Unstable Angina Pectoris As A Trigger In Development Of Acute Coronary Accidents: Myth Or Reality?


Clinical, morphological and functional determinants of the course of acute forms of ischemic heart disease’s (IHD) are of considerable interest in contemporary cardiology. The latest especially applies to «intermediate» forms of destabilization of IHD, such as unstable angina (UA) and acute non-Q-wave forms of myocardial infarction (n-Q-w AMI). Increased interest of investigators to this pathology is due to the high risk of ACUTE MYOCARDIAL INFARCTION’s morbidity. In the Ukraine, particularly in able-bodied age patients, morbidity forms 116 out of 100000 of population[1]. Certain heterogeneity of the clinical and pathogenic links of destabilization, the lack of its common conception[2], which was expressed in different degree in patients with diagnosed unstable angina (UA), had in it’s turn influence on subsequent course of the disease to a certain extent. In many aspects this is due to the fact, that until today UA remains as a clinical symptom complex, which can be faintly corroborated by objective criteria, but it is sufficiently menacing in the development of acute coronary pathology. The problem is important also in view of the high expense treatment level of patient in an observation period of 5 years, which makes up to $49.581 with a half lesser expenses for analogous program in patients with stable angina[3].

The use of stress tests in contemporary urgent cardiology assumes ever-greater spread; particularity for the help they give in the objectification of diagnostics, the determination of coronary reserve and functional state of myocardium in patients with destabilization of IHD under conditions of tress tests use.

Methods:
Examined patients: 580 patients, admitted in cardio reanimation unit and infarction department, were diagnosed according to the World Health Organization criteria of acute myocardial infarction (AMI),[9] clinical evidence, data of ECG-examination and enzyme's level (aspartataminotransferasa, lactatedehydrogenasa, creatine phosphokinasa). UA was diagnosed in 385 patients within 2-3 days (males, mean age 50,7±1,3 years). Non-Q-w AMI was defined in 140 patients (males with a mean age of 57,6±2,6 years), in 55 patients the organic damage of myocardium was not confirmed and the case of functional pathology-neurocirculatory asthenia was diagnosed (NCA.) (Males mean age was 34,6±3,7 years). Patients with Q-w AMI and circulatory deficiency II, III stages were not included.

Taking into consideration the heterogeneous rank of patients with UA, they were distributed into the following subgroups: the subgroup of subsequent prolonged stable course of angina at the stage of an annual follow-up (group S-207 (53,8%) of patients), the subgroup with periodical episodes of destabilization at the early post hospital stage, which ultimately concluded with relative stabilization (group DS - 35 (9,1%) of patients), the subgroup with relative stabilization at the early post hospital stage which later on nevertheless tend to destabilization (group SD- 108 (28,0%) of patients), the subgroup with constantly relapsing episodes of destabilization at the post hospital stage (group D- 35 (9,1%) of patients).

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Distribution of patients with UA was performed according to angina at onset (AO) and progressing angina (AP) (group AO- 88 (22.8%) of patients) and angina, progressed against a background of previous anamnesis of ischemia (group AP- 297 (77.3%) of patients). The group of patients with UA, in which later on during hospital care an AMI developed irrespective on adequate therapy, was analyzed separately (group UA AMI- 33 (8.6%) of patients).

**Investigation protocol**: Survey of all patients was performed in 3-5 days under the conditions of angina attack absence, beginning with TEES as the safest and most informative stress test. BE as an exercise tolerance test was used after the definition of loading tolerance and coronary reserve's reduction. Stress-EchoCG test was performed during TEES and BE.

**Transesophageal electrocardiostimulation**: performance of TEES corresponded to the standard protocol, began with generally accepted 12-lead and 35-lead from chest's anterior surface ECG registration. After transnasal insertion of pacing catheter electrode in esophagus, it was fixed at the level of the most complete contact with the left atrium, under the control of transesophageal ECG, approximately at 35-45 cm distance of electrode's length. The stimulation was started with 160 beats/min and was increased by 20 beats/min, maximal frequency established was 160 beats/min, and the duration of each testing frequency was 2 minutes. The test was stopped and evaluated as positive by the arising of angina attack and/or by horizontal ST-segment depression (1-2 mm from the baseline). The analysis of ECG-changes was performed in standard 12-lead and 35-lead from chest’s anterior surface electrocardiogram (ECTG) registration.

The transesophageal electrocardiostimulators used were SP-3 (TEMED, Poland) and HYV-1s (Ukraine), in the capacity of remote polygraph RFT Bioset 3000 (Germany).

**Bicycle ergometry**: BE was performed using Mingograf-81 (Siemens-Elema Germany-Sweden) and BE-01 (Ukraine), the initial voltage of BE depended on the results of TEES and after the stopping of TEES at the frequency of 100-120 beats/min read 10 W, at the frequency of 140 beats/min and more - 25 W. A subsequent increase of voltage was discrete; stepping interval was 10 W in the first case and 25 W - in the second. Criteria of BE's stopping was analogous to TEES. Analysis of ECG-changes was performed in standard 12 leads. In cases of signs of ischemia appearance in TEES and BE, a qualitative dynamics analyze was made the number of leads with signs of ischemia (NST), a summary of ST-segment depression (EST) and mean of ST-segment depression (AST).

**Echocardiography analysis**: Stress-EchoCG was performed using SSH-40A (Toshiba, Japan), SAL-38-AS (Toshiba, Japan), LS-5000 (Picker, USA), NINTERSPEC (USA) under M and B-regime, in 2- and 4-chamber imaging in parasternal and apical views with registration of end-diastolic and end-systolic volumes (EDV and ESV), EF and estimated with the use of semiautomatic graph analyzer Cardio-200 (Kontron, Germany) of segmental contractility on 5, 12, 48 segments.

**Holter monitoring**: Holter monitoring (HM) was performed using such recorders: Marquette Electronics Inc.) (USA) according to generally accepted method in the modified V2- and V5-leads during a period of 24 hours.

**Analyzed statistics**: The investigation results were analyzed using the Student’s t-criterion as a valid mathematical model in “Statistics for Windows” program, the 5.0 version (StatSoft, USA).

**Results**: Clinical analysis: In the group, as a whole, studied patients were characterized by duration of a previous IHD's history of 5.6±0.2 years. Most often gripping (46.6%) and crush (48.6%) pain were registered, less often - smart (23.1%), dull (16.5%) and lancinating (18.9%) pain, which occurred behind the sternum wall (52.4%) and radiated into the left arm (38.6%), arms (8.6%), the scapula (29.0%) and the neck (7.6%). Pain was registered after the patient has walked for approximately 50 m in 17.6% of cases, 100 m - in 12.7% and > 100 m - in 41.4% of cases. Very slow walking provoked pain in 7.6% of cases, slow walking - in 47.2%, fast walking - in 16.5%. Other causes: upstairs walking (53.1%), emotion (56.9%), at rest (43.4%), at night (34.8%), according to weather (35.8%). Nitroglycerin was used by 78.6% of patients, which built up an average of 9.7±1.5 tablets per 24 hours. Duration of the pain syndrome was 14.9±4.5 min, the frequency of episodes was 5.8±0.8 per 24
hours. The breathlessness was registered in 26.5% of cases during a load, in 3.8% at rest, in 12.1% during emotion. Post infarction cardiococclerosis was registered in 44.1% of cases, arterial hypertension - in 34.3%, diabetes mellitus - in 5.3%, 54.4% of patients smoked actively, in 2.8% of patients an alcohol usage was noted, overweight was in 35.1% of patients, negative inheritance (one of the parents suffered from AMI and hypertension) - in 32.1%.

According to ECG data, greater part of patients (52.7%) was already admitted with negative T-waves, ST-segment elevation (3.5%), bundle-branch block (6.6%) and extrasystoles (27.9%).

**Stress tests:** Results of TEES performed in 385 patients with UA, 112 patients with n-Q-w AMI and 22 patients with NCA are listed in Table I. The test was positive in 319 (82.8%) patients with UA, in 96 (85.7%) patients with n-Q-w AMI and negative in NCA patients. Already at first investigations it was noted, that the patients of AO-subgroup, compared to patients of AP-subgroup, differed by reliably higher frequency of stimulation's stopping (p<0.001) as listed in Table I. The mentioned trend remained during a period of one year of observation, until the second investigation took place. The patients with UA, in whom later on an AMI developed reliably, differed already from the entire UA group according to results of the first investigation, which remained henceforward. The subgroup DS differed from all analyzed subgroups of destabilization and destabilization course of illness on remote posthospital stage at the first investigation according to frequency data of TEES' stopping. That subgroup was approximated to patients with UA and AMI later on developed. The subgroup of patients with n-Q-w AMI was notable for the greatest reduction of coronary circulation during TEES, which was analogous to the patients with UA and in spite of therapy later on developed AMI (Table I).

According to results of BE, already from the outset of the procedure, the subgroup S was characterized by having greater load level of tolerance when compared with the subgroup D (p<0.001), SD (p<0.05), DS (p<0.001). Against a background of a long-term therapy, a reliable increase of BE's voltage was defined in the subgroup S (p<0.001), DS (p<0.05), decrease - in the subgroup D (p<0.001) and SD (p<0.01) as displayed in Table I. Already at the beginning, a load tolerance was higher in the AO-subgroup as compared with the AP-subgroup (p<0.001), and a considerable decrease of carried out work in the subgroup with developed AMI as compared with AP (p<0.001) increased (p<0.05) later on in contrast to AP.

**Analysis of quantitative indices of myocardial ischemia:** Dynamics of ischemia against a background of stress tests indicates predominance of quantitative indices of ischemia reaction (EST, NST, AST) against a background of stress tests' performance (TEES and BE) in UA patients and in spite of therapy developed AMI (p<0.001) as listed in Table II. Considerable divergences were not defined during analysis of EST of patients with UA and non-Q-w AMI in 12-ECG leads (p<0.2).

During a determination of ischemia in dynamics by using TEES, no distinction in AO- and AP-subgroups was found, as listed in Table II. During a long-term follow-up of patients with UA considerable decrease of EST (p<0.01) and AST (p<0.05) may be found in the subgroup S, a decrease of EST in the subgroup D (p<0.02), and an absence of dynamics in SD and DS-subgroups (p<0.5). It should be noted that performing BE's allowed to define a greater inadequacy of coronary circulation by simulation of ischemia concerning EST-index, which predominated in that subgroup over an index of patients from AP (p<0.2). Subsequently, an adequate decrease of those indices was put into effect during a long-term follow-up (p<0.05).

**Echocardiography:** Analysis of general ejection fraction (EF) as an integral index of contractility in different UA patients subgroups indicates, that in the presence of the same trend to decrease at a height of TEES and BE load in AO patients - subgroup, the values of EF reached their maximum at rest and modeling of ischemia, especially during TEES performance (p<0.001). The greatest decrease of EF at a height of stress tests was noted in developed AMI patients in spite of therapy, the index predominated even over the dynamics of EF in with non-Q-w AMI patients (p<0.001) as listed in Table III.

**Holter monitoring:** According to Holter monitoring’s readings, duration of painless ischemia episodes did not significantly change in UA, which appeared in forms of AO and AP (p>0.5), significantly reduced when AMI developed against a background of UA in hospital (p<0.001). On the other hand during AMI, compared to AO and AP the duration of
painless ischemia episodes increased (p<0.001). The analyze of different readings of duration’s courses of illness showed, that in groups with UA in the form of D and DS, with great inclination to destabilization, were characterized compared to S and SD forms by considerable increase in painless ischemia episode duration (p<0.01). The probability of painless ischemia development in those groups was similar; substantially increase of patients in D and DS groups (p<0.02).

In the Ukraine, epidemiological analyses carried out in the past few years shows increase prevalence of UA throughout the country from 42.0 up to 46.8 and morbidity – from 22.7 to 32.3 upon 100.000 of the population. The problem of “intermediate” forms of IHD at the stage of acute coronary accident formation, takes on special significance in view of it’s ability to influence the active etiopatogenetic correction of the state of such a patient, which is practically impossible in the case of a patient suffering from AMI, where in terms of already formed necrosis areas the main interest is the limitation of it’s expansion. Task of modern cardiology may as well be the formation of two directions: prevention of AMI development during a population examination, active diagnostics of the “intermediate” form of destabilization with wide use of stress tests, including the cases of UA and non Q myocardial infarction, reexamination of means of treatment for IHD by introducing the so called “aggressive” technology, which includes surgical myocardial revascularization methods.

Adding to the features of the progressive process of destabilization, depending to the stress tests results, the dynamical indexes of echocardiography and Holter monitoring researches it is wise to add the following results. While carrying out transesophageal electrocardiostimulation it was marked that patients with AO, AP and UA with AMI, developed subsequently, already in the acute period distinguished by the different frequency of stimulation stopping. This included the DS groups, which approached patient with UA and AMI that developed latter on. When carrying out transesophageal electrocardiostimulation on patients suffering from non-Q AMI, they differed by a greater coronary blood flow reduction. Bicycleergometry results for the S group, already at the beginning of the stress test, was characterized as an increased level of tolerance load compared to the group D, SD and DS. Tolerance load at the beginning of the stress test was also high in patients with AO compared to patients with AP, on the other hand essential decrease in the tolerance load was noticed in groups with AMI, which occurred, compared to AP latter on (unlike AP the group) increased. The dynamic of the general E.F, as an integral contractility index, testify in favor of equal tendency of decrease when carrying out both transesophageal electrocardiostimulation and bicycleergometry, in the presence of a more positive changes in the AO group. The greatest E.F decrease on the height of stress tests was noticed in with non-Q AMI patients. According to the Holter monitoring data, the duration of painful ischemia fundamentally had no change either in the AO non-in the AP groups, on the other hand a considerable decrease was noticed when AMI occurred on a background of UA during hospitalization. On the contrary, in AMI patients compared to the AO and AP groups painless ischemia episodes increased. The analyses of different course of illness showed, the UA groups in the forms of D and DS, which means a great inclination to destabilization, was characterized compared to the S and SD forms by great predominance of painful myocardial ischemia episodes. The probability of painless ischemia formation corresponded in the latest groups and substantially increased in the D and DS groups. Thus, in patients with UA and AMI, essential features in coronary reserve restriction is possessed, which determinates the course of illness as a whole and the subsequent destabilization process during a long term observation, which in it’s turn allows the objectification of clinical and functional UA classification.
Table 1: Results of TEES' and BE's stopping in patients with acute coronary accidents in 1st and 2nd studies

<table>
<thead>
<tr>
<th>Groups</th>
<th>Results</th>
<th>STRESS-TESTS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TEES (beats/min)</td>
<td>BE (W)</td>
</tr>
<tr>
<td>NCD</td>
<td>158.0±0.5</td>
<td>153.4±4.3</td>
</tr>
<tr>
<td>UA</td>
<td>145.5±1.9</td>
<td>80.6±2.8</td>
</tr>
<tr>
<td></td>
<td>138.9±1.8</td>
<td>&lt;0.02</td>
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<tr>
<td></td>
<td>87.9±3.0</td>
<td>&gt;0.05</td>
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<tr>
<td>n-Q-w AMI</td>
<td>133.3±3.0</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Groups</th>
<th>Results</th>
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<tbody>
<tr>
<td></td>
<td>STRESS-TESTS</td>
</tr>
<tr>
<td></td>
<td>TEES (beats/min)</td>
</tr>
<tr>
<td></td>
<td>NCD</td>
</tr>
<tr>
<td></td>
<td>154.0±2.2</td>
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<tr>
<td></td>
<td>&gt;0.1</td>
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<tr>
<td></td>
<td>&lt;0.05</td>
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<tr>
<td></td>
<td>141.4±2.7</td>
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<td></td>
<td>&gt;0.1</td>
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<tr>
<td></td>
<td>20.0±2.4</td>
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<tr>
<td></td>
<td>133.3±3.9</td>
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<tr>
<td></td>
<td>&lt;0.02</td>
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<tr>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>147.0±2.6</td>
</tr>
<tr>
<td></td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>148.3±3.3</td>
</tr>
<tr>
<td></td>
<td>&gt;0.05</td>
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<tr>
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<td>120.0±3.4</td>
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<tr>
<td></td>
<td>&lt;0.001</td>
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<tr>
<td></td>
<td>105.4±4.2</td>
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<tr>
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<td>117.0±4.3</td>
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<tr>
<td></td>
<td>87.7±3.3</td>
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<tr>
<td></td>
<td>66.2±2.9</td>
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<td>87.7±3.3</td>
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<tr>
<td></td>
<td>66.2±2.9</td>
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</tbody>
</table>

Table 2: Dynamics of quantitative indices of ischemia (EST, NST, AST) during performance of TEES and BE in patients with acute coronary accidents at the 1st and 2nd studies

<table>
<thead>
<tr>
<th>Groups</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Stress-Tests</td>
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<tr>
<td></td>
<td>TEES (35 leads of ECTG)</td>
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<tr>
<td></td>
<td>EST</td>
</tr>
<tr>
<td>NCD</td>
<td>125.9±1.5</td>
</tr>
<tr>
<td></td>
<td>23.3±1.6</td>
</tr>
<tr>
<td></td>
<td>24.1±2.4</td>
</tr>
<tr>
<td></td>
<td>21.8±2.3</td>
</tr>
<tr>
<td></td>
<td>26.2±2.2</td>
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<td></td>
<td>23.2±2.0</td>
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<tr>
<td></td>
<td>39.0±3.9</td>
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<td></td>
<td>23.0±3.4</td>
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<td>26.2±2.5</td>
</tr>
<tr>
<td></td>
<td>16.7±2.1</td>
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<tr>
<td></td>
<td>22.5±2.8</td>
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<tr>
<td></td>
<td>32.7±3.0</td>
</tr>
<tr>
<td></td>
<td>27.9±2.3</td>
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<td></td>
<td>27.1±2.4</td>
</tr>
<tr>
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<td>27.4±2.9</td>
</tr>
<tr>
<td></td>
<td>26.9±2.9</td>
</tr>
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</table>

Table 3: Ejection fraction as an integral index of contractility during performance of TEES and BE in patients with acute coronary accident at the 1st and 2nd studies

<table>
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<tr>
<th>Groups</th>
<th>Results</th>
<th>Ejection Fraction (%)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>At rest</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TEES</td>
</tr>
<tr>
<td>UA</td>
<td>1</td>
<td>51,1±1,3</td>
</tr>
<tr>
<td>UA</td>
<td>2</td>
<td>56,4±0,7</td>
</tr>
<tr>
<td>AO</td>
<td>1</td>
<td>58,2±1,4</td>
</tr>
<tr>
<td>AO</td>
<td>2</td>
<td>61,7±1,3</td>
</tr>
<tr>
<td>PA</td>
<td>1</td>
<td>47,8±1,1</td>
</tr>
<tr>
<td>PA</td>
<td>2</td>
<td>54,3±0,7</td>
</tr>
<tr>
<td>UA AMI</td>
<td>1</td>
<td>49,0±2,5</td>
</tr>
<tr>
<td>UA AMI</td>
<td>2</td>
<td>45,5±2,6</td>
</tr>
<tr>
<td>S</td>
<td>1</td>
<td>52,5±0,7</td>
</tr>
<tr>
<td>S</td>
<td>2</td>
<td>58,7±0,8</td>
</tr>
<tr>
<td>D</td>
<td>1</td>
<td>49,0±1,7</td>
</tr>
<tr>
<td>D</td>
<td>2</td>
<td>52,4±1,9</td>
</tr>
<tr>
<td>SD</td>
<td>1</td>
<td>48,4±1,2</td>
</tr>
<tr>
<td>SD</td>
<td>2</td>
<td>51,8±1,2</td>
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<tr>
<td>DS</td>
<td>1</td>
<td>47,0±1,6</td>
</tr>
<tr>
<td>DS</td>
<td>2</td>
<td>53,9±1,9</td>
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<tr>
<td>n-Q-w</td>
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<td>47,7±1,8</td>
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</table>

Table 4: Dynamics of indices of painful and painless myocardial ischemia in patients with acute coronary accidents according to data of Holter monitoring.

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>Myocardial ischemia (quantity of episodes and duration)</th>
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<tr>
<td></td>
<td>Painful AMI</td>
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<tr>
<td></td>
<td>Quantity (24 hours)</td>
</tr>
<tr>
<td>AO</td>
<td>3,02±0,61</td>
</tr>
<tr>
<td>PA</td>
<td>2,50±0,52</td>
</tr>
<tr>
<td>UA AMI</td>
<td>2,00±0,39</td>
</tr>
<tr>
<td>S</td>
<td>2,38±0,51</td>
</tr>
<tr>
<td>D</td>
<td>4,33±0,72</td>
</tr>
<tr>
<td>SD</td>
<td>1,25±0,38</td>
</tr>
<tr>
<td>DS</td>
<td>2,60±0,58</td>
</tr>
</tbody>
</table>

|        | Painless ischemia                                         |
|        | Quantity (24 hours) | Duration (min) |
|        | 4,80±0,87 | 66,0±3,94 |
|        | 4,19±0,56 | 41,0±3,1 |
|        | 11,0±2,14 | 298,0±59,6 |
|        | 3,00±0,43 | 71,8±15,6 |
|        | 6,00±1,41 | 147,6±25,8 |
|        | 4,00±0,89 | 38,7±8,9 |
|        | 6,17±1,42 | 200,0±38,6 |

References: