Adherence to Medical Treatment in Elderly Patients with Coronary Artery Disease in the Settings of Primary Outpatient Care

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Aim. To study medication adherence in elderly patients with coronary artery disease (CAD) in primary care practice.

Material and methods. The study conducted in out-patient clinic of Moscow city. 293 elderly (⩾65 years) patients with established CAD included. The following patient data obtained via electronic medical record system: demography, medical history, modifiable risk factors and prescribed pharmacotherapy. Level of medication adherence measured by Morisky scale (MMAS-8) via telephone survey.

Results. According to Morisky scale high adherence was identified in 146 (49.8%) elderly patients, moderate adherence – in 99 (33.8%) patients, low adherence – in 48 (16.4%) patients. Analysis of specific questions of the scale done in non-adherent patients revealed signs of unintentional non-adherence due to forgetfulness (45.9%) and signs of intentional non-adherence due to patients feeling worse (35.8%) or better (28.4%). By means of dichotomic interpretation of Morisky scale results the population under research was divided into two groups: 147 (50.2%) non-adherent patients and 146 (49.8%) – totally adherent patients. These groups were comparable in terms of sex (female 71.2 vs 68.0%; p>0.05) and age (median 73.5 vs 73.0 years; p>0.05) distribution, and medical history: myocardial infarction (39.0% vs 38.8%), atrial fibrillation (37.0 and 41.5%), chronic heart failure (90.4% vs 91.2%), diabetes (26.7% vs 24.5%). There were fewer smokers in adherent group (0.7% vs 6.5%; p<0.05). As primary antianginal pharmacotherapy adherent and non-adherent patients were equally prescribed beta-blockers (75.3% vs 75.5%; p>0.05). Drugs that improve prognosis were also prescribed comparably: antiplatelets (66.4% vs 61.9%; p>0.05), anticoagulants (36.3% vs 44.9%; p>0.05), statins (82.2% vs 79.6%; p>0.05), renin-angiotensin system inhibitors (89.0 and 87.8%; p>0.05). Adherent patients had lower mean values of lipids: total cholesterol (4.7±1.2 vs 5.2±1.4 mmol/l; p<0.05) and low density cholesterol (2.4±0.9 vs 2.8±1.2 mmol/l; p<0.05). Non-adherent elderly patients made more visits to general practitioner (median 5 vs 3 visits; p<0.05). Share of patients receiving drugs within supplementary pharmaceutical provision program was comparable in both groups (53.7% vs 50.7%; p>0.05).

Conclusion. Half of elderly patients with CAD are non-adherent to treatment in primary care setting. Medical history and structure of pharmacotherapy do not influence level of adherence in this population. Among adherent patients fewer individuals smoke and mean values of lipids are lower. Non-adherent elderly patients cause higher load on general practitioner, supplementary pharmaceutical provision program provided no better adherence in the population under research.

Keywords: ischemic heart disease, medication adherence, elderly patients.

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Actuality

Despite significant progress in the research of cardiovascular diseases (CVDs) cardiovascular mortality rates in the Russian Federation (RF) continue to be ones of the highest in Europe. In 2017 cardiovascular mortality rates amounted to 150 cases per 100,000 of the population in the USA and Europe and 550 cases per 100,000 in Russia with coronary artery disease (CAD) being the most frequent reason [1,2].

Increase in the share of elderly and senile-aged persons in population along with the life expectancy prolongation was noted as far back as the second half of the 20th century. CVD prevalence is increased steadily together with population aging, that is why the problem of the management of elderly patients with cardiovascular pathology is especially actual [3].

More than a half of all hospitalizations due to CVDs can be attributed to patients aged 65 years and older, these diseases are also the main cause of disability and the quality of life deterioration in such category of patients [4].

Majority of guidelines for stable CHD treatment in the patients of elderly and especially senile ages are based on the data received in randomized controlled studies dealt with younger patients, however the profit of medical treatment and the importance of low-density lipoprotein cholesterol (LDL-C) and blood pressure target levels achievement in old patients is out of question among experts [5].

When speaking of pharmacotherapy efficacy one has to consider such important item as the patients' adherence to treatment. In accordance with the World Health Organization data the patients' adherence to long-term treatment is amount to 50% in developed countries while it is significantly lower in developing states [6]. Many foreign studies have demonstrated the medication adherence in elderly CAD patients to be in average of 30-50% [7-11]. Age by itself is not as a rule a predictor for low adherence, however old patients have more factors to its development, such as: comorbidities, large number of drugs with difficult regimens of their intake, adverse reactions, cognitive, amnestic and depressive disorders, inadequate social assistance and some other factors [10-13]. At that low adherence to the prescribed treatment is closely related to poor clinical outcomes and higher treatment expenses for elderly patients with CAD [10,14-16].

The treatment adherence of patients with CVD is below the desired level and this problem is generally underestimated [17]. There is the obvious deficiency of the factual data concerning levels of the adherence to treatment among the patients of elderly and senile ages. Lack of such information makes it difficult to develop and implement effective measures aimed at the improvement of existing situation.

It should be noted that the problem of the treatment adherence has already drawn attention of the leading domestic experts. In particular, the guidelines of the Ministry of Health of the RF devoted to the medical treatment of the elderly and senile patients suggest the "7 steps" algorithm, which includes the obligatory estimation of the risk for low adherence in such patients [18]. Necessity of the detecting of the patients with low adherence in out-patient practice was also underlined in other domestic guidelines [19,20].

So, assessment of the real prevalence of poor treatment adherence among elderly patients along with disclosure of the factors influencing adherence are of great actuality. The aim of our study was to evaluate the adherence to medical treatment in elderly patients with CAD in the out-patient care settings.

Material and methods

The study was conducted in a large out-patient medical-and-preventive health care center of Moscow, it was a part of a retrospective-prospective program of pharmacoepidemiological trials aimed at the improvement of CAD treatment quality including the enhancing of patients' adherence at the primary level of medical care.

At the first step of the study we have performed the retrospective collection of the data from randomly selected medical records, allocated in the digital form in the EMIAS unified database, of the out-patients with the diagnosis of CAD followed-up by a cardiologist of the health care center (leading center and four affiliated branches).

Inclusion criteria were the age ⩾65 years [21] and verified stable CAD. Exclusion criteria were the follows: acute coronary syndrome and/or revascu-

larization during the last 6 months, participation in other clinical research. Taking into account these criteria we have selected 580 medical charts of elderly patients with CAD.

At the first stage we studied a case history, available clinical data, laboratory tests results (lipid profile, glycemic status), concomitant diseases (dislipidemy, diabetes mellitus, chronic kidney disease) and a history of revascularization. The behavioral risk factors of CVD were fixed if they were noted in medical records (smoking status, physical activity and dietary habits). We also registered the medical treatment prescribed to elderly patients by cardiologists of the health care center and receiving drugs within the supplementary pharmaceutical provision (SPP) program.

At the second stage we estimated the adherence of the patients to the prescribed treatment (no later than within 3 months from the including in the study). A validated questionnaire - the Morisky Green Adherence Scale (an 8-item version) was used for the assessment of the patients' adherence. The interrogation of the patients was conducted by phone. It should be noted that estimation of the CVD patients' adherence with the help of different questionnaires (scales) is widely distributed abroad as a simple, convenient and rather reliable method [22,23]. The widely used 4- and 8-item versions of the Morisky Green Medication Adherence Scale (MMAS-4 and MMAS-8), which was primarily developed and validated for hypertensive patients, are ones of such questionnaires. The 8-item version of the Morisky scale is characterized by higher validation in comparison with the 4-item one: reliability (described by the Cronbach's alpha coefficient) α=0.83 vs 0.61, sensitivity = 0.93 vs 0.81, specificity = 0.53 vs 0.44; it also keeps high correlation with the validation criteria [24,25]. Series of studies have demonstrated the maintenance of universality along with significant increase in the sensitivity of the 8-item Morisky scale [26].

In accordance with the second stage results a total of 293 patients who had completely answered the scale questions were selected. The patients' answers on the Morisky questionnaire were appraised by the standard method: each question of the scale supposed an answer in the "YES" (0 points)/"NO" (1 point) format, except for the 5th question which appraised inversely and also for the 8th question which had the form of the Likert scale and was only appraised by 1 score point in the case of the answer "NEVER". The adherence to treatment was estimated by the scores summation and was considered low at the score of <6, mean at the score of 6-7 and high at the score of 8. We also used a simplified Morisky scale: a patient was considered adherent at the score of 8 and non-adherent at the score of less than 8 [27].

The information was then transferred from medical documents and questionnaires to individual registration cards. To anonymize personal data each patient was assigned a three-figure number, the data were further recorded in electronic database. Statistical treatment was performed with the help of statistical libraries SciPy 0.13.3 and NumPy 1.8.2 for Python 3.4 (Python Software Foundation, Delware, USA). Each continuous quantity was characterized by mean (M) and standard deviation (SD) or median (Me) and interquartile range (25%; 75%) according to the type of distribution. The hypothesis of normal distribution was verified using the Shapiro-Wilk test. The statistical significance of differences between the two groups was checked by the Student t-test and the nonparametric Mann-Whitney U-test. To verify the hypothesis of the equality of the mean values of the studied parameters in several groups the Kruskal-Wallis H-test was used. Qualitative variables were estimated by the Pearson χ^2 test and by the calculation of p-levels of significance. Distinctions were considered significant at $p<0.05$.

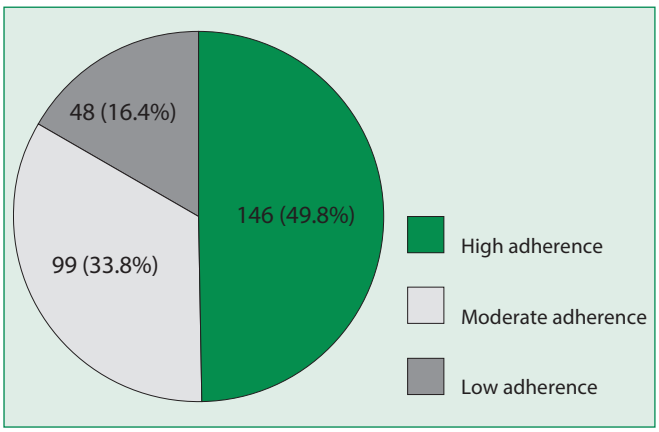

Figure 1. Levels of adherence to pharmacotherapy in interviewed elderly patients with ischemic heart disease

Results and discussion

The total of 293 elderly patients with verified stable CAD, who had answered all questions of the Morisky-Green scale (the 8-item version), were enrolled in the final analysis. The inquiry results are presented in Figure 1. In accordance with the Ju.V. Lukina et al. data 40.8% of 130 CVD patients from the out-patient register "PROFIL", who had been tested by the Morisky-Green 8-item scale, were found to be highly adherent, 36,9% revealed moderate level of adherence and 22.3% were poorly adherent to treatment [28]. It should be however noted that the population was differed from that one in our study by a number of characteristics, first of all by age and medical history.

The detailed analysis of answers to some MMAS-8 questions revealed the signs of unintentional non-adherence caused by forgetfulness which is no wonder taking into account the characteristics of the studied population (Fig.2). However, rather big part of the patients had also demonstrated intentional medication non-adherence. In particular, 35.8% and 28.4% of the respondents were inclined to self-contained withdrawal or change of a prescribed drug dose in the cases of the improvement or deterioration of health state, respectively. 36.5% of the patients were discontent with a dose regimen. Authors of the "PROFIL" register also reported that 23.5% and 23.6% of the patients, respectively, were inclined to change the dosage regimen at the improvement or deterioration of health state [28].

For further analysis the binary algorithm of the Morisky scale results interpretation was used: patients with low and middle levels of adherence were clustered in one group of non-adherent patients. So, in accordance with the dichotomic interpretation of the scale results 147 (50.2%) persons were classified as non-adherent to medical treatment and 146 (49.8%) – as absolutely adherent. Our results are partly corresponded with the T.V. Fovanova et al. data, who had demonstrated that 61.1% of patients with arterial hypertension and CAD, examined in Moscow out-patient clinics, revealed poor adherence to prescribed treatment (score ⩽3 by the 4-item Morisky scale) [29]. However, this study dealt with the younger patients' population and only half of the patients had CAD.

It is interesting that 50% of the non-adherent patients had gained 7 score points, that is to say had stopped within a step from high adherence. What had prevented these patients from such a step? In accordance with the data presented in Figure 3 the main fault lies in intentional non-adherence.

This finding deserves attention, as it indicates what measures for the enhancing of adherence must be firstly focused at. Many foreign researchers underline

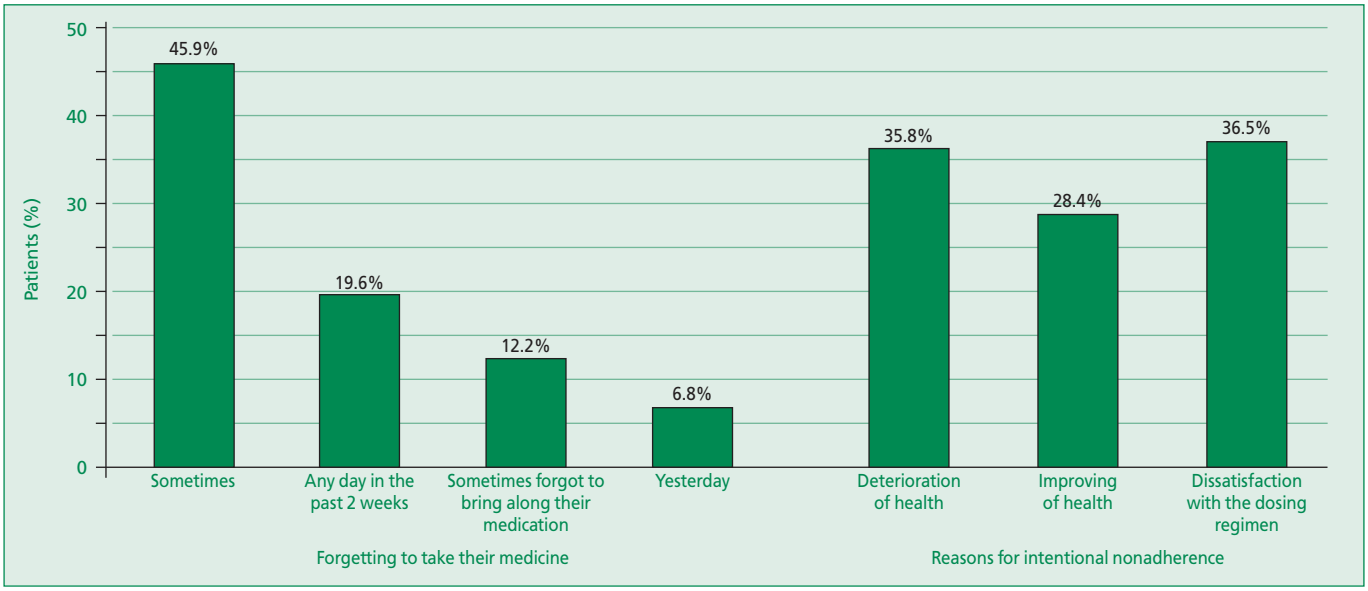

Figure 2. The proportion of patients' negative responses to the questions of the Morisky scale about forgetfulness and intentional nonadherence (n=293)

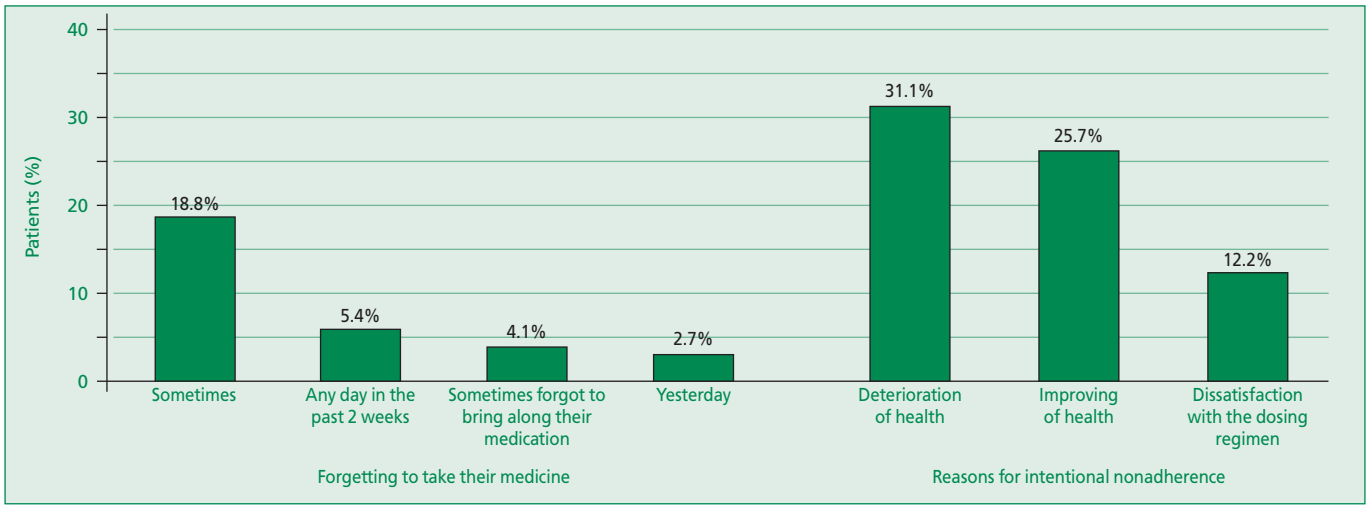

Figure 3. The proportion of negative responses from patients with 7 points for the Morisky-Green scale (n=74)

importance of the analysis of reasons for low adherence in the elderly population for the more feasible choice of interventions such as educational programs aimed at the intentional non-adherence correction and changing of behavioral factors which lead to unintentional non-adherence [10].

In the foreign literature non-adherence risk factors associated with patients are well-studied. However there is no consensus on this question. Among risk factors for poor adherence authors mark off young age, male sex, low income, desolation, smoking, depression and others [30].

In our study the groups of adherent and non-adherent patients were comparable by the principal demographic and anamnestic characteristics (Table 1). The share of men was slightly higher in the group of non-adherent patients (32.0% vs 28.8%, p>0.05). Both mean age and the share of senile-aged patients (75 years and older) were similar. The groups were also comparable by the predominant comorbidities.

Unfortunately it was difficult to analyze behavioral risk factors in adherent and non-adherent patients due to the lack of such information in medical documents. An exception to this was the smoking status, which was incidentally noted in medical charts. This allowed to reveal that the share of smokers was 10-time higher in the group of non-adherent old patients (6.5% vs 0.7%; p=0.006).

One of the important aspects of adherence is the quality of prescribed medical treatment. Some domestic researchers suppose take this into account in dealing with the problem [31]. Thus, the next step of our study was to analyze the medical treatment prescribed to elderly patients with CAD. Adherent and non-adherent patients were compared by the prescription rates of the drugs used in CAD treatment. Table 2 lists drugs of the first line which have antianginal action (beta-blockers and calcium antagonists) and also drug groups which are used for cardiovascular events prevention (antiplatelet agents and anticoagulants, statins, angiotensin-converting-enzyme inhibitors (ACEi) and angiotensin-2 receptor antagonists (ARA). Incidence of fixed drug combinations prescription was also analyzed.

The positive fact was that almost all the patients were prescribed preparations influencing the hemostasis system. The anticoagulant prescription rate correlated with a number of patients with atrial fibrillation. Other patients were prescribed antiplatelet agents. The lipid-lowering therapy (statins) was only prescribed in 80.9% of the patients (n=237) with no statistically significant difference in the prescription rates between the groups of adherent and non-adherent patients. The renin-angiotensin-aldosterone system inhibitors were mentioned in 88.4% of doctors' recommendations (n=259): the shares of ACEi and ARA were amounted to 43.0% (n=126) and 45.4% (n=133), respectively; yet sartans up to date have no solid evidential base concerning CAD prognosis. The incidence rates of both drug groups prescription were not differed in the studied populations.

Table 1. Main demographic and anamnestic characteristics of adherent and non-adherent to pharmacotherapy in elderly patients with coronary artery disease

Parameter	Adherent (n=146)	Non-adherent (n=147)
Men, n (%)	42 (28.8)	47 (32.0)
Age, years	73.5 (70; 79)	73 (70; 81)
Age ⩾75 years, n (%)	66 (45.2)	68 (46.3)
Arterial hypertension, n (%)	138 (94.5)	139 (94.6)
History of myocardial infarction, n (%)	57 (39.0)	57 (38.8)
Stable angina pectoris, n (%)	110 (75.0)	112 (76.2)
Chronic heart failure, n (%)	132 (90.4)	134 (91.2)
Diabetes mellitus, n (%)	39 (26.7)	36 (24.5)
Dyslipidemia, n (%)	23 (15.8)	23 (15.7)
Chronic kidney disease, n (%)	35 (24.0)	25 (17.0)
Atrial fibrillation, n (%)	54 (37.0)	61 (41.5)
Bronchial asthma/COPD, n (%)	12 (4.1)	10 (3.4)

Data are presented as Me (25%;75%), unless noted otherwise
p>0,05 for all intergroup comparisons
COPD – chronic obstructive pulmonary disease

Table 2. Frequency of prescription of the main groups of cardiovascular drugs in in adherent and non-adherent elderly patients with coronary artery disease

Parameter	Adherent (n=146)	Non-adherent (n=147)
Antiplatelet agents, n (%)	97 (66.4)	91 (61.9)
Anticoagulants, n (%)	53 (36.3)	66 (44.9)
Statins, n (%)	120 (82.2)	117 (79.6)
ACEi/ARA, n (%)	130 (89.0)	129 (87.8)
• ACEi, n (%)	67 (45.9)	59 (40.1)
• ARA, n (%)	63 (43.2)	70 (47.6)
Beta-blockers, n (%)	110 (75.3)	111 (75.5)
Nondihydropyridine calcium blockers, n (%)	5 (3.4)	3 (2.0)
Dihydropyridine calcium blockers, n (%)	65 (44.5)	69 (46.9)
Fixed drug combinations, n (%)	19 (13.0)	12 (8.2)

p>0.05 for all intergroup comparisons

ACEi – angiotensin-converting-enzyme inhibitors, ARA – angiotensin II receptor blockers

Beta-adrenoblockers were reasonably the first in line in antianginal pharmacotherapy (75.4%, n=221), while calcium antagonists causing bradycardia were prescribed in 2.7% of the cases (n=8). Dihydropyridines in their turn were recommended to 45.7% of the patients (n=134). The ratio of the prescribed drug groups was kept in almost equivalent proportions in the adherent and non-adherent patients.

Fixed drug combination prescription is one of the ways to raise adherence. Unfortunately, incidence of such prescriptions in the studied population was only 10.6% (n=31). It was lower in the group of non-adherent patients but we have revealed no statistically significant distinctions.

It is remarkable that adherent patients more often underwent coronary artery bypass graft (CABG) surgery – 8.2% vs 2.7% (p=0.019), there were no such distinctions in the case of percutaneous coronary intervention (PCI) (30.8% vs 32.0%; p=0.416). This finding may possibly be explained by the more severity of CABG surgery which makes patients pay more attention to treatment.

So, the presented data concerning demographic characteristics, medical history and the structure of medical treatment of adherent and non-adherent elderly patients testifies to the comparability of the groups. This allows to reasonably evaluate the results of the patients' treatment as a next step of the study. In this connection we had studied the results of a number of instrumental and laboratory examinations of adherent and non-adherent patients to analyze modifiable physiological and biochemical risk factors (Table 3).

Patients of both groups were in general overweight. We had not found any significant distinctions in the systolic and diastolic blood pressure values; however, this may be explained by more scrutinous fulfillment of recommendations before a visit to cardiologist, which definitely influences these parameters [32].

Concerning biochemical risk factors the studied population was consistent by the levels of glycated hemoglobin, fasting plasma glucose and some indices of plasma lipid profile (triglycerides, HDL-C). However, the levels of total cholesterol (TC) and LDL-C were significantly higher in the group of non-adherent patients as compared to adherent ones.

At the final stage of our study we estimated a number of cardiologist and general practitioner appointments by elderly patients during 12 months

Table 3. Modifiable risk factors in adherent and non-adherent elderly patients with coronary artery disease

Parameter	Adherent (n=146)	Non-adherent (n=147)
Body mass index, kg/m^2	29.6±4.9	29.2±4.7
CBP, mm Hg	136.1±16.7	135.4±19.2
DBP, mm Hg	79.1±8.9	77.9±10.1
TC, mmol/l	4.7±1.2	5.2±1.4*
LDL-C, mmol/l	2.4±0.9	2.8±1.2*
Triglycerides, mmol/l	1.5±0.9	1.5±0.8
HDL-C, mmol/l	1.4±0.3	1.4±0.3
Glicated hemoglobin, %	6.9±1.3	6.8±0.9
Fasting plasma glucose, mmol/l	6.4±2.6	6.1±1.6

Data are presented as M±SD

*p<0.05 in comparison with the group of adherent patients

SBP – systolic blood pressure, DBP – diastolic blood pressure, TC – total cholesterol, LDL-C – low-density lipoprotein cholesterol, HDL-C – high-density lipoprotein cholesterol

Table 4. Use of resources of the health care system in primary outpatient care in in adherent and non-adherent elderly patients with coronary artery disease

Parameter	Adherent (n=146)	Non-adherent (n=147)
Cardiologist appointments, n	3 (2; 6.75)	3 (2; 6)
General practitioner appointments, n	3 (1; 8)	5 (2; 9)*
ADS, n (%)	74 (50.7)	79 (53.7%)

Data are presented as Me (25%; 75%), unless noted otherwise

*p<0.05 in comparison with the group of adherent patients

and also the participation in the supplementary pharmaceutical provision (SPP) program. (Table 4).

The patients of both groups were revealed to visit cardiologist equally as often, which was possibly explained by the comparable severity of heart diseases. Non-adherent patients attended general practitioner more often than adherent ones. It was also found out that SPP did not increase adherence in out-patients with heart diseases, which is in line with the Fofanova et al results [29].

Conclusion

50.2% of out-patients with CAD are not adherent to medical treatment. Predominant comorbidities and the structure of drugs prescription within CAD medical treatment did not influence elderly patients' adherence in out-patients settings. A number of smokers and patients with increased levels of TC and LDL-C was higher among non-adherent elderly patients with CAD. Non-adherent patients less often underwent the CABG surgery. Non-adherent elderly patients had to more often visit general practitioner. The presence of recommended drugs in the list of supplementary pharmaceutical provision did not increase adherence in the studied population.

Relationships and Activities: none.

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