Original Research

Clinical and Angiographic Characteristics of Patients with Acute Coronary Syndrome Associated with Sudden Cardiac Death

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Introduction: Sudden death (SD) is in most cases due to cardiac causes, mainly secondary to ischemic heart disease. However, the angiographic characteristics in SD survivors in the context of an acute coronary syndrome (ACS) remain controversial. The aim of this study was to evaluate the clinical and angiographic characteristics of patients who suffered cardiac arrest during an ACS.

Methods: We evaluated 46 patients with SD related to ACS, who were divided into two groups according to their presentation: an ST-elevation myocardial infarction (SD-STEMI) group and a non ST-elevation myocardial infarction (SD-NSTEMI) group. Consecutive STEMI patients without SD served as a double size-matched control group. We compared the clinical and angiographic characteristics and the in-hospital mortality between groups.

Results: Patients in the SD-NSTEMI group (n=13) were older and had a higher incidence of hypertension. The left anterior descending coronary artery was the most frequent culprit vessel in all groups. SD-STEMI patients (n=33) had a higher prevalence of proximal coronary culprit segment involvement than did the non-SD STEMI group (75% vs. 36.3%, p<0.001). The SD-NSTEMI group was characterized by multivessel and multi-segment disease. Outcomes were similar for both SD groups.

Conclusion: SD in patients with NSTEMI occurred in patients who were older, with more cardiovascular risk factors, diffuse and multivessel coronary disease, complex coronary lesions, and a lower rate of angioplasty success as compared with the STEMI group. SD STEMI patients had a significant higher association with proximal coronary acute occlusion than STEMI patients without SD.

Sudden death (SD) from cardiac causes is estimated to account for approximately 50 percent of all deaths from cardiovascular causes.[1] Anatomic findings at autopsy include acute changes in coronary plaque morphology, such as thrombus, plaque disruption, or both, in 50% of cases of sudden coronary death, whereas in hearts with myocardial scars and no acute infarction, active coronary lesions are identified in 46% of cases.[2]

Pathological findings in patients in whom death occurred within a sudden ischemic event are well established.[3] However, the angiographic characteristics of SD survivors in the context of an acute coronary syndrome (ACS) remain controversial.[4]

This study aimed to analyze the clinical characteristics, coronary angiographic findings and hospital survival of patients resuscitated after a sudden cardiac arrest with ACS.

Methods

Patients and data collection

Patients who recovered from cardiac arrest with ACS and were admitted to La Paz University Hospital from 2007 to 2011 were included. Data were collected retrospectively from a prospective database of the Coronary Care Unit, and the clinical and angiography records. Clinical characteristics, electrocardiographic (ECG), echocardiographic and angiographic findings were analyzed. Patients were included if they survived cardiac arrest due to acute coronary thrombosis or severe coronary lesions seen on angiography. Patients without coronary disease on angiography were excluded from the current analysis. Patients were divided into two groups according to their presentation: 1) an ST-elevation myocardial infarction (SD-STEMI) group, and 2) a non ST-elevation myocardial infarction (SD-NSTEMI) group. For the same time period, consecutive STEMI patients without SD were included as a double size-matched control group. Patients with ischemic changes on the ECG and no lesions on coronary angiography were excluded from further data analysis.

Definitions

SD was defined as a cardiac arrest that occurred suddenly and unexpectedly in a patient who was in otherwise stable condition, with no premonitory heart failure, MI, or other clear cause of death within 24 hours from symptom onset. ACS was defined by ECG ischemic changes and clinical presentation. STEMI was defined as elevation of the ST segment on the ECG (≥2 mm of ST-segment elevation in the precordial leads or ≥1 mm in other leads), elevated troponin, and acute coronary thrombosis on angiography. NSTEMI was defined by the presence of ischemic changes on the ECG, elevated troponin, and severe coronary lesions on angiography.

Statistical analysis

The SPSS 19.0 (SPSS Inc., USA) statistical software package for Windows was used. Continuous variables were expressed as mean ± standard deviation and were analyzed using Student's t-test. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Kaplan–Meier survival curves and log-rank test were used to analyze the in-hospital mortality at 30 days. For all tests, $p<0.05$ (2-sided) was considered significant.

Results

From September 2007 to September 2011, 130 SD resuscitated patients were admitted to the Coronary Care Unit in our hospital. From patients referred to the catheterization laboratory with a clinical suspicion of acute coronary disease, 46 consecutive patients with angiographic coronary artery disease were included: 33 patients in the SD-STEMI group and 13 patients in the SD-NSTEMI group. All patients received therapeutic hypothermia according to the internal institutional protocol.

Clinical characteristics

The clinical characteristics of the patients are listed in Table 1. Patients with SD-NSTEMI were older than patients with SD-STEMI (68.5 ± 13.2 vs. 59.9 ± 13.6 years, $p=0.031$), and had a higher incidence of hypertension (40.6% vs. 84.6%, $p<0.001$). The remaining clinical parameters, including sex distribution, diabetes and smoking habits, were similar. Left ventricular ejection fraction (LVEF) did not show any statistically significant difference ($p=0.9$).

Angiographic characteristics

We found a significant association between severe multivessel disease, considered as the culprit in acute ischemic events, and SD-NSTEMI clinical presentation (Table 2). In the SD-STEMI group, the most common culprit vessel was the left anterior descending (LAD) artery, although the difference did not reach statistical significance. The number of affected vessels with severe coronary disease that were not considered culprits for the ACS did not show a significant association. In the non-STEMI group, there was a higher incidence of permeable (TIMI II-III) culprit vessels (76.9% vs. 32.1, $p=0.006$). SD-STEMI patients had an incidence of TIMI flow grade 0-I of 67.9% ($p=0.009$), associated with angiographic thrombus grade 3-4 in 73.3% of cases ($p<0.001$). A proximal focal lesion was significantly more frequent in the SD-STEMI group than in SD-NSTEMI patients (75% vs. 30.8%, $p=0.008$). In the SD-NSTEMI group, the association with multi-segment disease was stronger than in the SD-STEMI group (38.5% vs. 3.1%, $p=0.005$). In the SD-STEMI group, a type A or B lesion (American Heart Association classification) was more frequent (81.3% vs. 23.1%, $p<0.001$) whereas type C lesions were more frequent in the SD-

Table 1. Clinical characteristics of patients in the three groups.

	SD-STEMI (n=33)	SD-NSTEMI (n=13)	non-SD STEMI (n=80)	p*	p†
Age (years)	59.9 ± 13.6	68.5 ± 13.2	62.13 ± 14.3	0.031	0.44
Male sex	29 (90.6)	9 (69.2)	65 (81.3)	0.32	0.58
Hypertension	13 (40.6)	11 (84.6)	38 (47.5)	<0.001	0.53
Diabetes	8 (25)	6 (46.2)	34 (30)	0.28	0.08
Current smoking	18 (56.3)	5 (38.5)	51 (63.8)	0.33	0.45
Previous PCI	4 (12.1)	3 (23.7)	9 (11.3)	0.35	1
Previous infarction	4 (12.1)	4 (30.7)	8 (10)	0.13	0.74
Treatment:					
Aspirin	30 (90.9)	13 (100)	78 (97.7)	0.26	0.15
Thienopyridine	33 (100)	9 (69.2)	77 (96)	<0.001	0.55
Beta-blockers	15 (45.4)	4 (30.7)	49 (61.5)	0.14	0.14
ACEI / ARB	8 (24.2)	7 (53.8)	55 (69.3)	0.052	<0.001
Statins	24 (72.7)	11 (84)	74 (92.7)	0.39	0.011
LVEF	42.0 ± 15.0	45.0 ± 13.8	35.9 ± 20	0.9	0.12
Killip-Kimbal:					
I	9 (27.2)	2 (15.3)	50 (62.5)	0.39	<0.001
II	3 (9)	2 (15.3)	12 (15)	0.47	0.54
III	5 (15.1)	3 (23)	2 (2.5)	0.52	0.02
IV	16 (48.3)	7 (53.8)	8 (10.6)	0.74	<0.001

Values are given as n (%) or mean ± standard deviation. *SD-STEMI vs. SD-NSTEMI group. †SD-STEMI vs. non-SD STEMI group. ACEI – angiotensin-converting enzyme inhibitors; ARB – angiotensin II receptor blocker; LVEF – left ventricular ejection fraction; PCI – percutaneous coronary intervention; SD – sudden death; STEMI – ST-elevation myocardial infarction.

Table 2. Angiographic characteristics.

	SD-STEMI (n=33)	SD-NSTEMI (n=13)	non-SD STEMI (n=80)	p*	p†
Culprit vessel:					
Right coronary	12 (37.5)	3 (23.1)	29 (36.3)	0.4	1
Left anterior descending	14 (43.8)	4 (30.8)	34 (42.5)	0.5	1
Left circumflex	5 (15.6)	0	10 (12.5)	0.9	0.76
Multivessel	0	5 (38.5)	0	0.001	
Number of affected vessels:					
One-vessel disease	18 (54.5)	5 (38.5)	36 (45)	0.3	0.41
Two-vessel disease	7 (21.2)	3 (23.1)	27 (33.8)	0.9	0.25
More than one-vessel disease	10 (30.3)	7 (53.8)	37 (46.2)	0.9	0.14
TIMI flow 2-3	9 (32.1)	10 (76.9)	12 (15)	0.006	0.18
TIMI flow 0-1	19 (67.9)	2 (15.4)	64 (80)	0.009	0.019
Angiographic thrombus:					
Grade 1-2	8 (26.7)	11 (84.6)	13 (16.3)	<0.001	0.42
Grade 3-4	22 (73.3)	1 (7.7)	63 (78.8)	<0.001	0.23
Coronary culprit lesion segment:					
Proximal	24 (75.0)	4 (30.8)	29 (36.3)	0.008	<0.001
Middle	6 (18.8)	2 (15.4)	39 (48.8)	0.9	0.003
Distal	1 (3.1)	0	5 (6.3)	0.9	0.67
Multi-segment disease	1 (3.1)	5 (38.5)	2 (2.5)	0.005	1
Thrombus aspiration	6 (18.8)	0	20 (25.0)	0.16	0.62
AHA lesion classification:					
A-B	26 (81.3)	3 (23.1)	66 (82.5)	<0.001	0.79
C	4 (12.5)	9 (69.2)	10 (12.5)	<0.001	1
PCI successful	23 (71.9)	5 (38.5)	74 (92.5)	0.032	0.005
IABP requirement	6 (18.1)	1 (7.6)	1 (1.3)	0.37	0.002

Values are given as n (%). *SD-STEMI vs. SD-NSTEMI group. †SD-STEMI vs. non-SD STEMI group. AHA – American Heart Association; IAPB – intra-aortic balloon pump; PCI – percutaneous coronary intervention.

NSTEMI group (69.2% vs. 12.5%, p<0.001). In the SD-STEMI group, the PCI success was higher than in the SD-NSTEMI group (71.9% vs. 38.5%, p=0.032).

Non-SD STEMI vs. SD-STEMI patients

We included 80 patients in the non-SD STEMI group. The clinical characteristics did not show any statistically significant difference between non-SD STEMI and SD-STEMI patients (Table 1). The culprit vessel did not show statistical differences between the groups, (Table 2) and the LAD was the vessel most frequently affected in both groups (p=1). Almost half of the patients had compromise of only one vessel (SD-STEMI 54.5% vs. non-SD STEMI 45%, p=0.41). The lesion was located in the proximal vessel in 75% of the SD-STEMI group and 36.3% of the non-SD STEMI group (p<0.001). The location was mid-vessel in 18.8% of the SD-STEMI group and 48.8% of the non-SD STEMI group (p<0.001). Distal culprit lesion location was found with similar frequency in both groups. On risk analysis, a proximal-vessel lesion location showed a statistically significant association with the SD-STEMI group (odds ratio [OR] 4.69, 95% confidence interval [CI] 1.92-11.43, p<0.001), whereas a mid-vessel lesion location showed an association with the non-SD STEMI group (OR 0.23, 95% CI 0.09-0.63, p<0.003).

Hospital outcomes

The hospital mortality was similar in both SD groups (53.8% in the NSTEMI group and 40.6% in STEMI patients, p=0.63; Figure 1). The main cause of death in both SD groups was related to hypoxic-ischemic encephalopathy (STEMI 23.7% vs. NSTEMI 46.1%, p<0.001). There were no significant differences between the causes of death in both groups (Table 3). Hospital stay was longer in the SD-STEMI group than in the STEMI group (7.2 ± 4.5 vs. 4.5 ± 7.5 days, p=0.043). Kaplan–Meier curves showed that in-hospital mortality was higher in the SD-STEMI group than in the non-SD STEMI group (42.5% vs. 3.8%, respectively, p<0.001; Figure 2).

Table 3. Hospital outcomes.

	STEMI (n=33)	NSTEMI (n=13)	p
Death (30 days)	13 (40.6)	7 (53.8)	0.63
Causes of death:	11 (34)	2 (15)	0.29
Hypoxic-ischemic encephalopathy	9 (27.3)	6 (46.1)	0.49
Multi-organ failure	2 (6.1)	1 (7.6)	0.75
Cardiogenic shock	2 (6.1)	0	0.54

Values are given as n (%).

Discussion

Cardiac arrest may be the first sudden manifestation of myocardial infarction. This is one of the first studies to describe exhaustively the coronary angiographic characteristics of this population. We found that SD-STEMI patients were younger, with more focal and proximal lesions, whereas non-STEMI patients were a sicker population with diffuse coronary disease. However, the in-hospital mortality was similar in both groups. Also, a positive significant relationship was observed between the acute proximal coronary thrombosis occlusion in the context of STEMI and the occurrence of sudden cardiac death in patients who survived. In our opinion, these findings reinforce the theory that myocardium at risk and the macro reentries around the large ischemic zones could generate malignant arrhythmias that cause sudden death episodes.[5-7] In experimental canine models, malignant ventricular arrhythmias were induced by proximal LAD occlusion in 37.5-61.9% of the cases.[5,6] In our study, this could be explained by the high incidence of proximal coronary occlusion in SD-STEMI patients, and the high incidence of diffuse coronary heart disease in SD-NSTEMI patients. In the context of STEMI, only one human study has confirmed this finding, whereas many others failed to demonstrate the role of the geography of the culprit lesion or occlusion in the mechanism of sudden death.[8]

According to the published literature, the incidence of sudden death and STEMI varies between 5.7% and 12.3%.[9,10] In NSTEMI patients, the incidence of ventricular tachycardia post-event was 25%, while that of sudden death in the follow-up was 1.5% to 6%.[11,12] In our population, STEMI presentation was the most frequent cause of sudden cardiac death related to acute coronary disease, with clinical and pathological findings similar to those previously described.[4,12] In an epidemiological analysis of acute coronary disease without SD, STEMI presentation was also more frequent than non-STEMI presentation.[9] The clinical characteristics of the STEMI group were similar to those described by Markusohn et al[14] and Lettieri et al,[15] with the fifth decade as the most frequent age of presentation, an incidence of cardiovascular risk factors of around

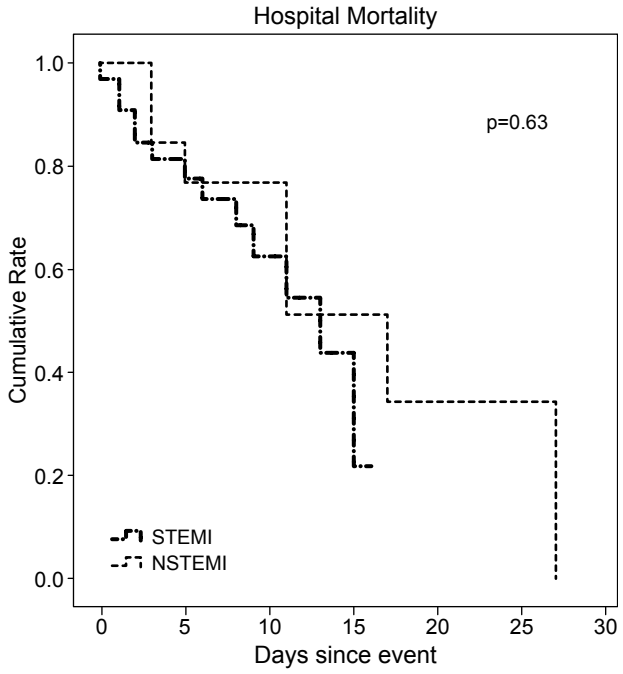

Figure 1. Hospital 30-day mortality comparing SD-STEMI vs. SD-NSTEMI. Kaplan–Meier curves showed no differences in hospital mortality between the two sudden death groups (p=0.63). Cox regression analysis also found no association between the groups and mortality (p=0.43).

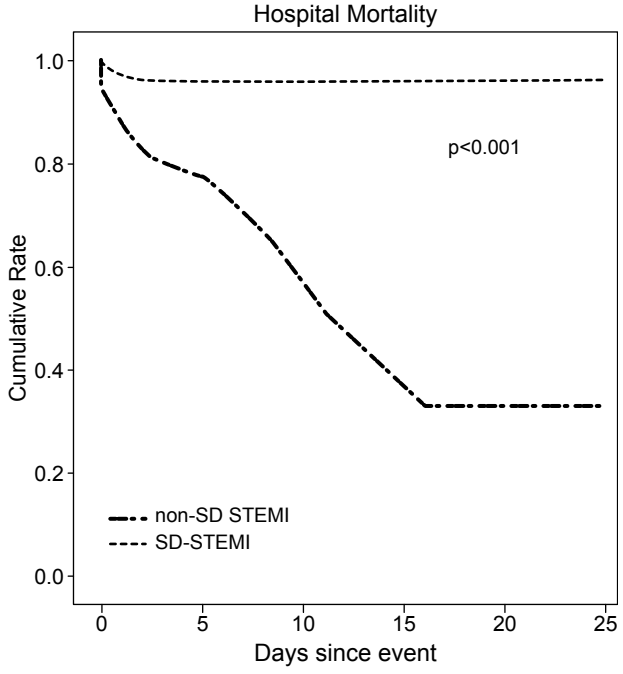

Figure 2. Hospital 30-day mortality comparing SD-STEMI vs. non-SD STEMI. Kaplan–Meier curves showed that in-hospital mortality was higher in the SD-STEMI group than in the non-SD STEMI group (42.5% vs. 3.8%, respectively, p<0.001). Cox regression analysis found a hazard ratio of 13.7 (95% confidence interval 4-46.9, p<0.001) for the association between SD-STEMI and mortality.

50% of patients,[14] and an incidence of previous coronary artery disease between 9% and 11.9%.[15,16] In an epidemiological analysis of ACS without SD, the STEMI population was younger and had less cardiovascular risk factors than NSTEMI patients,[17,18] although LVEF at admission was similar for both groups. In our study similar clinical features were found. Compared with the work of Bendz et al, our STEMI population had a lower LVEF.[13] We think that this could be related to more severe ischemia during cardiac arrest, the resuscitation maneuvers (including defibrillation), and a systemic inflammatory response after cardiac arrest.

In various series that included patients with STEMI but without SD, the LAD was the most frequently affected coronary vessel, in almost 50% of patients, followed by the right coronary artery in 30% of cases.[9,10] In our study, STEMI groups most frequently presented one-vessel disease, with focal lesions and angiographic thrombus. This has a correlation with the rate of thrombus aspiration and the pathological findings previously reported.[3,19,20] NSTEMI patients showed diffuse coronary disease in most cases, with complex coronary lesions and a lower classification of angiographic thrombus. These findings were correlated with a high frequency of successful angioplasty in STEMI patients and a better outcome.

Patients who had an ACS without SD had lower hospital mortality compared to our population (1.9% vs. 40.6%).[14] This was probably related to the high incidence in sudden death patients of hypoxemic encephalopathy and multisystem organ failure.[21,22] Although in-hospital mortality in this study was lower than in other studies previously reported, this may be the result of therapeutic hypothermia, which probably improved the outcome.[23-25] In our experience, therapeutic hypothermia with a target temperature of 32-34˚C is safe and may improve outcomes after cardiac arrest.[26,27] These conclusions are concordant with other recent studies.[28]

This study has several limitations. First, it was a retrospective study and some data were collected from clinical records, which may have reduced the quality of the information. Second, the small number of patients could have obscured statistical differences between groups in some variables in which a trend towards a significant difference was observed.

Conclusion

There are differences in clinical presentation and angiographic findings between patients who suffer

SD associated with STEMI or NSTEMI syndromes. Patients who had SD with NSTEMI are older, with more cardiovascular risk factors, diffuse and multivessel coronary disease, complex coronary lesions and a lower rate of angioplasty success, although no significant differences were found in 30-day mortality. Sudden cardiac death related to STEMI syndrome had a significantly higher association with proximal acute coronary occlusion compared to the STEMI group without SD.

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