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Sustained ventricular arrhythmias in unstable angina patients: Results of the ARIAM Database

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
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Summary

Background: The aim of this study was to investigate patients with unstable angina (UA) and the predictive factors of these arrhythmias and to determine whether this complication behaves as an independent variable with regard to mortality, increased length of stay in an ICU/CCU, and the performance of percutaneous coronary intervention (PCI).

Material/Methods: The retrospective cohort study included all patients diagnosed with UA and included in the Spanish "ARIAM" database between June 1996 and December 2005. Univariate and multivariate analyses were performed to evaluate the factors associated with these arrhythmias. 17,616 patients were included.

Results: Sustained ventricular tachycardia (SVT) occurred in 0.5%. The factors associated with its development were age, cardiogenic shock, and non-sustained ventricular tachycardia. SVT was associated with mortality (adjusted *OR*: 9.836, 95%*CI*: 1.81–53.33). Ventricular fibrillation (VF) occurred in 1%. In the multivariate study the variables that persistently associated independently with the development of VF were gender, Killip class, and high degree atrioventricular block (HDAVB). VF was associated with higher mortality (27.1% vs. 0.9%). Nevertheless, VF was not seen to be a variable independently associated with mortality in UA patients. Only VF was an independent variable in length of stay (adjusted *OR*: 2.059, 95%*CI*: 1.175-3.609). Neither SVT nor VF were independent variables associated with PCI.

Conclusions: Patients with UA complicated by SVT or VF represent a special high-risk subgroup with poor prognosis, which could lead to their being stratified towards a poor prognosis subgroup.

key words: **unstable angina • mortality • mean stay • percutaneous coronary intervention • atrioventricular block • arrhythmias**

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Background

Currently, a clear distinction is made between acute coronary syndrome (ACS) in non-ST-segment-elevation acute coronary syndrome (NSTE-ACS) and in acute ST-segment-elevation myocardial infarction (STEMI) in view of their physiopathology and management [1]. The epidemiology, prognosis [2], and management [1] of NSTE-ACS have been widely studied. Nevertheless, unstable angina (UA) is included in NSTE-ACS and, despite its importance and prevalence, has been barely studied. Both sustained ventricular tachycardia (SVT) and ventricular fibrillation (VF) are arrhythmias that have been shown to be prognostic in STEMI, and there are studies that demonstrate that these arrhythmias entail an aggravation of prognosis in NSTE-ACS. Nevertheless, there are only some sporadically described cases of these arrhythmias in UA and there are no studies evaluating their genesis and the prognosis they confer upon UA. Another interesting fact is the clear recommendation that exists in the conduct of percutaneous coronary intervention (PCI) in patients with high-risk UA, although for the moment this is still unrealistic. The appearance of these arrhythmias may probably stratify these patients directly towards high-risk patients in whom, due to the appearance of this arrhythmia, PCI could be indicated.

To this end, the objectives of this article are to evaluate: 1) the factors associated with the development of SVT and VF in patients with UA during their stay in intensive care units or coronary care units (ICU/CCU), 2) whether the presence of SVT or VF is associated with an increase in mortality during their stay in an ICU/CCU, 3) whether these arrhythmias are associated with an increase in the mean stay of UA patients during admission to an ICU/CCU, and 4) whether these arrhythmias are associated with the performance of PCI.

Material and Methods

Type of study: The ARIAM database

This was a descriptive cohort study carried out on a retrospective cohort that comprised all patients included in the database of the ARIAM (*Análisis del Retraso en el Infarto Agudo de Miocardio*, "Analysis of Delay in Acute Myocardial Infarction") project, a multicentre Spanish study designed as an internal quality improvement project in the treatment of ischemic heart disease [3–8]. The ARIAM project is limited to ICU/CCU of 129 hospitals in Spain. The ARIAM database includes all patients admitted to an ICU/CCU with diagnosis of ACS, be it acute myocardial infarct or unstable angina. This database satisfactorily passed an audit by the government of Andalusia of Spain as a database for STEMI. Case inclusion was prospective, although data interpretation and the development of the study were also retrospective. The study period was from June 1996 to December 2005. The follow-up period of this cohort study is limited exclusively to stay in an ICU/CCU. This study follows the ethical and privacy guidelines of the independent ethics and research committees related to the ARIAM project.

Variables studied

In this study, all patients diagnosed with UA who were admitted to an ICU/CCU and were only monitored during their stay in the ICU/CCU were selected. UA was defined as pain with evolving coronary characteristics, lasting more than 20 minutes at rest, with progressive characteristics in terms of intensity, duration, and a lower level of effort, and confirmed by enzymatic criteria with normality in the values of the different biomarkers used, i.e. creatine phosphokinase (CK), MB fraction of CK (CK-MB), or the different troponins. The definition and classification of UA of the Study Group on Angina Pectoris of the Ischemic Cardiopathy and Coronary Units Section of the Spanish Society of Cardiology of 1995 [9] was applied. UA was classified as: 1) Recent-onset effort angina: UA of less than 30 days' evolution; to be included as unstable, the symptoms must correspond to an advanced functional degree (III or IV) of the Canadian classification. 2) Progressive or increasing angina: this refers to a worsening of the symptoms with increased frequency, intensity, or duration of the angina episodes. 3) Rest angina: this appears spontaneously, without an apparent triggering. 4) Prolonged angina: this could be the culmination of any of the preceding forms, with a duration of more than 20 minutes, and no development of Q-wave necrosis, and 5) Post-infarct angina: this appears after the first 24 hours of an acute myocardial infarct and during its first month of evolution [9].

All patients presenting an increase in some of the biomarkers in the ranges suggested by the different laboratories of the different hospitals were excluded from the study.

Two subgroups were formed to evaluate the mean stay in the ICU/CCU: 1) suitable mean stay, defined as a stay with a duration of ≤2 days, and 2) prolonged mean stay, defined as a stay with a duration of >2 days. This definition of suitable and prolonged mean stay was made because the median mean stay of UA patients in our population is two days.

Age was studied from the quantitative and qualitative standpoints and was also categorized into the following age groups: 1) less than 55 years, 2) from 55 to 64 years, 3) from 65 to 74 years, 4) from 75 to 84 years, and 5) 85 years and older [10]. The treatment which was administered was the responsibility of the attending physician in each case and was based on the generally accepted criteria during the study period [6].

The following variables were studied: 1) cardiovascular risk factors, 2) the type of unstable angina, 3) seriousness on admission, evaluated by means of the score of the Acute Physiology and Chronic Health Evaluation II (APACHE II) [11] during the first 24 hours, 4) the worst functional class during the patient's stay in the emergency area, ICU/CCU, according to the Killip and Kimball classification [12], TIMI score [(2)], 5) mortality and mean stay, 6) complications, and 7) treatment given.

HDAVB was defined as a third degree atrioventricular block or a second degree block which required a temporary or permanent pacemaker. VF is classified as 1) primary VF, which includes all VF and torsade de pointes developed both during and prior to ICU/CCU admission, occurring in the 48 hours following the appearance of symptoms in stable patients with Killip and Kimball class 1, and 2) secondary VF, defined as occurring after another VF episode or when the Killip and Kimball classification is over 1, or over 48 hours

after the start of the ischemic event. Developments of any kind of VF were also studied (including the sum of primary and secondary VFs)

Statistical analysis

The statistical analysis merely seeks to explore and evaluate combinations of factors, and in no case does it purport to formulate an "absolutely or universally predictive" study or explain a reality, and thus any considerations related to adjustment of the distribution curves of the different variables are minimized, and no analysis of the diagnosis of the models is made, it being understood that for our purposes, binary logistic regression achieves sufficiently robust estimators. The Spanish version of the SPSS-13 statistics application was used. The following analyses were performed:

a) A descriptive analysis for quantitative variables was performed by means of central tendency measurements and dispersion measurements and for qualitative variables by means of the distribution of absolute and relative frequencies.
b) Two univariate analyses were performed to detect combinations or differences between patients with UA, according to whether or not they presented SVT or VF, with mortality.
c) Four multivariate analyses were performed: 1) to detect predictive factors or those associated with the development of SVT and VF and to evaluate whether the presence of SVT or VF is associated with: 2) mortality, 3) prolonged mean stay and 4) the the performance of PCI.

The dependent variables or results studied were the development of SVT and VF, mortality during their stay in the ICU/CCU, prolonged mean stay, and performance of PCI.

The multivariate analysis included all variables that presented statistically significant differences or were clinically relevant. The crude and adjusted odds ratios (*OR*) of each independent variable and their 95% confidence intervals (95%*CI*) were determined in the multivariate analysis. The multivariate analyses were performed by binary logistic regression, evaluating the existence of confounding variables and the possible interaction between different independent variables. The numerical data are presented as the mean ± standard deviation (*SD*). Qualitative variables are expressed as absolute numbers and percentages. A value of $p<0.05$ is regarded as statistically significant.

RESULTS

Descriptive study

From the appearance of the Spanish ARIAM database in 1993 until December 2005, 94,140 patients with ACS were included. During the selected study period, 17,616 (24.2%) patients were diagnosed with UA, with none of them presenting enzymatic increase (CK-MB or troponin, according to the time of admission and the determination performed in each hospital), thus representing our study population. Of the 17,616 patients diagnosed with UA, 12,335 (70%) were male and the median age was 67 years (mean age: 65.11±11.55 years). During the different years of the database, there was no significant changes in the percentage of admissions or mortality (1.2%). The delay in care between the onset of symptoms and arrival at the hospital was 269.38±174.20 minutes (median: 135 minutes). The mean APACHE II score was 8.81±7.55 points (median: 7). The TIMI score was only determined in 4,754 patients, with a mean value of 1.98±1.12 points (median: 2 points). 57.6% of patients (10,145) presented previous myocardial ischemia (Table 1). Neither SVT nor VF were seen to be independent variables associated with the conduct of PCI.

Development of SVT

Of the population with UA, 82 (0.5%) patients experienced SVT. Four patients required prehospital defibrillation. Patients with UA complicated by SVT were older (median: 70 vs. 67 years) and predominantly male. There were no significant differences in the type of angina between patients with and without SVT. Patients with SVT presented a higher Killip class, TIMI scores, and APACHE II. There were no differences in terms of cardiovascular risk factors, although there was an association of SVT with previous AMI (crude *OR*: 1.705, 95%*CI*: 1.057–2.752) (Table 1). As for management prior to the event studied, the patients without SVT had coronary angiographies more frequently. Patients with UA complicated by SVT presented more complications such as cardiogenic shock, episodes of systemic high blood pressure, and other arrhythmias (primary VF, secondary VF, non-sustained ventricular tachycardia, and supraventricular tachyarrhythmias). Patients with UA complicated by SVT required more diagnostic techniques such as echocardiography, coronary angiography, and pulmonary artery catheter implantation and more therapeutic techniques such as cardiopulmonary resuscitation, mechanical ventilation, electric cardioversion, and implantation of an intraaortic counterpulsation balloon. There were no differences in coronary revascularization techniques (PCI in patients with and without SVT: 15.2% vs. 17.4%, $p=0.401$). SVT was associated significantly with the use of certain treatments, such as antiarrhythmics, parenteral inotropic drugs, diuretics, and the use of magnesium. In the multivariate analysis the following variables remained associated independently of the development of SVT: age, development of cardiogenic shock, and the presence of non-sustained ventricular tachycardia (Table 2). The mean stay was greater in patients with SVT, but SVT was not shown to be an independent variable associated with prolonged mean stay. The patients with UA who presented with SVT had higher mortality; these patients with SVT had a crude *OR* for mortality of 14.051 (95%*CI*: 6.839-28.895). In the global population with UA, SVT was seen to be a variable associated with mortality, with an adjusted *OR* for mortality of 9.836 (95%*CI*: 1.814-53.333).

Ventricular fibrillation

The presence of VF was detected in 7174 patients, with VF in 71 of these patients (1%), being primary VF in 58 patients (0.8%) and secondary VF in 13 patients (0.19%). Patients with VF had a mean age of 65.00±11.55 years (median: 65 years). In males, VF was associated more frequently with higher Killip class, previous angina, SVT, supraventricular tachyarrhythmias, and HDAVB. There was an association with more complications, such as cardiogenic shock. Patients with VF required a higher implantation of provisional pacemakers, a greater frequency of cardiopulmo-

Table 1. Univariate analysis of the presence of Sustained VT.

Variables	Absence of SVT		Presence of SVT		*P*
Age (years)	64.98±11.51		68.37±10.28		0.016
Female sex	4200	(29.9%)	9	(12.9%)	0.014
APACHE II	8.81±7.42		15.22±21.36		0.001
TIMI	1.47±0.94		1.97±1.02		0.001
Mortality	143	(1.0%)	19	(27.1%)	0.000
Type of Angina					N.S
	790	(16.8%)	5	(11.9%)	
	542	(11.5%)	2	(4.8%)	
	1422	(30.2%)	14	(33.3%)	
	1403	(29.8%)	16	(38.1%)	
	2.0	(92%)	1	(2.4%)	
	282	(6.0%)	4	(9.5%)	
	183	(3.9%)	0	(0.0%)	
Killip and Kimball					0.0001
Factors and previous cardiovascular interventions	11635	(85.5%)	39	(55.7%)	
	1226	(9.0%)	9	(12.9%)	
	593	(4.4%)	8	(11.4%)	
	153	(1.1%)	14	(20.0%)	
Smoking	3361	(26.4%)	20	(28.6%)	N.S
Former smoker	3613	(26.4%)	22	(31.4%)	N.S
HBP	7453	(54.5%)	35	(50.0%)	N.S
Diabetes	3883	(28.4%)	23	(32.9%)	N.S
Hypercholesterolemia	5697	(41.6%)	34	(48.6%)	N.S
Stroke	726	(5.3%)	5	(0.0%)	N.S
previous MCI	4510	32.9%)	31	(45.6%)	0.036
Previous angina	46494	(47.4%)	38	(55.9%)	N.S.
Stent angioplasty	1190	(8.7%)	10	(14.3%)	N.S
Acute aortocoronary graft	87	(1.2%)	2	(2.9%)	N.S
Vascular surgery	66	(0.9%)	1	(1.4%)	N.S
Exercise test	2999	(21.9%)	27	(38.6%)	0.002
Coronary angiography	3649	(26.7%)	27	(38.6%)	0.027
Complications					
Right heart failure	53	(0.4%)	0	(0.0%)	N.S
Cardiac tamponade	7	(0.1%)	1	(1.4%)	0,040
Arterial hypertension	433	(3.2%)	2	(2.9%)	N.S
Cardiogenic shock	232	(1.7%)	13	(18.6%)	0.000
Primary ventricular fibrillation	0	(0.0%)	58	(82.9%)	0.000
Secondary ventricular fibrillation	0	(0.0%)	13	(18.%)	0.000
Ventricular tachycardia in bursts	71	(1.0%)	3	(4.3%)	P 0.034
Persistent sinusoidal tachycardia	112	(0.8%)	2	(2.9%)	P N.S
Supraventricular tachyarrhythmias	692	(5.1%)	10	(14.3%)	P 0.003
Severe bradyarrhythmias	299	(2.2%)	2	(2.9%)	P N.S

Table 1 continued. Univariate analysis of the presence of Sustained VT.

Variables	Absence of SVT		Presence of SVT		*P*
High degree atrioventricular block	139	(1.0%)	3	(4.3%)	P N.S
Difficult control angina	1806	(13.2%)	15	(21.4%)	P 0.051
Evolution to AMI	48	(0.4%)	8	(11.4%)	0,000
Pericarditis	40	(0.3%)	0	(0.0%)	N.S
Anoxic encephalopathy	14	(0.1%)	4	(5.7%)	0.000
Swan-Ganz	63	(0.5%)	4	(5.7%)	0.000
Echocardiography	2298	(16.8%)	26	(37.1%)	0.000
Cardiopulmonary resuscitation	99	(0.7%)	27	(38.6%)	0.000
Mechanical ventilation	236	(1.7%)	24	(34.3%)	0.000
Cardioversion	85	(0.6%)	39	(55.7%)	0.000
Pericardiocentesis	4	(0.0%)	0	(0.0%)	N.S
Temporary pacemaker	82	(0.6%)	2	(2.9%)	0,068
Intraaortic counterpulsation balloon	58	(0.4%)	1	(1.4%)	N.S
Antiarrhythmics	771	(5.6%)	24	(34.3%)	0.000
Antiaggregants	13207	(96.5%)	64	(91.4%)	0.037
Prophylactic heparin	2283	(28.6%)	20	(28.6%)	N.S
Therapeutic heparin	5160	(71.9%)	54	(77.1%)	N.S
Intravenous betablockers	879	(6.4%)	14	(20.0%)	0,000
Oral beta-blockers	7362	(53.8%)	31	(44.3%)	N.S
Intravenous nitroglycerine	11311	(82.6%)	58	(82.9%)	N.S
Oral nitrates	8119	(59.3%)	40	(57.1%)	N.S
Calcium channel blockers	4384	(32.0%)	35	(50.0%)	0.002
ACE inhibitors	4861	(35.5%)	33	(47.1%)	N.S
Inotropes	513	(3.7%)	19	(27.1%)	0.000
Digoxin	254	(3.5%)	4	(5.7%)	N.S
Intravenous vasodilators	211	(1.5%)	2	(2.9%)	N.S
Diuretics	1942	(4.2%)	20	(28.6%)	0.002
Magnesium	60	(0.8%)	4	(5.7%)	0.003
Lipid-lowering agents	3029	(22.1%)	10	(14.3%)	N.S

Table 2. Multivariate analyses on the development of SVT. Variables that persist associated with the development of SVT.

	p	OR	95%CI for OR	
Cardiogenic shock	0.000	6.077	2.359	15.655
Non-sustained TV	0.000	14.63	5.646	37.953
Age	0.001	1.015	1.006	1.024
Constant	0.001	0.003		

nary resuscitation, more mechanical ventilation, and more echocardiography and they were given more PCI (17.1 vs. 5.6%, $p<0.0001$). In the multivariate study it was observed that the variables that persisted and which were independently associated with the development of VF were gender, Killip class, and the development of HDAVB (Table 3). The patients who presented with VF had greater mortality (27.1% vs. 0.9%, crude *OR*: 41.35, 95% *CI*: 23.12–73.96). Nevertheless, VF was not seen to be an independent variable associated with mortality in the population with UA. Mean stay was shorter in patients without VF (2.88±3.99 vs.

Table 3. Univariate analysis of the presence of VF.

Variables	Absence of VF		Presence of VF		*P*
Woman	4200	(29.9%)	9	(12.9%)	0.002
Type of angina					
Initial	790	(16.8%)	5	(11.9%)	
Progressive	542	(11.5%)	2	(4.8%)	
Rest	1422	(30.2%)	14	(33.3%)	
Prolonged	1403	(29.8%)	16	(38.1%)	0.436
Variant	92	(2.0%)	1	(2.4%)	
Post-MCI	282	(6.0%)	4	(9.5%)	
Secondary	183	(3.9%)	0	(0.0%)	
Previous ischemic diagnosis	8118	(60.6%)	39	(73.6%)	0.069
Killip					
1	11635	(85.5%)	39	(55.7%)	
2	1226	(9.0%)	9	(12.9%)	0.000
3	593	(4.4%)	8	(11.4%)	
4	153	(1.1%)	14	(20.0%)	
Cardiovascular risk factors					
Smoking	3361	(24.6%)	20	(28.6%)	0.490
Former smoker	3613	(26.4%)	22	(31.4%)	0.345
HBP	7453	(54.5%)	35	(50.0%)	0.473
Diabetes	3883	(28.4%)	23	(32.9%)	0.429
Cholesterol	5697	(41.6%)	34	(48.6%)	0.274
Stroke	726	(5.3%)	5	(7.1%)	0.422
Family history	1154	(8.4%)	2	(2.9%)	0.126
Previous angina	6488	(47.4%)	44	(62.9%)	0.011
Previous MCI	4515	(33.0%)	26	(37.1%)	0.451
Previous angioplasty	694	(9.7%)	10	(14.3%)	0.219
Previous stent	503	(7.0%)	8	(11.4%)	0.155
Previous aortocoronary graft	805	(5.9%)	7	(10.0%)	0.194
Right heart failure	53	(0.4%)	0	(0.0%)	1.000
Cardiac tamponade	7	(0.1%)	1	(1.4%)	0.040
Severe systemic HBP	433	(3.2%)	2	(2.9%)	1.000
Shock	232	(1.7%)	13	(18.6%)	0.000
Infectious process	151	(1.1%)	7	(10.0%)	0.000
Pulmonary thromboembolism	1	(0.0%)	0	(0.0%)	1.000
Systemic embolism	12	(0.1%)	0	(0.0%)	1.000
Anoxic encephalopathy	14	(0.1%)	4	(5.7%)	0.000
Psychic intolerance	179	(1.3%)	0	(0.0%)	1.000
Septal rupture	1	(0.0%)	0	(0.0%)	1.000
Thrombophlebitis	19	(0.3%)	1	(1.4%)	0.177
Pneumothorax + haemothorax	5	(0.1%)	1	(1.4%)	0.057
Bacteremia	14	(0.2%)	0	(0.0%)	1.000

Table 3 continued. Univariate analysis of the presence of VF.

Variables	Absence of VF		Presence of VF		*P*
Sepsis	5	(0.1%)	1	(1.4%)	0.057
Cardiac perforation-tamponade	1	(0.0%)	0	(0.0%)	1.000
Sustained Tv	62	(0.5%)	6	(8.6%)	0.000
Tv in bursts	71	(1.0%)	3	(4.3%)	0.034
Persistent Ts	112	(0.8%)	2	(2.9%)	0.114
SV tachyarrhythmias	692	(5.1%)	10	(14.3%)	0.003
Severe bradyarrhythmia	299	(2.2%)	2	(2.9%)	0.669
HDAVB	139	(1.0%)	3	(4.3%)	0.036
Ischemia-embolism	9	(0.1%)	0	(0.0%)	1.000
Swan-Ganz	63	(0.5%)	4	(5.7%)	0.000
CPR	99	(0.7%)	27	(38.6%)	0.000
Mechanical ventilation	236	(1.7%)	24	(34.3%)	0.000
Cardioversion	4384	(32.0%)	35	(50.0%)	0.002
Pericardiocentesis	211	(1.5%)	2	(2.9%)	0.295
Echocardiography	2298	(16.8%)	26	(37.1%)	0.000
Implantation of temporary pacemaker	1942	(14.2%)	20	(28.6%)	0.002
Counterpulsation balloon	771	(5.6%)	24	(34.3%)	0.000
Antiaggregants	13207	(96.5%)	64	(91.4%)	0.037
Prophylactic heparin	2283	(31.8%)	20	(28.6%)	0.608
Therapeutic heparin	5160	(71.9%)	54	(77.1%)	0.422
IV betablockers	879	(6.4%)	14	(20.0%)	0.000
Oral betablockers	7362	(53.8%)	31	(44.3%)	0.119
IV nitroglycerine	11311	(82.6%)	58	(82.9%)	1.000
Angiotensin converting enzyme inhibitors	4861	(35.5%)	33	(47.1%)	0.044
Parenteral inotropics	513	(3.7%)	19	(27.1%)	0.000
Digoxin	254	(3.5%)	4	(5.7%)	0.316
Antivitamin K	235	(1.7%)	0	(0.0%)	0.635
Difficult angina	1806	(13.2%)	15	(21.4%)	0.051
Lipid-lowering agents	3029	(22.1%)	10	(14.3%)	0.147
Cardiac rehabilitation	33	(0.5%)	0	(0.0%)	1.000

5.60±6.19 days, $p<0.0001$). VF was seen to be an independent variable and a predictor of prolonged mean stay (adjusted *OR*: 2.059, 95% *CI*: 1.175–3.609).

Discussion

Our population of UA represents a sample with characteristics similar to other databases, although it only comprises patients with a diagnosis of UA, in other words with no elevation of cardiac biomarkers. This is why it is difficult to compare the population of this study and those of other databases, as existing ones include patients with NSTE-ACS [13–17], and not patients with an exclusive diagnosis of UA. In any case, we consider the study sample, and therefore its findings, to be significant and extrapolatable, at least for our purposes.

The interest in SVT and VF is clear when occurring in an STEMI, modifying the prognosis and therefore representing

Table 4. Multivariate analyses, variables that remain associated with the development of VF.

	p	Adjusted OR	95%CI for OR	
FEMALE SEX	0.001	0.311	0.152	0.636
KILLIP 1	0.0001	1		
KILLIP 2	0.042	2.140	1.028	4.457
KILLIP 3	0.001	3.760	1.714	8.248
KILLIP 4	0.0001	22.588	11.536	44.230
HDAVB	0.0001	10.617	3.884	29.018
Constant	0.0001	0.008		

a greater-risk subpopulation [18–20]. An increase in mortality after 30 days and 6 months was also observed in patients with NSTE-ACS who experienced this complication [21], although currently there are no studies that analyze the existence of these arrhythmias as complications of UA or the factors that may be associated with its development and whether this complication implicitly entails a worse prognosis. There are only studies that describe the existence of these arrhythmias in UA as sporadic findings [22] and as predictors of arrhythmias before cardiac surgery [23]. In this study we found that 0.5% of UA cases were complicated with SVT, a low frequency of presentation compared with STEMI or NSTE-ACS, which nevertheless is understandable if we take into account that our population was exclusively UA patients. In STEMI, factors associated with the development of SVT were lower baseline systolic pressure, intravenous lidocaine use before enrollment, higher Killip class, faster baseline heart rate, and advanced age [20], whereas in NSTE-ACS, previous high blood pressure, chronic obstructive pulmonary disease, prior myocardial infarction, and the presence of changes in the ST segment were predictors [21], which represents a subgroup of patients with greater morbidity and probably with greater coronary ischemic disease. In our population we found age, the development of cardiogenic shock, and the presence of non-sustained ventricular tachycardia to be factors that remain associated with the development of SVT, factors that really suggest a more extensive ischemia and greater comorbidity; in short, a subgroup of patients with greater severity. Similarly, the presence of SVT behaves as a predictive variable independent of mortality. The development of SVT thus shows us a subpopulation of greater seriousness and at higher risk, which might help us to stratify this population and address more active PCI policies. Similarly, our VF frequency was 1%, with being female, the presence of HDAVB, and Killip and Kimball degree presenting as factors associated with development, thus representing a subgroup of greater seriousness, and probably with greater myocardial ischemia.

It is interesting that most of the cases described in the literature of UA complicated by SVT or VF occur in patients with UA and episodes of coronary vasospasm; however, this does not correspond to the findings obtained in our study, where its appearance was greater in prolonged angina. Interestingly, there were no differences with regard to treatment by means of oral beta-blockers, with the administration of intravenous beta-blockers, antiarrhythmics, and magnesium being greater in patients with SVT and VF. In other words, the generation of these arrhythmias entails a worsening of the prognosis (whether due to the actual seriousness of the myocardial ischemia or even acceptable as a complication of the actual arrhythmia), although these patients received very little PCI during their admission to the ICU/CCU. Despite the acknowledged benefit of early PCI in patients with high-risk NSTE-ACS, and which is recommended by different therapeutic guidelines, it is evident that we still cannot apply it to the whole population [24]; therefore, and despite having high-risk subpopulations, the exclusive presence of SVT or VF could stratify these patients and address immediate reperfusion policies for them. However, the therapeutic guidelines [1] do not provide for this complication as a special high-risk subgroup, and it should probably be analyzed whether these patients present in themselves a special high-risk subgroup and therefore stratify these patients directly to high risk.

Another interesting fact is the excess in time of mean stay involved in these arrhythmias, ascribable to greater seriousness and/or a probably unsuitable wait until PCI. Early PCI would probably lead to a shortening of the mean stay and a reduction in costs.

Limitations

The ARIAM registry is an observational study and a cause-effect relationship cannot be established. It is not a completely continuous database, and cases of UA are lost. The ARIAM database was designed initially to analyze the delay in thrombolytic treatment, not to analyze arrhythmias in UA; therefore the variables collected focus more specifically on this point, and exhaustiveness may be lacking in some variables. It must be mentioned that there has been an evolution in ischemic heart disease since 1996 with regard to therapeutic recommendations, variability in the management in different hospitals, and in definitions over the years. In view of the broad study period, in many centers we may only know the data on CK, but not on troponins, and therefore there may be patients with a diagnosis of UA included who were really NSTE-ACS patients, although in recent years (since the value of the troponins has been known) it has the same frequency of admission and similar mortality as in previous years, probably because the population is similar. The evolution and follow-up of the patients is limited to their stay in the ICU/CCU. We do not know the exact moment of the development of these arrhythmias.

CONCLUSIONS

Patients with unstable angina complicated by SVT or VF represent a special high-risk subgroup with poor prognosis, which could lead them to be stratified towards a poor-prognosis subgroup.

APPENDIX A

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REFERENCES:

1. Braunwald E, Antman EM, Beasley JW et al, American College of Cardiology; American Heart Association: Committee on the Management of Patients With Unstable Angina. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction – summary article: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on the Management of Patients With Unstable Angina). J Am Coll Cardiol, 2002; 40(7): 1366–74
2. Antman EM, Cohen M, Bernink PJ et al: The TIMI risk score for unstable angina/non-ST elevation MI: a method for prognostication and therapeutic decision making. JAMA, 2000; 248: 835-42
3. Álvarez Bueno M, Vera Almazán A, Rodríguez García JJ et al: Concept, development and objectives of project ARIAM. Med Intensiva, 1999; 23: 273–80
4. Aguayo de Hoyos E, Reina Toral A, Colmenero Ruiz M et al: Analysis of delays in the treatment of acute coronary syndrome. Data in the Registry ARIAM. Med Intensiva, 1999; 23: 280–87
5. Reina Toral A, Aguayo de Hoyos E, Colmenero Ruiz M, Camacho Víctor A, Medina García P, Fernández Sacristán MA. Mortality in acute myocardial infarction. Med Intensiva; 1999; 23: 288–93
6. González Díaz F, Guerrero Gómez FJ, Martínez Coronel JF et al: Fribrinolytic agents in the project ARIAM. Exclusion reasons and complications. Med Intensiva 1999; 23: 294–300
7. Rosell Ortiz F, Mellado Vergel FJ et al: Acute coronary syndrome (ACS) with elevated ST segment: consensus strategy for early reperfusion. The Public Enterprise for Health Emergencies and the ARIAM Project Andalusia Med Intensiva, 2007; 31: 502–9
8. Ruiz-Bailén M, Pola Gallego de Guzmán MD, Éxposito Ruiz M et al: Atrioventricular block in unstable angina. Results of the ARIAM registry. Med Intensiva, 2006; 30(9): 432–39
9. Azpitarte Almagro J, Cabadés A, O'Callaghan A et al: Angina de pecho. Concepto y clasificación. Rev Esp Cardiol, 1995; 48: 373–82
10. Ruiz Bailén M, Aguayo de Hoyos E, Ramos-Cuadra JA et al, and ARIAM Group: Influence of age of management and clinical evolution of patients with acute myocardial infarction of Spanish population. Int J Cardiol, 2002; 85: 285–96
11. Knaus WA, Draper EA, Wagner DP, Zimmerman JE: APACHE II: A severity of disease classification system. Crit Care Med, 1985; 13: 818–29
12. Killip T III, Kimball JT: Treatment of myocardial infarction in a coronary care unit: a two year experience with 250 patients. Am J Cardiol, 1967; 20: 457–64
13. Scirica BM, Moliterno DJ, Every NR et al: Differences between men and women in the management of unstable angina pectoris. (The GUARANTEE registry). Am J Cardiol, 1999; 84: 1145–50
14. Kim C, Schaaf CH, Maynard C, Every NR: Unstable angina in the Myocardial Infarction Triage and Interventon Registry (MITI): short and long term outcomes in men and women. Am Heart J, 2001; 141: 73–77
15. Cannon CP, Weintraub WS, Demopoulos LA et al, TACTICS (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy) – Thrombolysis in Myocardial Infarction 18 Investigators: TACTICS (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy)–Thrombolysis in Myocardial Infarction 18 Investigators. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. N Engl J Med, 2001;;344(25): 1879–87
16. Inhibition of platelet glycoprotein IIb/IIIa with eptifibatide in patients with acute coronary syndromes. The PURSUIT Trial Investigators. Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy. N Engl J Med, 1998; 339(7): 436–43
17. Boch X, López de Sá E, López Sendón J et al: Perfil clínico, pronóstico y variabilidad en el tratamiento del síndrome coronario agudo sin elevación del segmento SR. Datos del registro PEPA. Rev Esp Cardiol, 2003; 56: 346–53
18. McMurray J, Kober L, Robertson M et al: Antiarrhythmic effect of carvedilol after acute myocardial infarction: results of the Carvedilol Post-Infarct Survival Control in Left Ventricular Dysfunction (CAPRICORN) trial. J Am Coll Cardiol, 2005; 45(4): 525–30
19. Ruiz-Bailen M, Aguayo de Hoyos E, Ruiz-Navarro S et al, ARIAM Group: Ventricular fibrillation in acute myocardial infarction in Spanish patients: Results of the ARIAM database. Crit Care Med, 2003; 31: 2144–51
20. Al-Khatib SM, Stebbins AL, Califf RM et al, GUSTO-III trial: Sustained ventricular arrhythmias and mortality among patients with acute myocardial infarction: results from the GUSTO-III trial. Am Heart J, 2003; 145(3): 515–21
21. Al-Khatib SM, Granger CB, Huang Y et al: Sustained ventricular arrhythmias among patients with acute coronary syndromes with no ST-segment elevation: incidence, predictors, and outcomes. Circulation, 2002; 106(3): 309–12
22. D'Agate DJ, Schwartz R, Lazar JM: Coronary vasospasm-induced ventricular tachyarrhythmias. J Invasive Cardiol, 2002; 14(10): 609–14
23. Ascione R, Reeves BC, Santo K et al: Predictors of new malignant ventricular arrhythmias after coronary surgery: a case-control study. J Am Coll Cardiol, 2004; 43(9): 1630–38
24. Bhatt DL, Roe MT, Peterson ED et al, CRUSADE Investigators: Utilization of Early Invasive Management Strategies for High-Risk Patients With Non-ST-Segment Elevation Acute Coronary Syndromes: Results From the CRUSADE Quality Improvement Initiative. JAMA, 2004; 292: 2096–104