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Sustained Ventricular Tachycardia as a Marker of Inadequate Myocardial Perfusion during the Acute Phase of Myocardial Infarction

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Summary

Background: Sustained ventricular tachycardia (VT) complicating the acute phase of myocardial infarction (AMI) is a quite rare event but with short-term unfavorable prognosis. The clinical characteristics as well as the therapeutic implications have not yet been well defined.

Hypothesis: This paper attempts to prove that VT may be considered a marker of inadequate myocardial perfusion after thrombolysis.

Methods: To assess the clinic-electroangiographic characteristics and prognosis of patients with VT occurring within the first 4 days of an AMI, a case-control study was carried out in 23 patients from a total of 1,100 patients (1.9%) hospitalized with AMI between March 1993 and July 1997. These patients were compared with a control group of 131 patients hospitalized consecutively. A statistical analysis was made using the chi-square test, *t*-test, and logistic regression.

Results: There were no differences among groups with regard to age, gender, and area of necrosis. Average time for the onset of VT was 26 h (range 0–92 h). Sixteen patients underwent coronary angiography: 4 patients had left main coronary artery disease, 2 had single-vessel disease, 8 had lesions in two vessels, and 2 had triple-vessel disease. Univariate analysis showed that patients with VT had a higher incidence of creatine phosphokinase (CPK)-MB peak > 300 UI/l (61 vs. 30%; $p < 0.001$), more frequent occurrence of previous AMI (48 vs. 17%; $p < 0.001$), and acute intraventricular conduction disorders (26 vs. 4%; $p < 0.001$). Furthermore, these patients suffered ischemia previous to VT more frequently (65 vs. 11%; $p < 0.0001$), and had a greater mortality rate than that in the control group (35 vs. 4%; $p < 0.0001$). In the multivariant analysis, the variables related to the occurrence of VT were CPK-MB peak > 300 IU/l (OR 5.9; 95% CI 1.6–21), acute intraventricular conduction disorders (OR 9.02; 95% CI 1.7–48), and ischemia immediately prior to VT (odds ratio [OR] 19.64; 95% confidence interval [CI] 5.3–73).

Conclusions: Ventricular tachycardia may be considered a marker of inadequate myocardial perfusion after thrombolysis; therefore, a more aggressive revascularization treatment in these patients would be advisable. The profile of patients with AMI, hospitalized in the coronary care unit, who will likely suffer from VT is previous AMI, CPK-MB peak > 300, acute intraventricular conduction disorders, Killip > I, and ischemia previous to VT.

Key words: ventricular tachycardia, myocardial infarction, inadequate perfusion

Introduction

The prognosis and electrophysiologic mechanisms of sustained ventricular tachycardia (VT) that occur in the subacute and chronic phase of an acute myocardial infarction (AMI) have been widely studied both in experimental and human models.[1, 2] However, during the acute phase of AMI, most efforts have been focused on ventricular fibrillation.[3–5] Recently, a subanalysis of the Global Utilization of Streptokinase and t-PA for Occluded coronary arteries (GUSTO) trial has defined the clinic-electroangiographic characteristics of patients who suffered from VT during the 48 h following an AMI.[6] This study assessed the significance, prognosis, and

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therapeutic implications of VT in the acute phase of AMI, but they found no relationship between VT and ischemia immediately previous to this arrhythmia. Wolfe *et al.* found a relationship between polymorphic VT and ischemia.[7] The purpose of our study was to assess the significance of VT in the acute phase of AMI and its possible relation to immediately previous ischemia.

Methods

Patients

Between January 1993 and July 1997, 1,100 patients with AMI were hospitalized in the coronary care unit of our hospital.

Data on demographic and clinic characteristics, laboratory results, and complications during the patients' hospitalization were collected prospectively on a form designed for that purpose. The diagnosis of AMI was based on clinical symptoms (chest pain for > 30 min), electrocardiogram (ECG) changes, and serial increases in creatine kinase (CPK) levels and its MB isoenzyme (CK-MB). All patients were monitored using a cardiac station capable of storing the ECG tracings for 24 h and reproducing them at any time on three different channels.

Coronary angiography was performed during the patients' hospital admission when they experienced the episode of VT. Prophylaxis with lidocaine was not administered to any patient. Beta-blocker treatment was used in 50% of patients in the control group and in 30% of patients who suffered VT. These drugs were not used if there was any contraindication such as heart failure, heart blockade, or chronic bronchitis. These patients were followed up until they were discharged from the coronary care unit. Data of the 23 patients with VT were compared with the control group (131 patients with AMI but without VT, hospitalized consecutively during the first 6 months of 1997).

Definitions

Sustained ventricular tachycardia was defined as a regular wide-complex tachycardia (≥120 ms), lasting > 30 s or leading to a hemodynamic compromise, at a rate of > 120 beats/min.

Ventricular tachycardia was considered polymorphic (PVT) when QRS complexes had variations in polarity and width. Patients with ventricular fibrillation immediately before an episode of VT, patients who had VT after 4 days in hospital, and those with any major cardiopathy associated with ischemic heart disease (valvular heart disease, etc.) were excluded from the study. These exclusion criteria were established to avoid any condition that could favor the appearance of VT.

Indirect reperfusion criteria are defined as a decrease in the ST segment of > 50% and the occurrence of maximum CPK peak before 14 h from the onset of AMI symptoms. Ischemia occurring previous to the VT episode was based on the occurrence of persistent angina despite thrombolytic therapy, the occurrence of post AMI angina regardless of ECG changes, or as a silent increase or decrease in the ST segment immediately before VT.

An extensive infarction was defined as CK-MB peak level > 300 IU/l.

Statistical Analysis

Numerical data are shown as mean value ± standard deviation. Differences between both groups were compared using the chi-square test and the Student's *t*-test. A logistic regression analysis was performed to obtain the independent variables associated with occurrence of VT. A logistic regression analysis was also performed to determine the variables associated with an increased risk of mortality. The CPK-MB values were transformed into a dichotomic variable to obtain greater sensitivity and specificity; 300 IU/l was chosen as the "cutoff" value.

The level of statistical significance was $p < 0.05$. Statistical analysis was made using the Statistical Package for Social Sciences (SPSS, Inc., Chicago, Ill., USA).

Results

Of 1,100 patients admitted to the coronary care unit with a diagnosis of AMI, 23 had an episode of VT during the first 4 days. Another six patients had an episode of VT between 5 and 27 days, but were not included in this study. In total, they represent 2% of all patients admitted consecutively due to AMI. Ten patients were not included either because they had ventricular fibrillation (VF) previous to VT, or because they did not suffer from AMI according to the above-mentioned criteria. Moreover, another two patients were excluded for severe aortic stenosis associated with an episode of ischemic heart disease.

Table I shows clinical and demographic characteristics. There were 20 men and 3 women, with an average age of 65 ± 9 (51–82). Eleven patients had previous AMI. The locations of AMI were 6 anterior-septal-lateral, 12 posterior-inferior, 3 non-Q AMI, and 2 with mixed allocations. Nine patients received thrombolytic treatment with tissue plasminogen activator, 8 received streptokinase, and 6 did not undergo thrombolysis because they did not meet the criteria: in 3 cases the ECG lesion was subendocardial and in 3 cases the evolution time of AMI was > 12 h.

The average time for thrombolysis was 4 h and 40 min. Eleven patients (48%) showed indirect reperfusion criteria and 12 (52%) had no evidence of such criteria.

The clinical situation of these patients according to Killip's classification was as follows: 26% were in Killip class I, 52% were in class II, 9% in class III, and 13% suffered from cardiogenic shock. The average ejection fraction of these patients, calculated by either ventriculography or transthoracic echocardiography, was 44% (24–63%).

Occurrence of an acute intraventricular conduction disorder by right or left bundle-branch block was observed in six pa-

TABLE I Clinical characteristics of patients with ventricular tachycardia

No. patients/ gender	Age	Previous AMI	Location of AMI [a]	Fibrinolysis	Time [b]	Fibrinolysis CPK/MB IU/l	Rep. Crit [c]	Killip class [d]	EF (%)
1/ M	76	+	Anterior-septal	t-PA	4 h	6800/806	+	II	28
2/ M	65	+	Inferior	t-PA	4 h	3170/376	+	II	34
3/ M	74	+	Posterior-lat.	t-PA	8 h	6925/799	+	II	47
4/ M	79	0	Inferior & RV	SK	6 h	1776/293	0	II	50
5/ M	51	0	Inferior	SK	4 h	3875/545	+	II	45
6/ M	56	0	Posterior-inf.	SK	5 h	4300/430	+	I	58
7/ M	76	0	Posterior-lat.	No	NA	5022/567	0	IV	NA
8/ M	52	0	Anterior-septal	SK	14 h	NA	0	IV	NA
9/ M	72	+	Anterior	SK	5 h	1379/140	0	III	55
10/ M	66	0	Inferior	t-PA	90 min	6190/472	0	I	40
11/ F	69	+	Anterior-septal	No	NA	370/37	0	I	24
12/ M	66	+	No Q	No	NA	NA	+	II	30
13/ F	55	+	Inferior	t-PA	70 min	4355/608	+	II	55
14/ M	62	0	Anterior	t-PA	150 min	5725/500	0	II	34
15/ M	59	0	Inferior	t-PA	5 h	2118/	+	I	61
16/ M	73	0	Posterior-inf.	t-PA	5 h	3155/443	+	II	63
17/ M	58	+	Inferior	t-PA	2 h	736/71	0	I	50
18/ F	82	+	Inferior	No	NA	3494/350	0	III	NA
19/ M	48	+	Anterior	SK	6 h	3590/397	0	II	30
20/ M	70	0	No Q	No	NA	418/65	0	I	NA
21/ M	70	0	Posterior-inf.	SK	5 h	3560/501	+	II	38
22/ M	69	0	Posterior-inf.	SK	4 h	3355/405	+	II	45
23/ M	67	+	No-Q	No	NA	NA	0	IV	NA

[a] Electrocardiographic AMI location.

[b] Time from the onset of symptoms to the start of the fibrinolysis procedure.

[c] Reperfusion criteria defined as decrease of the ST segment > 50% and CPK peak before 14 h from hospital admission.

[d] Maximum Killip during hospitalization.

Abbreviations: AMI acute myocardial infarction, CPK = creatine kinase, MB = MB fraction, Rep Crit = reperfusion criteria, EF = ejection fraction, F = female, M = male, RV = right ventricular, lat. = lateral, inf. = inferior, t-PA = tissue plasminogen activator, SK = streptokinase, NA = nonavailable or nonapplicable data, + = yes, 0 = no.

tients (26%). Ventricular tachycardia was polymorphic in 1 case, monomorphic in 20 cases, and in 2 cases the polymorphic VT became monomorphic.

Average time from onset of symptoms of ischemic heart disease until the occurrence of arrhythmia was 26 h (onset–92 h) (Table II). Fifteen patients (65%) had ischemia previous to VT. Sixty-nine percent of patients underwent coronary angiography: 4 (17%) patients had main left coronary artery disease, 2 (9%) had single-vessel disease, 8 (35%) had double-vessel disease, and 2 (9%) had triple-vessel disease. The overall mortality of this group of patients, who presented with an episode of VT during the acute phase of AMI, was 35%.

Univariate Analysis of Patients with Ventricular Tachycardia

Table III shows the results of the univariate analysis comparing the patient's characteristics with and without VT. No statistically significant differences were found regarding age, gender, thrombolysis, reperfusion criteria, or location of AMI.

Patients with VT have more extensive infarctions due to a higher CPK-MB peak (> 300 IU/l) (61 vs. 30%; p = 0.0006), higher Killip's class at admission (Killip > I, 74 vs. 30%; p = 0.0001), background of previous AMI (48 vs. 17%; p = 0.0008), and acute intraventricular conduction disorder (26 vs. 4%; p = 0.0004). Furthermore, these patients had ischemia immediately before VT more frequently (65 vs. 11%; p = 0.0001). The mortality rate in this group of patients was also higher (35 vs. 4%, p = 0.0001).

Logistic Regression

As shown in Table IV, the following variables, CPK-MB peak (odds ratio [OR] 5.9; 95% confidence interval [CI] 1.6–21), acute intraventricular conduction disorders (OR 9.02; 95% CI 1.7–48), and previous ischemia (OR 19.64; 95% CI 5.3–73), were independent predictors for the occurrence of VT during the acute phase of AMI. The other variables analyzed (age, gender, history of previous AMI, fibrinolysis, reperfusion criteria, Killip's classification) were not independent predictors for the occurrence of VT.

TABLE II Angiographic characteristics of ventricular tachycardia

Patient No.	T. symptoms arrhythmia [a]	Previous ischemia [b]	Death	Coronary angiography
1	4 h	+	+	No
2	40 h	0	0	AD 100%; Cx 60%
3	8 h	+	0	D1 80%; OM1 75%; OM2 90%
4	92 h	+	+	No
5	6 h	0	0	RC 100%; PTCA ineffective
6	40 h	0	0	No
7	38 h	0	+	No
8	16 h	0	+	AD occluded; Cx100%; OM1 60%
9	24 h	+	+	RC 90%; AD 70%
10	30 h	+	0	RC 70%; PD 70%
11	Unspecific	+	+	CD occluded; LM 60%
12	30 min	+	0	LM 100%; AD occluded
13	72 min	+	0	RC 95%; AD 60%
14	150 min	+	0	AD occluded; RC 50%
15	72 h	0	0	No
16	31 h	0	0	No
17	Onset	+	0	PD occluded; Cx occluded
18	12 h	+	0	No
19	90 h	0	+	RC,AD & Cx occluded
20	24 h	+	0	Cx 90%; AD and D1 75%
21	6 h	+	0	LM 70%, AD,Cx,RC 70%
22	4 h	+	0	Cx and OM2 90%. PTCA
23	24 h	+	+	LM 90%; 3 vessels

[a] Time from onset of AMI to occurrence of VT.
[b] Ischemia previous to VT.
Abbreviations: AD = anterior descendent, Cx = circumflex, Om1 = oblique marginal 1st branch, Om2 = oblique marginal 2nd branch, RC = right coronary, LM = left main coronary artery, D1 = first diagonal, PTCA = percutaneous transluminal coronary angioplasty,+ = yes, 0 = no.

TABLE III Clinical characteristics and mortality rate in patients with and without SVT. The values shown are means ± standard deviation. Absolute values are the number of patients and the percentages they represent are given in parentheses.

	AMI without VT (n = 131)	AMI with VT (n = 23)	RR	CI 95%	p Value
Age	62 ± 11	65 ± 9			0.24
Gender (M/F)	98 / 33	20 / 3	0.50	0.17–1.57	0.20
MB > 300 (%)	39 (30)	14 (61)	4.2	1.70–10.23	0.0006
Previous AMI (%)	22 (17)	11 (48)	3.36	1.63–6.7	0.0008
Fibrinolysis (%)	69 (53)	17 (74)	2.24	0.93–5.38	0.05
Reperfusion (%) [a]	59 (45)	11 (48)	1.10	0.51–2.33	0.80
BBB	6 (4)	6 (26)	4.18	2.03–8.59	0.0004
Ischemia previous to VT (%)	15 (11)	15 (65)	7.76	3.62–16.57	0.0001
Killip>I (%)	40 (30)	17 (74)	4.82	2.01–11.52	0.0001
Deaths (%)	6 (4)	8 (35)	5.33	2.75–10.30	0.0001

[a] Existence of reperfusion criteria; decrease of the ST segment >50% and CPK peak before 14 h from hospital admission.
Abbreviations: M= male, F = female, CK-MB = creatine kinase > 300 IU/l, BBB = bundle-branch block, CI = confidence interval, RR = relative risk.

Univariate Analysis of Intracoronary Unit Mortality

Table V shows the differences between survivors and nonsurvivors in the coronary care unit. Statistically significant differences were found in the existence of acute intraventricular conduction disorders, Killip > I, and ischemia previous to VT. Presence of VT was less frequent (11%) in the survivor group than in the nonsurvivor group (57%).

TABLE IV Results from logistic regression: Independent predictors of the incidence of sustained ventricular tachycardia (n = 23)

Variable	Correlation factor	Odds ratio	CI 95%	p Value
Constant	−2.86			0.03
BBB	2.19	9.02	1.7–48	0.009
Ischemia previous to VT	2.97	19.64	5.3–73	0.0001
MB peak > 300 IU/l	1.78	5.90	1.6–21	0.005

Abbreviations as in Table III.

TABLE V Univariate analysis for the mortality rate (n = 154)

	Non-survivors (n = 14)	Survivors (n = 140)	RR	CI 95%	p Value
Age > 65 (%)	11 (78)	65 (46)	3.76	1.09–12.96	0.02
Previous AMI (%)	6 (43)	27 (20)	2.75	1.02–7.37	0.04
Fibrinolysis (%)	9 (64)	77 (55)	1.42	0.50–4.05	0.50
Reperfusion (%) [a]	3 (21)	67 (48)	0.32	0.09–1.12	0.05
BBB	6 (43)	6 (4)	8.87	3.68–21.32	0.0001
Killip > I	12 (86)	45 (32)	10.21	2.36–44	0.0001
Ischemia previous to VT	7 (50)	23 (16)	4.13	1.56-10.89	0.002
SVT	8 (57)	15 (11)	7.59	2.90-19.85	0.0001

[a] Reperfusion criteria defined as a decrease of the ST segment > 50% and CPK peak before 14 h from hospital admission.
Abbreviations: BBB = bundle-branch block, Killip >1 = maximum Killip class during hospitalization, SVT = sustained ventricular tachycardia.

Logistic Regression for Mortality (Table VI)

Of all the variables analyzed, only the presence of acute intraventricular conduction disorder and Killip > I were independent predictors of intracoronary care unit mortality. The presence of VT also reached statistical significant level (p = 0.02), and this condition caused mortality to increase almost 5-fold (OR = 4.64).

TABLE VI Logistic regression for the mortality rate (n = 154)

	Correlation factor	Odds ratio	p Value
Constant	−0.97		0.18
BBB	1.85	6.39	0.01
VT	1.53	4.64	0.02
Killip > I	1.72	5.59	0.04

Abbreviations as in Table V.

Discussion

Sustained Ventricular Tachycardia as a Marker of Inadequate Myocardial Perfusion

Various studies have shown the association of sinus bradycardia and accelerated idioventricular rhythm with the occurrence of myocardial reperfusion,[8,9] as well as the lack of specificity of the ventricular arrhythmias as reperfusion markers.[10–12] However, it is not completely clear whether VT is a marker of inadequate myocardial perfusion after thrombolysis;[13] therefore, a more aggressive attitude has been recommended in these patients based on their high mortality rate. This high mortality rate is partially due to known data: these patients have ventricular function failure more frequently, and VT is a marker of extensive AMI as it has a higher CPK peak.[14] However, the direct relationship between VT and previous ischemia is still unclear.

This relationship can be inferred from indirect data:

1. Patients with a history of AMI who are more susceptible to VT usually have the AMI-related artery occluded[15,16]
2. Patients with ventricular arrhythmias have Thrombolysis in Myocardial Infarction (TIMI) 0 flow more frequently and TIMI 3 post thrombolysis less frequently[6]
3. Percutaneous transluminal coronary angioplasty on the AMI-related artery, even in the absence of active ischemia or viable myocardium, is an effective tool for controlling VT episodes refractory to other treatments[17]
4. Wolfe *et al*. also found that percutaneous angioplasty is not only effective as a treatment for VT, but also seems to be effective in the prevention of recurrence of polymorphic VT, especially when associated with persistent angina.[7,17,19]

Our data suggest the existence of a direct relationship between VT and ischemia previous to this arrhythmia. The previous ischemia is an independent predictor for the occurrence of VT. Therefore, this tachyarrhythmia may be considered a marker of inadequate myocardial perfusion (Figs. 1, 2). Furthermore, this type of patient frequently shows heart disease in which more than one vessel is involved.

Wolfe *et al.*[7] stated that sometimes VT occurring during the acute phase of AMI is associated with ischemia that is polymorphic. We have not checked these data in our studying in which monomorphic VT was prevalent.

Possible Mechanism of Ventricular Tachycardia

It is known that VT following the acute phase of AMI is produced by a reentry mechanism[20,21] that is generated subendocardially in most cases[22] although it may also be subepicardical. However, during the first hours of AMI, when the scar in the myocardial tissue is not yet formed, VT could be due to other mechanisms.

Thus, Rodriguez and Cinca[23] described, in an experimental model, the mechanisms that trigger ventricular arrhythmias

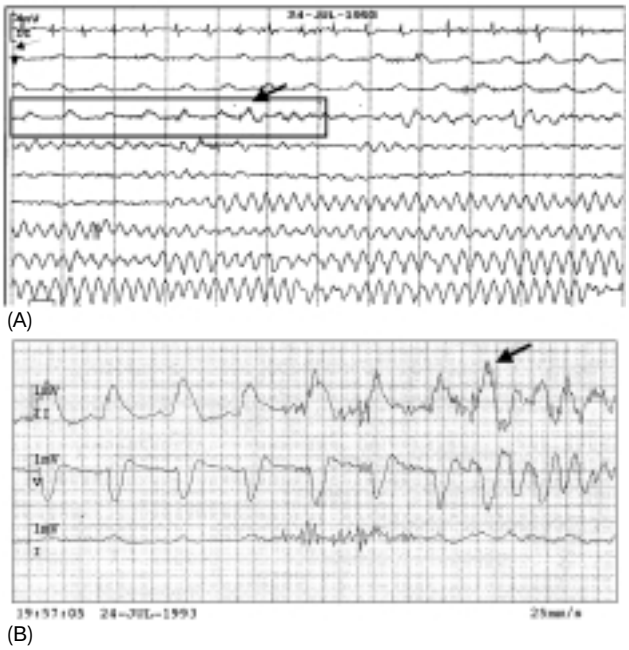

FIG. 1 Patient No. 20. (A) Digital tracing showing the beginning of a polymorphic ventricular tachycardia (VT) (thick arrow) after 35 heart beats from the onset of silent ischemia (thin arrow). (B) Enlargement of the VT onset (arrow). Notice the existence of a monophasic potential that indicates the severe degree of the ischemia.

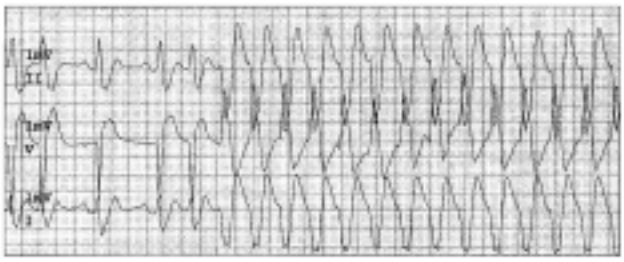

FIG. 2 Patient No. 23. Ventricular tachycardia with right bundle-branch block morphology in this patient with persistent angina. Notice the ST-segment displacement in the precordial lead.

following ischemia. It is known that two periods of arrhythmia appear during an episode of ischemia.[24] The first period starts almost immediately after coronary occlusion and lasts approximately 30 min (phase I), while the second period occurs a few hours later, lasting between 24 and 48 h (phase II). Subsequently, the first period is divided into another two: I_A and I_B.[25] It is also known that ischemia involves various metabolic and ionic changes, such as acidosis and increase in extracellular potassium,[26] that may produce disorders in the electrophysiologic properties of the myocardium[27, 28] and are the final cause of arrhythmias through several mechanisms, depending on the phase of the coronary occlusion.

Thus, in phase I_A, reentry seems to play a major role in the genesis of the arrhythmia, although focal mechanisms in the Purkinje cells have also been suggested.[29] In phase I_B, the mechanism of the arrhythmias is unclear. Although intramural reentry may be involved in their occurrence, the progressive accumulation of catecholamines that occurs in this phase[30] has led us to believe that such neurotransmitters could induce focal mechanisms such as an abnormal automatism.

Arrhythmias in phase II seemed to have their origin in the abnormal automatism or in the activity produced by postdepolarization of subendocardial Purkinje fibers.

This last phase occurs from 6 to 72 h after the coronary occlusion.[31] After this time, arrhythmias gradually decrease in frequency, but the action potential remains, which makes the occurrence of reentry arrhythmias possible.[20]

Prognostic and Therapeutic Implications

Since VT is a marker of myocardial ischemia, the usual severity of the coronary lesions in these patients and the high mortality rate would make it advisable to perform a more aggressive revascularization treatment.[6, 13] Moreover, other usual procedures, such as early use of beta blockers[13, 32] and angiotensin-converting enzyme inhibitors[33, 34] must be taken into account. It has not as yet been proven whether other usual procedures, such as early implantation of a defibrillator, would be effective.[35]

Study Limitations

A 12-lead ECG was not performed during all the episodes of tachycardia, as some patients were cardioverted immediately. Theoretically, this may have led us to mistake VT for an auricular origin tachycardia with an aberrant conduction. However, it seems reasonable to assume that a broad QRS tachycardia that occurs in the acute phase of AMI is a VT. The presence of supraventricular tachycardias with aberrant conduction during the acute phase of AMI that are hemodynamically not well tolerated is quite unusual. On the other hand, we did not perform coronary angiography in all patients.

Another limitation is that we analyzed patients who had VT between Days 3 and 4 post AMI and in whom ischemia may not have played a major role in the genesis of the arrhythmia. Nevertheless, as has been demonstrated experimentally,[23] it is still possible to suffer ventricular arrhythmias secondary to ischemia during this period.

Conclusions

The likelihood of the development of VT that complicates AMI is higher in patients with previous AMI, CPK-MB peak > 300 IU/l, acute intraventricular conduction disorders, Killip > I, and ischemia previous to VT.

Patients who present with an episode of VT during the acute phase of AMI have a high mortality rate, as this arrhythmia is an independent predictive factor. Ventricular tachycardia may be considered a marker of inadequate myocardial perfusion after the performance of thrombolytic therapy.

Therefore, a more aggressive revascularization treatment in these patients would be advisable.

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