

# The Importance of a Normal ECG in non-ST Elevation Acute Coronary Syndromes

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## Abstract

**Background:** Admission ECG has a major impact on the diagnosis and management of non-ST elevation acute coronary syndromes (ACS).

**Purpose:** To assess the impact of the admission ECG on prognosis over non-ST ACS.

**Population:** Prospective, continuous, observational study of 802 non-ST ACS patients from a single center. Patients were divided in 2 groups: A (n=538) – Abnormal ECG and B (n=264) – Normal ECG. Normal ECG was synonymous of sinus rhythm and no acute ischemic changes. A one-year clinical follow up was performed targeting all causes of mortality and the MACE rate.

**Results:** Group A patients were older ( $68.7 \pm 11.7$  vs.  $63.4 \pm 12.7$ Y,  $p < 0.001$ ), had higher Killip classes and peak myocardial necrosis biomarkers. Furthermore, they had lower left ventricular ejection fraction (LVEF) ( $52.01 \pm 10.55$  vs.  $55.34 \pm 9.51\%$ ,  $p < 0.001$ ), glomerular filtration rate, initial hemoglobin, and total cholesterol levels. Group B patients were more frequently submitted to invasive strategy ( $63.6$  vs.  $46.5\%$ ,  $p < 0.001$ ) and treated with aspirin, clopidogrel, beta blockers and statins. They also more often presented normal coronary anatomy ( $26.2$  vs.  $18.0\%$ ,  $p = 0.45$ ). There was a trend to higher in-hospital mortality in group A ( $4.6$  vs.  $1.9\%$ ,  $p = 0.054$ ). Kaplan-Meier analysis showed that at one month and one year ( $95.1$  vs.  $89.5\%$ ,  $p = 0.012$ ) survival was higher in group B and the result remained significant on a Cox regression model (normal ECG HR 0.45 (0.21 – 0.97)). There were no differences regarding the MACE rate.

**Conclusion:** In our non-ST elevation ACS population, a normal ECG was an early marker for good prognosis. (Arq Bras Cardiol 2010; 94(1) : 24-32)

**Key Words:** Electrocardiography; Diagnostic; Reference Standards; Prognosis.

## Introduction

The ECG represents one of the most important tools in acute coronary syndromes (ACS), differentiating two clinical entities, the ST-elevation and the non-ST elevation ACS, with consequent different management strategies. It remains at the present time an inexpensive, readily available and non-invasive test.

ST-segment depression and T wave changes are electrical markers of unstable coronary artery disease<sup>1,2</sup>.

According to two risk score analysis for non-ST elevation ACS, ECG variables were an important tool. In TIMI (*Thrombolysis In Myocardial Infarction*) risk score, an ECG binary variable, the presence or absence of ST depression, was a risk factor for a composite result of death or ischemic events, around 14 days after the ACS<sup>3</sup>, and in the GRACE (Global

Registry of Acute Coronary Events) score, ECG remained at six months an independent predictor for overall mortality<sup>4</sup>.

The number of leads with ST depression and the magnitude of ST depression on the admission ECG correlated with the severity of ischemia, and was a marker for a worse outcome, as reported by Holmvang et al<sup>5</sup> in the FRISC II (Fragmin and Fast Revascularization During Instability in Coronary Artery Disease) sub-analysis<sup>5</sup>.

ST depression was a relatively frequent finding in ACS patients, as almost 40% of a total of 55.000 patients in the Crusade registry presented this ECG abnormality<sup>6</sup>. Although there are doubts regarding the value of T wave inversion as a marker of ischemia, it has been acknowledged that anterior deep symmetrical T wave inversion was a marker for disease on the left anterior descending artery or main stem territory, as reported by Zwann et al<sup>7</sup>. Holmvang et al<sup>5</sup> concluded that in addition to the female gender, ST depression and T wave inversion in five leads were independent predictors of death or re-infarction, 30 days after randomization, in the TRIM (Thrombin Inhibition In Myocardial Ischemia) sub-study<sup>5</sup>.

Both American and European guidelines published in 2007 over non-ST elevation ACS recommend admitting a patient

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for an invasive strategy in the presence of presumably new ST depression (not T wave inversion) on the admission ECG<sup>8,9</sup>.

On the other hand, a normal ECG does not exclude an ACS, as previously reported by McCarthy *et al*, as almost 5% of patients discharged from the emergence room with a normal ECG had an acute ischemic event<sup>10</sup>.

In this context, we decided to analyze, in a single center coronary care unit, the prognostic value of a normal ECG in non-ST elevation ACS patients.

## Population and methods

### Study population

The present study was a continuous, observational, and prospective analysis of 1459 consecutive admissions for ACS, between May 2004 and December 2006, on a single coronary care unit. We excluded 130 records as they were readmissions. The final population consisted of 1329 patients. Of these, we selected 802 patients with a diagnosis of unstable angina or non-ST elevation acute myocardial infarction. The remaining population consisted of 445 patients with ST-elevation ACS, and 37 with a paced electrical rhythm ACS. Forty five patients were eliminated due to incomplete data.

Non-ST elevation acute myocardial infarction was defined by the presence of ischemic chest pain lasting more than five minutes, and positive cardiac biomarkers (troponin I) with or without ECG ischemic changes (namely ST depression or T wave inversion).

Unstable angina was defined either by new onset angina (at least class III CCS), progressive angina, or angina at rest, with or without ECG ischemic changes.

We analyzed standardized records during admission that included demographic, clinical, electrical, echocardiographic and laboratorial data. Medical therapy, catheterization data, in-hospital course and discharge medication were also recorded.

The population was divided in two groups, based on the admission ECG. Group A included 538 patients that presented an abnormal ECG; group B included 264 patients that presented a normal ECG. An abnormal ECG had at least one of the following changes: atrial fibrillation, ST depression, ST elevation, T wave inversion, or “de novo” bundle branch block.

This investigation conforms to the principles outlined in the Declaration of Helsinki. The protocol was approved by our institutional ethics committee, and all patients gave written informed consent to participate in the study.

### ECG analysis

ST depression had to be at least 1 mm in two contiguous leads to be considered and it was measured 60 ms after the J point. ST elevation had to be at least 2 mm in lead V1-V2 to be considered and 1 mm in any other lead, with the duration of at least 0.08 s. ST depression was not considered in the presence of left ventricular hypertrophy with strain, bundle branch block, paced rhythms, or if they were present on a

previous ECG; T wave inversion had to be also at least 1 mm, and all leads were considered except aVR.

Sinus rhythm was defined by the presence of a positive P wave in I, II, and aVL and negative in aVF, with an axis in the frontal plane between 0° and +90°. Atrial fibrillation was defined by an “irregularly irregular” ventricular rhythm, with associated *f* waves (irregular baseline undulation with variable amplitude, with a rate of 350 – 600/min).

Left bundle branch block (LBBB) was identified by a typical QRS morphology (R in V6, qRS in V1) with a duration superior to 120 ms, and right bundle branch block was defined by a QRS greater than 120 ms and a RsR' pattern in V1.

The ECG considered for the analysis was the one performed at the admission in the emergency room, or in the coronary care unit, previous to the start of the treatment.

Electrocardiographic characteristics were classified as “de novo” if they were not present in the most recent electrocardiogram before presentation, or if there was no prior electrocardiogram available. An abnormal ECG was considered in the presence of at least one ischemic change, bundle branch block or atrial fibrillation.

Pace rhythm was not contemplated in this analysis and the presence of Q waves were not considered either, due to missing data in the database.

### Follow up

We performed a median clinical follow up of 19 months after hospital discharge. The information was collected by phone call, from hospital records or at the outpatient clinic. The primary endpoints were all-cause mortality and the combined result of cardiovascular death, non-fatal myocardial infarction, re-admission for unstable angina, and unscheduled percutaneous coronary intervention – MACE. We also recorded the occurrence of acute myocardial infarction, re-admission for heart failure and stroke.

### Statistical Analysis

Continuous data are presented as mean and standard deviation and compared with the Student t-test. Categorical variables are reported as frequencies and percentages, and the  $\chi^2$  or the exact Fisher tests were used when appropriate to compare them.

The cumulative survival curves were constructed with the use of the Kaplan-Meier method and groups were compared with the Log rank test. The observational period started at hospital discharge and lasted for one year.

A multivariate Cox regression analysis was performed for the all-cause mortality endpoint at the end of the first year. Variables that were significant at the bivariate level or that had a clinical relevance were included in the model.

All statistical tests were two-tailed and a p value less than 0.05 was deemed significant. The analysis was performed with the SPSS 15 (*Statistical Package for Social Sciences*) from SPSS Inc, Chicago, IL.

## Results

### Baseline characteristics

Table 1 presents baseline characteristics for both groups. We observed that patients with a normal ECG were younger ( $63.4 \pm 12.7$  vs.  $68.7 \pm 11.7$  years,  $p < 0.001$ ), and more often admitted due to unstable angina (33.0 vs. 24.9 %,  $p = 0.017$ ). There were no significant differences with respect to risk factors for cardiovascular disease, cardiovascular history and previous medication.

### Hemodynamic, electrical and laboratory data

This data is presented in Table 2. Normal ECG patients were more often at lower Killip Kimball classes at admission, had a lower risk profile, and had a higher left ventricular ejection fraction (LVEF) ( $55.3 \pm 9.5$  vs.  $52.0 \pm 10.6\%$ ,  $p < 0.001$ ).

Regarding rhythm, 83.7 % of group A patients were in sinus rhythm. The most frequent ischemic finding was T wave inversion (36.6%), as ST depression was only present in a ¼ of patients. An admission left bundle branch block was present in 8.9% of them.

Abnormal ECG patients also had a higher peak value of cardiac biomarkers, lower glomerular filtration rate (assessed by the Cockcroft et Gault formula), and lower minimum hemoglobin during hospital stay.

### In-Hospital Management

Sixty-three percent of normal ECG patients compared to 46.5% of abnormal ones were submitted to an invasive strategy during admission ( $p < 0.001$ ) – Table 3.

Aspirin, clopidogrel, statins and beta-blockers were more frequently used in normal ECG patients, whereas abnormal

**Table 1 - Baseline Characteristics**

	A-Abnormal ECG	B - Normal ECG	p	OR (95% CI)
Number of patients	538	264		
Male gender (%)	363/538 (67.5)	185/264 (70.1)	0.46	0.88 (0.64 – 1.22)
Age (Mean, SD)	$68.7 \pm 11.7$	$63.4 \pm 12.7$	<0.001	
Admission diagnosis (%)				
NSTEMI	404/538 (75.1)	177/264 (67.0)	0.017	1.12 (1.02 – 1.24)
UA	134/538 (24.9)	87/264 (33.0)	0.017	0.76 (0.60 – 0.95)
Risk Factors Cardiovascular Disease (%)				
Diabetes	168/528 (31.8)	75/264 (28.4)	0.33	1.12 (0.89 – 1.41)
Dyslipidemia	376/503 (74.8)	185/245 (75.5)	0.82	0.99 (0.91 – 1.08)
Hypertension	381/513 (74.3)	185/246 (75.2)	0.78	0.99 (0.90 – 1.08)
Current Smoking habits	79/537 (14.7)	51/262 (19.5)	0.087	0.76 (0.55 – 1.04)
Cardiovascular history (%)				
Previous infarction	101/467 (21.6)	53/236 (22.5)	0.80	0.96 (0.72 – 1.53)
Previous PCI	65/515 (12.6)	33/255 (12.9)	0.90	0.98 (0.66 – 1.44)
Previous Heart Failure	7/191 (3.7)	3/136 (2.2)	0.45	1.66 (0.43 – 6.31)
Previous Stroke	38/527 (7.2)	9/263 (3.4)	0.34	2.11 (1.04 – 4.29)
Previous Medication (%)				
Aspirin	159/364 (43.7)	94/179 (52.5)	0.052	0.83 (0.69 – 1.00)
Other anti-platelet	59/364 (16.2)	26/179 (14.5)	0.61	1.12 (0.73 – 1.71)
Beta-Blocker	107/364 (29.4)	46/179 (25.7)	0.37	1.14 (0.85 – 1.54)
ACE inhibitors	153/364 (42.0)	80/179 (44.7)	0.56	0.94 (0.77 – 1.15)
Statins	110/364 (30.2)	68/179 (38.0)	0.070	0.80 (0.62 – 1.102)
Diuretics	15/57 (26.3)	172/729 (23.6)	0.64	1.16 (0.63 – 2.14)
Nitrates	95/364 (26.1)	38/179 (21.2)	0.22	1.23 (0.88 – 1.71)

STEMI – ST elevation acute myocardial infarction; NSTEMI – non ST elevation acute myocardial infarction; UA unstable angina; PCI percutaneous coronary intervention; ACE angiotensin converting enzyme

ECG patients were more frequently prescribed diuretics and nitrates 24 hours after admission.

At discharge there were no differences between groups with the exception of beta-blockers, which were more often used in group B patients.

#### Cath Lab Data

Normal ECG patients had a higher rate of a normal coronary angiogram (26.2% vs. 18.0%,  $p=0.045$ ) – Table 4.

There were no differences with respect to the anatomic lesions and the rate of percutaneous revascularization. When a percutaneous coronary intervention was performed, group B patients were more often treated with a drug-eluting stent.

#### Outcome

The lost to follow up rate was 4.5%, which means that data were available for 737 patients discharged from the hospital.

**Table 2 - Hemodynamic, electrical and laboratory data**

	A – Abnormal ECG	B – Normal ECG	P
Hemodynamic data on admission			
Heart rate, bpm (mean, SD)	76.7 ± 18.4	76.2 ± 8.3	0.65
Systolic blood pressure, mmHg (mean, SD)	142 ± 24.6	143 ± 23.7	0.65
Diastolic blood pressure, mmHg (mean, SD)	73.9 ± 14.8	77.4 ± 13.3	0.001
Killip-Kimball class I (%)	427/506 (84.4)	242/259 (93.4)	0.001
Killip-Kimball class II (%)	68/506 (13.4)	14/259 (5.4)	0.001
Killip-Kimball class III/IV (%)	11/506 (2.2)	3/259 (1.2)	0.32
TIMI risk score ≤ 2 (%)	231/538 (42.9)	139/264 (52.7)	0.01
TIMI risk score 3 – 4 (%)	228/538 (42.4)	101/264 (38.3)	0.27
TIMI risk score ≥ 5 (%)	79/538 (14.7)	24/264 (9.1)	0.026
LVEF (Mean, SD)	52.0 ± 10.6	55.3 ± 9.5	<0.001
Body mass index (kg/m <sup>2</sup> )	27.4 ± 4.3	28.0 ± 5.3	0.08
Electrical data on admission (%)			
Sinus Rhythm	442/528 (83.7)	264/264 (100)	<0.001
AF	62/528 (11.7)	0/264 (0)	
T wave inversion	193/528 (36.6)	0/264 (0)	
ST elevation	19/528 (3.6)	0/264 (0)	
ST depression	134/528 (25.4)	0/264 (0)	
LBBB	21/528 (4.0)	0/264 (0)	
RBBB	47/528 (8.9)	0/264 (0)	
Laboratory (mean, SD)			
Peak Troponin I, U/l	14.7 ± 26.2	8.6 ± 15.4	0.002
Peak MBCK mass, U/l	54.7 ± 95.4	39.1 ± 74.3	0.037
Total cholesterol, mg/dl	188.1 ± 54.0	198.3 ± 47.6	0.025
LDL cholesterol, mg/dl	125.9 ± 37.1	134.8 ± 35.3	0.006
Glomerular filtration rate ml/min	64.4 ± 4.2	75.5 ± 37.3	0.003
Admission glycemia, mg/dl	153.3 ± 89.3	146.8 ± 92.0	0.40
Admission hemoglobin, g/dl	13.5 ± 1.7	13.9 ± 1.6	0.016
Minimum hemoglobin, g/dl	12.0 ± 1.8	12.7 ± 1.7	<0.001

AF – atrial fibrillation; LBBB – left bundle branch block; RBBB – right bundle branch block; LVEF – left ventricular ejection fraction

There was a trend for a higher in-hospital mortality among abnormal ECG patients (4.6 vs. 1.9%,  $p=0.054$ ), which became significant at 30 days and at one year after the ACS (Figure 1.1).

The MACE rate at one year was not significantly different for both groups (18.9 vs. 14.8%,  $p=0.16$ ), although there were also a trend for a worse outcome for abnormal ECG patients (Figure 1.2).

By the end of the first year, abnormal ECG patients had a higher re-infarction and re-admission for heart failure rate - Table 5.

If we analyzed solely the group of patients with a non-ST elevation acute myocardial infarction, we observed that the stratification proposed for the normal ECG patients remained significant for the overall survival at one year (87.7 vs. 94.5%, log rank  $p = 0.019$ ) (Figure 1.3)

If we selected only the patients with ST depression or T wave inversion and compared them to the normal ECG ones, we observed that the survival curve for the T wave inversion patients was similar to the normal ECG patients, but the ST depression patients had a worse outcome (Figure 1.4).

**Table 3 - In Hospital management:**

	In the first 24 hours			Medication at discharge		
	n = 538	n = 264	p	n = 513	n = 259	p
	Group A Abnormal ECG	Group B Normal ECG		Group A Abnormal ECG	Group B Normal ECG	
Invasive Strategy (%)	250/538 (46.5)	168/264 (63.6)	<0.001			
Gp IIb/IIIa inhibitors (%)	264/538 (49.1)	138/264 (52.3)	0.39			
Levosimendan (%)	11/538 (2.0)	3/264 (1.1)	0.36			
Diuretic (%)	184/538 (34.2)	49/264 (18.6)	<0.001			
ASA (%)	505/538 (93.9)	257/264 (97.3)	0.03	428/513 (83.4)	215/259 (83.0)	0.88
Clopidogrel (%)	337/538 (62.6)	186/264 (70.5)	0.029	173/513 (33.7)	101/259 (39.0)	0.15
Beta Blockers (%)	415/538 (77.1)	232/264 (87.9)	<0.001	365/513 (71.2)	206/259 (79.5)	0.012
ACE inhibitors (%)	481/538 (89.4)	244/164 (92.4)	0.17	431/513 (84.0)	218/259 (84.2)	0.96
Statins(%)	523/538 (97.2)	263/264 (99.6)	0.022	484/513 (94.3)	238/259 (91.9)	0.19
Nitrates (%)	259/538 (48.1)	103/264 (39.0)	0.015			

Gp – glycoprotein; ASA – acetyl salicylic acid; ACE – angiotensinogen converting enzyme;

**Table 4 - Cath lab data**

	A – Abnormal ECG	B – Normal ECG	OR (95% CI)	P
Normal Coronary arteries *	45/250 (18.0)	44/168 (26.2)	0.69 (0.47 – 0.99)	0.045
1 vessel coronary disease *	101/250 (40.4)	55/168 (32.7)	1.2 (0.95 – 1.61)	0.11
2 vessel coronary disease *	40/250 (16.0)	34/168 (20.2)	0.79 (0.52 – 1.20)	0.27
3 vessel coronary disease *	62/250 (24.8)	33/168 (19.6)	1.26 (0.87 – 1.84)	0.21
Fully revascularized*	97/205 (47.3)	52/124 (41.9)	1.13 (0.88 – 1.46)	0.34
Partially revascularized*	36/205 (17.6)	23/124 (18.5)	0.95 (0.59 – 1.52)	0.82
Not revascularized*	72/205 (35.1)	49/124 (39.5)	0.89 (0.67 – 1.18)	0.42
Stent*	127/250 (50.8)	70/168 (41.7)	1.22 (0.98 – 1.51)	0.067
Drug-eluting Stents*	90/126 (71.4)	59/70 (84.3)	0.85 (0.73 – 0.98)	0.043
Surgical Revascularization*	16/538 (3.0)	8/264 (3.0)	0.98 (0.43 – 2.26)	0.97

\*%; PCI – percutaneous coronary intervention

FIG 1.1

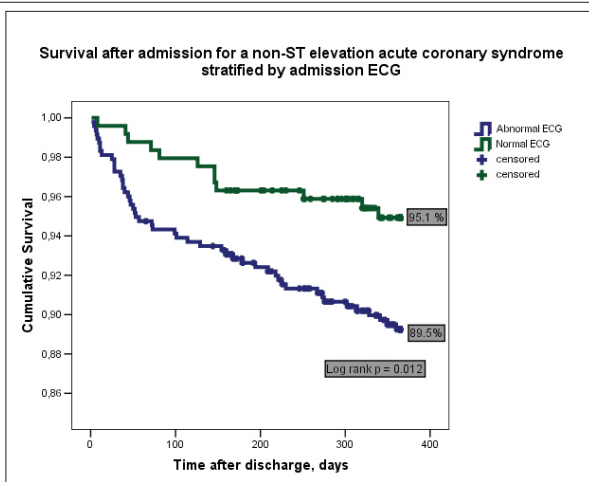


FIG 1.3

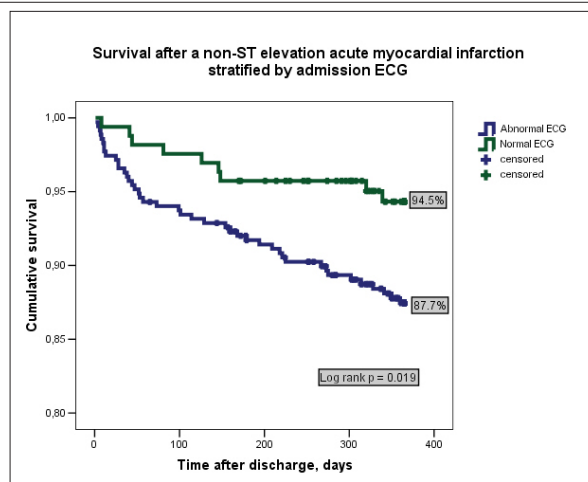


FIG 1.2

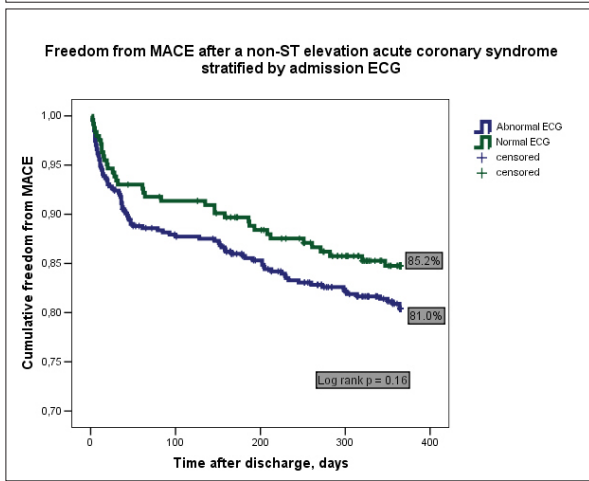
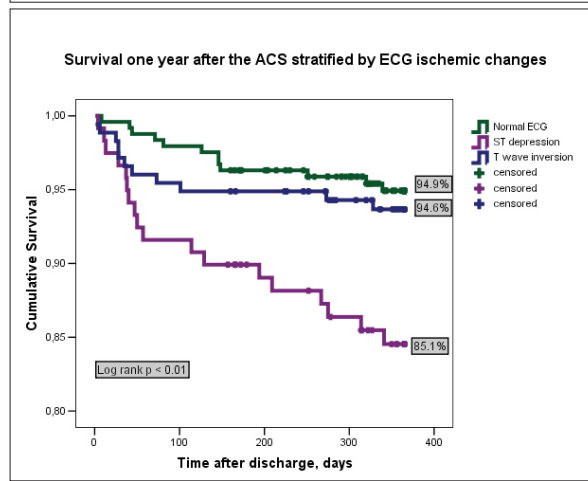


FIG 1.4



**Figure 1 – Kaplan-Meier Curves.** Fig. 1.1 – Kaplan-Meier Curves – One year survival after a non-ST elevation ACS stratified by admission ECG. Fig. 1.2 – Kaplan-Meier Curves – One year freedom from MACE after a non-ST elevation ACS stratified by admission ECG. Fig. 1.3 – Kaplan-Meier Curves – One year survival after a non-ST elevation acute myocardial infarction stratified by admission ECG. Fig. 1.4 – Kaplan-Meier Curves – One year survival after a non-ST elevation ACS, stratified by admission ECG ischemic changes.

**Table 5 - Outcomes in the hospital and 1 year after discharge:**

	A – Abnormal ECG	B – Normal ECG	OR (95% CI)	p
Length of stay (days)	5.3 ± 3.0	5.2 ± 2.7		0.65
In-Hospital Mortality (%)	25/538 (4.6)	5/264 (1.9)	2.45 (0.95 – 6.34)	0.054
Overall Mortality 30 days (%)	13/476 (2.7)	1/244 (0.4)	6.66 (0.88 – 50.64)	0.033
Overall Mortality 6 months (%)	35/476 (7.4)	9/244 (3.7)	1.99 (0.97 – 4.08)	0.052
Overall Mortality 1 year (%)	50/476 (10.5)	12/244 (4.9)	2.14 (1.16 – 3.93)	0.011
MACE 1 year (%)	90/476 (18.9)	36/244 (14.8)	1.28 (0.90 – 1.83)	0.16
Cardiovascular mortality 1 year (%)	34/476 (7.1)	5/244 (2.0)	3.49 (1.38 – 8.80)	0.004
Re-Infarction 1 year (%)	42/476 (8.8)	11/244 (4.5)	1.96 (1.3 – 3.73)	0.036
Heart Failure 1 year (%)	38/491 (7.7)	8/247 (3.2)	2.39 (1.13 – 5.04)	0.017
Stroke 1 year (%)	11/484 (2.3)	4/246 (1.6)	1.34 (0.45 – 4.34)	0.56

MACE: major adverse cardiovascular endpoints; PCI: percutaneous coronary intervention  
 \*Not programmed during hospital stay

### Multivariate Analysis

The outcome for overall mortality at one year was adjusted according to a Cox regression model that included normal ECG, age over 65 years, glomerular filtration rate under 60 ml/min, troponin I over 0.20 U/L, previous diabetes and higher Killip class at admission (Table 6). This model showed an adjusted 55% relative risk reduction of death one year after the ACS for the patients with a normal ECG.

### Discussion

When our data were compared to others published in the literature we observed a lower rate of ST-depression (16.7%), versus T-wave inversion (24.1%) for the global population. With respect to a sub-analysis from the GUSTO-IIb (Global Use of Strategies To Open Occluded Arteries in Acute Coronary Syndromes) study, of 12,142 randomized patients, 4263 (35.1%) had ST-depression, versus 2723 (22.4%) with T-wave inversion<sup>1</sup>. An even higher rate of ST depression was observed in a recent trial, the ICTUS (Invasive versus Conservative Treatment in Unstable Coronary Syndromes) study, in which almost 50% of the population had ST-depression at admission<sup>11</sup>. This difference could be explained, in our opinion, by the overall risk profile of the patients. To be eligible for the ICTUS trial, patients had to present positive cardiac biomarkers, and to be randomized to the GUSTO IIb trial, all the population needed to present a baseline ECG with ischemic changes. On the contrary, with respect to prognosis, our data seemed to be in agreement with those from the GUSTO trial, as ST-depression patients had a far worse outcome at 30 days, when compared to those with T-wave inversion.

With respect to atrial fibrillation, in our series, it was present in 7.7% of the overall population, which was a similar value when compared to recent data, such as the one reported by Lopes et al<sup>12</sup>.

### Baseline Data

One of the first observations of our analysis was that we associated a normal ECG with good prognostic variables during an admission for a non-ST elevation ACS, such as younger age, male gender, higher left ventricular ejection fraction, better renal function and consequent lower TIMI risk scores. It was noteworthy in fact that these patients, although presenting a lower global cardiovascular risk, were more often admitted for an invasive strategy, which probably reflected the paradoxical management strategy for real-world patients, as previously reported by Zia et al<sup>13</sup>. We observed that a stress test was performed in 29.1% of the population, and this result had an obviously important impact on the treatment option (data not shown).

This lower risk translated, as expected, into a higher percentage of normal coronary angiograms (nearly a quarter of the total population). This is a high value when compared to data from higher-risk randomized controlled trials, but it was a similar value to that observed in the RITA 3 (*Randomized Intervention Trial on unstable Angina*) trial, where in a lower risk population, 28% of patients allocated for an invasive strategy had a normal coronary angiogram<sup>14</sup>.

**Table 6 - Multivariate Cox regression analysis for overall mortality at one year after the ACS**

Variables	HR	P value	95% C I
Normal ECG	0.45	0.04	0.21 - 0.97
Troponin I > 0.2 (U/l)	1.17	0.68	0.55 - 2.47
Age ≥ 65 years	2.54	0.02	1.14 - 5.65
Diabetes	2.17	0.01	1.19 - 3.96
Killip Kimball III / IV	1.07	0.95	0.14 - 7.86
GRF ≤ 60 ml/min	1.18	0.61	0.63 - 2.21

Contrary to what was expected, our stratification does not seem to have influenced the MACE rate at the end of the first year. The present study had a small sample size of only 802 patients, with few events in the follow up, and consequent influence on prognosis. When data were separated with respect to the individual endpoints of the combined MACE result, both the cardiovascular mortality and the myocardial infarction rates remained significantly lower in the subgroup of patients with a normal ECG (Table V). Contrarily, the re-admission rates for unstable angina and the non-programmed coronary revascularization were higher among the normal ECG patients. The cause of this difference is difficult to explain, but it could be related to the higher rate of complications associated with an invasive procedure and the percutaneous revascularization, which have also been reported in the most recent randomized controlled trials over management strategy in non-ST elevation ACS<sup>11</sup>.

### Risk Stratification

Risk stratification is a crucial step in ACS, with major implications on patient management and prognosis. Many risk scores and factors have been published in the literature during the last decade, to help attain a more precise clinical decision. ECG has been a longtime useful tool for understanding, at the electrical level, an ACS.

At the emergency department, we observed that in our population, 22 % of patients with a normal ECG will have a NSTEMI, which on a practical level forces the clinician to achieve a precise clinical and biochemistry characterization, considering that a normal ECG may not be such an innocent finding, after all. We consider that ischemic changes are dynamic and that they could have missed detection in our series of normal ECG patients due to logistic reasons, and so the 22% of patients may be over-represented.

Risk assessment is a temporal multi-step analysis, with decisions being taken at admission, during hospital stay, and even at the cath lab. A patient should be rationally "understood" at a global level, and one of the most crucial decision steps is taken at the Emergency Department, which influences not only the diagnostic assessment, but also aggressive medical therapy and the option for an invasive strategy.

That was the reason to include easy well-known variables into our multivariate model, in an attempt to understand the relative power of each. We concluded that a normal ECG, along with age and diabetes, were the only early independent predictors of prognosis. The troponin I cut-off used was 0.2 U/ml, which is our local laboratory cutoff for a positive result. We also observed that this lower threshold was not as powerful as data derived from ECG analysis. Similar results have been also reported by Holmvang *et al* in the series from the TRIM (Thrombin Inhibition In Myocardial Ischemia) sub-study<sup>15</sup>.

Nevertheless, we observed (data not shown) that if we adjusted the model to include treatment variables and coronary anatomy, a normal ECG no longer had statistical significance. This meant that ECG loses importance on a global analysis, for clinical and treatment-derived variables, and even for troponin I data, with a cut-off determined from a ROC curve.

Although we have constructed a combined ECG variable, in our population, as also reported by previous authors, ST depression remained the most important ECG-derived information regarding prognosis.

## Limitations

We did not have available data on the presence of Q waves at the admission ECG. Our follow up was a clinical one and

unfortunately, we did not have data on the evolution of the electrical variables. Moreover, there were no data on the medication at the time of follow up, which could clearly have influenced outcome.

## Conclusions

A normal ECG in the spectrum of non ST elevation ACS is an early marker for mid-term good prognosis and remains an important variable in the 21<sup>st</sup> century for ACS patients. Nevertheless, the ECG, although important, was not enough to attain a global characterization of our patients' risk profile.

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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## Study Association

This study is not associated with any post-graduation program.

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