients. Inducibility for SMVT was similar in reperfused and non-reperfused patients without prior documentation of sustained VT or VF (56% vs 58%, p=ns). However, in the secondary prevention group inducibility for SMVT was significantly lower in reperfused patients as compared to non-reperfused patients (56% vs 79%, p=0.001).

Ventricular tachycardia cycle length

In 37 (11%) out of 351 patients with inducible SMVT, one or more induced VTCL was unknown, these patients were excluded from VTCL analyses. In the remaining 314 patients, the mean CL was 280 ± 61 ms (Table 2). In 161 (51%) patients, at least one monomorphic fast VT (CL ≤ 250) was induced.

Table 2. Difference of Mean Cycle Length of Induced Monomorphic Ventricular Tachycardias by *t* Tests.

	n	Mean CL	Difference* (95% CI)	*P* Value
All patients	314	280±61	NA	NA
Nonreperfused	258	287±63	NA	NA
Reperfused	56	247±40	40 (27–53)	<0.001
Thrombolysis	23	260±37	27 (2–53)	0.038
Primary PCI	33	238±40	49 (27–70)	<0.001

CI indicates confidence interval; CL, cycle length; NA, not applicable; and PCI, percutaneous coronary intervention.

* When compared with nonreperfused patients.

Reperfused patients had a shorter mean CL of the induced VT than non-reperfused patients (247 ± 40ms vs. 287 ± 63ms, p<0.001, Table 2). This difference was even more pronounced when patients who underwent primary PCI were compared to non-reperfused patients (238 ± 40ms vs. 287 ± 63ms, p<0.001). Patients treated with thrombolysis also had a significantly shorter mean CL than non-reperfused patients, but the difference was smaller (260 ± 37ms vs. 287 ± 63ms, p=0.038). After exclusion of patients on amiodarone during EPS the induced VTCL remained significantly shorter in reperfused patients (244 ± 40ms vs. 274 ± 58ms, p<0.001). Of importance, reperfused patients were more often inducible for very fast VT (CL ≤ 250ms) than non-reperfused patients (71% vs. 47%, p=0.001, Figure 1). The difference was mainly attributable to patients treated with primary PCI, while patients treated with thrombolysis had a similar percentage of very fast VT, as compared to non-reperfused patients. Univariate and subsequent

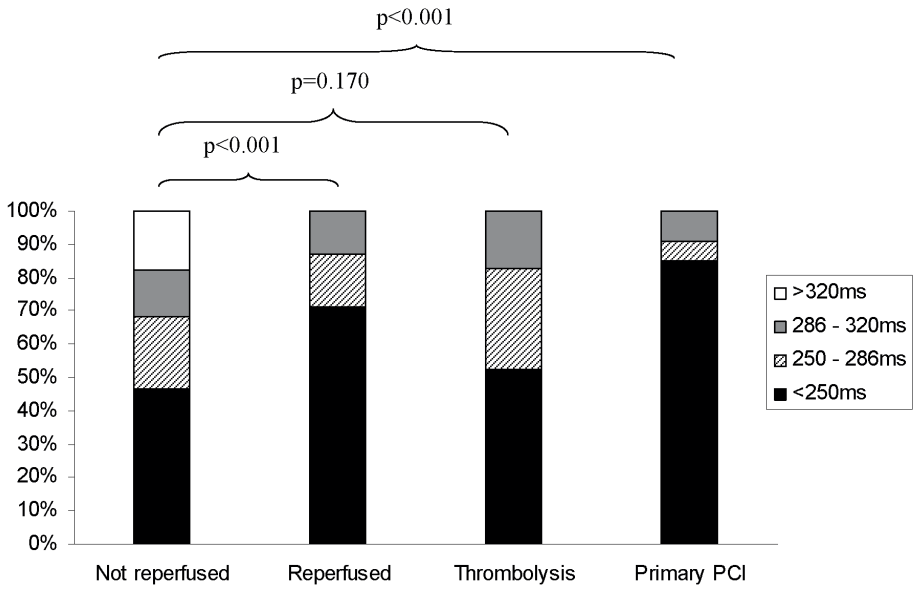

Figure 1.
Cycle length of the fastest induced monomorphic ventricular tachycardia, categorized into 4 subgroups. Percentages are for all patients with induced monomorphic ventricular tachycardia in the specific group. PCI indicates percutaneous coronary intervention.

multivariate analysis identified the following five variables as independently affecting the mean CL of induced VTs: no reperfusion, QRS > 120 ms, presenting arrhythmia, use of amiodarone and age. After adjustment, no reperfusion at MI was correlated with 17 ms (95%-CI 0-34 ms, p=0.048) increase in VT CL at EPS (Figure 2).

Spontaneous ventricular tachycardia

The 172 primary prevention ICD recipients were followed for a median of 28 months (IQR 11 – 45). During follow-up, spontaneous VT, triggering appropriate ICD therapy was observed in 51 (30%) patients. The cumulative incidence of first appropriate therapy was 13% (95% CI 8-18%) at one year, 22% (95% CI 15-28%) at two years, and 30% (95% CI 22-39%) at three years follow-up.

The three year cumulative incidence of first appropriate device therapy was 36% (95% CI 26-47%) in non-reperfused patients and 18% (95% CI 7-29%) in reperfused patients (Figure 3). Cox regression modeling demonstrated that non-reperfused patients exhibited a more than doubled risk for spontaneous VT (hazard ratio 2.2, 95% CI 1.2- 4.3, p=0.010).

The 334 secondary prevention ICD recipients were followed for a median of 37 months (IQR 9 – 68). Spontaneous VT occurred in 170 (51%) patients. The three year cumulative incidence of first appropriate device therapy was 38% (95% CI 32-44%) in

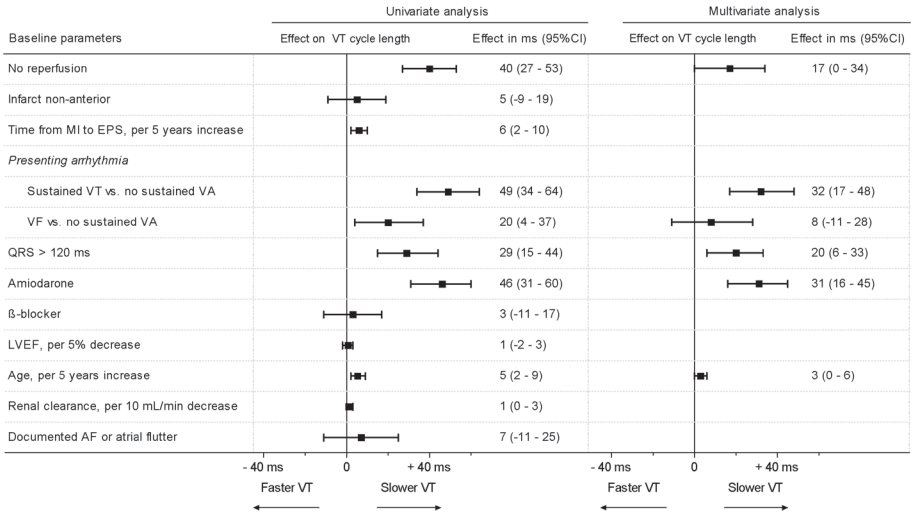

Figure 2.
Forest plot of the effect of baseline parameters on the mean cycle length of induced monomorphic ventricular tachycardias (VT). For example, in multivariate analysis, patients who did not receive reperfusion therapy at the index myocardial infarction on average had a 17-ms (95% confidence interval [CI], 0 to 34 ms) longer Vt cycle length (ie, a slower Vt), as compared with patients who did receive reperfusion therapy. AF indicates atrial fibrillation; LVEF, left ventricular ejection fraction; EPS, electrophysiology study; VA, ventricular arrhythmia; and VF, ventricular arrhythmia.

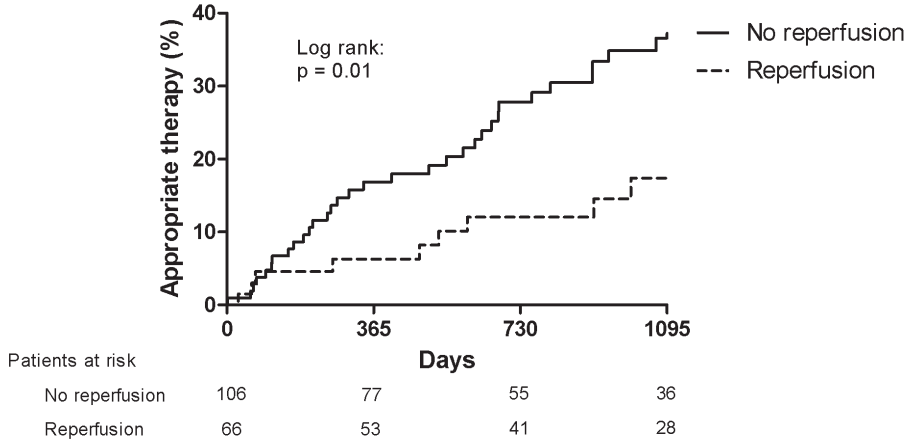

Figure 3.
Kaplan-Meier curve for the occurrence of first appropriate implantable cardioverter-defibrillator therapy in patients with primary-prevention implantable cardioverter-defibrillator with reperfusion versus no reperfusion at prior acute myocardial infarction.

non-reperfused patients and 26% (95% CI 12-39%) in reperfused patients (Figure 4). In this population with prior sustained ventricular arrhythmia, MI treatment did not significantly correlate with the occurrence of spontaneous VT during follow-up (hazard ratio 1.4, 95% CI 0.9-2.3).

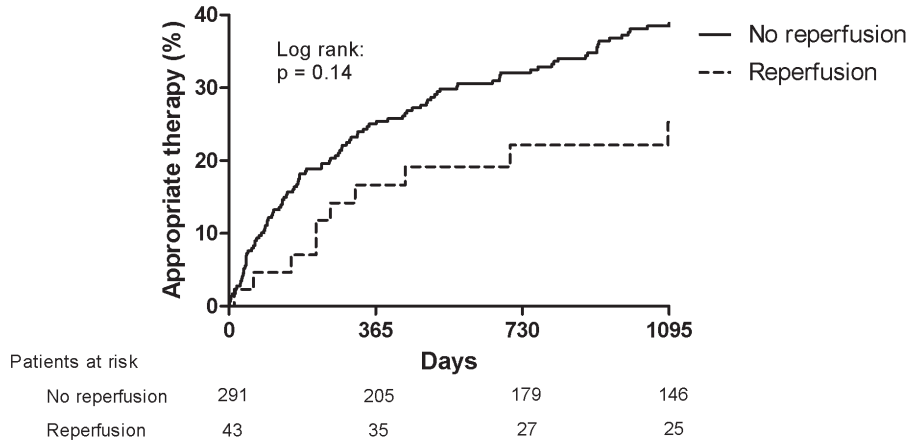

Figure 4.
Kaplan-Meier curve for the occurrence of first appropriate implantable cardioverter-defibrillator therapy in patients with secondary-prevention implantable cardioverter-defibrillator with reperfusion versus no reperfusion at prior acute myocardial infarction.

DISCUSSION

Early reperfusion therapy for acute MI has dramatically increased over the last decenniums and is likely to influence the chronic arrhythmogenic substrate for reentrant tachycardias after infarct healing.

The current study evaluates the effects of early reperfusion during acute MI on VT inducibility, induced VT CL and occurrence of spontaneous VT late after the index MI. Reperfused patients who presented with sustained VT or VF were less likely inducible for monomorphic VT as compared to non-reperfused patients. Reperfused and non-reperfused patients without prior sustained arrhythmia had comparable VT induction rates; however reperfused patients were less likely to experience spontaneous VT during follow-up. Among inducible patients VTCL of induced VTs was significantly shorter and inducible VT was more often very fast VT (CL ≤ 250 ms) in reperfused patients. These differences were even more pronounced in patients treated with primary PCI as compared to thrombolytic therapy. After adjustment for potential confounders, treatment of the index MI appeared to have an independently significant effect on the mean CL of induced VTs.

Early reperfusion during MI and inducibility of VT

Former studies performed before the widespread availability of reperfusion therapy have demonstrated that in patients with coronary artery disease VT was inducible in 92% of patients who presented with sustained VT and in 83% of patients who presented with cardiac arrest due to VF.[8] Accordingly, 79% of the non-reperfused patients in our study who presented with sustained VT or VF were inducible for monomorphic VT. In contrast, in only 56% of reperfused patients with documented VT or VF monomorphic VT was inducible. Although all patients had a chronic substrate as spontaneous arrhythmias occurred in the absence of a reversible cause the sensitivity of an EPS for substrate assessment after reperfusion therapy seems to be low. This finding is of clinical importance if EPS is performed for the evaluation of patients who present with unexplained syncope due to non-documented VT or during ablation procedures of VT if non-inducibility of monomorphic VT is considered as endpoint for ablation.

Acute reperfusion has resulted in a lower prevalence of spontaneous and induced ventricular arrhythmias in the acute phase of MI..[4, 21-23] In small series, 9-48% of patients receiving thrombolysis were inducible for ventricular arrhythmias as compared to 88-100% of patients without reperfusion therapy.[24, 25] However, the arrhythmogenic substrate causing late ventricular arrhythmias may develop over time. In our series, EPS was performed in the chronic healing phase of MI. Of interest, non-reperfused and reperfused patients without prior spontaneous arrhythmia showed high inducibility rates of 58% and 56%, respectively. However, during follow-up the three year cumulative incidence of appropriate device therapy was 36% in non-reperfused patients and only 17% in reperfused patients. This finding suggest that despite the presence of an arrhythmogenic substrate the value of EPS to predict VT occurrence is lower in reperfused patients as compared to non-reperfused patients.

Effect of early reperfusion and inducible VTCL

Early reperfusion during MI results in myocardial salvage and reduced mortality during follow-up.[3] Histological studies in patients and animal models of acute MI have shown that the duration of coronary artery occlusion is proportionally correlated to the size and transmural extent of myocardial scar.[4, 5, 26] Scar size and geometry are important determinants for the reentrant circuit geometry and may contribute to occurrence and cycle length of VT.[9, 27]

We recently demonstrated that reperfused patients referred for ablation of recurrent VT late after MI appeared to have smaller and less confluent electroanatomical scars with thick layers of surviving myocardium found at histology. Interestingly, the CL of spontaneous and induced VTs was shorter in reperfused than in non-reperfused patients likely due to the observed differences in scar geometry after reperfusion therapy.[13] The association between acute reperfusion therapy and shorter inducible VTCL was con-

firmed and extended, as the present study is conducted in a large population of post-MI patients also including patients without previously documented ventricular arrhythmia. In addition, we adjusted for all baseline characteristics that affect induced VTCL.

Limitations

Our study was performed in a selected population of ICD recipients with prior MI and low LVEF, who are not representative for the general population with prior MI. In addition, our cutoff of 9 hours for early reperfusion is arbitrarily chosen. Furthermore, we studied induced VTs, and our findings do not necessarily apply to spontaneous VTs. However, in the previous study by Wijnmaalen et al., spontaneous VTs were taken into account and similar differences were found, as compared to induced VTs. Finally, therapy for acute MI was not randomly assigned and time from MI to EPS differs between groups, which could have resulted in selection bias. However, since primary PCI has been shown to be the preferred treatment for acute MI, a study in which patients would be randomly assigned to primary PCI, thrombolysis or conservative treatment is ethically unacceptable and therefore, selection bias is now inevitable in studying the effects of reperfusion. To correct for it, we adjusted for baseline characteristics using linear regression and could demonstrate that reperfusion independently affects the CL of induced VTs.

CONCLUSION

There are important differences in VT inducibility, induced VTCL and occurrence of spontaneous VT in the chronic phase of MI between patients with and without successful reperfusion during acute MI. Reperfused patients who present with sustained VT/VF are less likely inducible for monomorphic VT. Despite similar VT induction rates in patients without prior documented sustained arrhythmias, reperfused patients are at lower risk for spontaneous VT. However, early reperfusion is associated with faster induced VT.

These findings suggest important differences in the chronic arrhythmogenic substrate after reperfusion, which gives rise to faster VT and which might be less reliably assessable by EPS.

CLINICAL PERSPECTIVE

Early reperfusion during myocardial infarction (MI) results in myocardial salvage and improved ventricular function, but it also influences the specific dimensions and geometry of myocardial fibrosis and thus the propensity for ventricular arrhythmia occurring late after MI. Recently, it has been demonstrated that reperfusion is associated with smaller, less confluent myocardial scars that appear to give rise to faster spontaneous and induced ventricular tachycardias (VTs) in patients referred for VT ablation late after MI. The present study comprised a large population of post-MI patients referred for electrophysiological evaluation and implantation of implantable defibrillators, without previously documented ventricular arrhythmia. In this population, reperfusion during MI affects inducibility, spontaneous occurrence, and cycle length of VTs. Monomorphic VT was inducible in only 56% of reperfused patients as compared with 79% of nonreperfused patients with documented VT or ventricular fibrillation. Reperfused and nonreperfused patients without prior sustained arrhythmia had comparable VT induction rates, but reperfused patients were less likely to have spontaneous VT during follow-up, suggesting that the value of electrophysiological study to predict VT occurrence is lower in reperfused patients as compared with nonreperfused patients. Finally, induced VTs were faster in reperfused patients. These findings probably reflect a different chronic arrhythmogenic substrate in reperfused patients, manifest by faster VTs and less reliably assessed by electrophysiological study.

REFERENCE LIST

1. Josephson M, Wellens HJ. Implantable defibrillators and sudden cardiac death. Circulation 2004;109(22):2685-91.
2. Heidenreich PA, McClellan M. Trends in treatment and outcomes for acute myocardial infarction. 1975-1995. Am J Med 2001;110(3):165-74.
3. The effects of tissue plasminogen activator, streptokinase, or both on coronary-artery patency, ventricular function, and survival after acute myocardial infarction. The GUSTO Angiographic Investigators. N Engl J Med 1993;329(22):1615-22.
4. Miyazaki S, Fujiwara H, Onodera T, Kihara Y, Matsuda M, Wu DJ, Nakamura Y, Kumada T, Sasayama S, Kawai C. Quantitative analysis of contraction band and coagulation necrosis after ischemia and reperfusion in the porcine heart. Circulation 1987;75(5): 1074-82.
5. Reimer KA, Lowe JE, Rasmussen MM, Jennings RB. The wavefront phenomenon of ischemic cell death. 1. Myocardial infarct size vs duration of coronary occlusion in dogs. Circulation 1977;56(5):786-94.
6. Tarantini G, Cacciavillani L, Corbetti F, Ramondo A, Marra MP, Bacchiega E, Napodano M, Bilato C, Razzolini R, Iliceto S. Duration of ischemia is a major determinant of transmurality and severe microvascular obstruction after primary angioplasty. a study performed with contrast-enhanced magnetic resonance. J Am Coll Cardiol 2005; 46(7):1229-35.
7. Thiele H, Kappl MJ, Linke A, Erbs S, Boudriot E, Lembcke A, Kivelitz D, Schuler G. Influence of time-to-treatment, TIMI-flow grades, and ST-segment resolution on infarct size and infarct transmurality as assessed by delayed enhancement magnetic resonance imaging. Eur Heart J 2007;28(12):1433-9.
8. Prystowsky EN, Miles WM, Evans JJ, Hubbard JE, Skale BT, Windle JR, Heger JJ, Zipes DP. Induction of ventricular tachycardia during programmed electrical stimulation. analysis of pacing methods. Circulation 1986;73(2 Pt 2):II32-II38.
9. Ciaccio EJ, Ashikaga H, Kaba RA, Cervantes D, Hopenfeld B, Wit AL, Peters NS, McVeigh ER, Garan H, Coromilas J. Model of reentrant ventricular tachycardia based on infarct border zone geometry predicts reentrant circuit features as determined by activation mapping. Heart Rhythm 2007;4(8):1034-45.
10. Marchlinski FE, Callans DJ, Gottlieb CD, Zado E. Linear ablation lesions for control of unmappable ventricular tachycardia in patients with ischemic and nonischemic cardiomyopathy. Circulation 2000;101(11): 1288-96.
11. Verma A, Marrouche NF, Schweikert RA, Saliba W, Wazni O, Cummings J, Abdul-Karim A, Bhargava M, Burkhardt JD, Kilicaslan F, Martin DO, Natale A. Relationship between successful ablation sites and the scar border zone defined by substrate mapping for ventricular tachycardia post-myocardial infarction. J Cardiovasc Electrophysiol 2005;16(5):465-71.
12. Peters NS, Coromilas J, Severs NJ, Wit AL. Disturbed connexin43 gap junction distribution correlates with the location of reentrant circuits in the epicardial border zone of healing canine infarcts that cause ventricular tachycardia. Circulation 1997; 95(4):988-96.
13. Wijnmaalen AP, Schalij MJ, von der Thüsen JH, Klautz RJM, Zeppenfeld K. Early reperfusion during acute myocardial infarction affects ventricular tachycardia characteristics and the chronic electroanatomical and histological substrate. Circulation 2010; 121(17):1887-1895.

14. Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, Domanski M, Troutman C, Anderson J, Johnson G, McNulty SE, Clapp-Channing N, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 2005; 352(20):225-37.

15. Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G. A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. N Engl J Med 1999;341(25): 1882-90.

16. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, Daubert JP, Higgins SL, Brown MW, Andrews ML. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med 2002; 346(12):877-83.

17. Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. Eur Heart J 2007;28(20):2525-38.

18. Van de Werf F, Bax J, Betriu A, Blomstrom-Lundqvist C, Crea F, Falk V, Filippatos G, Fox K, Huber K, Kastrati A, Rosengren A, Steg PG, et al. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation. the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J 2008;29(23):2909-45.

19. Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, Gregoratos G, Klein G, Moss AJ, Myerburg RJ, Priori SG, Quinones MA, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). J Am Coll Cardiol 2006;48(5):e247-e346.

20. Aliot EM, Stevenson WG, mendral-Garrote JM, Bogun F, Calkins CH, Delacretaz E, Della BP, Hindricks G, Jais P, Josephson ME, Kautzner J, Kay GN, et al. EHRA/HRS Expert Consensus on Catheter Ablation of Ventricular Arrhythmias. developed in a partnership with the European Heart Rhythm Association (EHRA), a Registered Branch of the European Society of Cardiology (ESC), and the Heart Rhythm Society (HRS); in collaboration with the American College of Cardiology (ACC) and the American Heart Association (AHA). Heart Rhythm 2009;6(6):886-933.

21. de Chillou C, Sadoul N, Bizeau O, Feldmann L, Gazakure E, Ismail M, Magnin-Poull I, Blankoff I, Aliot E. Prognostic value of thrombolysis, coronary artery patency, signal-averaged electrocardiography, left ventricular ejection fraction, and Holter electrocardiographic monitoring for life-threatening ventricular arrhythmias after a first acute myocardial infarction. Am J Cardiol 1997;80(7):852-8.

22. Hohnloser SH, Franck P, Klingenheben T, Zabel M, Just H. Open infarct artery, late potentials, and other prognostic factors in patients after acute myocardial infarction in the thrombolytic era: A prospective trial. Circulation 1994;90(4):1747-56.

23. Hohnloser SH, Klingenheben T, Zabel M, Schopperl M, Mauss O. Prevalence, characteristics and prognostic value during long-term follow-up of nonsustained ventricular tachycardia after myocardial infarction in the thrombolytic era. J Am Coll Cardiol 1999;33(7):1895-902.

24. Kersschot IE, Brugada P, Ramentol M, Zehender M, Waldecker B, Stevenson WG,

Geibel A, De ZC, Wellens HJ. Effects of early reperfusion in acute myocardial infarction on arrhythmias induced by programmed stimulation: a prospective, randomized study. J Am Coll Cardiol 1986;7(6):1234-42.

25. Sager PT, Perlmutter RA, Rosenfeld LE, McPherson CA, Wackers FJ, Batsford WP. Electrophysiologic effects of thrombolytic therapy in patients with a transmural anterior myocardial infarction complicated by left ventricular aneurysm formation. J Am Coll Cardiol 1988;12(1):19-24.
26. Matsuda M, Fujiwara H, Onodera T, Tanaka M, Wu DJ, Fujiwara T, Hamashima Y, Kawai C. Quantitative analysis of infarct size, contraction band necrosis, and coagulation necrosis in human autopsied hearts with acute myocardial infarction after treatment with selective intracoronary thrombolysis. Circulation 1987;76(5):981-9.
27. Ciaccio EJ, Costeas C, Coromilas J, Wit AL. Static relationship of cycle length to reentrant circuit geometry. Circulation 2001;104(16):1946-51.