# ROLE OF SERUM ISCHEMIA MODIFIED ALBUMIN (IMA) IN COMBINATION WITH hs-TROPONIN T TO DIAGNOSE ON PATIENTS WITH NON-ST SEGMENT ELEVATION ACUTE CORONARY SYNDROME

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**Abstract**

***Background:*** Early diagnosis of acute coronary syndrome (ACS) is significant to treatment and prognosis. It helps to reduce death and complications. What is the value from a combination of ischemia modified albumin (IMA) and hs-Troponin T(hs-TnT) for diagnosis of non-ST segment elevation acute coronary syndrome (NSTE-ACS)? ***Objectives:*** Determining the concentration of IMA and hs-TnT in patients with NSTE-ACS; Determining sensitivity and specificity when combining IMA and hs-TnT in diagnosis of non-ST segment elevation acute coronary syndrome. ***Subjects and Method:*** 75 patients were hospitalized in Hue Central Hospital with chest pain, presenting non-ST segment elevation acute coronary syndromes. Diagnosis of non-ST segment elevation acute coronary syndromes was done on 37 of those as in a patients group; 38 others were chosen as a controls group. Cross-sectional study with comparison was applied. ***Results:***- In 2 tests at different time points, the concentration of hs-TnT and IMA in patients group with NSTE-ACS was higher compared with that in the controls group (median: 0.065ng/mL >0.006ng/mL and 0.162ng/mL >0.0055ng/mL); Average IMA concentration in patients group was 93.49± 89.56 IU/mL (median: 58.57IU/mL) and higher compared with the controls group which reaches 15.01 ± 9.87 IU/mL (median:11.735IU/mL). It resulted in a statistical significance p<0.001.- The cut off point of hs-TnT was > 0.014 ng/mL and IMA>28.68 IU/ML, reaching a sensitivity at 88.9% and a specificity at 100%, AUC = 0.97, p < 0.001, 95% CI = 0.915 – 1.00. **Conclusion**: Combination of IMA and hs-TnT results in a high value for diagnosis of non-ST segment elevation acute coronary syndromes.

***Key words:*** IMA, hs-Troponin T, ACS, NSTE-ACS, UA, NSTEMI

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## 1. BACKGROUND

ACS is a dangerous disease in internal medicine emergency. It needs to be diagnosed and treated timely. According to WHO, 7.3 million people in the world die yearly from coronary arterial diseases [16]. According to the America Heart Association, there are 515,000 cases of myocardial infarction each year, in which 205,000 cases relapse [6]. In Europe, in every 6 men and every 7 women, there is one death from myocardial infarction[4]. In 2010 in England, rate of death from myocardial infarction patients is 39.2% in men and 17.7% in women [12]. ACS is more and more a popular pathology in Vietnam. Although there is no specific statistics, number of patients of heart diseases and especially of ACS is increasing. According to a study by Nguyễn Lân Việt, rate of hospitalized patients of ACS at the Vietnam National Heart Institute reaches 4.6% [5].

There are still difficulties in diagnosis of NSTE-ACS such as untypical clinical syndromes, unclear ECG images, late interference of biological markers in blood after myocardial necrosis.In the past years, a lot of new biological markers have been researched regarding their values for diagnosis and prognosis of death and major heart incidents. As a result, it helps to make early diagnosis accurately and timely, playing an important role in treatment and reduction of death rate and complications in patients with ACS [13].

Markers are different regarding release time and back-to-normal time. Therefore, it's necessary to combine biological markers in diagnosis of ACS. Combination of Ischemia Modified Albumin (IMA) and hs-Troponin T(hs-TnT) is one option for a valuable test and an ideal cardio-marker. Because the test quickly shows its results, it's an ideal option for early diagnosis of ACS, leading to a choice of early treatment for patients: either coronary arterial interference or antithrombotic therapy[10]. What is the value from a combination of IMA and hs-TnT for diagnosis of NSTE-ACS? We implemented the

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study "***Role of serum IMA in combination with hs-TnT to diagnose on patients with non-ST segment elevation acute coronary syndrome*** " with 2 objectives:

*1. Determining concentration of IMA and hs-TnT to diagnose on patients with non-ST segment elevation acute coronary syndrome (NSTE-ACS)*

*2. Determining the sensitivity and specificity when combining IMA and hs-TnT for diagnosis of NSTE-ACS*

## 2. SUBJECTS AND METHOD

### 2.1. Subjects

75 patients were hospitalized in Hue Central Hospital with chest pain, presenting non-ST segment elevation acute coronary syndromes. They were selected for 2 groups: 37 of those are for the patients group , diagnosed based-on the ESC Guidelines 2015 and the 38 others were in the controls group.[11].

### 2.2. Method

Cross-sectional study with comparison was applied.

Basic data was recorded: age, sex, occupation, adress, time of hospitalization, factors of risk, etc.

Electrocardiogram (ECG), cardio-ultrasonic test, coronary arterial imaging (if applicable) were done.

Other tests: standard vein test for IMA and hs-TnT test were done twice, 6 hours in between.

### 2.3. Management of data

Software SPSS 20.0 s applied.

## 3. RESULTS

Through the study on 75 patients presenting NSTE-ACS, we determined that 37 of them have NSTE-ACS and the 38 others belonged to the controls group.

### 3.1. Common characters of the subjects

**Table 1.** Ages and sexes

| Characters n | | Total ( n=75) | Groups | | | | | p |
|---|---|---|---|---|---|---|---|---|
| | | % | Controls group ( n=38) | | Patients group (n=37) | | | |
| | | | n | % | n | % | | |
| Ages | Average | 67.4±13.5 | | 65.1 ± 13.6 | | 69.8± 13.1 | | 0.129 |
| | Min:Max | 36:101 | | 37:101 | | 36:91 | | |
| Sexes | Male | 34 | 45.3 | 17 | 44.74 | 17 | 45.95 | 0.916 |
| | Female | 41 | 54.7 | 21 | 55.26 | 20 | 54.05 | |
| Rate Male/Female | | 0.83 | | 0.81 | | 0.85 | | |

*Remark:* The average age in 2 groups was equivalent. Number of female subjects was bigger than male subjects, but the difference was quite small.

**Table 2.** Reason and time duration from occurrence to hospitalization

| Reasons and time for hospitalization n | | Total (n=75) | | Controls group (n=38) | | Patients group (n=37) | | |
|---|---|---|---|---|---|---|---|---|
| | | % | n | % | n | % | | |
| Reasons for hospitalization | Chest pain | 66 | 88 | 30 | 78.9 | 36 | 97.3 | p=0.028 |
| | others | 9 | 12 | 8 | 21.1 | 1 | 2.7 | |
| Time duration from occurrence to hospitalization | <6 hrs | 27 | 36 | 8 | 21.1 | 19 | 51.4 | p<0.001 |
| | 6-12 hrs | 32 | 42.7 | 14 | 36.8 | 18 | 48.6 | |
| | >12 hrs | 16 | 21.3 | 16 | 42.1 | 0 | 0 | |

*Remark:* The patients are hospitalized mainly because of chest pain and time duration from occurrence to hospitalization was mainly less than 6 hours

### 3.2. Concentration of hs-TnT at 2 time points and IMA

**Table 3.** Concentrations of biological enzymes in groups

| Changes of biological enzymes | | Total (n=75) | Controls group (n=38) | Patients group (n=37) | p |
|---|---|---|---|---|---|
| hs-TnT in 1st time (ng/mL) | average | 0.4748 ± 1.4033 | 0.0115 ±0.0226 | 0.8012±1.5782 | <0.001 |
| | median | 0.01 | 0.006 | 0.065 | |
| | 25%:75% | 0.004:0.079 | 0.001:0.0105 | 0.0085:1.0585 | |
| | min:max | 0.001:8.053 | 0.001:0.111 | 0.001:8.053 | |
| hs-TnT in 2nd time (ng/mL) (N=74) | average | 0.4748 ± 1.4033 | 0.0343±0.1627 | 0.9397±1.9096 | <0.001 |
| | median | 0.014 | 0.0055 | 0.162 | |
| | 25%:75% | 0.0038:0.1893 | 0.001:0.01325 | 0.01725:1.105 | |
| | min:max | 0.001:10 | 0.001:1.010 | 0.001:10 | |
| IMA (IU/mL) | average | 53.88 ± 74.16 | 15.01 ± 9.87 | 93.49 ± 89.56 | <0.001 |
| | median | 30.99 | 11.735 | 58.57 | |
| | 25%:75% | 11.31:58.57 | 6.73:23.64 | 38.87:101.69 | |
| | min:max | 4.10: 383.52 | 4.1:36.77 | 22.74:383.52 | |

*Remark:* The concentrations of hs-TroponinT at 2 time points and IMA in the patients group were higher compared with those in the controls group.

### 3.3. Concentration of IMA and hs-Troponin in diagnosis of NSTE-ACS

**Graph 1.** ROC curve of hs-Troponin T and IMA in diagnosis of NSTE-ACS

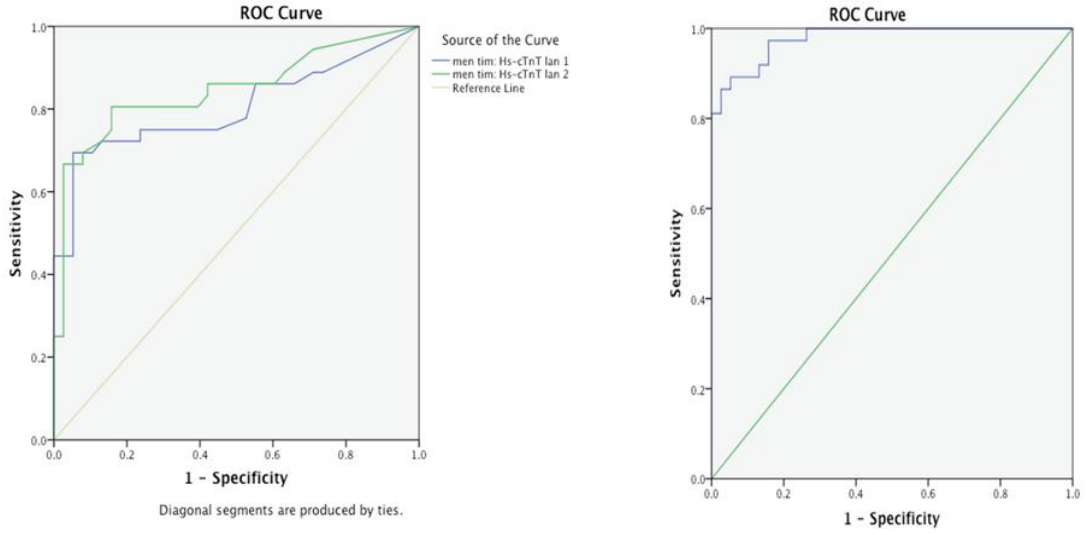


**Table 4.** Cross-sectional point, sensitivity, specificity, AUC of IMA and hs-TnT in diagnosis of NSTE-ACS

| | Value | Sensitivity (%) | Specificity(%) | AUC | Significancep | 95% CI |
|---|---|---|---|---|---|---|
| hs-TnT in 1st time (0h) (ng/mL) | 0.0145 | 72.2 | 86.8 | 0.80 | <0.001 | 0.70- 0.91 |
| hs-TnT in 2nd time (6-12h) (ng/mL) | 0.015 | 80.6 | 84.2 | 0.85 | <0.001 | 0.75- 0.94 |
| IMA (IU/ml) | 28.68 | 91.9 | 86.8 | 0.98 | < 0.001 | 0.95 – 1.00 |

*Remark:* Compared with hs-TnT at the 2 time points, sensitivity in IMA was higher and specificity in IMA was equal.

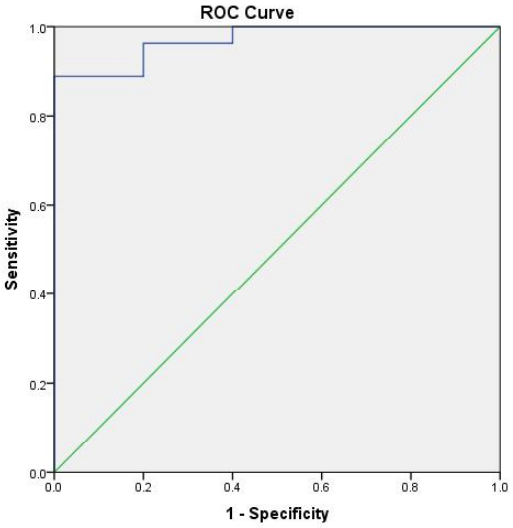
**Table 5.** Cross-sectional point of hs-TroponinT and IMA at risk of NSTE-ACS

| Factors | | OR | 95% CI | Significance p |
|---|---|---|---|---|
| IMA (IU/ml) | ≤ 28.68 | 1 | 16.54- 338.38 | < 0.001 |
| | > 28.68 | 74.8 | | |
| Hs-cTnT 1 (ng/mL) | ≤ 0.014 | 1 | 5.43- 58.45 | < 0.001 |
| | > 0.014 | 17.8 | | |
| Hs-cTnT 2 (ng/mL) | ≤ 0.014 | 1 | 6.65- 73.41 | <0.001 |
| | > 0.014 | 22.1 | | |

### 3.4. Combination of hs-TroponinT and IMA in diagnosis of NSTE-ACS

**Table 6.** hs-TroponinT and IMA in diagnosis of NSTE-ACS

| hs-TnT >0.014 ng/ mL | Value | Sentitivity(%) | Specificity(%) | AUC | Significance p | 95% CI |
|---|---|---|---|---|---|---|
| IMA (IU/ml) | 28.68 | 88.9 | 100 | 0.97 | < 0.001 | 0.915 – 1.00 |




**Graph 2.** ROC curve of IMA and hs-TroponinT in diagnosis of NSTE-ACS

Remark: the best cross-sectional point of IMA is> 28.68 IU/mL and hs-TroponinT is > 0.014ng/mL.

## 4. DISCUSSION

### 4.1. Common characters in groups of subjects

Age is one of the risk factors of ACS and also a prognosis factor in ACS. In our study, the average age of subject groups was 69.8±13.1. Patients with ACS were normally above 60 years old. Our study's results were similar to those by other national and international researchers. The average age of subjects in the study by Giao Thị Thoa was 65.74±14.51, by Nguyễn Tá Đông 66.61±11.19, by Anna Wudkowska and partners 63±12. Numbers of male and female subjects in our study were almost equal. [1], [3], [7].

The patients were hospitalized mainly because of chest pain, occupying 97.3%. In the patients group, time duration from occurrence to hospitalization was mainly less than 12 hours. In our study, number of hospitalized subjects with this time duration < 6 hours occupied 51.4% and >6 hours 49.6%. In comparison with other researchers: Giao thị Thoa (2014) < 6 hours: 30.6% and > 6 hours: 69.4%; Nguyễn Tá Đông (2016) < 6 hours: 14.63% and > 6 hours: 85.37%; there was obviously a big difference between the patients groups and controls groups in regarding of the time duration< 6 hours from occurrence to hospitalization. And compared with their studies, there are also differences regarding time factor due to low awareness of illness, financial background, health care and transportation conditions amongst areas [1], [3].

### 4.2. Concentration of IMA and biological enzymes in diagnosis of NSTE-ACS

NSTE-ACS consists of non-ST segment elevation myocardial infarction (NSTEMI) and unstable angina (UA). In order to diagnose myocardial infarction, it requires an increase of markers which indicate myocardial injures. Troponin has high sensitivity and specificity, but it may indicate false positive values and is not effective at 100%. Thus, it is necessary to utilize different markers simultaneously in diagnosis [15].

Our results indicated that the concentration of hs-Troponin T and IMA in the patients group was higher compared with the control group. We maked 2 tests with markers in order to obtain better possibilities for the diagnosis of ACS. The concentration of hs-Troponin T in blood serum of the patients group in 2 tests was higher compared with the controls group. The average concentration of hs-Troponin T is 0.8012 ± 1.5782 ng/mL (median: 0.065 ng/mL) and 0.9397±1.9096 ng/mL (median: 0.162 ng/mL). This result was many times higher compared with normal indicators. This result was similar to those in studies by Nguyễn Tá Đông and Bùi Thị Thanh Hiền [1], [2]. From our results, the concentration of hs-Troponin T in the first test was > 0.014ng/mL, it refers to an increasing risk of NSTE-ACS at 17.8, [95% CI=5.43- 58.45; p<0.001]; the concentration of hs-Troponin T in the second test was > 0.014ng/mL, it refers to an increasing risk of NSTE-ACS at 22.1 [ 95%CI=6.65- 73.41; p< 0.001].

The average concentration of IMA in patients groups was 93.49 ± 89.56 IU/mL, median was 58.57 IU/ml. This indicator was higher compared with the controls group. The best cut off point of IMA in diagnosis of NSTE-ACS was > 28.68 IU/ml, AUC = 0.98, 95% CI= 0.95-1.00; sensitivity reaches 91.9% and specificity reaches 86.8%. In patients with concentration of IMA > 28.68 IU/ml,the risk of NSTE-ACS increased 74.8 times compared with those with lower indicators. According to the results by Nguyễn Tá Đông, the average concentration of IMA in diagnosis of myocardial infraction is 43.40 ± 23.98IU/mL and the best cut off point was >30.28IU/mL[1]. In the study by C.Bhakthavatsala Reddy (2014), the concentration of IMA in patients with unstable angina was 89.00 ± 7.76IU/mL and in those with myocardial infraction was 87.50± 9.62IU/mL; there were no differences from 2 subject groups with the sensitivity of IMA at 92% and the specificity at 87% [8]. According to a research on NSTE-ACS by Anna Wudkowska (2010), in the patients group positive with Troponin, the concentration of IMA was 95.2 ±12.8IU/mL; meanwhile it reached 94.0±17.9IU/mL in the group which is negative with Troponin; there were no differences from the two groups [7]. In a research by Ramazan Gũven and partners (2016), the concentration of IMA in the patients group with NSTE-ACS and the patients group with NSTEMI was 41.4 ± 0.08 IU/mL and 45.4 ±0.08IU/mL respectively; the results were similar from the two groups, but there were differences compared with the controls group (the concentration of IMA in the controls group is 40.4± 0.04, p=0.006, the sensitivity reached 61.2%, the specificity reached 87.5% and the best cross-sectional point was 44,3 IU/mL [14].

### 4.3. Combination of hs-Troponin T and IMA in diagnosis of NSTE-ACS

Markers are different regarding release time and back-to-normal time. Therefore, it's necessary to combine biological markers in diagnosis of ACS. [15].

In our study, when combining hs-TroponinT >0.014ng/mL and IMA > 28.68 IU/mL, it results in a

sensitivity at 88.9% and a specificity at 100% , AUC = 0.97, p < 0.001, 95% CI=0.915 – 1.00. In a research by Ramazan Gũven and partners, the combination of Troponin and IMA indicated a sensitivity at 75% and a specificity at 82.9%; the indicators reached higher value when a biological marker was used [14]. In a research by Mutrie,the combination of IMA and Troponin indicated a sensitivity at 85% (65-96) [9].

## 5. CONCLUSION

Concentration of biological markers hs-Troponin T and IMA in the patients group with NSTE-ACS increases highly compared with the indicators in the controls group. The best cross-sectional point which is used for diagnosing NSTE-ACS is 28.68 IU/mL for IMA, is >0.014ng/mL for hs-TnT. The sensitivity reaches 88.9%, the specificity reaches100%, AUC = 0.97, p < 0.001, 95% CI= 0.915 – 1.00.

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