

# Evaluation of a New Diagnostic Algorithm for Acute Coronary Syndrome Using High-Sensitivity Troponin T Assay

## *Evaluación de un nuevo algoritmo diagnóstico para el síndrome coronario agudo con determinación de troponina T de alta sensibilidad*

JUAN P. COSTABEL<sup>1</sup>, DIEGO CONDE<sup>1,2</sup>, FLORENCIA LAMBARDI<sup>1</sup>, ANDREA CORRALES BARBOZA<sup>1</sup>, AUGUSTO LAVALLE COBO<sup>1</sup>, MARTÍN ARAGÓN<sup>1</sup>, MARCELO TRIVI<sup>MTSAC, 3</sup>

### ABSTRACT

**Introduction:** Chest pain represents 5 to 10% of annual visits to emergency departments. Its diagnosis is sometimes difficult, with the added problem of inappropriate discharge of patients with acute coronary syndrome or unnecessary hospitalizations. This has led to the development of different algorithms for the evaluation of these patients.

**Objective:** The aim of this study was to validate, in terms of safety and length of hospital stay, a novel algorithm incorporated in our center, which includes measurement of high-sensitivity troponin T in patients with suspected acute coronary syndrome.

**Methods:** The study included 528 consecutive patients attending the emergency department with suspected acute coronary syndrome and evaluated according to the chest pain unit protocol. Clinical and laboratory variables and functional tests were analyzed. Follow-up at 30 days was performed in all the patients.

**Results:** After observation, 90.7% of the patients were discharged and 1.25% presented a cardiovascular event during follow-up, represented by percutaneous coronary intervention and hospitalization due to acute coronary syndrome. The specificity of the global algorithm for the diagnosis of acute coronary syndrome was 97% with a negative predictive value of 99%. Emergency department length of stay was  $4.5 \pm 2.5$  hours for all the patients.

**Conclusion:** The novel algorithm incorporated in our center with measurement of high-sensitivity troponin T in patients with suspected acute coronary syndrome has proved to be safe, as it prevents the discharge of patients with acute coronary syndrome and at the same time reduces emergency department length of stay.

**Key words:** Acute Coronary Syndrome - Chest Pain Units - High-sensitivity Troponin T

### RESUMEN

**Introducción:** El dolor precordial representa el 5% al 10% de las consultas anuales en los departamentos de emergencias; su diagnóstico suele ser dificultoso y a ello se le suma el problema que implican la externación de pacientes con patología coronaria aguda o las internaciones innecesarias. Esto ha llevado al desarrollo de diferentes sistemáticas para la evaluación de estos pacientes.

**Objetivo:** Validar en términos de seguridad y tiempos de estadía hospitalaria un nuevo algoritmo incorporado en nuestro centro que incluye la medición de troponina T de alta sensibilidad en pacientes con sospecha de síndrome coronario agudo.

**Material y métodos:** Se incluyeron 528 pacientes que consultaron en el servicio de emergencias con sospecha de síndrome coronario agudo y se les realizó el protocolo de unidad de dolor. Se analizaron variables clínicas, de laboratorio y el resultado de las pruebas funcionales efectuadas. En todos los pacientes se efectuó seguimiento a los 30 días.

**Resultados:** El 90,7% de los pacientes fueron externados luego de la observación y al seguimiento el 1,25% había presentado un evento cardíaco, representado por angioplastia coronaria e internación por síndrome coronario agudo; la especificidad del algoritmo global para el diagnóstico de síndrome coronario agudo fue del 97% y el valor predictivo negativo fue del 99%. El tiempo de estadía en el servicio de emergencias del total de los pacientes fue de  $4,5 \pm 2,5$  horas.

**Conclusión:** El nuevo algoritmo incorporado en nuestro centro con determinación de troponina T de alta sensibilidad en pacientes con sospecha de síndrome coronario agudo demostró que es seguro al evitar la externación de pacientes que cursaban un síndrome coronario agudo y, a la vez, requiere una corta estadía hospitalaria en el servicio de emergencias.

**Palabras clave:** Síndrome de Brugada – Arritmias cardíacas - Andrógenos - Finasterida.

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Address for reprints: Dr. Juan Pablo Costabel - Blanco Encalada 1543 - (1428) Ciudad Autónoma de Buenos Aires, Argentina  
e-mail: jpcostabel@icba.com.ar

Instituto Cardiovascular de Buenos Aires

<sup>MTSAC</sup> Full Member of the Argentine Society of Cardiology

<sup>1</sup> To apply as full member of the Argentine Society of Cardiology

<sup>1</sup> Department of Cardiovascular Emergency Care

<sup>2</sup> Coronary Care Unit

<sup>3</sup> Department of Cardiology

## Abbreviations

|    |                       |     |                   |
|----|-----------------------|-----|-------------------|
| CA | Coronary angiography. | ECG | Electrocardiogram |
|----|-----------------------|-----|-------------------|

## INTRODUCTION

Chest pain represents 5 to 10% of annual visits to emergency departments and nearly 25% of hospitalizations. Its diagnosis is sometimes difficult, with the added problem of inappropriate discharge of patients with acute coronary syndrome or unnecessary admissions to the coronary care unit (30% to 70% of cases). (1-4)

Over the last decades, different protocols have been developed for evaluating patients with chest pain and suspected acute coronary syndrome. Most of them include observation of patients for a few hours and serial measurement of myocardial injury biomarkers. (5-8)

High-sensitivity troponin has proved to be useful for the evaluation of this type of patients, mainly due to its high negative predictive value and rapid positive result in cases of myocardial injury. (9-18)

The goal of our study was to validate a novel algorithm, in terms of safety and length of stay, used in our center since 2012, which includes measurement of high-sensitivity cardiac troponin T in patients with suspected acute coronary syndrome.

## METHODS

A prospective study was conducted from September 1 to February 30, 2013, which included patients who attended the emergency department with suspected acute coronary syndrome and who were evaluated according to the chest pain unit protocol.

### Inclusion criteria

Patients > 18 years attending the emergency department with suspected acute coronary syndrome.

### Exclusion criteria

- Definite acute coronary syndrome.
- Non-cardiac chest pain.
- Admission indicated by another physician.
- Need for transfer of patient due to lack of beds.
- Patient refusal to stay for observation.
- Impossibility of follow-up.

### Definitions

Suspected acute coronary syndrome:

- a) Probable angina with normal electrocardiogram (ECG) or unspecific abnormalities (ST-segment depression or T-wave inversion < 1 mm, straight ST-segment, flat T-wave, signs of ventricular hypertrophy, early repolarization pattern, presence of Q-waves, poor R-wave progression in the precordial leads, conduction blocks and abnormal previous ECGs).
- b) Non-ischemic chest pain with unspecific ECG abnormalities.

### Events

The primary endpoint included major cardiac events defined as: cardiac death, percutaneous coronary intervention or

coronary artery bypass graft surgery, or hospitalization due to acute coronary syndrome.

### Chest pain unit protocol

Patients with suspected acute coronary syndrome were temporarily admitted to the chest pain unit, where they were evaluated by means of anamnesis, physical examination, ECG and measurement of high-sensitivity cardiac troponin T, according to the management algorithm (Figure 1).

The evaluation period for each patient depended on the time from the last episode of chest pain to consultation. According to international recommendations, high-sensitivity cardiac troponin T has a positive predictive value > 97% and a negative predictive value > 98% for the diagnosis of myocardial infarction when measured 6 hours after the last episode of chest pain. Therefore, in this setting, patients were discharged from the emergency department when high sensitivity cardiac troponin T was negative ( $\leq 14$  ng/L). In patients in whom the last episode of chest pain occurred less than 6 hours before consultation, two negative troponin T measurements were necessary to rule out myocardial infarction.

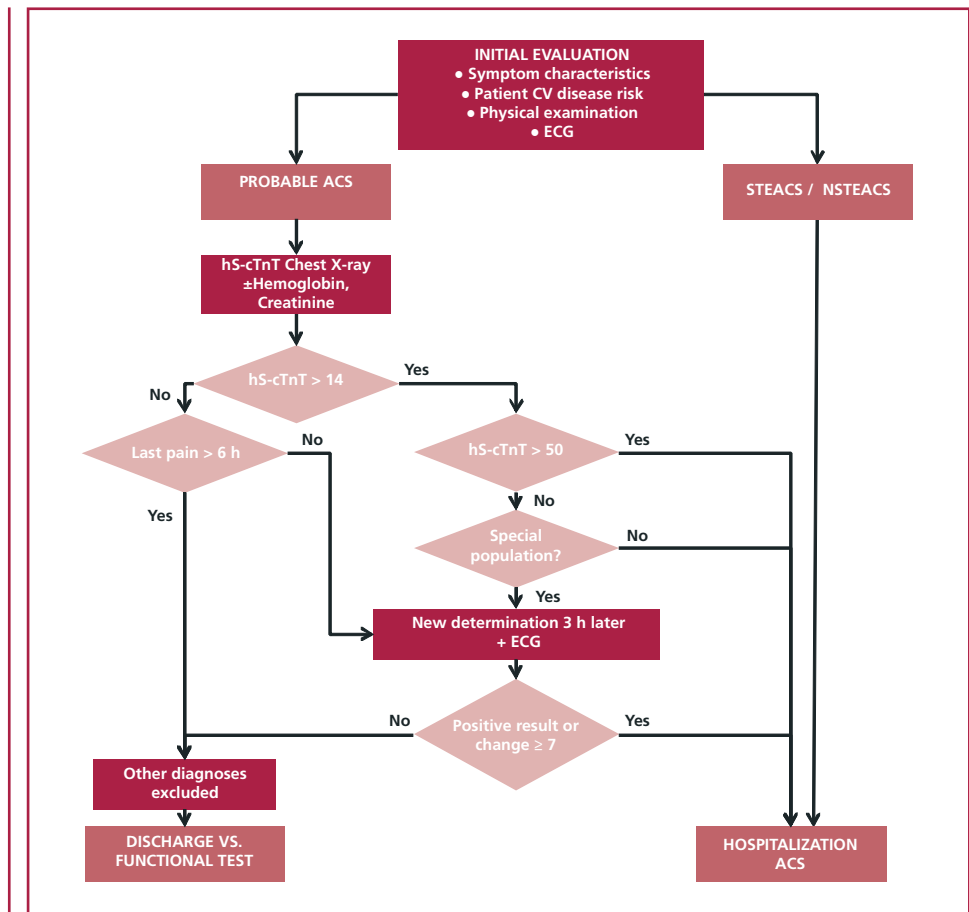
If troponin T level was > 14 ng/ml, the patient was admitted to undergo further examinations. In patients with chronically elevated troponin T levels, as in those with previous coronary artery disease, uncontrolled hypertension, age > 70 years, chronic heart failure or kidney dysfunction, a second determination of troponin T was necessary to define the strategy. Even in these cases, patients with a first determination of troponin T > 50 ng/L were hospitalized, since although these patients belong to special populations, they rarely attain these values. (14-18)

The second blood sample was taken 3 hours after the first measurement to achieve good sensitivity and an adequate variability curve. A change in troponin level > 7ng/L between the first and the second measurement was considered significant based on the study by Reichlin et al., who reported that the change in absolute value for the diagnosis of myocardial infarction is more accurate than the relative change. (18) Patients were hospitalized with the diagnosis of acute coronary syndrome when the variation between the first and the second determination of troponin T was > 7 ng/L. When the variation was < 7 ng/L and the first determination was < 14 ng/L, the patient was discharged and if the first determination was > 14 ng/L, a functional test was recommended.

In essence, patients with recurrent chest pain classified as having "definite" angina, those who developed heart failure or acute ischemic abnormalities in the ECG and/or presented elevated high-sensitivity cardiac troponin T levels during the evaluation were hospitalized with the diagnosis of acute coronary syndrome.

Finally, if the results of all the tests performed during the evaluation were normal, a functional test was indicated during the observation period or in the ambulatory setting. This indication was decided at the discretion of the physician and according to the immediate availability of the functional test in the institution. In this setting, the patient was either hospitalized with a positive result or discharged if the test was negative.

**Fig. 1.** Management algorithm. CV: Cardiovascular. ECG: Electrocardiogram. ACS: Acute coronary syndrome. STEACS: ST-segment elevation acute coronary syndrome. NSTEMACS: Non-ST segment elevation acute coronary syndrome. hs-cTnT: High sensitivity cardiac troponin T. CXR: Chest x-ray.



**Follow-up**

In all the patients included in the study follow-up at 30 days was performed in the outpatient clinic or by telephone.

**Statistical analysis**

Discrete variables are expressed as percentages and continuous variables as mean with its corresponding standard deviation or median with its corresponding P25-P75 interquartile range, according to their distribution. The K-S test was used to analyze normality. Discrete variables were compared using the chi square test and continuous variables were analyzed using Student’s t test or the Mann-Whitney test according to sample distribution. A two-tailed p value < 0.05 was considered statistically significant. All statistical analyses were performed using Statistix 8.0 software package. All patients gave their informed consent before participating in the study.

**RESULTS**

During the period analyzed, 1550 chest pain consultations were recorded, 34% (528 patients) of which fulfilled the criteria of suspected acute coronary syndrome. Ninety-eight percent of these 528 patients completed the follow-up evaluation at 30-days. Mean age was 58 ± 13 years and 58% were men (Table 1).

Eighty-five percent of patients had at least one cardiovascular risk factor and 54% had two or more. A history of coronary artery disease was present in 22%

of patients, with an overall population TIMI risk score of 1 (P25 0 P75 2) and a GRACE risk score of 92 ± 24.

Fifteen percent of patients underwent a functional test as part of the initial observation before hospitalization was decided. Finally, 90.7% of patients were discharged from the emergency department after completing the observation and 9.3% were admitted to the coronary care unit.

During follow-up, 6 of the patients discharged presented a cardiovascular event, defined as hospitalization for acute coronary syndrome in 3 cases and, in the remaining 3 patients, as a scheduled percutaneous coronary intervention due to ischemia in the functional test. No cardiovascular surgeries or all-cause deaths were reported. This means that 98.8% of the patients discharged did not present events.

The reasons for admitting 49 patients were elevated troponin levels in 90% of cases, recurrent chest pain in 4%, a positive functional test in 4%, and ECG changes in 2%. Coronary angiography (CA) was performed as the first diagnostic strategy in 65% of patients. In the remaining patients, CA was performed to those patients with functional stress test positive for ischemia (20%). Sixty-five percent of patients underwent a percutaneous coronary intervention due to the presence of significant stenosis and 2 patients

| Variable                                    | Overall value | Hospitalized<br>(n = 49) | Discharged<br>(n = 479) | p         |
|---|---------------|--------------------------|-------------------------|-----------|
| Male gender, n (%)                          | 306 (58)      | 27 (55)                  | 279 (58)                | 0.671     |
| Age, years                                  | 58 ± 13       | 62 ± 12                  | 55.4 ± 14.3             | 0.172     |
| Cardiovascular risk factors                 |               |                          |                         |           |
| Diabetes, n (%)                             | 63 (12)       | 1 (2)                    | 62 (13)                 | 0.041     |
| Hypertension, n (%)                         | 200 (38)      | 26 (54)                  | 174 (36)                | 0.021     |
| Current smoke or former smoker, n (%)       | 205 (39)      | 31 (63)                  | 174 (36)                | 0.013     |
| Dyslipidemia, n (%)                         | 237 (45)      | 32 (65)                  | 205 (43)                | 0.002     |
| History of coronary artery disease          |               |                          |                         |           |
| Percutaneous coronary intervention, n (%)   | 60 (11.5)     | 11 (22)                  | 49 (10)                 | 0.011     |
| Myocardial infarction, n (%)                | 42 (8)        | 1 (2)                    | 41 (8.5)                | 0.122     |
| Coronary artery bypass graft surgery, n (%) | 27 (5.3)      | 4 (8)                    | 23 (4)                  | 0.413     |
| History of other cardiovascular diseases    |               |                          |                         |           |
| Cardiomyopathy, n (%)                       | 10 (1.8)      | 0                        | 10 (2)                  | 0.223     |
| Heart failure, n (%)                        | 10 (1.8)      | 0                        | 10 (2)                  | 0.223     |
| Cardiovascular medication                   |               |                          |                         |           |
| Aspirin, n (%)                              | 105 (20)      | 17 (35)                  | 88(18)                  | 0.006     |
| Beta blockers, n (%)                        | 89 (17)       | 20 (42)                  | 69 (14)                 | 0.000002  |
| Statins, n (%)                              | 110 (21)      | 17 (35)                  | 93 (19)                 | 0.012     |
| Risk scores                                 |               |                          |                         |           |
| TIMI  | 1 (0-2)       | 1 (0.75-4)               | 1 (0-2)                 | 0.063     |
| TIMI > 2, n (%)                             | 67 (12.7)     | 17 (35)                  | 50 (10)                 | 0.0000036 |
| GRACE                                       | 92 ± 24       | 102 ± 45.6               | 89.2 ± 27               | 0.091     |

**Table 1.** General characteristics of the study population. Analysis of the differences between hospitalized and discharged patients

required coronary artery bypass graft surgery. Discharge diagnoses were: acute coronary syndrome in 39 patients (80%), pericarditis in 3, pulmonary thromboembolism in 1, stable angina in 1 and non cardiac chest pain in 5.

Emergency department length of stay was  $4.5 \pm 2.6$  hours for all the patients. In 50% of patients who consulted after more than 6 hours from the last chest pain episode, emergency department length of stay was  $2.9 \pm 2$  hours. In the rest of the patients, mean time from the last episode to consultation was  $5.1 \pm 2.8$  hours ( $p = 0.352$ ).

When the characteristics of the patients hospitalized were compared with those not hospitalized, the prevalence of hypertension, smoking habits and dyslipidemia was greater and diabetes was lower in hospitalized patients. The previous use of beta blockers, aspirin and statins was more common and the number of patients with a TIMI risk score of at least moderate risk was greater in hospitalized patients (35% in hospitalized patients vs. 10% in discharged patients,  $p = 0.0000036$ ). In hospitalized patients, chest pain was characterized as oppressive and was less altered by respiration or movements (Table 2).

The specificity of the global algorithm for the di-

agnosis of acute coronary syndrome was 97% with a positive predictive value of 81.4% and a negative predictive value of 98.7% (Table 3).

## DISCUSSION

This study demonstrates that the algorithm used for the evaluation of patients with suspected acute coronary syndrome is acceptably safe, and that patients with low short-term risk may be rapidly discharged from the emergency department. The impact of this algorithm is important, as the initial evaluation of these patients, which represent between 30 and 40% of medical consultations due to chest pain, is difficult because of the presence of “probable angina” and a non-diagnostic ECG, resulting in a considerable use of resources and time spent until a diagnosis is made. (1-3)

The rate of events among patients discharged from the emergency department was low and similar to the one reported by international publications in other chest pain units. Only 1.2% of patients presented a major cardiac event at 30 days. (6-8, 19, 20) This was not due to a greater hospitalization rate, as the percentage of patients hospitalized (9.3%) is also similar to the one reported worldwide.

**Table 2.** Types of patient presentation. Differences between hospitalized and discharged patients

| Variable                         | Overall value | Hospitalized (n = 49) | Discharged (n = 479) | p      |
|----------------------------------|---------------|-----------------------|----------------------|--------|
| SBP, mm Hg                       | 128 ± 17      | 129 ± 24              | 121 ± 16             | 0.301  |
| DBP, mm Hg                       | 73 ± 11       | 80 ± 14               | 70.5 ± 10.7          | 0.181  |
| HR, bpm                          | 72 ± 11       | 69 ± 6.6              | 72 ± 11.2            | 0.271  |
| Type of pain                     |               |                       |                      |        |
| Oppressive, n (%)                | 200 (38)      | 25 (51)               | 175 (36)             | 0.042  |
| Non-oppressive, (%)              | 322 (61)      | 23 (47)               | 299 (62)             | 0.031  |
| Pain location                    |               |                       |                      |        |
| Retrosternal, n (%)              | 116 (22)      | 10 (21)               | 106 (22)             | 0.782  |
| Precordial, n (%)                | 163 (31)      | 17 (35)               | 146 (30)             | 0.542  |
| Other location, n (%)            | 242 (47)      | 21 (44)               | 221(48)              | 0.661  |
| Pain propagation                 |               |                       |                      |        |
| Epigastric region, n (%)         | 63 (11.9)     | 0                     | 63 (13)              | 0.013  |
| Lower jaw, n (%)                 | 42 (0.8)      | 0                     | 42 (0.9)             | 0.061  |
| Upper limbs, n (%)               | 84 (16.1)     | 7 (14)                | 77 (16)              | 0.741  |
| Interscapular, n (%)             | 45 (8.5)      | 7 (14)                | 38 (8)               | 0.121  |
| Prolonged (> 20 minutes), n (%)  | 179 (34)      | 17 (35)               | 162 (33)             | 0.901  |
| FC IV, n (%)                     | 459 (87)      | 31 (64)               | 428 (89)             | 0.0001 |
| Reproducibility                  |               |                       |                      |        |
| Palpation, n (%)                 | 89 (17)       | 8 (15)                | 81 (17)              | 0.910  |
| Inspiration, n (%)               | 100 (19)      | 0                     | 100 (20)             | 0.0007 |
| Movements                        | 79 (15)       | 0                     | 79 (16.5)            | 0.004  |
| Pain-to-consultation time, hours | 5.5 (2-8)     | 13 (1-36)             | 5.5 (2-8)            | 0.881  |
| > 6 hours, %                     | 50            | 50                    | 50                   |        |

SBP: Systolic blood pressure. DBP: Diastolic blood pressure. HR: Heart rate. bpm: Beats per minute. FC: Functional class.

**Table 3.** Diagnosis and management of the patients evaluated, considering 30-day outcome

| Diagnosis                      | Total (n = 528) | Discharge (n = 479) | Hospitalization (n = 49) |
|--------------------------------|-----------------|---------------------|--------------------------|
| Non cardiac chest pain         | 433             | 428                 | 5                        |
| Acute coronary syndrome        |                 |                     |                          |
| Unstable angina                | 11              | 6                   | 5                        |
| AMI                            | 33              | 0                   | 33                       |
| Pericarditis - myopericarditis | 47              | 43                  | 4                        |
| Stable angina                  | 4               | 2                   | 2                        |

AMI: Acute myocardial infarction.

Several authors have published the diagnostic usefulness and safety of performing early functional tests in patients with chest pain and low initial risk. (21, 22) However, the presence of severe coronary artery disease was considered as a positive diagnosis in the usefulness analysis, a situation that is not always associated with acute coronary events. Functional tests provide valuable information for patient assessment, but there is no clear evidence that performing it before discharge is decisive. In our experience, the use of the new algorithm was associated with a low rate of functional test utilization, probably associated to the

fact that high sensitivity troponin, together with the low risk of the patients evaluated, afford more safety.

The use of our algorithm reduced mean emergency department length of stay compared to the one reported by other studies, without difference in patient safety. In the ROMICAT II study, which evaluated the benefits of contrast-enhanced computed tomography coronary angiography to rule out acute coronary syndromes, 50% of patients were discharged within 8.6 hours, while in our study the patients were discharged after 4.5 hours. (23) In the study by Botto et al. performed at our institution before high-sensitivity troponin was available, 88% of patients were discharged after 13 ± 7 h, and the rate of events was similar to the one found in the current registry. Although the benefits of chest pain units in terms of cost-effectiveness have been previously reported by several publications (1-5, 20-24), the best strategy has not been defined yet. It is reasonable to assume that a reduction in hospital stay may promote greater availability of emergency department beds and reduce the costs of medical care, but this analysis was not performed.

Our algorithm is similar to the one proposed by the European Society of Cardiology, with the difference that we have defined the cutoff values of troponin which are essential for decision-making. This

constitutes the greatest collaboration of our study to medical practice. (24)

### Study limitations

Most of the patients analyzed were low-risk patients; thus, it would be interesting to evaluate the usefulness of the method in patients with higher baseline risk.

It should be noted that this study was conducted in a tertiary cardiac care center, managed by cardiologists trained in coronary artery disease and its types of presentation. In this sense, the new algorithm should be tested in general emergency departments

### CONCLUSION

The novel algorithm used in our center, which included measurement of high-sensitivity cardiac troponin T in patients with suspected acute coronary syndrome has proved to be safe, preventing the discharge of patients with acute coronary syndrome and reducing emergency department length of stay in this population.

### Conflicts of interest

None declared.

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