

Predicting Survival with Reperfusion Arrhythmias during Primary Percutaneous Coronary Intervention for Acute Myocardial Infarction

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Abstract

Background: The significance of arrhythmia occurring after successful recanalization of an occluded artery during treatment following primary percutaneous coronary intervention for ST-segment elevation myocardial infarction is controversial.

Objectives: To study the association of reperfusion arrhythmia with short and long-term survival.

Methods: We used a prospective registry of consecutive STEMI patients undergoing PPCI. Patients with an impaired epicardial flow (TIMI flow grade < 3) at the end of the procedure were excluded.

Results: Of the 688 patients in the study group, 22% were women. Mean (\pm SD) age of the cohort was 61 (\pm 14) years and frequent co-morbidities included diabetes mellitus (25%), dyslipidemia (55%), hypertension (43%) and smoking (41%). RA was recorded in 200 patients (29%). Patients with RA had lower rates of diabetes (16% vs. 30%, $P < 0.01$) and hypertension (48% vs. 62%, $P < 0.01$), and a shorter median pain-to-balloon time (201 vs. 234 minutes, $P < 0.01$) than patients without RA. Thirty day mortality was 3.7% and 8.3% for patients with and without RA, respectively ($P = 0.04$). After controlling for age, gender and pain-to-balloon time the hazard ratio for mortality for patients with RA during a median follow-up period of 466 days was 0.46 (95% confidence interval 0.23–0.92).

Conclusions: The occurrence of RA immediately following PPCI for acute STEMI is associated with better clinical characteristics and identifies a subgroup with a particularly favorable prognosis.

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Early recanalization of an acutely occluded coronary artery and restoration of normal blood flow are the main treatment goals in patients with ST-segment acute myocardial infarction. However, despite successful recanalization by either thrombolytic agents or primary percutaneous transluminal coronary intervention, a substantial number of patients still fail to achieve complete and sustained myocardial reperfusion. Furthermore, even patients with an apparently normal epicardial flow might not achieve tissue reperfusion, which impacts negatively on prognosis. Arrhythmias occurring during restoration of epicardial flow (reperfusion arrhythmias) are thought to indicate myocardial reperfusion [1]. However, a recent study suggested that RA is associated with worsening of left ventricular function [2]. We hypothesized that RA occurring immediately after coronary reperfusion, as opposed

to arrhythmia occurring later within the first 24 hours, may carry more prognostic significance. Therefore, we wished to study the association of RA with patients' characteristics as well as with short and long-term prognosis in patients with STEMI undergoing angiographically successful PPCI, and to examine the value of RA as an easy-to-obtain tool in predicting outcome in these patients.

Patients and Methods

This prospective study included consecutive STEMI patients (initial ST-segment elevation of ≥ 1 mm in at least two contiguous electrocardiogram leads) undergoing PPCI at a tertiary care center during the period April 2002 to December 2005. Patients were included if they achieved adequate epicardial flow (TIMI flow grade 3) at the end of the procedure. For patients presenting more than once during the study period, only the later event was included. Data on demographic and clinical variables as well as on angiographic characteristics and treatment were collected prospectively. Arrhythmias were recorded immediately after angioplasty. Reperfusion arrhythmias were defined as accelerated idioventricular rhythm or ventricular tachycardia, or multiple ventricular ectopic beats appearing immediately (within 1 minute) after balloon deflation and not documented prior to recanalization. Median follow-up time was 460 days and mortality data were extracted from the national register.

Statistical analysis

Continuous variables were compared using Student's *t*-test for independent groups and the chi-square statistic was used for comparison of dichotomous variables. Survival curves were calculated using the Kaplan-Meier method. Cox regression analysis was used for long-term survival with adjustments for covariates and with mortality as the dependent variable. Death and end of follow-up were used as censors.

Results

Of the 688 patients, 22% were women. Mean (\pm SD) age of the cohort was 61 (\pm 4) years and frequent co-morbidities included diabetes mellitus (25%), dyslipidemia (55%), hypertension (43%) and smoking (41%). The infarct-related artery was the left anterior descending in 49%, circumflex in 13% and right coronary in 38%.

STEMI = ST-segment elevation myocardial infarction
 PPCI = primary percutaneous coronary intervention
 RA = reperfusion arrhythmia

Table 1. Baseline characteristics

	Patients with RA (n=200)	Patients without RA (n=488)	P
Age (yrs) (\pm SD)	60 \pm 12	61 \pm 14	0.12
Female (%)	37 (19)	115 (24)	0.15
Diabetes mellitus (%)	32 (16)	140 (29)	< 0.01
Hypertension (%)	66 (33)	222 (45)	< 0.01
Smoking (%)	91 (46)	200 (41)	0.53
Pain to balloon time (min) (\pm SD)	243 \pm 171	319 \pm 264	< 0.01
Infarct-related artery			
Left anterior descending (%)	90 (45)	248 (51)	0.28
Circumflex (%)	32 (16)	59 (12)	
Other (%)	78 (39)	181 (37)	
No. of diseased vessels			0.03
One	61 (30)	159 (32)	
Two	58 (30)	181 (37)	
Three	81 (40)	148 (31)	
IIb/IIIa inhibitors use (%)	99 (50)	219 (45)	0.27
Left ventricular dysfunction*			0.06
Mild or preserved function	70 (37)	205 (46)	
Moderate	63 (33)	113 (26)	
Severe	54 (30)	122 (28)	

* As assessed by echocardiography within 72 hours of presentation.

Reperfusion arrhythmias were recorded in 200 patients (29%) and included mainly accelerated idioventricular rhythm (71% of all RA). Table 1 compares the baseline, event characteristics and angiographic differences between patients with and without RA.

Thirty day mortality was 3.7% and 8.3% for patients with and without RA, respectively ($P = 0.04$). The hazard ratio for mortality during the entire follow-up period among patients with vs. those without RA was 0.46 (95% confidence interval 0.26–0.80, $P < 0.01$) [Figure 1].

After controlling for age, LV dysfunction and number of diseased vessels, the hazard ratio was 0.49 (95% CI 0.23–1.02, $P = 0.48$); further controlling for diabetes mellitus, hypertension, time to balloon, and gender attenuated the above risk reduction (HR 0.67, 95% CI 0.32–1.47, $P = 0.33$).

Discussion

Reperfusion arrhythmias have been recognized as a marker of restoration of antegrade flow since Goldberg et al. [3] registered AIVR during intracoronary thrombolytic therapy, and their usefulness for assessing myocardial reperfusion after thrombolytic therapy followed [1]. The value of AIVR as a marker of reperfusion or infarct-related artery patency was further established by several groups [4,5]. Gressin and colleagues [6] showed that the early occurrence (< 6 hours) of AIVR was a specific (76%) sign of a patent infarct-related coronary artery after thrombolytic therapy.

LV = left ventricular
CI = confidence interval
HR = hazard ratio
AIVR = accelerated idioventricular rhythm

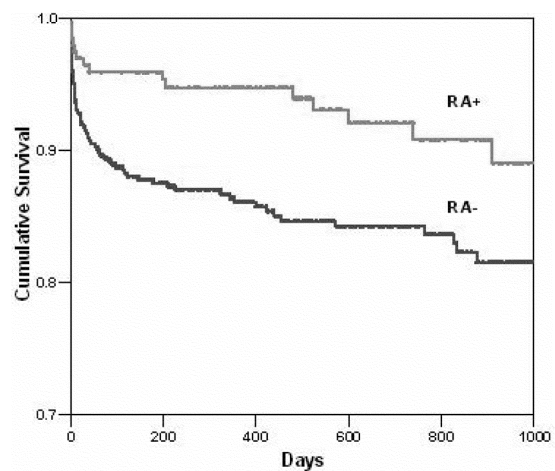


Figure 1. Kaplan-Meier survival curves for patients with (RA+) and without (RA-) reperfusion arrhythmias

Although coronary artery patency correlates with prognosis, even in patients with a normally restored TIMI grade 3 flow, tissue reperfusion at the myocardial level is a finer prognostic determinant [7,8]. We previously linked tissue level reperfusion with reperfusion arrhythmias occurring immediately following PPCI in STEMI patients [9]. In that study ST-segment resolution was positively associated with the occurrence of RA. Engelen and team [2] studied RA over a 24 hour period and found that their occurrence is associated with worsening left ventricular function and pointed out that RA probably represent myocardial cellular injury. However, the authors' definition of RA over a 24 hour period is too broad and thus invariably included late ventricular arrhythmias, known to predict adverse ventricular function and outcome [10]. In the present much larger study, we correlated RA occurring immediately post-PPCI with both baseline and angiographic characteristics and survival. Reperfusion arrhythmias were not associated with age or gender. Patients without RA had a higher prevalence of diabetes and hypertension but the same rate of multivessel disease. Thus, the occurrence of RA does not necessarily identify patients with a better coronary risk profile. Longer pain-to-balloon time was associated with a decreased RA rate. This is in accordance with the prognostic significance of time to reperfusion even in patients achieving good epicardial flow after PPCI [11]. These results further substantiate our main findings.

RA seem to be a powerful tool for predicting short-term prognosis since patients with RA had less than half of the 30 day mortality rate than those without RA. We assume that the link to better prognosis is that RA signify tissue level reperfusion better than previously shown. RA were not correlated with a lesser degree of LV dysfunction. There was even a lower proportion of patients with mild dysfunction or preserved function among patients in the RA group. However, LV function assessment was done in the acute phase, usually within 24 hours from presentation, and such early assessment may not be an optimal measure of the quality of reperfusion. RA patients fared better than the non-RA patients even though they had a somewhat worse LV

dysfunction. Furthermore, controlling for LV dysfunction in a multivariate analysis did not diminish the prognostic value of RA. This finding has clinical implications with regard to patient management post-angioplasty. RA also predicted lesser long-term risk.

After controlling for multiple variables known to affect prognosis, the predictive power of RA was reduced. Nevertheless, since the point-estimate for the hazard ratio was well below unity, there is a fair chance that with a larger sample size RA will be shown to independently predict survival. We believe that in patients without reperfusion arrhythmia there is a need to consider adjunctive strategies that may enhance microvascular reperfusion and lessen reperfusion injury.

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