ORIGINAL ARTICLE

Prognostic Value of Corrected QT Interval and its Correlation with Cardiac Troponin T in Non-ST-Elevation Acute Coronary Syndrome

SUSANA C. LLOIS[MTSAC, 1], FRANCISCO L. GADALETA[MTSAC, 1], VÍCTOR A. SINISI[MTSAC, 1], PABLO AVANZAS[2], JUAN C. KASKI[2]

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Address for reprints:
Dra. Susana C. Llois
Hospital Interzonal General de Agudos "Eva Perón"
Servicio de Cardiología
Ricardo Balbín 3200
(1650) San Martín
Provincia de Buenos Aires
República Argentina
Tel. 54 011 4768-8904
e-mail: scllois@intramed.net

ABSTRACT

Background
Presence of different risk groups in non-ST-elevation acute coronary syndrome (NSTE-ACS), indicate the need for new tools to perform early diagnosis and prognostic stratification. In this sense, it has been shown that the corrected QT interval prolongation is an independent risk marker in NSTE-ACS with or without acute ischemic changes. However, there is scarce information about its relationship with other variables of known prognostic value, such as cardiac troponins.

Objective
The purpose of this study was to assess the correlation between prolongation of corrected QT interval and cardiac Troponin T in NSTE-ACS.

Methods
This prospective study included 106 patients admitted with NSTE-ACS. The corrected QT interval was measured at admission ECG and at 6, 12, 18, 24, and 48 h post-admission. The cut-off point with best sensitivity and specificity to predict major clinical events was ≥0.458 sec. Cardiac Troponin T ≥0.04 ng/ml was considered positive for myocardial injury. The composite end-point of cardiac death, non-fatal myocardial infarction and recurrent angina were the major clinical events at 30 days post-discharge. Patients were divided into two groups, according to the presence (group A) or absence (group B) of these events. Corrected QT interval at admission and maximum corrected QT interval were correlated with cardiac Troponin T in each group. Multivariate regression analysis was carried out to identify independent predictors of major clinical events.

Results
The correlation coefficient between cardiac Troponin T and maximum corrected QT interval was 0.38 ($p < 0.001$) and maximum corrected QT ≥0.458 sec was an independent predictor of major clinical events [OR=4.1 (IC 95% 1.7-11.2) p=0.002] with a negative predictive value of 80.8%.

Conclusions
Maximum corrected QT interval correlated with cardiac Troponin T values and was an independent risk predictor in NSTE-ACS patients.

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Key words > Myocardial Ischemia - Prognosis - Electrocardiography - Troponin

Abbreviations >

AACEI	Angiotensin converting enzyme inhibitors	**NSTE-ACS**	Non-ST elevation acute coronary syndrome
ACS	Acute coronary syndrome	**QTc**	Corrected QT interval
cTnI	Cardiac troponin I	**QTc-max**	Maximum corrected QT interval
cTnT	Cardiac troponin T	**QTd**	QT interval dispersion
ECG	Electrocardiogram	**RA**	Recurrent angina
GA	Group A	**ROC**	Receiver Operating Characteristic curve
GB	Group B	**SD**	Standard deviation
MCE	Major clinical event	**UA**	Unstable angina

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[MTSAC] Full Member of the Argentine Society of Cardiology
[1] Department of Cardiology, Hospital Eva Perón. Buenos Aires, Argentina
[2] Cardiovascular Sciences Research Centre, St. George's, University of London, UK

BACKGROUND

Different risk groups in non- ST segment elevation acute coronary syndrome (NSTE-ACS) indicate the need of new tools to perform an early diagnosis and prognostic stratification in order to apply the most adequate treatment. (1-5)

There is ample evidence of specific myocardial injury markers such as cardiac troponin I (cTnI) and cardiac troponin T (cTnI) for short and long-term prognostic values of NSTE-ACS mortality and new infarction. (6-10)

On the other hand, the 12-lead electrocardiogram (ECG) is a first line, essential tool to assess these patients and detect the presence of variables with independent short and long-term prognostic value, such as abnormal ST segment. (1, 4, 5, 11, 12) The limitation of the abnormal ST is its low incidence on the admission ECG found in previous studies. It is more frequent to find an ECG without acute ischemic changes or with T wave changes that do not rule out an acute coronary syndrome (ACS) and is one of the causes for subdiagnosis. (4, 13)

Due to its universal availability, low cost and easy performance at the patient´s bedside, efforts are still made to find new diagnostic and prognostic variables in the 12-lead ECG.

Several studies have been published showing the prolonged corrected QT interval (QTc) as an independent risk marker in NSTE-ACS with or without acute ischemic changes, both at 30-day post- discharge or long-term follow–up. (14-16) However, there is scarce data of its relationship with other variables of known prognostic value as cardiac troponins. The purpose of this work was thus to evaluate the correlation between two independent prognostic variables, QTc and cTnT in NSTE-ACS.

METHODS

Clinical characteristics of the study population

This is a prospective, observational study of 135 patients admitted to the Coronary Care Unit with NSTE-ACS from May 22, 2003 to March 2, 2005. After application of inclusion and exclusion criteria, 106 patients were included for analysis.

Inclusion criteria were: male and female patients, >18 years, admitted with NSTE-ACS diagnosis, with or without acute ischemic ECG changes, classified as Braunwald´s subclass II-IIIB.

Exclusion criteria were:

1. ST-segment-elevation AMI criteria.
2. Flat T wave (< 0.2 mV).
3. Wide QRS (≥ 0.12 s)
4. Serum potassium ≤ 3.5 mEq/l.
5. Severe ventricular hypertrophy.
6. Valve disease or severe cardiomyopathy.
7. Patients receiving antiarrhythmic or QT interval modifying drugs
8. Wolff-Parkinson-White, atrial fibrillation, atrial flutter or frequent/bigeminate extrasystoles.

The study was approved by the local Ethics Committee and was performed on all patients who had given their written consent.

Patients with unstable angina (UA) and non-Q wave myocardial infarction were included in the study. Unstable angina was defined as typical angina chest pain without elevation of biochemical markers, and with or without ECG changes. Non-Q wave myocardial infarction was characterized by abnormal cTnT ≥ 0.04 ng/ml. No electrocardiographic signs of acute transmural infarction were observed in any case.

Upon admission to the hospital all patients received conventional treatment according to national and international consensus statements. (3-5)

A 12-lead ECG was performed at admission in all cases and then at 6, 12, 18, 24 and 48 h post-admission.

Blood samples were obtained after ≥ 6 hours since the beginning of the last episode of chest pain to assess cTnT.

Demographic variables at admission were age, gender, height, weight, arterial pressure, history of myocardial infarction, hypertension, diabetes mellitus, smoking, hypercholesterolemia, family history of coronary disease, cerebrovascular disease, and previous coronary revascularization. Medication before entering the study was also registered.

All patients were classified at admission according to the TIMI score for NSTE-ACS. (2)

After basal characterization, all patients were followed-up for 30 days after discharge.

Study endpoints

Major clinical events (MCE) observed up to 30 days post-discharge and considered as composite endpoint were: cardiac death, non-fatal myocardial infarction (defined by increased biochemical markers of myocardial injury, characteristic dynamic and evolving electrocardiographic changes and typical prolonged chest pain) and recurrent angina which led to cinecoronariography, and according to the results, the ensuing urgent revascularization treatment within 30 days of admission. Patients were divided into two groups according to the presence (group A) or absence (group B) of MCE.

Measurement of corrected QT interval

Two independent experienced researchers (F.G. and S.L.), not involved in decision making, performed QTc measurements using manual compasses as described in a previous study. (14) Measurements were done on each patient and the highest QTc measured in the ECGs within 48 h post-admission was considered as final value for analysis.

Bazett´s formula was used to calculate QTc according to heart rate. (17) QTc ≥ 0.450 s in men and ≥ 0.470 s in women were considered abnormally prolonged. Maximum QTc (QTc-max) was defined as the most prolonged value in each case, and QTc at admission and QTc-max were correlated with cTnT in each group.

Cardiac troponin T dosage

cTnT was measured in 98 patients and in all cases the sample was collected ≥ 6 h after the last angina episode. Authorized commercial electrochemoluminiscence assays were used for the determinations. Concentrations ≥ 0.04 ng/ml were considered to be positive for myocardial injury. A second measurement was done in patients in whom the first determination was negative.

Statistical analysis

Continuous variables with normal distribution are expressed as mean ± standard deviation (SD) and continuous variables with non-normal distribution are expressed as median (interquartile range). The Kolmogorov-Smirnov test was used

for the normality analysis of continuous variables. Unpaired Student´s t test or Mann-Whitney U test were used to compare continuous variables, as appropriate. Proportions were compared using the chi-square test or Fischer´s exact test if the number of expected values was < 5. Spearman´s correlation test was employed to establish the correlation between troponin and QTc-max values. Information on the presence of composite endpoint was obtained from all the patients. Binary logistic regression was used to determine independent predictors of composite end point. Parameter analysis by binary logistic regression was obtained using Wald´s test and forward stepwise selection with 0.05 inclusion and 0.1 exclusion probabilities. In addition to QTc, the variables included in the multivariate analysis were: the TIMI score, elevated cTnT, age, gender, history of infarction, ventricular dysfunction and cardiovascular risk factors as diabetes mellitus, hypercholesterolemia and smoking. Receiver Operating Characteristic (ROC) curves established the QTc cut-off values with the best sensitivity and specificity to predict the MCEs that determined the composite endpoint.

Patients were divided into two groups according to the presence (group A) or absence (group B) of MCEs.

Cardiac TnT ≥ 0.04 ng/ml and QTc of 0.458 s (given by the ROC curve) cut-off points were used for statistical analysis and clinical interpretation.

A p value < 0.05 was considered statistically significant.

Multivariate regression analysis was performed to identify independent predictors of MCE.

SPSS package for Windows version 15.0 (SPSS Inc., Chicago, Illinois) was used for statistical calculations.

RESULTS

From a population of 106 patients, 70% were men with mean age 58 ± 10 years; 43 patients (40.57%) belonged to group A (GA) because they had a MCE and 63 (59.43%) not presenting a MCE formed group B (GB).

Recurrent angina (RA) was the most frequent MCE. It was present in 35 patients (33%), followed by non-fatal myocardial infarction in 6 patients (5.6%) and cardiac death in 2 (1.9%) (Table 1).

Ninety seven percent with of the patients with RA (34/35 patients) required urgent revascularization treatment within de follow-up month; 17 underwent transluminal coronary angioplasty and 17 myocardial revascularization surgery.

Fifty seven of the 106 patients (53.7%) did not present acute ischemic changes in the admission or evolution ECGs. The remaining 49 (46.2%) presented changes: 36 patients had negative T waves (33.96%) and 13 abnormal ST segment (12.26%).

Median QTc at admission was 0.450 s (0.422-0.480) in GA and 0.439 s (0.417-0.453) in GB, with p = 0.12.

Prolonged QTc was found in 38/43 (83.37%) GA patients, whereas only in 26/63 (41.3%) GB patients (p < 0.001).

Median QTc-max was 0.487 s (0.459-0.534) in GA and 0.449 s (0.436-0.470) in GB (p < 0.001).

Eighty eight point five percent of the patients with RA (31/35) had prolonged QTc, same as the 100% patients with non-fatal myocardial infarction (6/6) and death (2/2).

Cardiac TnT dosage was positive in 24/43 (55.8%) GA patients and in 22/63 (34.9%) GB patients (p = 0.03).

Table 1. Distribution of major clinical events

MCE	Patients (n = 106)	%
Recurrent angina	35	33
Non-fatal AMI	6	5.6
Death	2	1.9

MCE: Major clinical event. AMI: Acute myocardial infarction.

The TIMI score at admission was calculated in all cases. Median TIMI score was 4 (2-5) in GA, and 3 (2-4) in GB (p = 0.1) (Table 2).

ROC curves were built to establish the QTc value that represented the cut-off point with greatest sensitivity and specificity to predict MCE. The cut-off value was 0.458 s with an area under the curve of 0.752; 95% CI 0.659-0.831; 61% positive predictive value and 80.8% negative predictive value (Figure 1).

Multivariate analysis showed that QTc-max 0.458 s was an independent predictor of MCE risk in this population, with OR = 4.1, p=0.002, and 95% CI 1.4 to 11.5. The rest of the included variables were not event predictors (Table 3).

The correlation between QTc-max and QTc at admission with cTnT in both groups resulted in a correlation coefficient of 0.38 between QTc-max and cTnTc, p < 0.001 (Figure 2).

DISCUSSION

Results showed a statically significant correlation between QTc-max and cTnT confirming the independent predictive values of prolonged QTc-max 0.458 to detect MCE in NSTE-ACS up to 30 days post discharge, indicating the highly negative predictive value of this variable. (14-16)

The 12-lead ECG is the first tool used in patients with suspected ACS. Four to 5% of the patients who consult for ACS compatible symptoms with ECG without acute ischemic changes and/or negative biomarkers are discharged without adequate diagnosis or treatment. (3-5, 13)

The prognostic value of abnormal ST segment in the admission ECG for short and long-term death and/or non-fatal myocardial infarction has been fully studied and demonstrated. (11, 18, 19) However, it is present in few cases. In the TIMI IIIB study and records, only 14.3% of 1416 included patients presented abnormal ST segment, 21.9% had inverted T wave and 54.9% no ECG changes. (11) Our series showed presence of abnormal ST segment in 12.26% of the cases. These data confirm the importance of new electrocardiographic variables with short and long-term prognostic value, such as the prolonged QTc. (14-16)

As a result of the ample evidence on the prognostic value of biological markers known as “troponins”, cTnT and/or cTnI, same as abnormal ST segment are

Variables	With events (n = 43) Group A	Without events (n = 63) Group B	p
Age (years)	59.1 ± 11.3	57.2 ± 9	0.052
Male, n (%)	29 (67.4)	41 (65.1)	0.8
Hypertension, n (%)	34 (79.1)	46 (73)	0.5
Hypercholesterolemia, n (%)	32 (74.4)	49 (77.8)	0.69
Smoking, n (%)	25 (58.1)	32 (50.8)	0.45
Diabetes, n (%)	6 (14)	14 (22.2)	0.28
LV dysfunction, n (%)	11 (25.6)	7 (11.1)	0.052
TIMI score	4 (2-5)	3 (2-4)	0.1
Biochemistry			
Positive cTnT, n (%)	24 (55.8)	22 (34.9)	0.03
ECG			
QTc at admission (s)	0.450 (0.422-0.480)	0.439 (0.417-0.453)	0.12
Prolonged QTc, n (%)	36 (83.7)	26 (41.3)	< 0.001
Maximum QTc (s)	0.487 (0.459-0.534)	0.449 (0.436-0.470)	< 0.001
Medication			
Aspirin, n (%)	43 (100)	63 (100)	1
Betablockers, n (%)	43 (100)	62 (98.4)	0.5
ACEI, n (%)	26 (60.5)	29 (46)	0.17
Nitroglycerin, n (%)	43 (100)	61 (96.8)	0.5

Data are expressed as mean ± standard deviation and as number (%).
TIMI score, QTc at admission and maximum QTc data are expressed as median (interquartile range).
LV: Left ventricle. cTnT: Cardiac Troponin T. ECG: Electrocardiogram. QTc: Corrected QT interval. ACEI: Angiotensin converting enzyme inhibitors.

Table 2. Analyzed variables according to the presence or absence of major clinical events

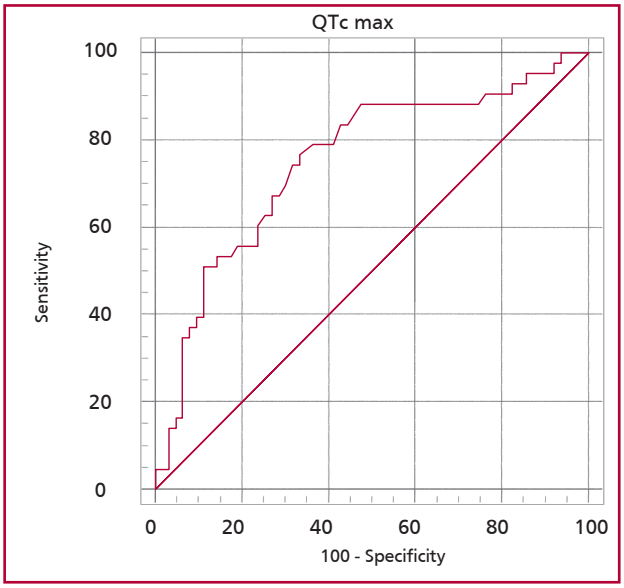

Fig. 1. ROC curve to establish the QTc value that represents the cut-off point with best sensitivity and specificity to predict MCE. Area under the ROC curve = 0.752. Standard error = 0.050, 95% confidence interval= 0.659 to 0.831. QTc > 0.458 s. Sensitivity: 76.7%. Specificity: 66.7%. Positive Likelihood Ratio: 2.3. Negative Likelihood Ratio: 0.35. Positive predictive value: 61.1%. Negative predictive value: 80.8%.

Table 3. Independent predictors of major clinical events†

	OR	p	95% CI	
			Lower limit	Upper limit
Prolonged QTc-max	4.1	0.002	1.4	11.5

* OR: Odds ratio. ORs were calculated considering QTc equal to 0.458s as reference cut-off point.
† The following variables were not predictors of events: TIMI score (p = 0.54), elevated cTnT (p = 0.9), age (p = 0.82), gender (p = 0.87), history of infarction (p = 0.8), presence of ventricular dysfunction (p = 0.24), diabetes mellitus (p = 0.12), hypercholesterolemia (p = 0.93) and smoking (p = 0.67).

included in diverse risk stratification scales, as the TIMI scale. (2, 6-10)

The purpose of our work was to investigate the degree of correlation between an electrocardiographic variable as QTc and a biological variable as cTnT, both of which are useful tools in NSTE-ACS early risk stratification.

In 2000, Döven et al correlated QT dispersión (QTd) with cTnT levels in NSTE-ACS patients. They found that QTd was greater in cases with elevated cTnT and postulated QTd as a non-invasive marker of myocardial injury and a useful variable to select high risk patients. (20)

Jernberg et al evaluated the prognostic value of continuous ST monitoring in simultaneous leads, either isolated or in combination with cTnT in NSTE-ACS patients. They concluded that presence of ischemic episodes, defined by abnormal ST segment ≥ 1mV during one minute or more of monitoring correlated with greater risk of infarction or death, and that the combination of continuous ST monitoring with cTnT determinations was a valuable tool for early risk stratification. (21)

Rushkin et al observed the highest transient QTc

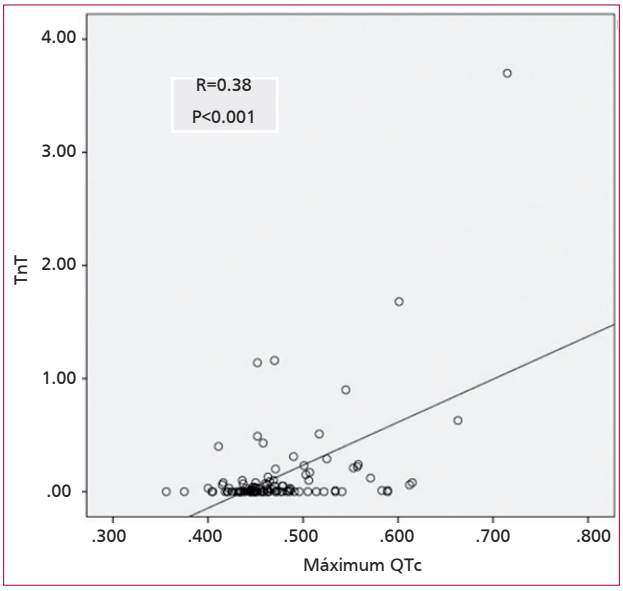

Fig. 2. Correlation between QTc-max and cTnT.

prolongation in non-Q wave AMI compared to UA patients, and concluded that the analysis of this variable could help to the early differentiation of UA from non-Q wave AMI, suggesting that QTc prolongation would not only be related to ischemia but also with the degree of necrosis. (22)

In 2003, Gadaleta et al published the results of 102 patients with UA and acute ischemic changes. They reported that a QTc ≥ 0.460 s in the admission ECG was an independent risk marker for clinical events such as cardiac death, non-fatal myocardial infarction and need for urgent revascularization at 30 day follow-up. Patients who died during follow-up had significantly more prolonged QTc than the rest of the patients. (14) They also analyzed QTc prolongation in NSTE-ACS patients without acute ischemic changes at admission, confirming its independent prognostic value when QTc is ≥ 0.458 s [OR 19 (95% CI 4.8-80.5)], $p < 0.001$ to predict MCE at 30 days. Even though it was not the aim of the study, this work showed a good correlation between prolonged QTc and cTnT. (16)

Jiménez-Candil et al studied QTc behavior in NSTE-ACS and concluded that prolonged QTc was an independent predictor of short and long-term risk. They observed a positive correlation between cTnT and QTc. (15) These investigators postulated a new risk scale for NSTE-ACS based on electrocardiographic variables with known predictive ability, and also included QTC ≥ 0.450 s, ST segment elevation and left atrial enlargement. (23)

Recently, Kenigsberg et al showed for the first time that QTc prolongation is the earliest electrocardiographic sign of early transmural ischemia, which was present in 100% of the studied cases. (24) These data not only change the classical concepts of ischemic cascade described by Nesto and Kowalchuk, but also confirm observations regarding the importance of measuring this electrocardiographic variable in NSTE-ACS patients. (25)

Study limitations

In our opinion, the most important limitations are the number of included patients and that their selection was conducted in only one center.

The study was performed with short-term follow-up (30 days).

Taking into account that in our sample the QTc cut-off point was calculated from the analysis of a ROC curve, results are only applicable to the study population, and thus more studies are required to assess the validity of this cut-off point in other populations.

QT interval measurements were manually performed by two independent experienced observers using a 12-lead conventional ECG at 25 mm/s speed and standard calibration. This could decrease the precision of the results; however, the relative error was calculated to minimize intra and inter-observer measurement variability. With respect to automatic measurements, no error-free mathematical algorithms have been achieved. For this reason, no regulatory office currently accepts automatic measurements without manual measurement corroboration. This is especially true when new molecules that could eventually prolong the QT interval are investigated.

CONCLUSIONS

In NSTE-ACS, QTc-max correlated with troponin levels and was an independent risk predictor. This evidence confirms our confidence in considering QTc as a useful and efficient tool for the prognostic stratification of NSTE-ACS, and its inclusion in future risk scales should therefore be considered.

Conflicts of interest

None declared

Acknowledgement

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RESUMEN

Valor pronóstico del intervalo QT corregido y su correlación con la troponina T cardíaca en el síndrome coronario agudo sin elevación del segmento ST

Introducción

La presencia de diferentes grupos de riesgo en el síndrome coronario agudo sin elevación del segmento ST (SCASEST) lleva a la búsqueda de nuevas herramientas para realizar un diagnóstico y una estratificación pronóstica precoces. Así, se ha mostrado que el intervalo QT corregido prolongado es un marcador independiente de riesgo en el SCASEST con cambios isquémicos agudos o sin ellos; no obstante ello, existen pocos datos sobre su relación con otras variables de reconocido valor pronóstico como las troponinas cardíacas.

Objetivo
Evaluar la correlación entre el intervalo QT corregido prolongado y la troponina T cardíaca.

Material y métodos
Se incluyeron prospectivamente 106 pacientes. Se midió el intervalo QT corregido en el ECG de ingreso y a las 6, 12, 18, 24 y 48 horas. El punto de corte con mejor sensibilidad y especificidad para predecir eventos clínicos mayores fue de ≥ 0,458 seg. Se efectuó la determinación de troponina T cardíaca y se consideró positivo el valor ≥ 0,04 ng/ml. Los eventos clínicos mayores observados hasta los 30 días del alta fueron muerte de causa cardíaca, infarto de miocardio no mortal y angina recurrente, que constituyeron el punto final combinado. Se dividió a los pacientes en dos grupos según la presencia (grupo A) o la ausencia (grupo B) de estos eventos. Se correlacionaron los valores del intervalo QT corregido de admisión y máximo con los de troponina T cardíaca de cada grupo. Se aplicó análisis multivariado de regresión logística para identificar predictores independientes de eventos clínicos mayores.

Resultados
El coeficiente de correlación del intervalo QT corregido máximo con la troponina T cardíaca fue de 0,38 ($p < 0,001$), y el intervalo QT corregido máximo ≥ 0,458 seg tuvo valor pronóstico independiente para eventos clínicos mayores [OR = 4,1 (IC 95% 1,7-11,2); $p = 0,002$] y valor predictivo negativo del 80,8%.

Conclusiones
En pacientes con SCASEST, el intervalo QT corregido máximo se correlacionó con los niveles de troponina y fue predictor independiente de riesgo.

Palabras clave > Isquemia miocárdica - Pronóstico - Electrocardiografía – Troponina

REFERENCES

1. Braunwald E. Unstable angina. A classification. Circulation 1989;80:410-4. http://doi.org/d2brg7
2. Antman EM, Cohen M, Bernink PJ, McCabe CH, Horacek T, Papuchis G, et al. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. JAMA 2000;284:835-42. http://doi.org/fngdg5
3. Anderson JC, Adams C, Antman EM, Bridges CR, Califf RM, Casey DE, et al. ACC/AHA 2007 Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction. J Am Coll Cardiol 2007;50:1-157. http://doi.org/csv24j
4. Bassand JP, Hamm CW, Ardissino D, Boersma E, Budaj A, Fernández-Avilés F, et al Guidelines for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes. Eur Heart J 2007;28:1598-660. http://doi.org/b5cff6
5. Bazzino O, Belardi J, Charask A, Doval HC, Gurfinkel E, Guzmán LA y col. Consenso de Síndrome Coronario Agudo Sin Elevación Inicial Persistente del Segmento ST. Rev Argent Cardiol 2005;73:1-62.
6. Hamm CW, Ravkilde J, Gerhardt W, Jørgensen P, Peheim E, Ljungdahl L, et al. The prognostic value of serum troponin T in unstable angina. N Engl J Med 1992;327:146-50. http://doi.org/fngfg3
7. Antman EM, Tanasijevic MJ, Thompson B, Schactman M, McCabe CH, Cannon CP, et al. Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. N Engl J Med 1996;335:1342-9. http://doi.org/frtnsd
8. Ohman EM, Armstrong PW, Christenson RH, Granger CB, Katus HA, Hamm CW, et al. Cardiac troponin T levels for risk stratification in acute myocardial ischemia. GUSTO IIA Investigators. N Engl J Med 1996;335:1333-41. http://doi.org/cqx93f
9. Morrow DA, Antman EM, Tanasijevic M, Rifai N, de Lemos JA, McCabe CH, et al. Cardiac troponin I for stratification of early outcomes and the efficacy of enoxaparin in unstable angina: a TIMI-11B substudy. J Am Coll Cardiol 2000;36:1812-7. http://doi.org/dfmc3m
10. Olatidoye AG, Wu AH, Feng YJ, Waters D. Prognostic role of troponin T versus troponin I in unstable angina pectoris for cardiac events with meta-analysis comparing published studies. Am J Cardiol 1998;81:1405-10. http://doi.org/cgc3xq
11. Cannon CP, McCabe CH, Stone PH, Rogers WJ, Schactman M, Thompson BW, et al. The electrocardiogram predicts one-year outcome of patients with unstable angina and non-Q wave myocardial infarction: results of the TIMI III Registry ECG Ancillary Study. Thrombolysis in Myocardial Ischemia. J Am Coll Cardiol 1997;30:133-40. http://doi.org/b233t4
12. Hamm CW, Braunwald E. A classification of unstable angina revisited. Circulation 2000;102:118-22. http://doi.org/jfp
13. Pope JH, Aufderheide TP, Ruthazer R, Woolard RH, Feldman JA, Beshansky JR, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. N Engl J Med 2000;342:1163-70. http://doi.org/c9htwj
14. Gadaleta FL, Llois SC, Lapuente AR, Batchvarov VN, Kaski JC. Prognostic value of corrected QT-interval prolongation in patients with unstable angina pectoris. Am J Cardiol 2003;92:203-5. http://doi.org/bg98qj
15. Jiménez-Candil J, González IC, González Matas JM, Albarrán C, Pabón P, Moríñigo JL, et al. Short- and long-term prognostic value of the corrected QT interval in the non-ST-elevation acute coronary syndrome. J Electrocardiol 2007;40:180-7. http://doi.org/c2c79v
16. Gadaleta FL, Llois SC, Sinisi VA, Quiles J, Avanzas P, Kaski JC. [Corrected QT interval prolongation: a new predictor of cardiovascular risk in patients with non-ST-elevation acute coronary syndrome]. Rev Esp Cardiol 2008;61:572-8. http://doi.org/bwfnkv
17. Bazett H. An analysis of the relationships of the heart rate. Heart 1920;7:353-70.
18. Savonitto S, Ardissino D, Granger CB, Morando G, Prando MD, Mafrici A, et al. Prognostic value of the admission electrocardiogram in acute coronary syndromes. JAMA 1999;281:707-13. http://doi.org/dtwng3
19. Diderholm E, Andrén B, Frostfeldt G, Genberg M, Jernberg T, Lagerqvist B, et al. ST depression in ECG at entry indicates severe coronary lesions and large benefits of an early invasive treatment strategy in unstable coronary artery disease; the FRISC II ECG substudy. The Fast Revascularisation during InStability in Coronary artery disease. Eur Heart J 2002;23:41-9. http://doi.org/bkvbvp
20. Döven O, Ozdol C, Sayin T, Oral D. QT interval dispersion: non-invasive marker of ischemic injury in patients with unstable angina pectoris? Jpn Heart J 2000;41:597-603. http://doi.org/dptgr2
21. Jernberg T, Lindahl B, Wallentin L. The combination of a continuous 12-lead ECG and troponin T; a valuable tool for risk stratification during the first 6 hours in patients with chest pain and a non-diagnostic ECG. Eur Heart J 2000;21:1464-72. http://doi.org/bkgbq8
22. Rukshin V, Monakier D, Olshtain-Pops K, Balkin J, Tzivoni D. QT interval in patients with unstable angina and non-Q wave myocardial infarction. Ann Noninvasive Electrocardiol 2002;7:343-8. http://doi.org/dbhbd6
23. Jiménez-Candil J, González Matas JM, Cruz González I, Hernández Hernández J, Martín A, Pabón P, et al. In-hospital prognosis in non-ST-segment elevation acute coronary syndrome derived using a new risk score based on electrocardiographic parameters obtained at admission. Rev Esp Cardiol 2010;63:851-5. http://doi.org/brfzrn
24. Kenigsberg DN, Khanal S, Kowalski M, Krishnan SC. Prolongation of the QTc interval is seen uniformly during early transmural ischemia. J Am Coll Cardiol 2007;49:1299-305. http://doi.org/brfzrn
25. Nesto RW, Kowalchuk GJ. The ischemic cascade: temporal sequence of hemodynamic, electrocardiographic and symptomatic expressions of ischemia. Am J Cardiol 1987;57:23C-30C. http://doi.org/fgb2t8