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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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ASSESSMENT OF CORONARY COLLATERAL CIRCULATION PREDICTORS AMONG PATIENTS WITH ACUTE CORONARY SYNDROME IN POPULATION GEORGIA

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Abstract.

Background: Coronary collateral circulation (CCC) has been shown to have a prognostic role in acute myocardial infarction (MI). We aimed to identify factors associated with CCC development in patients with acute myocardial ischemia.

Methods: In the present analysis, 673 consecutive patients aged 27 – 94 years (64.7+11.48) with acute coronary syndrome (ACS), who underwent coronary angiography within the first 24 hours after symptom onset were included. Baseline data, including sex, age, cardiovascular risk factors, medication, antecedent angina, prior coronary revascularization, EF%, blood pressure levels were obtained from patient medical records. The study individuals were divided into two groups: patients with Rentrop grade 0 to 1 were classified as the poor collateral group (456 patients), and the patients with grade 2 to 3 - as the good collateral group (217 patients).

Results: Prevalence of good collaterals of 32% was found. Odds of good collateral circulation increases with higher eosinophil count - OR=17.36 (95% CI: 3.25-92.86); history of MI (OR=1.76; 95% CI:1.13-2.75); multivessel disease - OR=9.78 (95% CI: 5.65-16.96); culprit vessel stenosis - OR=3.91 (95% CI: 2.35-6.52); presence of angina pectoris > 5 years - OR=5.55 (95% CI:2.66-11.57) and decreases with high N/L- OR=0.37 (95% CI:0.31-0.45) and male gender - OR=0.44 (95% CI:0.29-0.67). High N/L is a predictor of poor collateral circulation, with 68.4 sensitivity and 72.8% specificity (cutoff: $2.73*10^9$).

Conclusions: Relative chance of good collateral circulation increases with the higher number of eosinophils, presence of angina pectoris with duration of more than 5 years, history of past myocardial infarction, culprit vessel stenosis, multivessel disease, and reduces if patient is male and has high N/L ratio.

Peripheral blood parameters may serve as an additional simple risk assessment tool in ACS patients.

Key words. Coronary collateral circulation, predictors, acute coronary syndrome.

Introduction.

Coronary collateral Circulation (CCC) is an alternative source of blood supply to myocardium Jeopardized by the ischemia in chronic as well as acute coronary artery disease (CAD). Coronary collaterals exist in humans, even without CAD (so called native collaterals). Coronary collateral (CC) development exhibits wide inter individual variation. The initial formation of bypass arterial connections refers to embryonic period and affected mainly by genetic factors [1]. It has been shown up to 39% prevalence of visible coronary collaterals in a population free of CAD [2]. However, in non-obstructed epicardial artery blood flow through collaterals is minimal or equal to zero. Coronary artery stenosis and occlusion are dominant triggers for coronary collateral growth/remodeling [3-7]. Arteriogenesis or remodeling of preformed collateral vessels is leading mechanism of collateral development in stable CAD [4]. Main source of collateral circulation in acute settings is recruitment of pre-formed collaterals. However, acute ischemia is associated also with angiogenesis – formation of new capillary circulation around peri-ischemic area [8]. Interestingly, coronary collateral development reflects severity of CAD, and on the other hand, remodeled collateral network as an alternative source of blood supply has a protective effect with regard to jeopardized myocardium during ischemia. Several studies have addressed prognostic role of CCC in acute myocardial infarction (MI) [4,6,7,9-11]. It has been detected CCC preventive role against cardiogenic shock and left ventricular (LV) aneurism formation in MI patients [4]. Several factors other than pressure gradient along the native collaterals connecting to the constricted vessel may potentiate remodeling and development of collateral network, including white blood cell (monocytes, neutrophils, lymphocyte) recruitment and release of inflammatory mediators, growth factors (vascular endothelial growth factor, fibroblast growth factor, transforming growth factor β- [TGF-β]), MMP-s, chemokines [4,12]. However, they cannot fully explain the mechanisms of CCC formation. Factors influencing coronary collateral formation may play a role in prediction of prognosis in acute and chronic CAD patients.

We aimed to identify factors associated with CCC development in patients with acute myocardial ischemia.

Materials and Methods.

In the present analysis, 673 consecutive patients aged 27 – 94 years (64.7+11.48) with acute coronary syndromes and documented CAD were included. All study individuals underwent coronary angiography within the first 24 hours after symptom onset in the Department of Cardiology, SamgoriMediClinic (Tbilisi, Georgia) between January 2014 and January 2017.

Baseline data, including sex, age, cardiovascular risk factors: hypertension, diabetes mellitus (DM), dyslipidemia, transient ischemic attack (TIA), smoking status, relevant medication, antecedent angina pectoris, coronary revascularization (coronary artery bypass surgery- CABG or percutaneous coronary intervention -PCI) history, ultrasound parameters of left ventricular systolic and diastolic function such as: ejection fraction, regional wall motion abnormalities, also systolic and diastolic blood pressure levels were obtained from patient medical records.

Diabetes melitus was defined as a history of DM, the use of antidiabetic drugs or fasting plasma glucose levels of ≥7 mmol/L. Hypertension (HT) was defined as a history of HT or use of antihypertensive drugs, or a blood pressure ≥140/90 mmHg. Smoking status was defined as current smoking. The study protocol was approved by the local ethics committee.

Patients with renal dysfunction (serum creatinine level >132.6 μmol/L), severe valvular disease, myocardial or pericardial disease, and inconclusive angiography data were excluded from the study. Patients who were diagnosed with hematological disease, cancer, systemic inflammatory or autoimmune diseases, thrombocytopenia and the use of anticoagulant agents were also excluded from the study.

Angiographic evaluation and CC grading.

Coronary angiography was performed through the radial artery for all patients using the Seldinger technique. Each angiogram was interpreted by two experienced cardiologists who were blinded to the patient's clinical features and other diagnostic tests results.

CC vessels were graded according to Rentrop grading system of 0 to 3:

0 = no filling of any collateral vessel.

1 = filling of the side branches of the artery to be perfused by collateral vessels without visualization of the epicardial segment.

2 = partial filling of the distal epicardial segment by collateral vessels.

3 = complete filling of the distal epicardial segment by collateral vessels.

The study population was divided into two groups according to the Rentrop collateral score: patients with grade 0 to 1 collateral development were classified as the poor collateral group(456 patient); and patients with Rentrop grade 2 to 3 collateral development (217 patient) were classified as the good collateral group.

Biochemical and hematological parameters.

All patients were evaluated by hematological indices, such as High sensitive troponin (Microplate Reader RT-2100C), serum creatinine was measured by a blood counter (Humalyzer 3000), Redcell, platelet count, white blood cell (WBC) count, differential counts (neutrophil, lymphocyte, eosinophil, and monocyte) and percentages were analyzed using the automatic blood counter(Human Count 30^{TS}). All measurements were performed 30 min after blood collection. The neutrophil/ lymphocyte ratio (N/L) was calculated as the absolute count of neutrophils divided by the absolute count of lymphocytes.

Statistical Analysis.

Continuous variables are expressed as mean ± SD, and categorical variables as frequencies and percentage. Continuous variables were compared with the use of the two-tailed independent t test and variance homogeneity by Levene's test, and categorical variables with the use of the Fisher's Exact Test. P value < 0.05 was considered as statistically significant. Multivariable logistic regression analysis was performed to identify the independent predictors of CCC. Odds ratios (OR) with corresponding 95% confidence intervals were calculated using a forward stepwise regression. Receiver operating characteristic (ROC) analysis was used to detect the cut off value of N/L and eosinophil count in the prediction of CCC. Correlation analysis between continuous variables was performed using the Pearson correlation and Spearman correlation analyses was used for categorical variables. All statistical analyses were performed using SPSS version 23.

Results.

The distribution of patients according to acute coronary syndrome and CCC is given in Figure 1.

According to CC circulation, the difference between the groups is not statistically significant.

The distribution of patient's initial characteristics according to the collateral circulation is shown in the Table 1.

The group labeled as having "good collateral circulation" shows statistically significant high prevalence of older age, female gender, history of angina pectoris of more than 5 years, TIA, previous MI, multivessel disease, EF=<35%, and diastolic dysfunction, such as pseudo normal, or restrictive filling. The group labeled as "bad collateral circulation" reveals significantly higher prevalence of alcohol consumption, vascular stenosis inducing ischemia, EF>45%, and normal diastolic function.

Statistically significant difference in extent of CCC between STEMI, Non-STEMI and UA patients was not detected.

The Table 2 shows mean values of blood components and biochemical features for groups with good and bad collateral circulation.

Mean values of serum creatinine and eosinophils were significantly elevated in a group with good collateral circulation compared with the other group. However, mean values of lymphocytes and N/L were low.

ROC curve analysis showed that the eosinophil count is prognostic for good collateral circulation with 59.0% sensitivity and 63.6% specificity (cutoff:>$0.18*10^9$) (Figure 2); Area Under the Curve - AUC=0.613+.024 (95% CI:0.565-0.660), p<0.0001 (poor diagnostic accuracy).

According to the ROC curve analysis, the high N/L is the predictor of poor collateral circulation (Figure 3), with 68.4 sensitivity and 72.8% specificity (cutoff:>$2.73*10^9$); AUC =0.752+0.019(95%CI:0.714-0.790), p<0.0001 (fair diagnostic accuracy).

Based on multivariate logistic regression analysis, eosinophil count, presence of angina pectoris > 5 years, history of MI, and culprit stenosis were associated with an increased likelihood of "good collaterals" and high N/L increases the likelihood "bad collaterals" in the study population (Table 3).

The Table 3 shows the results of logistic regression analyses for the independent predictors of good CCC in the study subjects.

Regression analysis showed that the odds of good collateral circulation increases with the increased number of eosinophils, presence of angina pectoris with duration of more than 5 years, history of past MI, culprit vessel stenosis, multivessel disease, and is reduced if patient's gender is male and N/L is high.

Discussion.

Anastomoses between large coronary vessels /coronary collaterals have limited role in myocardium blood supply in individuals free of CAD. It has been shown wide variation in CC development in healthy subjects. Further investigations elucidated the role of genetic polymorphism in" native collateral" development as well as CC remodeling capacity. In other words, more developed "native" collateral network has higher potential for enlargement/ remodeling. The main stimulus for CCC remodeling is epicardial coronary artery stenosis. Arteriogenesis/enlargement of collateral vessels takes 3-4 weeks [13].

Table 1. *Patients' characteristics according to the collateral circulation.*

Factors		**Poor CCC N=456**	**Good CCC N=217**	**P**
		n (%) or (Mean±SD)	**n (%) or (Mean±SD)**	
AGE	Years (Mean±SD)	63.30±11.77	67.55±10.26	<0.0001
SEX	Female, n(%)	146(32.02)	90(41.47)	0.0162
	Male, n(%)	310(67.98)	127(58.53)	0.0162
Cardiovascular risk factors	Alcohol, n(%)	177(38.82)	64(29.49)	0.0184
	Smoking, n(%)	255(55.92)	112(51.61)	0.2948
	Hypertension, n(%)	346(75.88)	173(79.72)	0.2676
	DM, n(%)	92(20.18)	54(24.88)	0.1664
	Dyslipidemia, n(%)	186(40.79)	100(46.08)	0.1947
Angina pectoris	Documented, n(%)	218(47.81)	142(65.44)	<0.0001
	History of 1 Month, n(%)	120(26.32)	56(25.81)	0.8884
	History of 1 Year, n(%)	55(12.06)	25(11.52)	0.8398
	From 1 to 5year, n(%)	26(5.70)	18(8.29)	0.2039
	More than 5 years, n(%)	17(3.73)	43(19.82)	<0.0001
History of cardiovascular disease	TIA, n(%)	27(5.92)	19(8.76)	0.1737
	History of MI, n(%)	108(23.68)	86(39.63)	<0.0001
	History of PCI or CABG, n(%)	99(21.71)	46(21.20)	0.8801
Angiographic and procedural characteristics	LM, n(%)	15(3.29)	23(10.60)	0.0001
	LAD, n(%)	186(40.79)	145(66.82)	<0.0001
	RCA, n(%)	193(42.32)	149(68.66)	<0.0001
	LCX, n(%)	162(35.53)	115(53.00)	<0.0001
	Stenosis of Culprit vessel, n(%)	334(73.3)	178(82.21)	0.0125
	Culprit vessel identified	217(100)	438(96.05)	0.0030
	Multivessel disease, n(%)	45(9.87)	98(45.16)	<0.0001
LV function	EF >45% , n(%)	289(63.38)	111(51.15)	0.0025
	EF - 36-45%, n(%)	125(27.41)	75(34.56)	0.0580
	EF <=35%, n(%)	42(9.21)	31(14.29)	0.0479
	EF%(Mean±SD)	46.84±8.46	45.13±9.11	0.0205
	Wall motion abnormalities, n(%)	351(76.97)	180(82.95)	0.0760
Diastolic dysfunction	Normal, n(%)	88(19.30)	20(9.22)	0.0008
	Impaired relaxation, n(%)	241(52.85)	116(53.46)	0.8833
	Pseudonormal filling, n(%)	81(17.76)	54(24.88)	0.0311
	Restrictive Filling	8(1.75)	14(6.45)	0.0013
	Not identified, n(%)	38(8.33)	13(5.99)	0.2838

CABG - coronary artery bypass grafting; CCC- coronary collateral circulation, DM - DiabetisMelitus; EF - ejection fraction, LAD - left anterior descending; LM - left main coronary artery, LV - left ventricular; LCX - left circumflex; MI - myocardial infarction, PCI - percutaneous coronary intervention; RCA - right coronary artery, TIA - transitory ischemic attack; UA - unstable angina;

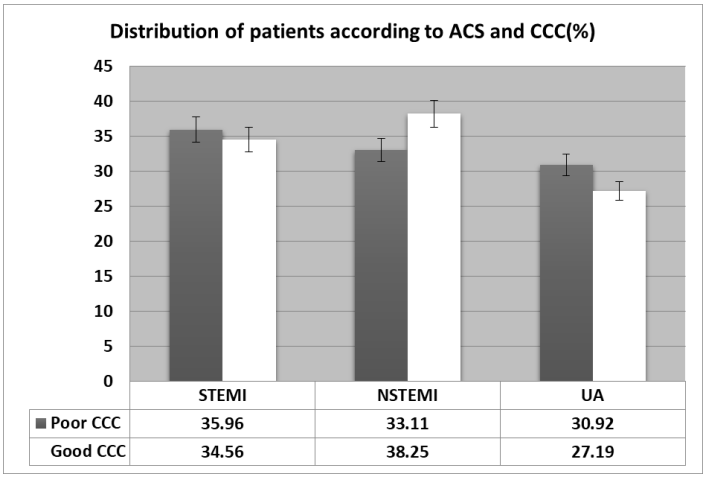

Figure 1. *Distribution of patients according to ACS and CCC.*

Table 2. *Peripheral blood components and biochemical features according to the collateral circulation.*

Factors	**Poor CCC(Mean±SD) N=456**	**Good CCC(Mean±SD) N=217**	**P**
Troponin ng/ml	7.51±13.74	5.91±10.23	0.1281
Creatinine, mmol/l	98.73±25.09	106.12±35.76	0.0021
Red blood cell count x10^{12}/l	4.33±0.51	4.32±0.55	0.8970
Platelet count x10^{9}/l	213.41±27.05	214.00±23.68	0.7731
WBC x10^{9}/l	8.76±2.27	8.98±2.59	0.2500
NC x10^{9}/l	5.94±1.84	4.78±1.93	<0.0001
EC x10^{9}/l	0.17±0.10	0.22±0.13	<0.0001
LC x10^{9}/l	2.04±0.89	2.25±0.90	0.0045
N/L	3.28±1.24	2.28±0.82	<0.0001
CCC- coronary collateral circulation; EC-Eosinophil count; LC - lymphocyte count; NC - neutrophil count; N/L - neutrophil-lymphocyte ratio; WBC - white blood cell count.			

Table 3. *Multivariable binary logistic regression analysis for the independent predictors of good CCC.*

Variables	**p**	**OR**	**95% C.I.for OR**	
EC	0.0009	17.36	3.25	92.86
N/L	0.0000	0.37	0.31	0.45
Male	0.0001	0.44	0.29	0.67
History of MI	0.0126	1.76	1.13	2.75
Multivessel disease	0.0000	9.78	5.65	16.96
Stenosis of Culprit vessel	0.0000	3.91	2.35	6.52
Presence of agina pectoris > 5 years	0.0000	5.55	2.66	11.57
CCC- coronary collateral circulation; CI, confidence interval, OR, odds ratio; EC-Eosinophil count; N/L - neutrophil-lymphocyte ratio.				

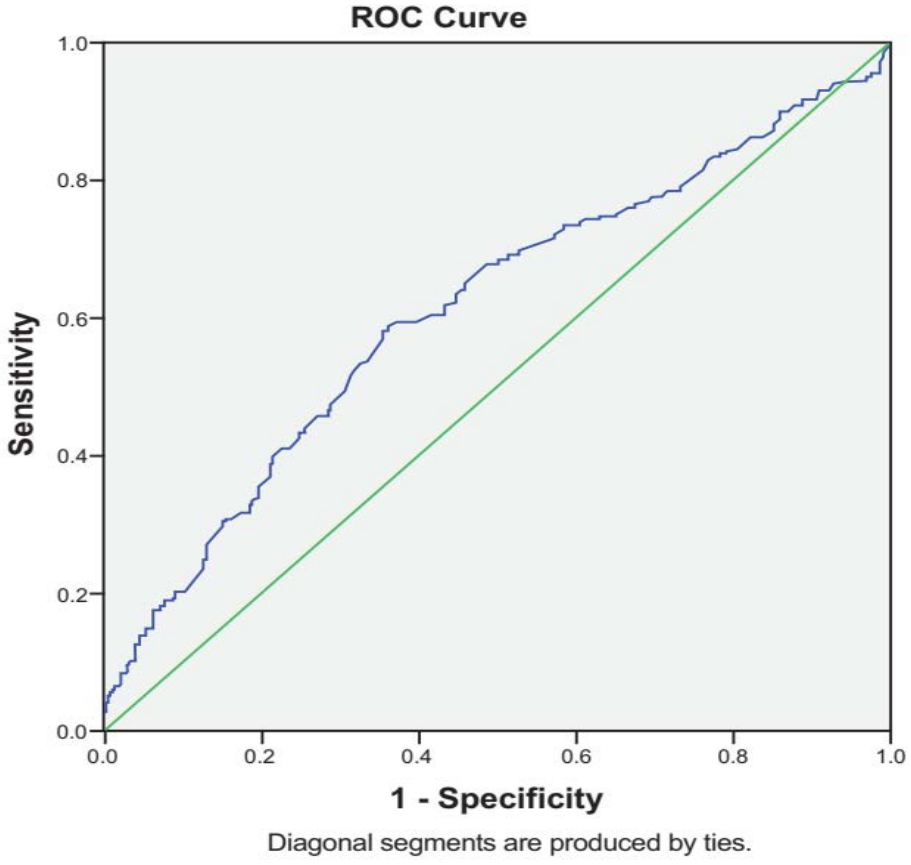

Figure 2. *ROC curves for EC value in the prediction of high-grade coronary collateral circulation.*

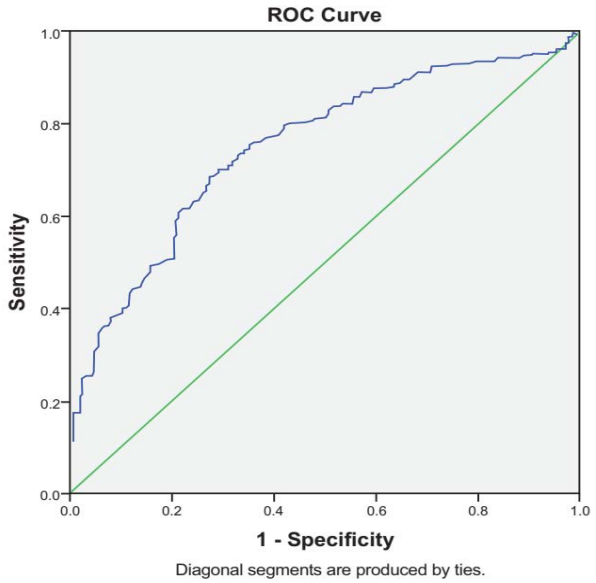

Figure 3. *ROC curves for N/L value in the prediction of high-grade coronary collateral circulation.*

The existence of gender differences in relation to the coronary collateral circulation and its determining factors is debatable [14]. Our study showed that the number of females who are in good collateral group is statistically higher than that of males and the male gender reduces the likelihood of developing collaterals.

Several studies have addressed CCC in Acute MI. In our study in patients with ACS who underwent PCI within 24 hours after symptom onset, the prevalence of visible good collaterals (Rentrop 2 or 3) was 32% without significant differences between study population (STEMI, NSTEMI, UA) . It has been detected 'good collaterals" (by high Rentrop scores) in 10-40 % of patient with acute MI [15]. In the study on coronary collateral appearance timing during STEMI [7], it has been shown that the presence of CC increases within the first 24 hours, with 19% of patients showing visible CC after 6 hours versus 40% of patients after 24 hours. After acute coronary occlusion, main mechanism of CC activation is recruitment of pre-formed collateral vessels. Angiogenesis (sprouting of capillaries) is another protective mechanism [16]. Among our study variables, history of angina > 5 years, age, occlusion of culprit artery, multivessel disease, identified culprit vessel, EF%, N/L ratio and eosinophil count appeared to be strongly associated with presence of good CCC (Rentrop 2-3). All other factors (DM, AH, dyslipidemia, smoking) have shown non-significant association with CCC occurrence in ACS patients included in our study. Similar findings were reported by other studies [16].

Pre-infarction angina may lead to the development of good CCC before acute MI and as a result, visible collaterals may appear in early MI. Antecedent stenosis of culprit artery (before acute occlusion by thrombus) may lead to CCC remodeling [17]. It has been shown that pressure gradients occurring due to chronic occlusion or dynamic stenosis act as triggers for collateral recruitment. Billinger et al. showed that repetitive, 2-min occlusions of a coronary artery increase CC flow and recruitment [9]. Regression analysis in our study revealed that history of angina is the independent predictor of good CCC in patients with ACS (OR- 4.83, 95% CI 2.44 – 9,56). Similar results were obtained by previously conducted studies [17].

It has been suggested that older age may result in low capacity of remodeling/arteriogenesis [1]. In contrast of previous study results, we have found that advanced age was associated with better CCC [18]. We may speculate that high prevalence of good CCC revealed in our study could be explained by the longer duration of CAD and high-grade chronic occlusion and related remodeling of preformed collateral arteries.

Our study indicated that angiographic evidence of culprit artery occlusion is a predictor of high grade CCC (Rentrop 2-3). We also found that multivessel disease is associated with "good collaterals". We suggested that more severe and frequent episodes of ischemia associated with multivessel disease may cause recruitment of pre-formed collateral arteries. Association of high grade CCC with identified culprit vessel detected by our study may be related to remodeling of collateral circulation both by stenotic lesion of epicardial artery and thrombus formation few days before occlusion. In contrast, in patients with unidentified culprit vessel low grade CCC may be associated with early spontaneous thrombolysis in epicardial artery without significant stenosis.

One of the variables associated with CCC development appeared to be EF%. Lower EF% in patients with "good collaterals" may be caused by more severe CAD in patients with high degree CCC as well as high prevalence of past MI in this group of individuals.

Based on our study results, eosinophil count and N/L ratio have been revealed to be independent predictors of the CCC. Previously it was reported that peripheral blood count parameters are associated with severity and prognosis of CAD, including acute MI [16,19,20-23].

Recent observations suggest that eosinophils may have a role in coronary atherosclerosis. The association between eosinophil count and increased risk for cardiovascular event has been indicated [20]. It has been shown that eosinophils play an important role in the development of thrombosis in patients with ACS [24,25]. Some of the eosinophil mediators activate thrombosis. Eosinophils synthesize mediators such as leukotriene C4 (a potent vasoconstrictor) and activate release of a number of vasoactive substances, including histamine, prostaglandin D2 and leukotrienes C4 and D4, from mast cells and basophils [26].

The study by Wang et al. revealed correlation between increased eosinophil count and high-grade CCC in patients with UAP [7]. The authors demonstrated that eosinophils can independently predict the presence of high-grade CCC with 72.5% sensitivity and 58.4% specificity (AUC: 0.681), in patients with UA. Verdoia et al. [27] concluded that high eosinophil count is not independently associated with the severity of CAD, but appears

to be confounded by their link with major cardiovascular risk factors. Our study showed 59.0% sensitivity and 63.6% specificity of eosinophil count in the prediction of high-grade coronary collateral circulation in ACS (STEMI, NSTEMI and UA) patients (low rate).

A number of studies demonstrated the association of cardiovascular risk with neutrophil count and N/L ratio. The N/L ratio is considered effective in predicting increased cardiovascular risk. A few studies have addressed the relationship between N/L and CCC. Nacar et al. [28] showed that high N/L is associated with poor coronary collateral circulation in patients with CTO (sensitivity of 95% and a specificity of 90% for the prediction of CCC). The similar result was reported by Kalkan et al [29]. It has been shown that N/L predicts poor CCC with 77% sensitivity and 65% specificity in CAD patients with CTO. According to the data of Siregar et al., higher N/L ratio is useful in predicting poor coronary collateral circulation in stable coronary heart disease with multivessel disease. The N/L ratio >1.99 was independently associated with impairment in coronary collateralization. This value had a sensitivity of 78.9% and specificity of 52% [21]. According to our study results, the high N/L is the predictor of poor collateral circulation with 68.4 % sensitivity and 72.8% specificity (cutoff:>2.73*10^9). Inflammatory processes inhibit nitric oxide (NO) production and reduce NO bioactivity, thereby inhibiting the formation of collaterals. Both the number of neutrophils and lymphocytes are inflammatory markers, and their ratio is an important predictor of the occurrence of collaterals [30,31].

Conclusion.

The likelihood of good collateral circulation increases with the increased number of eosinophils, presence of angina pectoris with duration of more than 5 years, history of past myocardial infarction, culprit vessel stenosis, multivessel disease, and decreases with the male gender and high N/L ratio.

Peripheral blood parameters may serve as an additional simple risk assessment tool in ACS patients considering that CCC has prognostic value in patients with ACS.

Conflict of interest.

Authors have no conflicts of interest to declare.

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Abstraqti

CigogiZe m[1], faRava z[1], TaboriZe i[2], lomia n[1], saaTaSvili g[1], SaraSiZe n[1].

[1] ivane javaxiSvilis saxelobis Tbilisis saxelmwifo universiteti, Tbilisi, saqarTvelo

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cnobilia koronaruli kolateraluri cirkulaciis (kkc) prognozuli roli mwvave Mmiokardiumis infarqtis gamosavalSi.

Cveni mizani iyo miokardiumis mwvave iSemiis mqone pacientebSi koronaruli kolateraluri sisxlZarRvebis ganviTarebasTan dakavSirebuli faqtorebis identificireba.

meTodebi. gamokvleul iqna 27-dan 94 wlamde asakis 673(64.7±11.48) Tanamimdevruli pacienti mwvave koronaruli sindromiT, romlebsac CautardaT koronaruli angiografia simptomebis dawyebidan pirveli 24 saaTis ganmavlobaSi. Seswavlil iqna sabaziso monacemebi - sqesi, asaki, gul-sisxlZarRvTa risk-faqtorebi, miRebuli medikamentebi, EF%, arteriuli hipertenzia, stenokardia da koronaruli revaskularizacia anamnezSi. gamokvleuli pirebi daiyo or jgufad: pacientebi 0-1 klasebiT Rentrop-is skalis mixedviT ganawilebuli iyvnen cudi kkc-s jgufSi (456 pacienti), xolo pacientebi 2-3 klasiT (217 pacienti) ganawilebuli iyvnen kargi kkc-s jgufSi. Sedegebi: dafiqsirda kargi uzrunvelyofis 32%-iani upiratesoba. kargi kkc-s Sansebis fardobas zrdis eozinofilebis raodenoba - OR = 17,36 (95% CI: 3,25-92,86); MI anamnezSi - OR=1.76 (95% CI: 1.13-2.75); mravalsisxlZarRvovani dazianeba - OR=9,78 (95% CI: 5,65-16,96); dainteresebuli arteriis stenozi - OR=3.91 (95% CI: 2.35-6.52); stenokardia > 5 weli - OR = 5,55 (95% CI: 2,66-11,57) da amcirebs - N/L - OR = 0,37 (95% CI: 0,31-0,45); mamrobiTi sqesi - OR = 0.44 (95% CI: 0.29-0.67). maRali N/L aris cudi kolateraluri sisxlis mimoqcevis maCvenebeli 68.4 mgrZnobelobiT da 72.8% specifikurobiT (Cutoff:2.73*109).

daskvnebi: kargi koronaruli kolateraluri sisxlis mimoqcevis albaTobas zrdis eozinofilebis raodenoba, stenokardiis arseboba 5 welze meti xnis ganmavlobaSi, miokardiumis infarqtis anamnezSi, dainteresebuli arteriis stenozi, mravalsisxlarRvovani daavadeba da mcirdeba, mamakacebSi da N/L-is zrdasTan erTad.

periferiuli sisxlis mniSvnelobebi SeiZleba gaxdes riskis Sefasebis damatebiTi martivi instrumenti ACS-is mqone pacientebSi.

sakvanZo sityvebi: koronaruli kolateraluri sisxlis mimoqceva, prediqtorebi, mwvave koronaruli sindromi.

Оценка предикторов коронарного коллатерального кровообращения у пациентов с острым коронарным синдромом в популяции Грузии

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Абстракт

Актуальность: Показана прогностическая роль коронарного коллатерального кровообращения (ККК) при остром ИМ.

Цель: выявление факторов, ассоциированных с развитием ССС у больных с острой ишемией миокарда.

Методы: В анализ были включены 673 последовательных пациента в возрасте от 27 до 94 лет (64,7+11,48) с острим коронарным синдромом (ОКС), которым была проведена коронароангиография в течение первых 24 часов после

появления симптомов. Были получены исходные данные, включая пол, возраст, сердечно-сосудистые факторы риска, медикаментозное лечение, EF%, стенокардия, артериальная гипертензия, коронарная реваскуляризация в анамнезе. Исследуемые лица были разделены на две группы: пациенты с 0–1-й степенями по шкале Rentrop были отнесены к группе плохого коллатеральной цируляции (456 человек), а пациенты со 2–3-й степенью (217 пациентов) — к группе хорошей.

Результаты: Обнаружено преобладание ККК - 32%.

Отношение шансов хорошего коллатерального кровообращения увеличивает количество эозинофилов - ОШ = 17,36 (95% ДИ: 3,25-92,86); ИМ в анамнезе - ОШ=1,76 (95% ДИ: 1,13-2,75); Многососудистое поражение - ОШ=9,78 (95% ДИ: 5,65-16,96); Стеноз виновного сосуда - ОШ=3,91 (95% ДИ: 2,35-6,52); Наличие стенокардии > 5 лет - ОШ = 5,55 (95% ДИ: 2,66-11,57) и снижение N/L- ОШ = 0,37 (95% ДИ: 0,31-0,45); Мужской пол - ОШ = 0,44 (95% ДИ: 0,29-0,67). Высокий N/L является предиктором плохого коллатерального кровообращения с чувствительностью 68,4 и специфичностью 72,8%. (Отсечка:>2,73*109). Высокий N/L является предиктором плохого коллатерального кровообращения с чувствительностью 68,4 и специфичностью 72,8%. (Отсечка:>2,73*109).

Выводы. Относительная вероятность хорошего коллатерального кровообращения увеличивает количество эозинофилов, наличие стенокардии продолжительностью более 5 лет, перенесенный инфаркт миокарда в анамнезе, стеноз виновного» сосуда, многососудистое поражение и снижается, если пол пациента мужской и N/ Л.

Показатели периферической крови могут служить дополнительным простым инструментом оценки риска у пациентов с ОКС.

Ключевые слова: коронарное коллатеральное кровообращение, предикторы, острый коронарный синдром.