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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

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თანამშრომლობითა და მისი პატრონაჟით

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

ТБИЛИСИ - НЬЮ-ЙОРК

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 and The International Academy of Sciences, Education, Industry and Arts (U.S.A.) 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.

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GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией и Международной академией наук, образования, искусств и естествознания (IASEIA) США 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.

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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.

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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).

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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.

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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).

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ავტორთა საყურადღებოდ!

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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.

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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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Содержание:

SST2 AS A PREDICTOR OF STATIN TREATMENT EFFICACY IN PATIENTS WITH MULTIPLE MYELOMA

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Abstract. The aim of the study: to investigate an interrelationship between pre-treatment circulating form of suppression of tumorigenicity-2 (ST2) level and one-year survival rate, cardiovascular events in subjects with multiple myeloma.

Methods: Ninety-seven subjects with full or partial remission of multiple myeloma were enrolled in the study. During observation period progression of multiple myeloma was proved in 25 patients, 5 persons were excluded for poor follow-up. 67 patients were included into statistical analysis. Patients were divided into 2 groups based on whether or not statins were included in their treatment: a statin group (n=31) and a no statin group (n=36). Among patients in the statin group, 19 patients received 20 mg/day atorvastatin and 12 patients received 40 mg/day atorvastatin. None of the patients had received any lipid-modulating medications, including statins or fibrates, before enrollment. Observation period was up to 1 year. Blood samples for biomarkers measurements were collected. ELISA method for measurements of circulating level of sST2, interleukin-6 and NT-pro-brain natriuretic peptide were used.

Results: Lipid lowering effect in statin user was associates with declined serum sST2 level, whereas in not statin users similar response was not appeared. No changes in hemodynamics and other biomarkers between both cohorts were found. Univariate logistic regression had exhibited that sST2 (odds ratio [OR] = 1.27; 95% CI = 1.04–1.39; P = 0.002), NT-proBNP (OR = 1.06; 95% CI 1.03–1.11; P < 0.05) and statin therapy (OR=1.05; 95% CI = 1.02–1.10; P = 0.03) predicted one-year cumulative CV events. After adjustment on statin therapy, sST2 remained independent predictor one-year cumulative cardiovascular events (OR = 1.11; 95% CI = 1.08–1.15; P = 0.01). When initial sST2 level has incorporated into prediction model, statin therapy was found as predictor for improving survival in patients with elevated serum sST2 level (>37 ng/ml).

Conclusion: Elevated pre-treatment sST2 level may by a powerful predictor of positive effect of statins on survival in patients with regression of multiple myeloma.

Keywords. sST2, interleukin-6, NT-pro-brain natriuretic peptide, multiple myeloma, statin, survival, prognosis.

Introduction.

Multiple myeloma (MM) is a plasma cell dyscrasia accounting for 1% of neoplastic diseases [1].

Cardiovascular disease is one of the most frequent comorbidities in MM patients [2]. Since the global population is aging, the prevalence of both MM and cardiovascular disease is expected to increase in the near future [3].

Cardiovascular disease in MM may derive from factors unrelated to the disease (age, diabetes, dyslipidemia, obesity), or those related to the myeloma (anemia, amyloidosis, hyperviscosity, renal dysfunction) and be related to the treatment of the disease [4].

It is difficult to estimate the actual incidence of chemotherapy-induced cardiovascular diseases, because current data about drug-induced cardiotoxicity were generated in clinical trials, from which patients with severe cardiovascular comorbidities were excluded. However, in real-life clinical practice, MM patients may suffer from cardiovascular diseases, have cardiovascular risk factors, and may have already received several cardiotoxic drugs [5].

Recommendations for management of patients with MM now include routine baseline risk stratification including ECG and echocardiography and administration of thromboprophylaxis drugs for patients treated with immunomodulatory drugs.

It is now well recognized that interactions between tumor cells and stromal cells in the tumor microenvironment play a determinant role in cancer initiation and progression [6]. The production of soluble growth factors, cytokines and chemokines by stromal cells in the presence of tumor cells is one among the several mechanisms by which the tumor microenvironment affects cancer cells. Among these soluble factors is interleukin-6 (IL-6) that promotes the self-seeding of circulating tumor cells and contributes to a stress response that protects tumor cells from drug action [7].

sST2 is a circulating form of suppression of tumorigenicity-2 (ST2) glycoprotein that is a member of the interleukin 1 receptor family. It serves as the receptor for IL-33, an IL-1–like cytokine that can be secreted by living cells in response to cell damage. IL-33 exerts its cardioprotective function by reducing cardiac fibrosis and inflammation [8]. sST2 can eliminate this cardioprotective function by acting to IL-33 and thus is considered an indicator of adverse outcome and a prognostic predictor for heart disease [9]. Moreover, it has been demonstrated that a higher sST2 level have prognostic properties for an increased incidence of cardiovascular events and mortality [10]. There are limited studies of sST2 in patients with multiple myeloma.

In our study, we aim to analyze the role of sST2 in the development of cardiovascular events, its value in screening and clinical decision making and its possible predictive application in follow-up as a “routine” test in an addition to established biomarkers, such as N-terminal pro-brain natriuretic protein (NT-proBNP) [11].

In this context there is possibility to use statins in dyslipidemic patients with regression of multiple myeloma to prevent unfavorable cardiovascular outcomes under control of sST2 level. The aim of the study: to investigate an interrelationship between pre-treatment sST2 level and one-year survival rate, cardiovascular events in subjects with multiple myeloma.

Design and Methods.

Ninety-seven out subjects with full or partial remission of multiple myeloma were enrolled in the study. During observation period progression of multiple myeloma was proved in 25 patients, 5 persons were excluded for poor follow-up. 67 patients were included into statistical analysis. All subjects gave their written informed consent to participation in the study. Diagnosis and staging of multiple myeloma were defined by current clinical practice guidelines [12]. To be achieving remission chemotherapy was used accordingly contemporary clinical guidelines. Patients were divided into 2 groups based on whether or not statins were included in their treatment: a statin group (n=31) and no statin group (n=36). Only patients with dyslipidemia were treated with statins. None of the patients had received any lipid-modulating medications, including statins or fibrates, before enrollment. Among patients in the statin group, 19 patients received 20-mg/day atorvastatin and 12 patients received 40-mg/day atorvastatin.

Echocardiography in B-mode was performed accordingly to Recommendation of American Society of Echocardiography on the scanner "MyLab 50" (Italy) using a transducer with a frequency of 2.5-3.5 MHz. End-diastolic and end-systolic left ventricle (LV) volumes were obtained using a two-dimensional reference sector according to Simpson's method, and LV ejection fraction (LVEF) was calculated by accordingly conventional methods [13].

All blood samples were collected after fasting in cooling vacutainer and after that it was immediately centrifuged (4°C for 6.000 × 15 min). After centrifugation serum was blind coded and stored at -70° until used. sST2, IL-6 and NTproBNP were measured by ELISA technique (ELISA kits manufactured by Clinical Diagnostics, USA; R&G, United Kingdom) used for examination. All determinations were done by duplicating. Fasting plasma glucose (FPG) was quantified by the glucose oxidase procedure; HbA1c was measured by ion-exchange high-performance liquid chromatography (HPLC; Bio-Rad, Hercules, CA, USA). Concentrations of total cholesterol (TC), low density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol were determined by direct enzymatic methods using Dimension Clinical Chemistry System (Dade Behring Inc, Newark, NJ). All measurements and blood sample for were collected at the same visit.

Clinical Events: Screening and Diagnostics. Clinical interviews were carried out every month for one year after baseline. The following are the clinical events verified: newly diagnosed strokes or TIAs; death for any reasons and sudden cardiac death; coronary ischemic events (myocardial infarction, unstable angina) that needed hospital admission for cardiovascular reasons, new-onset chronic heart failure. Newly diagnosed strokes were confirmed with CT. All clinical events were presented as cumulative.

Statistical Analysis. All statistical analyses were performed in SPSS for Windows v. 17.0 (SPSS Inc., Chicago, IL, USA). All values were given as mean and 95% confidence interval [CI] or median and percentiles. An independent group t-test was used for comparisons for all interval parameters meeting the criteria of normality and homogeneity of variance. For interval parameters not meeting these criteria, the non-paramentric Mann-Whitney test was used to make comparisons between the groups. Comparisons of categorical variables between the groups were performed using the Chi2 test, and the Fisher exact test. The potential factors that may be associated with cardiovascular events was identified first by the univariate analysis, then multivariate logistic regression analyses were used to identify the predict factors. A calculated difference of $p<0.05$ was considered significant.

Table 1. Baseline Clinical Characteristics.

Variables	Statin users (n=31)	Never statin users (n=36)	P-value
Age, years	61.14 [48.31; 71.12]	58.12±[48.82; 66.12	>0.05
Males, n (%)	15 (48.4)	22 (41.7)	>0.05
Hypertension, n (%)	5 (16.1)	6 (16.7)	>0.05
T2DM, n (%)	1 (3.2)	0 (0.0)	>0.05
BMI, kg/m^2	28.12 [24.54; 33.12]	26.27 [22.41; 30.98]	>0.05
Obesity, n (%)	4 (12.9)	4 (11.1)	>0.05
Overweight, n (%)	10 (32.3)	8 (22.2)	>0.05
Adherence to smoking, n (%)	1 (3.2)	2 (5.5)	>0.05
GFR, mL/min/1.73 m^2	99.27 [72.61; 122.80]	103.42 [79.99; 128.72]	>0.05
HbA1c, %	5.19 [4.69; 7.12]	5.02 [3.71; 5.94]	>0.05
Fasting blood glucose, mmol/L	6.08 [4.47; 6.79]	4.54 [3.98; 5.89]	>0.05
Creatinine, μmol/L	74.43 [50.82; 98.71]	70.28 [54.69; 92.35]	>0.05
sST2, ng/ml	32.48 [12.36; 44.82]	29.76 [22.8; 39.4]	>0.05
NT-pro-BNP, pg /mL	11.95 [3.42; 20.36]	12.45 [2.79; 24.44]	>0.05
IL-6, pg/ml	2.38 [0.81; 4.64]	2.22 [0.68; 4.01]	>0.05
ACEI or ARAs, n (%)	6 (19.4)	5 (13.9)	>0.05
Acetylsalicylic acid or clopidogrel, n (%)	27 (87.1)	26 (72.2)	>0.05
Metformin, n (%)	1 (3.2)	0 (0.0)	>0.05
Loop diuretics, n (%)	3 (9.7)	6 (16.7)	>0.05
Mineralcorticoid receptor antagonists, n (%)	2 (6.5)	4 (11.1)	>0.05

*Note: * - statistically differences between parameters in the two groups ($p<0.05$); CI – confidence interval; T2DM – type two diabetes mellitus, GFR - Glomerular filtration rate, BMI - Body mass index, BNP – brain natriuretic peptide, ACEI – angiotensin-converting enzyme inhibitor, ARAs – angiotensin-2 receptors antagonists.*

Table 2. Change in Clinical Characteristics According to Statin Treatment.

Variables	Statin users (n=31)			Never Statin users (n=36)		
	Baseline	At 12 months (% change)	P-value	Baseline	At 12 months (% change)	P-value
Total cholesterol, mmol/L	5.12 [4.29; 5.98]	4.24 [3.54; 5.12]	<0.01	4.83 [4.11; 5.61]	4.80 [4.23; 5.33]	>0.05
LDL-C, mmol/L	3.68 [2.04; 4.05]	2.01 [1.67; 3.59]	<0.01	2.72 [2.14; 3.21]	2.84 [2.11; 3.40]	>0.05
HDL-C, mmol/L	1.43 [1.02; 1.89]	1.46 [1.08; 1.80]	>0.05	1.54 [1.18; 1.89]	1.44 [1.12; 1.92]	>0.05
Systolic BP, mm Hg	125.44 [112.02; 138.89]	122.39 [110.33; 138.48]	>0.05	126.24 [113.20; 139.81]	125.34 [114.80; 139.14]	>0.05
Heart rate, beats per 1 min.	81.19 [70.94; 90.36]	74.04 [67.25; 90.18]	>0.05	79.08 [70.22; 88.16]	76.82 [70.12; 88.36]	>0.05
LVEF, %	57.17 [52.36; 61.10]	58.39 [53.98; 60.46]	>0.05	57.10 [53.01; 61.99]	52.50 [49.89; 55.12]	<0.05
E/Am, U	1.12 [0.89; 1.38]	1.10 [0.81; 1.34]	>0.05	1.19 [0.78; 1.35]	1.12 [0.81; 1.39]	>0.05
E/Em, U	6.82 [5.22; 8.40]	6.29 [4.88; 8.04]	>0.05	7.07 [6.02; 8.59]	8.98 [7.12; 10,36]	<0.05
sST2, ng/mL	32.48 [22.36; 44.82]	21.98 [9.38; 28.05]	<0.05	29.76 [22.80; 39.4]	34.52 [22.61; 45.98]	>0.05
NT-pro-BNP, pg /mL	11.42 [2.39; 19.82]	3.10 [1.07; 6.90]	<0.05	11.22 [4.36; 24.80]	4.91 [1.96; 12.99]	>0.05
IL-6, pg/mL	2.27 [0.34; 3.80]	7.60 [3.71; 9.23]	<0.05	2.22 [0.94; 4.39]	5.20 [1.26; 6.14]	>0.05

Table 3. Characteristics of multiple myeloma patients with vs without CV events.

Variables	Free-events subjects (n=49)	Subjects with CV events (n=18)	P-value
Age, years	59.21 [48.16; 68.32]	61.00 [52.12; 69.81]	>0.05
Males, n (%)	21 (42.9)	9 (50.0)	>0.05
Hypertension, n (%)	6 (12.3)	4 (22.2)	>0.05
Dyslipidemia, n (%)	27 (55.1)	11 (61.1)	>0.05
T2DM, n (%)	0 (0.0)	1 (5.5)	>0.05
BMI, kg/m^2	26.74 [25.69; 27.79]	27.40 [25.82-28.98]	>0.05
Obesity, n (%)	5 (10.2)	3 (16.7)	>0.05
Overweight, n (%)	13 (26,5)	5 (27,7)	>0.05
Adherence to smoking, n (%)	2 (4.1)	1 (5.6)	>0.05
GFR, mL/min/1.73 m^2	102.30 [79.4; 127.6]	101.05 [80.8; 142.8]	>0.05
HbA1c, %	5.01 [4.56; 5.98]	5.27 [4.98; 5.58]	>0.05
Fasting blood glucose, mmol/L	4.63 [4.09; 5.25]	4.80 [4.26; 5.65]	>0.05
Creatinine, μmol/L	68.71 [52.41; 86.12]	73.67 [50.25; 90.98]	>0.05
Total cholesterol, mmol/L	5.09 [4.28; 5.99]	4.77 [3.89; 6.12]	>0.05
LDL-C, mmol/L	2.94 [2.35; 4.01]	2.89 [2.54; 3.99]	>0.05
HDL-C, mmol/L	1.50 [0.98; 1.95]	1.50 [0.94; 1.32]	>0.05
sST2, ng/ml	24.17 [12.87; 27.48]	47.57 [21.36; 68.79]	<0.01
NT-pro-BNP, pg /mL	5.68 [2.36; 12.58]	23.8 [6.34; 36.4]	<0.01
IL-6, pg/ml	1.80 [0.32; 7.89]	2.95 [0.98; 9.36]	>0.05
Systolic BP, mm Hg	124.3 [115.6; 138.8]	129.0 [116.3; 142.0]	>0.05
Heart rate, beats per 1 min.	80.56 [70.22; 90.58]	79.43 [68.3; 94.48]	>0.05
LVEF, %	58.11 [51.25; 64.80]	55.84 [51.41; 59.65]	>0.05
E/Am, U	1.12 [0.74; 1.38]	1.17 [0.98; 1.32]	>0.05
E/Em, U	7.14 [5.45; 9.16]	9.29 [7.30; 11.17]	<0.05

*Note: * - statistically differences between parameters in the two groups (P<0.05); CI – confidence interval; T2DM – type two diabetes mellitus, GFR - Glomerular filtration rate, HDL-C - high-density lipoprotein cholesterol, LDL-C - Low-density lipoprotein cholesterol, BP – blood pressure, BMI - Body mass index, BNP – brain natriuretic peptide, LVEF - Left ventricular ejection fraction, U – unit, Em - early diastolic myocardial velocity, Am - late diastolic myocardial velocity, E – peak velocity of early diastolic left*

Results.

The baseline characteristic of both cohorts of the patients depending on treatment regime is presented in the Table 1. All patients were matched accordingly age, sex, cardiovascular events, diabetes presentation rate, serum biomarker concentration, and concomitant medications.

All of the patients in the statin group tolerated the treatment well, and no serious side-effects were reported during the follow-up period. The effect of both statin regimes is reported in the Table 2. One can see, lipid lowering effect in statin user was associates with declined serum sST2 level, whereas in not statin users similar response was not appeared. No changes in hemodynamics and other biomarkers between both cohorts were found.

Thirty-six cumulative clinical events occurred in 18 patients (26.9%) within the follow-up, with their distribution being as

follows: 2 cardiovascular deaths, 16 cardiac arrhythmias, 3 cardiac ischemic events, 1 stroke, 4 chronic heart failures and 10 hospital admissions for cardiovascular reasons. 2 deaths were not related with cardiovascular pathology.

Table 3 is reported characteristics of the multiple myeloma patients with vs without cardiovascular events. One can see, free-events subjects had lover levels of sST2, IL-6 and NT-proBNP than subjects with cardiovascular events. The data suggested that sST2 plasma levels were directly related to NT-pro-BNP ($r = 0.42$, $P = 0.03$). No relations were found in sST2 and IL-6.

Univariate logistic regression had exhibited that sST2 (odds ratio [OR] = 1.27; 95% CI = 1.04–1.39; $P = 0.002$), NT-proBNP (OR = 1.06; 95% CI 1.03–1.11; $P < 0.05$) and statin therapy (OR=1.05; 95% CI = 1.02–1.10; $P = 0.03$) predicted one-year cumulative CV events. After adjustment on statin therapy, sST2 remained independent predictor one-year cumulative cardiovascular events (OR = 1.11; 95% CI = 1.08–1.15; $P = 0.01$). When initial sST2 level has incorporated into prediction model, statin therapy was found as predictor for improving survival in patients with elevated serum sST2 level (>37 ng/ml). The results of the study have confirmed an assumption regarding statins' positive effect on survival in higher risk subjects with multiple myeloma. Although this is a preliminary result, probably, it is required more investigations to explain the role of pretreatment level of sST2 as independent predictor of long-term clinical outcomes in stable individuals with multiple myeloma.

Conclusion.

sST2 has a high predictive value in terms of prognosis and an additive value to natriuretic peptide measurement. The results of the study have exhibited that elevated pre-treatment sST2 level might be a powerful predictor of positive effect of statins on survival in patients with multiple myeloma.

Complementary prospective studies are still needed to confirm its prognostic value and to determine the target population for combined biomarker analysis and, maybe in the future, for using sST2 as a target for preventive treatment of cardiovascular events in patients with multiple myeloma.

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SST2 AS A PREDICTOR OF STATIN TREATMENT EFFICACY IN PATIENTS WITH MULTIPLE MYELOMA

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Abstract. The aim of the study: to investigate an interrelationship between pre-treatment circulating form of suppression of tumorigenicity-2 (ST2) level and one-year survival rate, cardiovascular events in subjects with multiple myeloma.

Methods: Ninety-seven subjects with full or partial remission of multiple myeloma were enrolled in the study. During observation period progression of multiple myeloma was proved in 25 patients, 5 persons were excluded for poor follow-up. 67 patients were included into statistical analysis. Patients were divided into 2 groups based on whether or not statins were included in their treatment: a statin group (n=31) and a no statin group (n=36). Among patients in the statin group, 19 patients received 20 mg/day atorvastatin and 12 patients received 40 mg/day atorvastatin. None of the patients had received any lipid-modulating medications, including statins or fibrates, before enrollment. Observation period was up to 1 year. Blood samples for biomarkers measurements were collected. ELISA method for measurements of circulating level of sST2, interleukin-6 and NT-pro-brain natriuretic peptide were used.

Results: Lipid lowering effect in statin user was associates with declined serum sST2 level, whereas in not statin users similar response was not appeared. No changes in hemodynamics and other biomarkers between both cohorts were found. Univariate logistic regression had exhibited that sST2 (odds ratio [OR] = 1.27; 95% CI = 1.04–1.39; P = 0.002), NT-proBNP (OR = 1.06; 95% CI 1.03–1.11; P < 0.05) and statin therapy (OR=1.05; 95% CI = 1.02–1.10; P = 0.03) predicted one-year cumulative CV events. After adjustment on statin therapy, sST2 remained independent predictor one-year cumulative cardiovascular events (OR = 1.11; 95% CI = 1.08–1.15; P = 0.01). When initial sST2 level has incorporated into prediction model, statin therapy was found as predictor for improving survival in patients with elevated serum sST2 level (>37 ng/ml).

Conclusion: Elevated pre-treatment sST2 level may by a powerful predictor of positive effect of statins on survival in patients with regression of multiple myeloma.

Keywords. sST2, interleukin-6, NT-pro-brain natriuretic peptide, multiple myeloma, statin, survival, prognosis.

SST2 КАК ПРЕДИКТОР ЭФФЕКТИВНОСТИ ЛЕЧЕНИЯ СТАТИНАМИ У ПАЦИЕНТОВ С МНОЖЕСТВЕННОЙ МИЕЛОМОЙ МАКРОЦИКЛА

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Целью настоящего исследования явилось исследование взаимосвязи между уровнем sST2 и выживаемостью, кардиоваскулярными событиями пациентов с множественной миеломой на протяжении 1 года.

Материалы и методы: в исследование включены 97 пациентов с регрессией множественной миеломы. Пациенты были разделены на две группы в зависимости от наличия статинов в их лечении: группа, получавшая статины ((n=31) и группа без статинов (n=36). В группе пациентов, получавших статины, 19 пациентов получали 20 мг аторвастатина в сутки и 12 пациентов получали 40 мг аторвастатина в сутки. До включения в исследование все пациенты не получали препараты, модулирующие липидный обмен, включая статины. Период наблюдения составил 1 год. Проводился забор крови для исследования биомаркеров. Уровень циркулирующего sST2, интерлейкина-6, NT-фрагмента мозгового натрийуретического пептида определяли с помощью иммунносорбентного метода.

Результаты. Гиполипидемический эффект статинов ассоциировался со снижением уровня sST2, хотя ответ у пациентов, получавших статины, был неодинаков. Не было выявлено значимых различий в гемодинамических показателях и других биомаркерах. С помощью универиантной логистической регрессии показано, что sST2 (отношение шансов [ОШ] = 1,27; 95% доверительный интервал [ДИ] = 1,04–1,39; p = 0,002), NT-proBNP (ОШ=1,06; 95% ДИ = 1,03–1,11; p < 0.05) и терапия статинами (OR=1,05; 95% CI = 1,02–1,10; p = 0,03) обладают предикторными свойствами кардиоваскулярных событий на протяжении 1 года. После лечения статинами sST2 остался независимым предиктором кумулятивных кардиоваскулярных событий (ОШ = 1,11; 95% ДИ = 1,08–1,15; p = 0,01). При включении уровня плазменного sST2 в прогностическую модель, лечение статинами показало предикторные свойства в улучшении выживаемости пациентов с множественной миеломой и уровнем плазменного sST2 выше 37 нг/мл.

Вывод: повышенный уровень sST2 может быть предикторном позитивного эффекта статинов на выживаемость пациентов с регрессией множественной миеломы.

Ключевые слова: sST2; интерлейкин-6; NT-фрагмент мозгового натрийуретического пептида; множественная миелома; статин; выживаемость; прогноз.