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The use of a clinical calculator to determine the rate of development of chronic kidney disease in elderly patients with type 2 diabetes mellitus

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Abstract

Aim – to develop an applied prognostic calculator for the rate of progression of CKD in elderly patients with type 2 diabetes, which makes it possible to identify a group of high rate of GFR reduction in conditions of routine outpatient admission.
Material and methods. 69 clinical indicators were studied, the interrelationships and significance of differences in parameters in the groups identified according to the original diagnostic parameter, the glomerular filtration rate reduction index with a threshold value of 3.83 ml/min/1.73 m^2 per year, above which the rate of progression of CKD was considered high.
Results. By using regression analysis, significant factors for the prognostic calculator were identified: the duration of diabetes and insulin therapy, concomitant diagnosis of obesity, pulse in the ankle artery, severe stage of polyneuropathy, risk group IV of hypertension, treatment with sulfonylureas, the number of antihypertensive drugs taken. When evaluating the information capacity and predictive ability of the calculator, the area under the AUC ROC curve was 0.89 (0.80; 0.99) p < 0.001, which characterizes the quality of the diagnostic technique as high.
Conclusion. The presented calculator gives the doctor the opportunity to identify a group of patients with the risk of rapid progression of CKD directly on an outpatient basis.
Keywords: old age, type 2 diabetes mellitus, chronic kidney disease, glomerular filtration rate, disease prognosis calculator, outpatient treatment of type 2 diabetes mellitus.
Conflict of interest: nothing to disclose.

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Применение клинического калькулятора для определения темпа развития хронической болезни почек у пожилых пациентов с сахарным диабетом 2 типа

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Аннотация

Цель – разработать прикладной прогностический калькулятор темпа прогрессирования хронической болезни почек (ХБП) у пациентов с СД 2 типа пожилого возраста, позволяющий в условиях рутинного амбулаторного приема выделить группу высокого темпа снижения СКФ.
Материал и методы. Изучено 69 клинических показателей, выявлены взаимосвязи и значимость различий параметров в группах, выделенных по оригинальному диагностическому параметру Индекс снижения скорости клубочковой фильтрации с пороговым значением 3,83 мл/мин/1,73м^2 за год, при превышении которого темп прогрессирования ХБП считался высоким.
Результаты. Путем применения регрессионного анализа выделены значимые факторы для прогностического калькулятора: длительность забо-

левания СД и инсулинотерапии, сопутствующий диагноз ожирения, пульс на лодыжечной артерии, выраженная стадия полинейропатии, IV группа риска артериальной гипертензии, лечение препаратами сульфонилмочевины, количество принимаемых гипотензивных препаратов. При оценке информативности и предсказательной способности калькулятора площадь под ROC-кривой AUC составила 0,89 (0,80; 0,99) p < 0,001, что характеризует качество диагностической методики как высокое.

Заключение. Представленный калькулятор дает врачу возможность непосредственно в амбулаторных условиях выделить группу пациентов с риском быстрого прогрессирования ХБП.

Ключевые слова: пожилой возраст, сахарный диабет 2 типа, хроническая болезнь почек, скорость клубочковой фильтрации, калькулятор прогноза заболевания, амбулаторное лечение сахарного диабета 2 типа.
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Список сокращений
АГ – артериальная гипертензия; АД – артериальное давление; ССЗ – атеросклеротические сердечно-сосудистые заболевания; АРМЭ – автоматизированное рабочее место врача-эндокринолога; ДИ – доверительный интервал; иАПФ – ингибиторы ангиотензин-превращающего фермента; иДПП-4 – ингибиторы дипептидилпептидазы 4 типа; ИМТ – индекс массы тела; иНГЛТ-2 – ингибиторы натрий-глюкозного котранспортера 2-го типа; ИС_СКФ – индекс снижения скорости клубочковой фильтрации; ОИМ – острый инфаркт миокарда; ОШ – отношение шансов; РАС – ренин-ангиотензиновая система; СКФ – скорость клубочковой фильтрации; СППВР – система поддержки принятия врачебных решений; СД – сахарный диабет; ФРСД – федеральный регистр больных сахарным диабетом; ХБП – хроническая болезнь почек; HbA1c – гликированный гемоглобин.

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INTRODUCTION

The steady increase in the number of senior and old people and the global aging of the population are among the most pressing medical and social problems of our time. According to the data of 2018, approx. 25.4% of the population in the Russian federation are aged over 60[1]. Following the demographic forecast of the Federal State Statistics Service, in 20 years the number of people in Russia aged over 60 will reach 37.3 million people (26.9% of the population)[2]. The increase in life expectancy affects the growth of various risk factors that aggravate the comorbid nature of the pathology, characteristic of this cohort of patients. [1]. A no less socially significant factor for the society is the prevalence of diabetes mellitus (DM) and its complications. As per the data of the Federal Diabetes Register (FDR), the total number of people with DM in the Russian Federation was over 4.96 million people (3.3% of the population of the country) as of January 1, 2023; among them the share of patients with type 2 DM is 92.3% (4.58 million people) [2]; and the share of senior patients in the type 2 DM cohort is 81.9% [3]. According to the results of the national epidemiological cross-sectional study NATION, the prevalence of DM in the cohort of senior patients is 6.72%, and the number of patients with non-diagnosed carbohydrate metabolism disorder reaches 6.05% [4]. This data sheds light on the real scale of the problem: over 12% of the population of senior people are highly likely to have some or other signs of disorders in the tolerance to carbohydrates or a manifested disease.

According to modern concepts, the main task of a physician in the treatment of diabetes is the active identification and adequate treatment of chronic vascular complications, including diabetic renal disease [5] and related comorbidities: dyslipidemia, arterial hypertension (AH), atherosclerotic cardiovascular diseases (ASCVD) [6]. The damage to renal tissue in diabetes mellitus is assessed within the framework of the supranosological concept of chronic kidney disease (CKD), which is defined as damage to nephrons that persists for three months or more due to the action of various etiological factors. The anatomical and histological basis of the pathological process is the replacement of normal renal cells with fibrosis, which leads to nephrosclerosis and ultimately to a decrease in excretory function [7]. According to modern concepts, diabetic kidney disease develops in close relationship with cardiovascular manifestations and should be considered within the framework of the cardiorenal continuum [8–10].

A significant feature of CKD in senior patients is the heterogeneity of pathological factors that influence the rate of progression of the process, as well as comorbid pathology, characteristic of the clinical portrait of most geriatric patients [11].

The register nature is the essential feature of this study. The clinical information base was the local register of patients with type 2 DM in outpatient medical institutions of Samara collected by means of digital tools[3]. According to the International Register of Clinical Trials https://clinicaltrials.gov/, in the year 2023 over 450,000 clinical trials were registered worldwide (over 64,000 are currently selecting the participants), based on the data from various registers [12]. Observational registry studies have significant advantages over classical randomized

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studies, since they allow for a one-time, broad coverage of a whole range of different risk factors in real clinical practice, as well as an objective assessment of their impact on the course and dynamics of the pathological process [13–15].

In most cases, the reference randomized design involves obtaining answers to one or two specific questions, assessing the effectiveness of a particular diagnostic or treatment method. For an elderly patient with concomitant diabetes, the polymorbid nature of the disease is almost a mandatory condition; the main disease is accompanied by hypertension, dyslipidemia and ASCVD that are closely associated with age. Identification of pathogenetic relationships and the mutual influence of many risk factors available to a doctor in a real outpatient setting on the dynamics of CKD development has become one of the main objectives of the presented work.

AIM

To develop an applied prognostic calculator for the rate of progression of CKD in elderly patients with type 2 diabetes mellitus, allowing to identify a group with a high rate of decline of GFR in the conditions of routine outpatient care.

In order to achieve this aim, the following tasks were identified.

1. Use regression analysis with the original diagnostic parameter RI_GFR[1] to evaluate clinical risk factors of fast progression of CKD in the cohort of senior patients with type 2 diabetes [16].

2. Conduct a comprehensive assessment of the significance of the influence of individual parameters of clinical status on the rate of progression of CKD in a cohort of senior patients with type 2 diabetes, and assign scores to the identified clinical predictors.

3. Build a ROC curve, estimate the AUX area, and create a classification matrix to assess the diagnostic significance of the proposed calculator.

MATERIAL AND METHODS

Survey Design. Observational cross-sectional survey of indicators of clinical status in the cohort of senior patients with type 2 diabetes.

Collection of primary medical information is performed in the computer software program "Endocrinologist's Automated Workplace ARME 2.0" [17], which processes and stores primary medical data of patients in digital form during outpatient visit. To participate in the survey, 118 outpatient consultations of elderly patients with type 2 diabetes were selected, which were exported to an Excel spreadsheet.

For the purposes of the analysis, 69 indicators of clinical status from the formalized protocol matrix of ARME 2.0 were used [18]. These include quantitative indicators, e.g. anthropometric data, clinical and laboratory data (among them data of home-based self-monitoring of arterial hypertension, data of glycaemia self-monitoring and its variability), history (including event occurrence dates), pharmacological data (insulin dose, Units; dose of antihyperglycaemic tabloids with percentage from maximum therapeutic dose; class and quantity of antihypertensive agents). Qualitative indicators include patient's chronic complications of diabetes mellitus and concomitant conditions, their stage as identified using the standard AH risk scale, and others.

In the ARME, the outpatient consultation protocol is formed as a structured electronic medical document. The process of export to Excel is automated with the use of the Power Query tool, the text values from pre-set lists are converted and validated against the nominal and ordinal scales. The case history data is stored as quantitative data of event occurrence in years, secondary diagnoses, as qualitative (presence or absence) or nominal (stage of progression) indicators. In the same way, quantitative and qualitative indicators of pharmacological treatment are processed: insulin treatment with indication of dose and duration of treatment, oral antihyperglycaemic agents of certain types (sulphonylureas, biguanides, DPP-4 inhibitors, SGLT-2 inhibitors with indication of percentage of the maximum dosage), antihypertensive agents from ACE inhibitor, RAS blockers, beta blockers, calcium channel antagonists, and diuretics.

Subject Group Characteristics. The survey subject is a cohort of senior patients with type 2 diabetes. The sample included 118 patients of the Caucasian race over 60 years of age, who were under dispensary observation with a diagnosis of type 2 diabetes in municipal medical organizations in Samara. Consent was received from all participants, all patients are registered in the FDR, the study is approved by the Ethics Commission of the Samara State medical University (Protocol No.199 dated April 3, 2019).

Inclusion criteria: patients with type 2 diabetes aged over 60, whose formalized consultation protocol contains data on levels of creatinine, HbA1c, glycaemia (laboratory and self-monitoring data), and at least 75% genera clinical parameters used to analyze the results, GFR in the range of 15–120 ml/min/1.73m^2.

Exclusion criteria: presence of acute exacerbations of diabetes, exacerbation of comorbidities at the moment of consultation, presence of concomitant chronic pathology affecting the renal function (anemia, gouty arthritis), terminal stage of CKD (GFR <15 ml/min/1.73m^2). The clinical characteristics of participants follow in **Table 1**.

Clinical methods. During an objective clinical examination of the study participants, a standard protocol for dispensary observation of a patient with type 2 diabetes was used including collection of complaints, determination of anthropometric parameters, measurement of the main hemodynamic indicators, auscultation of the circulatory and respiratory organs, abdominal palpation, determination of the characteristics of the pulse of the arteries of the lower extremities. The laboratory examination included determination of glycaemia, glycated hemoglobin (HbA1c), creatinine, and lipid profile.

[1] Pervyshin N.A. A way to determine the progression rate of chronic kidney disease in patient with type 2 diabetes using the diagnostic index of reduction of glomerular filtration rate. Patent for invention No. 2810369. Application: 2023113094 dated 21.05.2023; registration date: 27.12.2023. Bulletin No. 26. https://www.fips.ru/cdfi/fips.dll/ru?ty=29&docid=2810369

Subjects, n	118	
Sex (M/F), n (%)	31 (26%) / 87 (74%)	
Receiving insulin therapy, n (%)	102 (86%)	
Average age, years	67,98±5,96	67,0 [62,0; 71,25]
Duration of diabetes, years	12,37±8,08	11,0 [6,75; 15,0]
BMI, kg/m2	31,34±5,23	31,2 [27,55; 33,60]
HbA1c, %	8,61±2,62	8,0 [7,00; 9,10]
delta HbA1c = X-TL, %	1,78±2,66	1,1 [0,30; 2,60]
Creatinine, umol/l	89,95±25,05	92,80 [80,00; 106,90]
GFR CKD-EPI (ml/min/1.73 м²)	72,28±22,26	75,0 [53,0; 92,63]

Note: The data is presented as absolute and average values, and standard deviation
Примечания. Данные представлены в виде абсолютных и средних значений, стандартного отклонения.

Table 1. *Clinical characteristics of participants in the CKD study in type 2 diabetes*

Таблица 1. *Клиническая характеристика участников исследования ХБП при СД 2 типа*

Blood sampling required an exposure of at least 8 hours after the last meal, and was performed in the morning on an empty stomach. The level of glycated hemoglobin was determined by ion-exchange chromatography with an automatic biochemical analyzer using a standardized method. The GFR value was calculated in the medical decision-making module of the ARME automatically using the CKD-EPI formula.

Statistical analysis of data. To export the primary material from the ARME database to the Microsoft Excel file, an original query script was developed. During the export process, the values of the text fields on drug therapy are validated against nominal scales according to the drug class.

The software used for the statistical analysis was SPSS 25.0 (IBM Corporation, Armonk, New York, USA).

When checking the normality of the distribution of quantitative characteristics, a graphoanalytical method was used, which involves visual analysis of distribution histograms, as well as the determination of the Shapiro-Wilk and Kolmogorov-Smirnov criteria with the Lilliefors correction. Both parametric and non-parametric analysis methods were applied. Descriptive statistics for quantitative characteristics are presented as mean and standard deviation (M±SD) or, in case of large deviations from normality, as median and quartiles [Me (Q1; Q3)]. Nominal features were pre-coded with numbers and assigned appropriate labels, values are presented as the number of observations and percentage of the group size. Mann-Whitney, Student's tests, one-way ANOVA and Kruskal-Wallis analysis were used to compare quantitative features in groups. The frequencies of nominal features were compared with each other by calculating the Pearson Chi-square (χ^2) test and the two-tailed Fisher test. The strength of the relationships between clinical status indicators was determined using Spearman rank correlations for quantitative features and Kendall correlation (tau) for pairs of features on an ordinal and quantitative scale. Univariate logistic regression was used to quantify the contribution of individual clinical status indicators to the risk of rapid progression of CKD. The odds ratio was calculated (OR), 95% confidence intervals (95% CI), significance of differences (p).

For all types of analysis, results were considered statistically significant at $p < 0.05$.

Concept of RI_GFR. To assess the rate of progression of CKD in diabetes mellitus in a quantitative manner, the Department of Endocrinology and Geriatrics of Samara State Medical University proposed and developed the concept of reduction index in glomerular filtration rate[1] that is based on certain assumptions and has certain limitations in application. Firstly, it is assumed that the development of CKD in diabetes mellitus is irreversible and progressive; in a particular patient, the rate of progression of the pathology has a linear characteristic and is determined by a decrease in GFR with each year of the course of diabetes mellitus. Secondly, it is assumed that the duration of diabetes mellitus corresponds to the difference between the date of consultation and the date of registration of the patient with a verified diagnosis of diabetes mellitus. Moreover, in most real clinical situations, the diagnosis of diabetes is established much later than the pathogenetic processes associated with chronic hyperglycemia begin in the patient's body [4]. Thirdly, it is assumed that the initial GFR before the manifestation of diabetes in a particular patient was greater than or equal to 90 ml/min/1.73m^2.

Subject to the above conditions, the RI_GFR may be calculated as follows:

$$\textit{Reduction index of GFR (RI\_GFR)} = (90 - X) / \textit{number of years of diabetes,}$$

where X is the GFR value at the moment of consultation, 90 ml/min/1.73m^2 is the threshold value of the normal GFR.

Despite the fact that RI_GFR is a 'momentary' value, i.e. its calculation involves the GFR at a certain time in the course of progression of the diabetes, this parameter is a tool that allows us to give an objective quantitative characteristic of the rate of progression of CKD. The study of its associations with the parameters of the clinical status of patients allows identification of the factors that influence the dynamics of the pathological process.

RESULTS AND DISCUSSION

In the initial stages of the study, associations between clinical status indicators and RI_GFR were examined using correlation analysis [19]. Taking into account the identified relationships, an analysis of the significance of differences in parallel groups of different RI_GFR was performed with separation at the threshold value of 3.83 ml/min/1.73m^2 per year (upper quartile of the parameter distribution). While dividing the sample into groups of "Slow reduction of GFR" (RI_GFR ≤ 3.83 ml/min/1.73m^2 per year) and "Fast reduction of GFR" (RI_GFR > 3.83 ml/min/1.73m2 per year) certain parameters were found demonstrating significant ($p < 0.01$) differences: the patient's body mass index (BMI), glycaemia level as identified in the laboratory, duration of diabetes in years, amount of insulin received in units, amount of tabloid sulfonylurea drugs in per cent of

[1] Pervyshin N.A. A way to determine the progression rate of chronic kidney disease in patient with type 2 diabetes using the diagnostic index of reduction of glomerular filtration rate. Patent for invention No. 2810369. Application: 2023113094 dated 21.05.2023; registration date: 27.12.2023. Bulletin No. 26. https://www.fips.ru/cdfi/fips.dll/ru?ty=29&docid=2810369

Predictor	Degrees	OR, (95% CI)	P	b
Concomitant obesity	No/Yes	0,309 (0,104-0,915)	0,034*	-0,12
Duration of diabetes at the moment of consultation	Reference: 10+ years	1,00	1,000	0,00
	from 0 to 4.9 years / reference	110,00 (11,59-1043,94)	<0,001**	0,47
	from 5 to 9.9 years / reference	6,60 (1,21-36,10)	0,029*	0,12
Duration of insulin therapy	Reference: 5+ years	1,00	1,000	0,00
	from 0 to 4.9 years / reference	9,43 (1,99-44,59)	0,005**	0,22
Pulse of a. tibialis posterior	No/Yes	0,22 (0,06-0,84)	0,027*	-0,15
Severe stage of polyneuropathy	No/Yes	12,75 (1,03-157,14)	0,047*	-0,26
Sulfonylurea	No/Yes	4,82 (1,58-14,66)	0,006**	0,16
AH risk group IV	Yes / No	0,09 (0,02-0,45)	0,003**	-0,24
Number of anti-hypertension agents	1 agent / 2+ agents	0,19 (0,05-0,74)	0,016*	-0,16

*Notes. OR – odds ratio; CI – confidence interval; b – regression factor; p – variance significance; * – p < 0.05; ** – p < 0.01.*
*Примечания. ОШ – отношение шансов; ДИ – доверительный интервал; b – коэффициент регрессии; p – значимость различий; * – p < 0,05; ** – p < 0,01.*

Table 2. *The contribution of individual indicators of the clinical status to the rate of GFR decrease in the allocation of subgroups of nominal signs*

Таблица 2. *Вклад отдельных показателей клинического статуса в темп снижения СКФ при выделении подгрупп номинальных признаков*

Factor	Degrees	Score
Concomitant obesity	No	4
	Yes	2
Duration of diabetes at the moment of consultation	from 0 to 4.9 years	14
	from 5 to 9.9 years	8
	10+ years	4
Duration of insulin therapy	from 0 to 4.9 years	8
	5+ years	4
Pulse of a. tibialis posterior	No	4
	Yes	1
Severe stage of polyneuropathy	No	4
	Yes	9
Sulfonylurea	No	4
	Yes	7
AH risk group IV	No	4
	Yes	0
Number of anti-hypertension agents	1 agent	4
	2+ agents	1

Table 3. *Score values of the "Clinical calculator for the prognosis of rapid progression of CKD in elderly patients with type 2 diabetes"*

Таблица 3. *Значения баллов «Клинического калькулятора прогноза быстрого прогрессирования ХБП у пожилых пациентов с СД 2 типа»*

the maximum therapeutic dosage. The duration of the period during which the patient received insulin demonstrated an average level of significance ($p < 0.05$).

At the next stage, in order to determine the extent of influence of the identified clinical signs on the rate of decrease in GFR, a logistic regression analysis was performed. Evaluations were made of the odds ratio (OR), 95% of the confidence interval (95% CI), and their significance in the groups of fast and slow GFR reduction, which made it possible to identify diagnostically significant predictors of CKD progression in a cohort of senior patients with type 2 diabetes. These predictors included the following: minimum glycemic level in self-monitoring, duration of the diabetes, inclusion in group IV AH risk and treatment with sulfonylurea drugs (only the pharmacological class of the drug was considered without group specification), BMI, diagnosis of obesity, creatinine and glycaemia levels at admission, duration of insulin therapy, ankle artery pulse characteristics, treatment with calcium antagonists and complex AH treatment (with two or more anti-hypertension agents).

The logical continuation of the regression analysis was the development of a practical prognosis calculator to assess progress of CKD in senior patients with type 2 diabetes. For the sake of clarity and ease of use in clinical practice, quantitative variables are divided into subgroups of nominal features, one of which is taken as a reference (**Table 2**).

The selection of predictors for the calculator was carried out on the basis of a comprehensive assessment of clinical and statistical significance performed in the previous stages, taking into account the confounding effect (e.g., for the variables BMI ≥ 25 and the diagnosis of obesity). The numerical value of the points for each of the predictors was assigned taking into account the value of the regression coefficient (**Table 3**).

When determining the total score in a specific patient with type 2 diabetes, the obtained value corresponds to the personal risk of progression of CKD with RI_GFR > 3.83 ml/min/1.73m2 per year. The scale characteristics are as follows: limits from 20 (lower score) to 54 (upper score); with the condition of the binary prognosis function ('fast' or 'slow' progress of CKD) the cut-off score of 33 points is of significance; once it is exceeded, the risk of fast CKD progress is considered high.

To assess the diagnostic significance of the calculator, an analysis of the histogram of the distribution of outcomes depending on the total score was performed. (**Fig. 1**).

The analysis of the above diagram clearly demonstrates a clear division of groups of fast and slow progression of CKD at the level of the selected cut-off point.

In the assessment of the area under the ROC curve (AUC) the value of 0.89 (0.80; 0.99) $p < 0.001$ was obtained, which confirms the high diagnostic significance of the proposed calculator. The ratio of acceptable sensitivity parameters is associated with keeping a sufficiently high specificity, which forms a characteristic step shape of the curve (**Fig. 2**).

The parameters of the classification matrix of the calculator at the total score of 33 follow in **Table 4**.

The number of correctly identified patients with a high risk of CKD progression among senior patients with the true value of RI_GFR > 3.83 ml/min/1.73m^2 per year was 17 out of 21 (Se = 81%); the number of patients with the truly high RI_GFR among all predicted with the model was 17 out of 22 (positive predictive value, PPV = 77%). The number of correctly identified negative results (RI_GFR ≤ 3.83 ml/min/1.73m^2) was 53 out of 58 (Sp = 91%); the number of patients with the truly low RI_GFR among all predicted with the model was 53 out of 57 (negative predictive value, NPV = 93%). The accuracy of the mathematical model of the calculator was 89%.

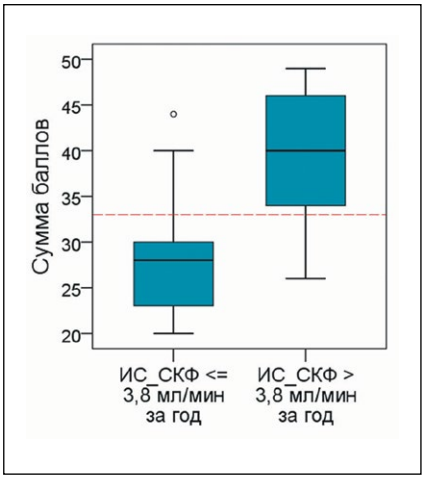

Figure 1. *Histogram of the distribution of outcomes from the GFR_RI with a threshold value.*

Рисунок 1. *Гистограмма распределения исходов ИС_СКФ с пороговым значением.*

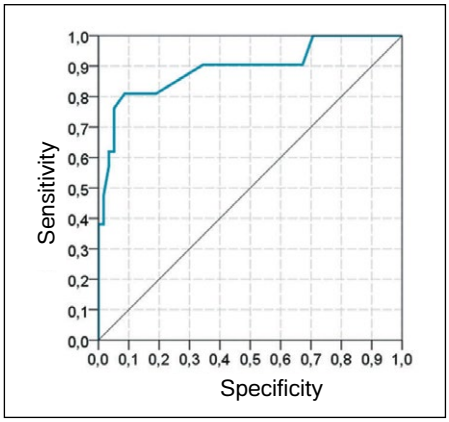

Figure 2. *The characteristic (ROC) curve of the "Clinical calculator for the prognosis of rapid progression of CKD in elderly patients with type 2 diabetes".*

Рисунок 2. *Характеристическая (ROC) кривая «Клинического калькулятора прогноза быстрого прогрессирования ХБП у пожилых пациентов с СД 2 типа».*

Figure 3. *QR code of the "Clinical calculator for the prognosis of rapid progression of CKD in elderly patients with type 2 diabetes".*

Рисунок 3. *QR-код «Клинического калькулятора прогноза быстрого прогрессирования ХБП у пожилых пациентов с СД 2 типа».*

The calculator is written in JavaScript, HTML, and CSS; the size of the program code is 13.7 kilobytes. There are no specific requirements as to hardware and software; the program is functional on any personal computer or mobile device with any installed web browser (Google Chrome, Yandex, etc.) running on any supported operating system. The computer program is available for doctors at the following URL

https://кафэндгер.рф/Клинические_калькуляторы/Геронтология/Риск_быстрого_прогрессирования_ХБП/QR-код.png or QR code (**Fig. 3**).

The calculator accuracy is determined by testing against clinical cases from routine laboratory practice. A random patient was selected from the general sample of XXX1949, age: 73, concomitant diagnosis: obesity (BMI 34 kg/m^2) (2 points), duration of diabetes: 7 years (8 points), no insulin therapy (8 points), preserved pulse on ankle artery (1 point), no severe manifestations of diabetic polyneuropathy (4 points), receiving therapy with sulphonyl urea agents (7 points), no high risk of hypertension (4 points), receiving complex antihypertension therapy with agents of two different classes (1 point). The total score for the patient was 35 points allowing for a poor prognosis of CKD with RI_GFR over 3.83 ml/min/1.73м^2 per year.

The applied use of the calculator in everyday clinical practice is possible in two variants. In the first scenario of a conventional patient admission, when the consultation protocol is filled out on paper, the doctor may enter the values of eight independent initial indicators into any personal computer or mobile phone with the installed program and clarify the risk of a high rate of progression of CKD in the patient. In the second scenario, when clinical work involves digital tools (e.g. ARME 2.0 software suite developed at the department of endocrinology and geriatrics of SSMU), the patient's initial medical data is stored and systematized in electronic form at the moment of admission. Since all independent variables used in the calculator are included in the standard of dispensary observation of a patient with diabetes, no additional work time is required from the doctor to enter specific parameters. In this case, the calculator determines the risk of rapid progression of CKD automatically and displays prompts for determining the regulations for dispensary observation and forming a trajectory of pharmacological treatment.

		Predicted RI_GFR		% of true values
		RI_GFR ≤ 3.83 ml/min/1.73m^2 per year	RI_GFR > 3.83 ml/min/1.73m^2 per year	
Observed RI_GFR	RI_GFR ≤ 3,83 ml/min/1.73m^2 per year	53	5	Sp=91%
	RI_GFR > 3.83 ml/min/1.73m^2 per year	4	17	Se=81%
Total, %		NPV=93%	PPV=77%	89%

Table 4. *Classification matrix of the "Clinical calculator for the prognosis of rapid progression of CKD in elderly patients with type 2 diabetes"*

Таблица 4. *Матрица классификации «Клинического калькулятора прогноза быстрого прогрессирования ХБП у пожилых пациентов с СД 2 типа»*

CONCLUSIONS

1. The registry study allowed an evaluation of the complex influence of multiple comorbid factors on the progression of CKD in old age in patients with type 2 diabetes, and provided a more detailed and accurate understanding of the patterns of development of diabetic kidney disease associated with age.

2. The use of a prognostic calculator for rapid progression of CKD in elderly patients with type 2 diabetes in a routine outpatient setting allows the physician to identify patients at risk of a high rate of decline in GFR, which is important for optimizing dispensary monitoring measures and timely prescription of medications with proven nephroprotective properties.

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Источник финансирования. Работа выполнена по инициативе авторов без привлечения финансирования.	***Study funding.*** The study was the authors' initiative without external funding.
Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с содержанием настоящей статьи.	***Conflict of Interest.*** The authors declare that there are no obvious or potential conflicts of interest associated with the content of this article.
Участие авторов. Первышин Н.А. – идея, дизайн исследования, сбор материала, статистический анализ. Булгакова С.В., Василькова О.Н., Лебедева Е.А. – общая концепция, обсуждение и клиническое обоснование результатов. Галкин Р.А. – обсуждение и клиническое обоснование результатов, формулировка выводов. Чертищева А.А. – обработка первичного клинического материала, написание текста. Все авторы одобрили финальную версию статьи перед публикацией, выразили согласие нести ответственность за все аспекты работы, подразумевающую надлежащее изучение и решение вопросов, связанных с точностью или добросовестностью любой части работы.	***Contribution of individual authors.*** Pervyshin N.A. – idea, research design, material collection, statistical analysis. Bulgakova S.V., Lebedeva E.A., Vasilkova V.N. – general concept, discussion and clinical justification of the results. Galkin R.A. – discussion and clinical justification of the results, formulation of conclusions. Chertischeva A.A. – processing of primary clinical material, writing the text. All authors gave their final approval of the manuscript for submission, and agreed to be accountable for all aspects of the work, implying proper study and resolution of issues related to the accuracy or integrity of any part of the work.

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