

SOURCES OF DIAGNOSTIC AND THERAPEUTIC INACCURACY IN ACUTE CORONARY SYNDROMES

GABRIELA EMINOVICI¹, I. MANIȚIU²

^{1,2}“Lucian Blaga” University of Sibiu

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Abstract: A document adopted by a consensus between the European Society and the American College of Cardiology in 2000, redefines the acute myocardial infarction as any quantity of myocardial necrosis caused by ischemia. Together with the appearance of new, sensitive biomarkers of myocardial infarction, little quantities of necrotic myocardium started to be detected and recognized as literally. The recent definition has changed the diagnosis central role, focusing the attention towards the troponine levels and lowering the importance of the old criteria (clinical scenery and EKG changes), allowing a larger scale of interpreting these criteria. Even before been accepted, the new definition of the myocardial infarction was questioned: only half of the doctors accept the diagnosis in the presence of the symptoms and the high troponine levels (in the absence of the EKG changes or high levels of CK and CK-MB). The essential criteria in the fight with the time, regarding the decision of reperfusion, remains still the ST elevation. Regarding the decision for trombolysis, the EKG changes remain sovereign. Which doctor had never been confronted in the emergency room with the next situation: thoracic pain and un-interpretable electrocardiogram? In these particular situations, which can lead to diagnosis confusions, the interpreting of the troponine elevation can solve some problems. Moreover, the correct diagnosis of this cases can have serious therapeutic benefits. Even in the case of a correct and in time diagnosis, the percent of the eligible patients who do not receive any reperfusion form is unacceptable high (approximate 50%, after the data received from the European Congress 2008). The aim of this paper is to interpret from this point of view (of the new definition and recent indications of reperfusion), the data of the patients which were hospitalized during the last two years (January 2007 - October 2009) in the Cardiology Department of the Emergency Clinical County Hospital, having the diagnosis at admission of Acute Coronary Syndrome (ACS).

Cuvinte cheie: infarct miocardic, noua definiție, troponina, reperfuție

Rezumat: Un document adoptat prin consens între Societatea Europeană și Colegiul American de Cardiologie în 2000, redefineste infarctul miocardic acut ca și orice cantitate de miocard necrozat cauzat de ischemie. Odată cu disponibilitatea a noi și sensibili biomarkeri de necroză miocardică, mici cantități de miocard necrozat pot fi detectate și recunoscute ca atare. Definiția recentă a schimbat rolul central diagnostic, focalizând atenția asupra troponinei și reducând greutatea vechilor criterii (scenariul clinic și modificările ECG, permițând o plajă largă de interpretare a acestor criterii). Chiar înainte de a fi acceptată, noua definiție a infarctului miocardic este pusă sub semnul întrebării: doar aproximativ jumătate dintre doctori acceptă diagnosticul în prezența simptomatologiei și a troponinei crescute (în absența modificărilor ECG sau a nivelurilor crescute de CK și CK-MB). Cine nu s-a confruntat însă în regim de urgență, cu următoarea situație: durere toracică cu ECG ne- sau greu interpretabil? În aceste situații particulare, pretabile la confuzii diagnostice, interpretarea ascensiunii troponinei poate tranșa dilemele. Mai mult, încadrarea corectă, la timp, a acestor cazuri, poate avea serioase beneficii terapeutice. Dar chiar pentru situațiile „norocoase”, ale unui diagnostic corect și la timp efectuat, procentul de pacienți eligibili ce nu primesc nici o formă de reperfuție este inacceptabil de înalt (aproximativ 50%, după datele culese la European Congress 2008). Scopul acestei lucrări este de a interpreta din acest punct de vedere (al noii definiții și recentelor indicații de reperfuție), datele pacienților internați pe perioada a aproape doi ani (2007- octombrie 2009), având diagnosticul de internare de Sindrom coronarian acut (SCA).

INTRODUCTION

A document adopted by consensus between the European Society of Cardiology and American College in 2000, redefined myocardial infarction as any amount of necrotic myocardium caused by ischemia. With the availability of new and sensitive biomarkers of myocardial necrosis, small amounts of myocardial necrosis can be detected and recognized as such. Definition recent diagnosis changed the central role, focusing

attention on reducing weight and cardiac troponin old criteria (clinical scenario and ECG changes, allowing a wide range of interpretation of these criteria). Even before it accepted the new definition of myocardial infarction is questionable: only about half of doctors accept the presence of symptoms and diagnosis of elevated cardiac troponin (in the absence of ECG changes or elevated levels of CK and CK-MB). The essential criterion in the fight time, in terms of the decision

¹Corresponding Author: Eminovici Gabriela, Clinical Hospital Emergency of Sibiu, Cardiology, 2-4 Bulevardul Corneliu Coposu street, Sibiu, România; e-mail: geminovici@ymail.com; tel +40-0722625639

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of reperfusion, remains supradenivelat ST. At least in terms of thrombolysis, ECG changes are not faced suverane.Cine but urgent, with following situation: chest pain with ECG interpretable us or hard?

In this particular situation, the price of diagnostic confusion, cardiac troponin rise can tranche interpretation dilemmas. Furthermore, correct classification at the time, these cases can have serious benefits for situations terapeutice.Dar even "lucky", the proper diagnosis and timely made, the percentage of eligible patients receive no reperfusion as unacceptable high (about 50%, after data collected at the European Congress 2008). The purpose of this paper is to interpret from this point of view (the new definition and recent indications of reperfusion), data of patients admitted during the nearly two years (2007 - October 2009), with admission diagnosis of acute coronary syndrome (ACS).

PURPOSE OF THE STUDY

The contents of this paper aims:

1. ACS, "false alarm"?
2. What is the use of cardiac troponin in ACS?
3. Angina with troponin positive - false diagnosis?
4. Vs. other biomarkers troponin
5. Troponin and other diagnostic criteria (compared to statistical indicators).
6. ACS and BRS: a controversial association.
7. Reperfusion therapy: underused?
Aborted MI or "masquerading" heart?

MATERIAL AND METHOD

Were considered in all patients admitted in the Cardiology Department of Hospital Clinic Sibiu County, in the period 01/01/2007 to 10/22/2009. This period was chosen purely pragmatic reasons, because cardiac troponin determination (and therefore the possibility of implementing new criteria for diagnosis) is made from early 2007. Among them were selected who presented at admission diagnosis of acute coronary syndrome. Respectively, from a total of 9633 patients hospitalized in this period, were selected from 734 patients with ACS, representing a rate of 7.62%.

RESULTS AND DISCUSSION

1. ACS, "false alarm"?

Of all patients hospitalized with suspected ACS, 65% dinagnostical discharge of AMI was at 9% of hospital discharge diagnosis was angina, and 26% of cases (67 patients were discharged with diagnoses noncoronariene).

Of those 67 diagnoses "noncoronariene so-called" STEM is involved only in 19 cases (of which 8 were BRS). The remaining 48 cases were provided by non-stem.

Cases of "fake stem" were mostly covered by various forms of heart failure: left ventricular failure - 12 cases, acute pulmonary edema - 8 cases, congestive heart failure - 6 cases, followed by: dilative cardiomyopathy - 3 cases, pulmonary embolism - 2 cases, 2 cases of myocarditis, pericarditis 1caz, Takotsubo syndrome - a case.

2. What is the use of cardiac troponin in acute coronary syndromes?

In the literature, is that, for patients who have not received any dose of biomarkers of necrosis, an almost 10% and troponin in particular, this percentage increases to 60%. In our study group, troponin was measured in the 18.1% of patients admitted with a diagnosis of ACS. 9.8% were troponin positive and negative was 8.3%. Patients who have not received any dose of biomarkers are in number 61, representing 8.3%, percentage assimilated data. Discharge diagnosis of heart was at 376 patients in whom troponin was not wrapping. Therefore, this

diagnosis is based on the old definition (WHO definition), which requires 2 / 3 criteria. If for Stem ECG remain sovereign, at least in terms of therapeutic decision for NSTEMI, biomarker test has become "the cornerstone". Low specificity of pain and ST-T changes and gives precedence biomarkers, specifically cardiac troponin. Of 379 patients only 58 were NSTEMI troponin wrapping. Of 48 patients with ACS and troponin BRS only seven were wrapping. However the percentage of NSTEMI patients without the biomarker dose is only 3.5%.

3. Angina with positive troponin-false diagnosis?

Troponin positive ACS is a combination which, as defined mean heart. Of 61 cases with positive troponin, only 53 were classified as stroke, the remaining eight being wrongly interpreted as an unstable majority.

Revising the diagnostic criteria under the new definition

- All patients were diagnosed with angina pain naturally,
- More than 3 were even supradenivelat ST
- One patient out of 8 with alternative diagnoses has noncoronariană pathology, pulmonary embolism respectively. Even this would be classified under the new criteria at least in category: MI type 2.

Given the reporting of cardiac troponin positivity in patients with admission diagnosis of ACS, it is reasonable not to perform cardiac troponin false positivity in the present batch (ultraselectionat).

4. Troponina vs. other biomarkers.

Protocols for the interpretation of cardiac biomarkers (American Association for Clinical Chemistry 2007 - Guidelines for use of biomarkers in ACS)

- Not suitable single marker.
- It is desirable to combine an early marker, sensitive (myoglobin) with one more specific and late (troponin).
- Excluding a timely diagnosis is a target variable depending on the probability per test, time from onset of pain
- Additional testing will be performed (or stress imaging) after MI was excluded.

The purpose of this chapter is to highlight the study group (734 patients with ACS) any differences between biomarkers in terms of statistici.S indicators were calculated sensitivity, specificity, positive predictive value, negative predictive value for each enzyme in parte.Comparația between the group diagnosed with myocardial infarction and the group without diagnosis at discharge, cardiac troponin is positive ($p < 0.01$), while for CK-MB and mioglobină could not establish such a correlation (for the present group, $p > 0.01$ for both biomarkers). Data obtained indicates troponin testing as the highest specificity. In terms of hierarchy, the result is not surprising. Biomarker troponin is the most specific and mioglobina has the highest sensitivity (data in agreement with the literature). Surprise result but in terms of value received. In literature, values reported for specific cardiac troponin does not fall below 90%. Although testing was performed on a batch ultraselectionat, with high probability of having the disease specificity of cardiac troponin is below the values reported in literature (about 78%). At least two explanations for this difference:

1. Este possible compliance at harvest (ie, a second dose at least 6h from onset) to reduce the number of false negative tests,
2. Diagnostical discharge has not been reviewed on this lot. But there are eight cases with positive troponin, assigned to other diagnoses, most of the discharge diagnosis of angina pectoris.

Revision under the new definition would reduce the number of false positives, specificity reaşezând value, as

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follows: sensitivity of cardiac troponin in the diagnosis of infarction is 57.7% while the specificity is 96.5%. Revised value for specificity is much closer to the literature by the correct classification of only 7 cases - 96.6%. Regarding other statistical indicators, that diagnostic accuracy, positive predictive value and negative - the comparison, even without revision is diagnostic for cardiac troponin. Therefore, it provides most of the cases correctly diagnosed (about 61%).

We studied two levels below significance of biomarkers in confirming or excluding the diagnosis of heart. Sure that the definition does not require the isolation of two biomarkers, but there is equivocal situations, the ECG or imaging criteria not working and the pain is low specificity. The purpose of cutting them would be good to know to what extent we can rely on positivity or negativity of the two biomarkers.

Therefore:

- + CK-MB positive troponin positive indicates a diagnosis of stroke in 99% ($p < 0.01$)
- + CK-MB negative troponin negative myocardial excluded in 95% ($p < 0.05$)
- + Mioglobina positive troponin positive indicates a diagnosis of heart in 95% ($p < 0.05$). Exclusion can not count on having two negative values of myocardial troponin and mioglobină. ($P > 0.05$). Mioglobinei Poor specificity probably justify this result.

5. Troponina versus other diagnostic criteria

The most common causes of ST supradenivelat are some statistics: SS, BRS, early repolarization and ventricular aneurysm in other STEM is third. SS and BRS keeps constant but instead on "the podium". Many of these conditions may be erroneously interpreted as myocardial infarction thrombolysis resulting in unwanted or inappropriate coronarografi emergency.

In our study group, observed that pain sensitivity is 89%, while specificity for diagnosis of chest pain of heart, a lot ultraselectionat with admission diagnosis of ACS is only 20% (one third of patients with pain and ACS are discharged without a diagnosis of heart). I tried to as a hierarchy of different ECG features in terms of performance testing. We calculated sensitivity and specificity of each element relative to the initial batch (ie those with ACS as the admission diagnosis). Although the calculation of performance testing for biomarkers was performed on different batches (only those on which the determination), at least indicative indicators can be compared to all elements involved in diagnosis.

In terms of diagnostic accuracy, ie the highest percentage of correct - provide ST elevation (66.8%), followed by pain and Q-wave (64%).

In subgroup with NSTEMI association: positive troponin + pain correlate with diagnosis of heart to the nearest 99% ($p < 0.01$). The subgroup with STEM correlation value is not as strong ($p = 0.05$), so be positive troponin correlated with the diagnosis of stroke with an accuracy of only 95%. If you do not take into account pain, virtually no correlation between troponin and diagnosis infarct. Pentru rest of the criteria for myocardial associations could not establish a statistical correlation ($p > 0.05$) for all these combinations.

6. SCA and BRS: a combination that can become problematic

Data from the literature argue that patients with MI and BRS were higher hospital mortality (22.6%) than patients without BRS (13.1%). This difference is due at least in part retention of reperfusion (drug or mechanically these patients). About half of patients with MI and BRS symptoms not typical (ie without chest pain are hospitalized). ST changes consistent (with QRS) and ST depression, V1-V3 on the merits of BRS were found to have high specificity (97%) confirmed the

diagnosis of myocardial enzyme.

When new, BRS descending artery occlusion is related to previous infarction with a large quantity "jeopardized." Moreover, previous BRS is a powerful marker of LV dysfunction associated loss of myocardium so may result in shock cardiogen. Întrebarea entry that arises is whether the combination of MI and BRS is treated in accordance with the guidelines or not.

In group present with ACS as the admission diagnosis, BRS was present in 48 patients, representing 6.5% of the total. Of those, only 20 have received final discharge diagnosis of AMI. 20 patients received discharge diagnosis of angina and the remaining eight were assigned to diagnoses noncoronariene.

1. We compared the other two groups, namely: ACS and ACS without ST ST supradenivelat supradenivelat, ACS BRS, in terms of proportion of events ultimately interpreted as noncoronariene. The comparison provided significant results in "favor" BRS ($p < 0.01$ for both groups).
2. In terms of risk profile, group BRS is associated with a high risk profile that association with diabetes, hypertension and heart failure.
3. Given the difficulty of framing BRS as ACS, I tried reporting this kind of pathology (or BRS) in total 9632 patients admitted to the ward from 01/01/2007 to 10/22/2009.

In a number of 682 patients (7.07%) was diagnosed with left bundle branch block (BRS). Of all patients with BRS, 35 patients (5.13%) had troponin wrapping. 31 of these patients, cardiac troponin values were below the considered pathological. The remaining four patients had levels considered above normal upper limta. Of these, 3 patients were discharge diagnosis of acute myocardial infarction and one patient had the discharge diagnosis of acute myocardial infarction. Of all patients with BRS, 26 patients (3.81%) had CK wrapping. In 17 patients of them, CK-MB values were above the upper limit considered normal (4.5 ng / ml). The remaining nine patients had CK values considered normal. Of the 17 patients with BRS and elevated CK-MB, only three were made at discharge diagnosis of acute myocardial infarction. The remaining 14 cases were interpreted as acute myocardial infarction.

1. No patient with ACS and BRS was not thrombolysed, although 20 of 48 were diagnosed with AMI at discharge. BRS is therefore included a significant proportion of cases among nontromboliză reasons.
2. In terms of evolution, there is also a higher percentage of patients with adverse developments in the group with ACS and BRS, lots to type stem or NSTEMI ACS.
3. Terapia reperfusion - underused?

In our study group 42.2% of patients with myocardial STEM as discharge diagnosis were thrombolysed. Sure that the percentage may reflect greater label, by adjusting the lot on the time of onset, age, contraindications thrombolysis.

Relationship with age: 66.70% of patients between 31-40 years with an indication of thrombolysis were thrombolysed; remaining percentages are as follows: 30% (41-50) 18.50% (51-60 years), 16 80% (61-70 years), 7.90% (71-75 years), 9.5% (76-80 years), 1% (81-90 years). But we found that age was not a major impediment to initiate thrombolysis. There were 10 patients, representing approximately 10% over 75 years, who were thrombolysed.

Relation to Sex: 68% of female patients were not thrombolysed, 51% of male patients were thrombolysed. Percentage of female patients who were not thrombolysed significantly higher than in male patients ($p < 0.01$). Tromboliticele used, in order of frequency were: streptokinase (58.75%), Alteplase (28.75 %), Tenecteplase (10%), Reteplase (2.5%). The percentage of patients sent for PCI in particular

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reflect the reality of logistical limitation in implementing this therapy. We calculated, however, and the percentage of patients who received reference purposes invasive revascularization: 15.4% of patients with AMI as discharge diagnosis and 6.2% of patients with angina, the diagnosis of extrenare. Of the 73 patients with AMI sent for PCI, 31 were previously thrombolysed.

In our study group, the presence of the following factors proved to have statistical significance in the netrombolizați group ($p < 0.01$) heart failure, hypertension, diabetes, BRS. Există several potential reasons for failure of thrombolysis in these patients, and lack of knowledge that reperfusion indications were extended to more complex groups (less studied in trials). For example, doctors hesitate to prescribe reperfusion in patients with atypical symptoms (shortness of breath instead of classic retrosternal pain). Patients with old myocardial infarction or CABG are also less subject to difficulties in interpretation supradenivelării reperfusion ST (old or new?). Patients with heart failure or diabetes symptoms are not typical, resulting in no further investigation ECG.

CONCLUSIONS

1. There is a "restraint" from physicians in the diagnosis of AMI according to new criteria.
2. Underspending cardiac troponin and CK-MB, and biomarkers of necrosis recommend the new definition is relevant to the lack of implementation.
3. One (or more than two determinations) may amount calculations "complicated" multivariable used in prognostic assessment.
4. Underestimated the true incidence of AMI is the correct diagnostic inconsistency. The percentage of "false ACS (ie, cases that were not completed in coronary diagnosis) is only 9%. Various forms of heart failure is the major manifestation in these patients.
5. Positive troponin correlates with the diagnosis of stroke with an accuracy of 99% ($p < 0.01$), which could not be found for other biomarkers ($p > 0.05$). The diagnostic review (ie, using new criteria), the specificity of cardiac troponin is similar to the literature (96.5%).
6. Findings combination of two values of biomarkers in confirming, excluding diagnosis of heart that is in favor: troponin + CK. Mioglobina in combination with troponin can be used for confirmation ($p < 0.05$), but can not be used for exclusion ($p > 0.05$).
7. Comparison in performance between elements ECG testing indicates that the component BRS provides the fewest false-positive cases, followed by ST depression and ST supradenivelat (89% vs. 75.4 vs. 66.5). Highest percentage of correct results it provides ST elevation (66.8% accuracy).
8. In the group with troponin wrapping, its positive predictive value was superior to other clinical and ECG evidence for both STEM and for NSTEMI.
9. Combination pain - troponin is superior to other combinations in the diagnosis of infarction ($p < 0.01$), probably by cross-fertilization (for pain, showed 89% sensitivity, while only 20% specificity).
10. The presence of BRS in patients with ACS is associated with an increased risk profile, with high probability of conservative treatment ($p < 0.01$) and highest proportion of hospital deaths (compared to the group with ST supradenivelat and NSTEMI).
11. Reperfusion was performed as follows: drug to 24.6%, invasive 16.9% to 7.2% combined. 65.6% following conservative treatment (group considered include both STEM and NSTEMI patients, but the hospital had AMI).

This diagnosis was considered a substitute for NSTEMI risk (as they would be guidelines only indication of revascularization).

12. Reported only in patients with STEM, these data are encouraging, that are similar to those in literature - 71% of patients with revascularized STEM.

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