



## CLINICAL PHARMACOLOGICAL APPROACH TO RATIONAL TREATMENT OF ISCHEMIC HEART DISEASE

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### ABSTRACT

*A cross-sectional pharmacoepidemiological study was performed at an outpatient clinic in Moscow. A total of 805 patients (mean age 68.9±9.9 years, 51.4% men) with a diagnosis of stable coronary heart disease were included. Demographic, medical history, and pharmacotherapy data were recorded. Physician adherence was assessed based on the degree of compliance of actually prescribed medication with the main provisions of clinical guidelines (class I). A pharmacotherapeutic index of compliance with clinical guidelines (PICCG) was proposed, calculated using the all-or-nothing approach and taking into account contraindications. To analyze adherence predictors, the patient population was divided into two groups based on the PICCG assessment.*

### INTRODUCTION

In the conditions of outpatient clinical practice of managing patients with stable coronary heart disease (CHD), drug prescriptions do not always correspond to the principles of modern clinical guidelines (CG). The global nature of this problem was first determined at the end of the last century based on the first results of a number of large pharmacoepidemiological studies (EU- ROASPIRE I-II [1], ATP Survey [2], etc.). The assessment of the results of the first two stages of the EUROASPIRE project by European experts was indicative - "collective failure of medical practice", which does not even need translation. However, in recent years, not only in Europe and the USA, but also in our country, certain successes have been achieved in solving the problem of introducing the principles of evidence-based cardiology into clinical practice [3-5].

### MATERIALS AND METHODS

The study was conducted at a large outpatient clinic in Moscow as a pharmacoepidemiological cross-sectional study. The object of the study was 2000 randomly selected outpatient cards of cardiac patients for 2023. The analysis included the documentation of 805 patients in accordance with the following inclusion criteria: age over 30



years, verified stable coronary heart disease, no participation in a clinical trial. Demographic and medical history data, as well as pharmacotherapy prescribed to patients by cardiologists were subject to registration. Information from the medical documentation was transferred to an individual patient registration card. The database was formed in MS Excel.

Physicians' adherence to drug treatment of stable coronary heart disease was analyzed within the framework of the CGs that were relevant at the time of the study [1]. The assessment was based on the principles of evidence-based medicine, reflecting the class of recommendations and the level of evidence (class I, levels A and B). In accordance with this postulate, a pharmacotherapeutic index of compliance with clinical recommendations (PICCR) was proposed, in the calculation of which 1 point was awarded for the prescription of each pharmacological group of class I and level A/B. In the CR, the following groups of drugs are of key importance: beta-blockers (BB) and/or calcium channel blockers (CCB), antiplatelet drugs (acetylsalicylic acid [ASA] or clopidogrel) and/or oral anticoagulants (OAC; with concomitant atrial fibrillation), statins and/or ezetimibe, angiotensin-converting enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARB; with a history of myocardial infarction [MI]). Adherence was assessed according to the "all or nothing" approach [2].

## RESULTS AND DISCUSSION

Statistical data processing was performed using IBM SPSS Statistics 16.0. Quantitative variables were described using the following parameters: mean (M), standard deviation (SD) or median (Me), and interquartile range (Q1; Q3). Qualitative variables were described by absolute and relative (in percent) frequency of accepting each of the possible values. The statistical significance of differences between groups was tested using standard statistical criteria (all criteria were two-sided). For quantitative variables with a distribution close to normal, Student's t-test for two independent samples was used; for quantitative variables with a distribution different from normal - Mann-Whitney U-test; to test the normality of distribution - Kolmogorov-Smirnov test; for qualitative variables - Pearson's 2 criterion. Multivariate analysis of physicians' adherence to CR was conducted using the logistic regression method. The significance level for all statistical criteria used was  $p < 0.05$ .

According to the World Health Organization, "any quality assurance system for medical care should have in its arsenal measures aimed at the rational use of drugs, scientifically based mechanisms for the implementation of the main provisions of the CG for the management of patients with various nosologies, as well as tools for regular supervision (audit) of the activities carried out in this regard" [2]. In other words, assessing the quality of drug treatment actually carried out in practice requires the creation of simple methods that can be used in the conditions of a specific medical institution. One of the options, which has already received recognition in world practice, is the use of complex indicators (indices) reflecting the compliance of the actual pharmacological treatment with the provisions of the CG, primarily with respect to drugs that must be prescribed in a particular clinical situation (class I recommendations). The composite performance score in several modifications is used as a key quality indicator in the American Heart Association program aimed at optimizing pharmacotherapy for patients who have had an MI - "Get With The Guidelines (GWTG)" [3].

Taking into account the above-described experience, FISKR was proposed for a comprehensive assessment of the compliance of drug prescriptions with the principles of



evidence-based pharmacotherapy for stable coronary artery disease. According to the assessment of physicians' adherence using FISKR, the general population of patients was divided into two groups. Group 1 (n=667; 82.9%) included patients who received pharmacotherapy in full compliance with the CG, and group 2 (n=138; 17.1%) included patients who were prescribed pharmacological treatment with deviations from the CG. Further, in order to find factors that could influence physicians' adherence to the CG, these groups were compared according to demographic and anamnestic characteristics.

It was found that the average age of patients receiving treatment in full compliance with the CG was lower ( $p=0.05$ ), but the gender difference was not statistically significant (although the number of female patients whose prescriptions corresponded to the CG was higher in absolute figures). The comparison results revealed a statistically significantly higher number of patients with stable angina, arterial hypertension (AH) and dyslipidemia in the group of patients receiving treatment in accordance with the CG. In turn, the proportion of patients with a history of MI in this group was lower. The next step of the scientific search was the selection of a number of variables for input into the multivariate analysis and the formation of a model of the influence of patient characteristics on the implementation of the CG. In this regard, it seemed appropriate to turn to similar studies that have already been conducted for a more accurate hypothesis construction.

In a recent review, C.J.G.M. Hoorn et al. attempted to systematize the results of studies conducted by 2023 on factors associated with higher or lower adherence to CR by physicians in real clinical practice of managing patients with cardiovascular pathology. Female gender and older age were identified as the main factors reducing the likelihood of high adherence to CR on the part of patients [2]. A similar effect of age on the degree of CR compliance was shown directly in the population of patients with coronary heart disease [3]. In turn, in the Swedish SWEDEHEART registry, age was not a significant factor, but female gender was associated with a lower frequency of prescribing the necessary preventive medications throughout the entire observation period [4].

Such a factor as the presence of stable angina in the patient lost its effect in the multivariate analysis. Among the factors that showed a significant impact on the degree of compliance of physicians with CR prescriptions, first of all, it is worth highlighting the patient's age: with its increase by 1 year, the chances of high physician adherence decrease by 3% ( $p = 0.009$ ). Similar data were obtained in a retrospective analysis of Canadian researchers who studied the features of prescribing prophylactic drugs to patients after MI (n = 8706). The odds ratio (OR) for an increase in age by 1 year was 0.98 (95% confidence interval [CI] 0.97-0.99) for BB; 0.97 (95% CI 0.97-0.98) for ACE inhibitors and ARBs; 0.94 (95% CI 0.93-0.95) for statins [5]. In the above-mentioned study by American authors, patient age was also a significant predictor of high adherence of specialists to the CR, assessed by a composite indicator (OR 0.93; 95% CI 0.91-0.94;  $p<0.0001$ ) [2]. A possible explanation may be that younger patients, as a rule, have fewer comorbidities, thereby facilitating the doctor's task in terms of more precise implementation of the CR. In addition, a higher risk of developing adverse reactions in elderly patients may also be a reason for deviation from the CR.



Among the anamnestic characteristics that positively influenced physicians' adherence to CR in our study were hypertension, dyslipidemia, CHF, and revascularization, the presence of which in a patient increased the chances of a high degree of physician compliance with CR by 3.89, 2.31, 1.95, and 2.14 times, respectively. Again referring to the results of the analysis by D.J. Kumbhani et al., we note hypertension (OR 1.08; 95% CI 1.04-1.12;  $p < 0.0001$ ) and dyslipidemia (OR 1.27; 95% CI 1.23-1.32;  $p < 0.0001$ ) as predictors of physician compliance with CR prescriptions.

## CONCLUSION

In outpatient practice, the level of adherence of cardiologists to the CG for drug treatment of stable coronary artery disease was satisfactory, amounting to 82.9% as assessed using the FISKR. Patient age was a significant independent factor influencing the degree of CG compliance. The presence of hypertension, CHF, dyslipidemia and revascularization in the patient's history increased the likelihood of high pharmacotherapeutic adherence of specialists, while a history of myocardial infarction, on the contrary, was associated with lower adherence of doctors. Identification of various factors influencing the degree of compliance with the main provisions of the CG should contribute to a more targeted development of measures and strategies for further improving the quality of pharmacological treatment of stable coronary artery disease in primary care.

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