# CARDIOVASCULAR EVENT ASSESSMENT IN PATIENTS WITH NONOBSTRUCTIVE CORONARY ARTERY DISEASE UNDERGOING DUAL ANTIPLATELET TREATMENT

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Nonobstructive coronary artery disease (NObCAD) is atherosclerotic plaque that would not be expected to obstruct blood flow or result in anginal symptoms. Although such lesions are relatively common, occurring in 10% to 25% of patients undergoing coronary angiography [1,2].

Nonobstructive coronary artery disease has historically been considered benign and clinically insignificant, however it was associated with a 28 to 44 percent increased risk of a major cardiac event such as a heart attack or death, in a new study presented at the American Heart Association's Quality of Care and Outcomes Research 2014 Scientific Sessions.

Nonobstructive CAD in acute coronary syndromes (ACS) has attracted much attention because of the relatively high incidence of adverse cardiovascular events if not appropriately diagnosed and treated [3,4].

Dual antiplatelet therapy (DAPT) consisting of aspirin and a $P2Y_{12}$ receptor antagonist is a fundamental component of acute coronary syndrome (ACS) management. However, DAPT of NObCAD remains a major topic of discussion and is of particular importance.

The aim of our study was to learn the differences in baseline presentation between NObCAD and obstructive coronary artery disease (ObCAD) subjects, to compare the likelihood of several clinical outcomes and the rate of primary endpoints between this groups.

**Material and methods.** Out study included 165 patients: 115 patients with NObCAD ACS, 50 – with ObCAD ACS. Inclusion criteria: age >18 year; Presence of any atherosclerotic stenosis greater than 20% but less than 50% in the left main coronary artery, and greater than 20% but less than 70% in any other major epicardial coronary artery. Exclusion criteria: Age<18 year; Antiplatelet treatment in past; Coronary revascularization in past; Absolute contraindications for antiplatelet treatment; After providing written informed consent, patients with NObCAD ACS were randomly assign in an 1:1 ratio in 2 group: Group A (n=55) received dual antiplatelet treatment with aspirin 100-160 mg once daily and clopidogrel 75 mg once daily for three months. Group B (n=60) received only aspirin 100-160 mg once daily for three months. 50 patients with ObCAD ACS entered in group C – controlled group, patients were treated according appropriate treatment guidelines.

Clinical, demographic and treatment data were investigated. Demographic variables included age and gender. Comorbidities included smoking, diabetes, hyperlipidemia, hypertension, obesity, and prior history of heart disease (angina, heart failure, myocardial infarction, coronary artery bypass grafting, and percutaneous coronary intervention), renal and liver disease. ECG changes and initial laboratory data were recorded. Laboratory analyses: CBC, urine test, serum lipid profile, fasting blood glucose and $HbA_1C$, creatinine and eGFR, liver enzymes were provided. All patients underwent coronary angiography. Data describing patient management included use of β-blockers, aspirin, ACE inhibitors or angiotensin receptor blockers, lipid-lowering agents.

We categorized each patient by CAD extent. To accomplish this, we categorized each patient by CAD severity in a single, double, or triple-vessel distribution: 1-, 2-, and 3-vessel nonobstructive CAD; and 1-, 2-, and 3-vessel obstructive CAD. Rates of MI, all-cause mortality, and the combined outcome during the full study period were calculated and compared by CAD extent.

Follow-up evaluations were performed at one, two and three months and 1 year. At these visits was assessed primary endpoints - MACE (Major adverse cardiac events): 1year hospitalization for Myocardial infarction or other cardiovascular causes after index angiography, cardiovascular death, revascularization, survival. We studied type and frequency of bleeding during treatment and follow up period. Severe bleeding was defined as fatal or intracranial hemorrhage, or bleeding cause hemodynamic compromise; moderate bleeding was defined as bleeding requiring transfusion not characterized as severe and mild asymptomatic bleeding.

All the analysis was calculated using the Statistical Package for Social Sciences (SPSS, version 22) software. A Student's t-test was used to compare the difference in the continuous variables between groups. A value of p<0.05 was considered to be statistically significant.

**Results and discussion.** Baseline characteristics of patients are displayed in Table 1.

NObCAD patients (group A and B), as compared to ObCAD subjects (group C) had less cardiovascular risk factors at baseline (including diabetes mellitus, hypertension, dyslipidemia, cigarette smoking).

As shows the analysis of data, after one year from an initiation of treatment, frequency of CVD in group A is 29.1%, in group B – 35% and in group C - 64%, and events frequency increased with CAD extension. Hospitalization for MI was significantly higher in group C: 16.4% in group A, 18.3% - in group B and 24% in group C. Revascularization rate was 10.9% in group A, 20% – in group B and 38% in group C. Cardiovascular death rate was significantly higher in group C. There were no significant difference between all 3 groups according bleeding frequency. All cases of bleeding was mild and asymptomatic.

Despite the prevalence of nonobstructive CAD identified by coronary angiography, little is known about its risk of adverse outcomes. More data on nonobstructive CAD patients and their longitudinal outcomes are essential for understanding their risks for adverse cardiac outcomes and potential therapeutic implications [5,6]. Differences in prognosis and baseline clinical presentation have been documented among patient with acute coronary syndrome and coronary artery disease with obstructive (ObCAD) or nonobstructive arteries (NObCAD), but the rates of events largely varied across single studies.

An unstable coronary plaque is the primary cause of the coronary syndrome. Thrombus formation occurs under conditions of high shear stress and is principally driven by platelet aggregation in acute coronary syndrome. Platelet aggregation during intracoronary thrombus represents the dramatic effects that antiplatelet therapies have on clinical outcomes [7].

Despite evidence of myocardial ischemia that is demonstrated after presenting with cardiac symptoms, an angiogram that shows nonobstructive CAD will ultimately result in little medical treatment. This approach is of concern to clinicians because many of these patients will continue to have symptoms that will lead to rehospitalization, repeated diagnostic testing [8].

*Table 1. Clinical characteristics of patients*

| Variables | Group A (n=55) | Group B (n=60) | Group C (n=50) |
|---|---|---|---|
| Age, mean | 58.2±8.9 | 61.3±9.02 | 63.2±7.4 |
| Female % | 38 (69.1%) | 35 (58.3%) | 21(42%) |
| Smoker % | 19(34.5%) | 15 (25%) | 21(42%) |
| Hypertension % | 35 (63.6%) | 35 (58.3%) | 41 (82%) |
| Diabetes Mellitus % | 9 (16.4%) | 11 (18.3%) | 17(34%) |
| Heart Failure | 11(20%) | 15(25%) | 11(22%) |
| History of atrial fibrillation % | 5(9.1%) | 4(6.7%) | 5(10%) |
| History of stroke % | 3(5.5%) | 2(3.3%) | 0 |
| COPD % | 0 | 2(3.3%) | 2(4%) |
| Dyslipidemia % | 29(52.7%) | 33(55%) | 37 (74%) |
| Chronic renal disease % | 4(7.3%) | 3 (5%) | 3(6%) |
| Liver disease % | 0 | 0 | 2(4%) |
| CAD extend | 1 vessel – 26(47.3%)<br>2 vessel - 11(20%)<br>3 vessel – 18 (32.7%) | 1 vessel - 36 (60%)<br>2 vessel-13(21.6%)<br>3 vessel–11 (18.3%) | 1 vessel - 9 (18%)<br>2 vessel - 21(42%)<br>3 vessel – 20 (40%) |

*Table 2. Clinical outcomes, adverse events and primary end points assessment*

| End points | Group A (n=55) | | | Group B (n=60) | | | Group C (n=50) | | |
|---|---|---|---|---|---|---|---|---|---|
| CAD extend | 1 vessel | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 |
| CVD events | 2 (3.6%) | 5 (9.1%) | 9* (16.4%) | 4* (6.7%) | 7* (11.7%) | 10* (16.7%) | 3 (6%) | 11* (22%) | 18* (36%) |
| Hospitalization for MI | 2 (3.6%) | 2 (3.6%) | 5 (9.1%) | 2 (3.3%) | 4 (6.6%) | 5 (8.3%) | 2 (4%) | 3 (6%) | 7* (14%) |
| Revascularization | 0 | 1 (1.8%) | 5* (9.1%) | 1 (1.7%) | 4* (6.6%) | 7* (11.7%) | 2* (4%) | 12* (24%) | 15* (30%) |
| Cardiovascular death | 0 | 0 | 0 | 0 | 1 (1.7%) | 2 (3.3%) | 1 (2%) | 3 (6%) | 2 (4%) |
| Bleeding | 2(3.6%) | | 1(1.8%) | | 1(1.7%) | 1(17%) | 1(2%) | | 1(2%) |

*\* - P<0.05*

The effect of dual antiplatelet therapy following an acute coronary syndrome was confirmed by the trials. Combined aspirin and clopidogrel therapy decreased the 1-year incidence of cardiovascular events by up to 20% compared with aspirin alone. Although a large volume of evidence supporting the use of dual antiplatelet therapy in patients with the acute coronary syndrome, there remains major uncertainty regarding the treatment of patients with NObCAD.

After data assessment we can tell, that the combination of clopidogrel and aspirin was not significantly more effective than aspirin alone in reducing the rate of myocardial infarction, but there was significant difference between groups regarding the CVD event rates, revascularization frequency and bleeding rate.

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## SUMMARY

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**Keywords:** nonobstructive coronary artery disease, acute coronary syndrome, dual antiplatelet therapy, cardiovascular events.

## РЕЗЮМЕ

### КАРДИО-ВАСКУЛЯРНЫЕ СОБЫТИЯ У ПАЦИЕНТОВ С НЕОБСТРУКТИВНЫМ КОРОНАРНЫМ ЗАБОЛЕВАНИЕМ НА ФОНЕ ДВОЙНОГО АНТИТРОМБОЦИТАРНОГО ЛЕЧЕНИЯ

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Цель исследования - определение различия в клинических данных больных необструктивным и обструктивным острым коронарным синдромом для сравнения частоты развития различных кардио-васкулярных событий и основных конечных точек.

Исследовано 165 пациентов: 115 - с необструктивным, 50 – с обструктивным заболеванием коронарных артерий. Критерии включения в исследование: возраст >18лет; наличие любого атеросклеротического стеноза, больше, чем 20%, но меньше чем 50% в левой главной коронарной артерии, и больше, чем 20%, но меньше чем 70% в любой другой главной эпикардиальной коронарной артерии. Пациенты распределены на три группы: группа А - 55 пациентов с необструктивным острым коронарным синдромом, которые получали двойное антитромбоцитарное лечение – аспирин 100-160 мг в день и клопидогрел 75 мг в день, группа В - 60 пациентов с необструктивным острым коронарным синдромом, которые получали аспирин 100-160 мг в день, группа С - 50 пациентов с обструктивным острым коронарным синдромом, которым проводилось стандартное лечение. Исследованы клинические и демографические данные (возраст и пол). Сопутствующие заболевания включали диабет, гиперлипидемию, гипертонию, ожирение и болезни сердца (стенокардия, сердечная недостаточность, инфаркт миокарда, проведенное коронарное шунтирование и чрескожное коронарное вмешательство), почечное заболевание и заболевание печени. Зарегистрированы изменения кардиограммы и начальные лабораторные данные. Пациенты категорированы по количеству поражённых коронарных артерий. Последующие обследования выполнены спустя один, два и три месяца и 1 год. Оценены основные конечные точки - серьезные неблагоприятные кардиальные события: госпитализация спустя год по причине инфаркта миокарда или других сердечно-сосудистых заболеваний, частота сердечно-сосудистой смерти, стентирование кровеносных сосудов, выживаемость. Изучены типы и частота кровотечения в период лечения и наблюдения. Оценка данных проведенного исследования позволяет сделать вывод, что комбинация клопидогрела и аспирина оказалась значительно более эффективной, чем аспирин в снижении частоты развития инфаркта миокарда, однако отмечалась значительная разница между группами относительно частоты кардио-васкулярных событий, кровеносной реваскуляризации и кровотечений.

რეზიუმე

კარდიოვასკულური მოვლენების შეფასება არაობ-
სტრუქციული კორონარული დაავადებით პაციენ-
ტებში, რომლებსაც უტარდებოდა დუალური ანტი-
აგრეგაციული მკურნალობა

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კვლევის მიზანს წარმოადგენდა კლინიკური მონა-
ცემების და პირველადი საბოლოო წერტილების შეს-
წავლა პაციენტებში არაობსტრუქციული კორონარუ-
ლი დაავადებით.

კვლევაში მონაწილეობდა 165 პაციენტი: 115 – არაო-
ბსტრუქციული და 50 – ობსტრუქციული კორონარ-
ული დაავადებით. პაციენტები დაიყო სამ ჯგუფად:
A ჯგუფში შევიდა 55 პაციენტი არაობსტრუქციული
კორონარული დაავადებით, რომელთაც უტარდებოდა
დუალური ანტიაგრეგაციული მკურნალობა: ასპირინი
100-160 მგ 1-ჯერ დღეში და 75 მგ კლოპიდოგრელი

1-ჯერ დღეში. B ჯგუფში შევიდა 60 პაციენტი არაო-
ბსტრუქციული კორონარული დაავადებით, რომლე-
ბიც დებულობდნენ მხოლოდ 100-160 მგ ასპირინს
1-ჯერ დღეში, C ჯგუფში მოხვდა 50 პაციენტი ობ-
სტრუქციული კორონარული დაავადებით, რომელთა-
ც უტარდებოდა გაიდლაინების მოწოდებული
მკურნალობა. ყველა პაციენტს ჩაუტარდა კორონარ-
ული ანგიოგრაფია. პაციენტები განაწილებულნი იყო
დაზიანებული კორონარების რაოდენობის მიხედვით.
შესწავლილია დემოგრაფიული მონაცემები, თანმხ-
ლები დაავადებები და ლაბორატორიული მონაცე-
მები: ჰემატოლოგია, ლიპიდები, უზმოდ გლუკოზა და
HbA1C, eGFR და კრეატინინი, ღვიძლის ფუნქციები.
შესწავლილია ძირითადი კარდიოვასკულური მოვ-
ლენების განვითარების სიხშირე: მიოკარდიუმის
ინფარქტი, რევასკულარიზაცია, კარდიოვასკულური
სიკვდილობა, ასევე სისხლდენის განვითარების ხა-
სიათი და სიხშირე. კვლევის შედეგებმა აჩვენა, რომ
დუალურმა ანტიაგრეგაციულმა მკურნალობამ არ
გამოავლინა სარწმუნო განსხვავება ასპირინთან შე-
დარებით მიოკარდიუმის ინფარქტის განვითარების
თვალსაზრისით, მაგრამ სარწმუნოდ შემცირდა კარ-
დიოვასკულური მოვლენების და სისხლდენის სიხ-
შირე.

# THE LEFT VENTRICULAR SYSTOLIC FUNCTION AMONG PATIENTS WITH STEMI AFTER DIFFERENT TYPES OF TREATMENT STRATEGIES

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Cardiovascular diseases (CVD) are remaining at the leading positions in the structure of morbidity and mortality in the world. Despite significant advances in modern cardiology in improving the treatment of patients with ischemic heart disease (IHD), its clinical form – acute myocardial infarction (AMI) is a potentially fatal event and cause of death among adults [1].

This pathology is classified by the World Health Organization as one of the most important non-communicable diseases. By definition, the acute myocardial infarction with stable ST segment elevation (STEMI) and non-ST segment elevation myocardial infarction (NSTEMI) differ only in patterns of acute ischemia and myocardial necrosis on ECG. In the future, it determines the treatment tactics, but does not affect the AMI diagnostic protocol [2].

The main method of STEMI treatment is the restoration of blood flow patency in the occluded infarct-dependent artery. This can be achieved by pharmacological method. There is used thrombolytic therapy or mechanically which involve primary percutaneous coronary intervention (PPCI), or a combination of these methods of pharmaco-invasive reperfusion strategy. The use of a particular method of reperfusion is determined by the time elapsed from the beginning of manifestations of AMI and the clinical situation. Primary percutaneous coronary intervention, in accordance with the recommendations, is the preferred treatment strategy for the first 120 minutes after the onset of clinical AMI manifestations [3].

Reperfusion is not always possible in real clinical practice. This is primarily due to the inevitable technical difficulties, and secondly, the late seek of patients for medical care. According to the registers, the percentage of reperfusion therapy ranges from 77% to 95% [4,5].

Left ventricular function is an important predictor of the AMI outcome. In the studies the determination of left ventricular ejection fraction was shown to be a powerful predictor of total mortality during the observation period. Even with the successful reperfusion, the problem of the development of adverse postinfarction left ventricular remodeling does not lose its relevance. Risk assessment of systolic dysfunction among patients with STEMI after different types of treatment strategies is an important task of practical cardiology, which determined the purpose of this study [6,7].

The aim of the study - determine parameters the left ventricular systolic function among patients with STEMI after different types of treatment strategies.

**Material and methods.** The results of the study are based on the data obtained from a comprehensive examination of 447