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Research Article

Critical aspects of the management of stable coronary artery disease in primary care practice or how to increase the efficacy of evidence-based pharmacological therapy?

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Abstract

Introduction: The publication describes a fragment of the pharmacoepidemiologic study conducted to review the quality of management of patients with stable coronary artery disease (SCAD) in primary care over a 12-year period. The aim of the study was to justify the application of standard operating procedures (SOPs). Such determinants of pharmacotherapy as non-pharmacological modification of cardiovascular risk factors (RFs) and medication adherence were analyzed.

Material and methods: A retrospective, cross-sectional, 3-stage (2006, 2011, 2018) study was conducted in a primary care setting of Moscow. As many as 3027, 1834, 805 patients with verified diagnosis of SCAD were included. Demographics, medical history, data on modifiable RFs and prescribed drug therapies were collected. At the third stage, medication adherence was measured, using the 8-item Morisky scale.

Results and discussion: Over a 7-year period, better control of modifiable RFs in coronary patients was revealed. The target levels of blood pressure were reached in 58.3% (+20.7%; $p < 0.05$) of the patients, total cholesterol – in 33.0% (+16.0%; $p < 0.05$), and low-density lipoprotein cholesterol – in 23.3% (+12.2%; $p < 0.05$). Two critical problems that determined still inadequate RFs control were identified. The attention of physicians to RFs and rates of non-pharmacological interventions remained low throughout the study. Information on lifestyle RFs was recorded in fewer than one-third of the subjects. The lipid profile was registered only in half of patients' histories. Non-adherence to pharmacotherapy was identified in 51.3% of patients.

Conclusion: Further increase in efficacy of pharmacotherapy might be provided by application of SOPs regarding the registration and correction of modifiable cardiovascular RFs, identification of non-adherent patients and promotion of medication adherence.

Keywords

coronary artery disease, medication adherence, non-pharmacological treatment, risk factors, standard operating procedures.

Introduction

This paper describes a fragment of the pharmacoepidemiologic study conducted to monitor the quality of management of stable coronary artery disease (SCAD) in primary care practice over a 12-year period. The aim of the study was to demonstrate the need to develop and apply standard operating procedures (SOPs) as a tool of the quality management system (QMS) of pharmacotherapy in primary healthcare facilities on example of a pharmacoepidemiologic analysis of the outpatient management of SCAD. The study focused on the processes that played the crucial role in providing adequate quality of care to coronary patients: identification, registration, and correction of modifiable cardiovascular risk factors; achievement of the target levels; pharmacological interventions; and medication adherence.

In the separate publication on the analysis of the prescribed drug therapies regarding relevant clinical practice guidelines (CPGs), the authors demonstrated the performance of the pharmacotherapeutic SOPs in primary healthcare settings. However, along with the positive trends, lacking efficacy of pharmacological interventions was observed. Few patients had risk factors target levels achieved, which became the basis to study other quality of SCAD management indicators. Among these were the attention of primary care physicians to cardiovascular risk factors, the effectiveness of their modification in compliance with relevant CPGs and medication adherence of coronary patients.

Material and methods

A pharmacoepidemiologic, retrospective, cross-sectional, cohort study was conducted in a primary healthcare facility of Moscow City. Over the 12-year period, three stages of the study were completed (in 2006, 2011 and 2018). As many as 3027, 1834 and 805 medical records of patients with SCAD were analyzed, respectively. The methodical approach applied was borrowed from the international project of the European Society of Cardiology – EUROASPIRE (Kotseva et al. 2017). Subject inclusion criteria were the same at all stages of the study: age over 30 years, verified diagnosis of SCAD, and non-participation in a clinical trial. The following data were collected: demographics, medical histories, information on modifiable cardiovascular risk factors (smoking and alcohol status, level of physical activity, diet; body mass index (BMI), blood pressure (BP), lipid profile, glycemic status), lifestyle and pharmacological interventions.

Additionally, at the third stage of the study, medication adherence was measured in 386 patients. The validated questionnaire – 8-item Morisky Medication Adherence Scale (MMAS-8) – was used. The patients were interviewed via telephone. The self-report method of assessing medication adherence in patients with cardiovascular disease (CVD) using various scales and questionnaires is widespread in international practice due to its simplicity, usability, and rather high reliability (Nguyen et al. 2014). MMAS-8 has good validation parameters: internal consistency reliability (described by Cronbach's alpha coefficient) $\alpha = 0.83$, sensitivity 0.93, specificity 0.53, and strongly correlates with validation criteria (Morisky et al. 2008; Lukina et al. 2016). Interpretation of MMAS-8 was carried out in a standard way. Each question of the scale implied an answer like "yes" (0 point) or "no" (1 point), except the 5th question, which was scored the opposite, and the 8th question, which was presented as Likert scale and scored 1 point only if the answer was "never". In this paper, a simplified dichotomous interpretation of the MMAS-8 was performed: adherent (8 points) or non-adherent (less than 8 points) (Tan et al. 2014).

All the data from medical records and questionnaires were transferred to patients' case report forms (CRF). The study database was constructed in MS Excel. Statistical data processing was performed using IBM SPSS Statistics V16.0 (IBM, Armonk, NY, USA). Continuous variables were expressed as mean (M), standard deviation (SD), first (Q1), second (Q2) and third (Q3) quartiles. Categorical variables were expressed as frequencies and percentages. Significance of the differences between the groups was estimated by standard statistical tests (two-sided). Independent *t*-tests were used for continuous variables distributed approximately according to the normal law; Wilcoxon rank-sum tests were used for continuous variables not distributed approximately according to the normal law. Kolmogorov-Smirnov normality tests were used to check the normality of distribution. Chi-square tests were used for categorical variables. The level of statistical significance was set at $p < 0.05$.

Results and discussion

The demographic characteristics and medical histories of patients with SCAD included at each stage of the study are presented in Table 1. Analyzing the changes over a 12-year period, it is worth highlighting an increased patients' mean age and proportion of males, as well as growing prevalence of myocardial infarction, atrial fibrillation, and heart failure in cardiovascular history of coronary patients.

Table 1. Demographics and medical histories of patients with stable coronary artery disease.

Characteristic	Stage 1 (N = 3027)	Stage 2 (N = 1834)	Stage 3 (N = 805)
Male gender, n (%)	1050 (34.7)	845 (46.1)†	414 (51.4)‡
Age (years), M ± sd (Q1, Q2, Q3)	65.5 ± 9.3 (59, 67, 72)	66.0 ± 9.7 (59, 66, 73)	68.9 ± 9.9‡ (62, 69, 72)
Age≥65 years, n (%)	1839 (60.8)	1013 (55.2)†	538 (66.8)‡
Stable angina pectoris, n (%)	2915 (96.3)	1633 (89.0)†	517 (64.2)‡
Myocardial infarction, n (%)	752 (24.8)	825 (45.0)†	414 (51.4)‡
Chronic heart failure, n (%)	1608 (53.1)	1383 (75.4)†	729 (90.6)‡
Arterial hypertension, n (%)	2763 (91.3)	1695 (92.4)	732 (90.9)
Atrial fibrillation, n (%)	306 (10.1)	369 (20.1)†	249 (30.9)‡
Diabetes mellitus, n (%)	385 (12.7)	384 (20.9)†	161 (20.0)

Note: † $p < 0.05$ compared with stage 1; ‡ $p < 0.05$ compared with stage 2.

As mentioned above, the analysis of the prescribed drug therapies regarding CPGs was performed within the study. The results demonstrated improved physician adherence to a guideline-recommended pharmacotherapy at stage 3 (2018) compared with stage 2 (2011) – 82.9% versus 58.7% ($p < 0.05$). So, it was reasonable to analyze the effectiveness of pharmacological interventions expressed as achievement of risk factor targets in patients with SCAD. It was revealed that the control of key parameters characterizing the manifestation of such risk factors as overweight, hypertension and dyslipidemia remained inadequate (Table 2). It became obvious that the reasons for poor performance regarding modification of the risk factors lied not only within the scope of evidence-based pharmacological treatment.

Table 2. The proportion of coronary patients with risk factor targets achieved.

Parameter	Stage 2 (2011)		Stage 3 (2018)	
	n/N	%	n/N	%
Body mass index	67/313	21.4	143/754	19.0
Blood pressure	665/1768	37.6	468/803	58.3‡
Total cholesterol	217/1268	17.0	150/454	33.0‡
LDL† cholesterol	68/613	11.1	68/292	23.3‡

Note: † low-density lipoprotein; ‡ $p < 0.05$ compared with stage 2.

On this point, the degree of physician attention to the identification and non-pharmacological intervention of modifiable cardiovascular risk factors was analyzed in detail. It is widely known that these measures are the groundwork for an effective pharmacotherapy. From this perspective, it was considered reasonable to evaluate the attention of primary care physicians to cardiovascular risk factors expressed as the registration rates of relevant information in outpatient records, but not just the prevalence of risk factors in the population (Table 3).

Table 3. Attention of primary care physicians to cardiovascular risk factors in patients with stable coronary artery disease.

Information on the risk factor registered in outpatient medical records	Stage 1 (N = 3027)	Stage 2 (N = 1834)	Stage 3 (N = 805)
Smoking status, n (%)	73 (2.4)	506 (27.6)†	229 (28.4)
Alcohol status, n (%)	9 (0.3)	394 (21.5)†	78 (9.7)‡
Diet status, n (%)	4 (1.3)	19 (2.3)†	12 (1.5)
Level of physical activity, n (%)	6 (0.2)	2 (1.1)	11 (1.4)‡
Body mass index, n (%)	394 (13.0)	313 (17.1)†	754 (93.7)‡
Blood pressure, n (%)	2918 (96.3)	1768 (96.4)	803 (99.8)‡
LDL§ cholesterol, n (%)	476 (15.7)	613 (33.4)†	292 (36.3)
Total cholesterol, n (%)	1347 (44.5)	1268 (69.1)†	454 (56.4)‡
Blood glucose, n (%)	559 (18.5)	514 (28.0)†	274 (34.0)‡
Glycosylated hemoglobin, n (%)	no data	18 (1.0)†	113 (14.0)‡

Note: † $p<0.05$ compared with stage 1; ‡ $p<0.05$ compared with stage 2; § low-density lipoprotein.

The results demonstrated complete "failure" in terms of primary care physicians' attention to modifiable risk factors regarding the CPGs for the management of SCAD. Particularly unsatisfactory was the attention of doctors to lifestyle risk factors through all the stages of the study. The recording of the relevant information was done extremely rarely. Unfortunately, some positive dynamics in capturing smoking and diet statuses, observed over the period of 2006–2011, received no further development over the next time period. Only the collection of parameters of BP (99.8%) and BMI (93.7%) in 2018 was adequate. At the same time, the key parameter of lipid profile – LDL cholesterol – was recorded in fewer than one-third of the patients through the entire observation period. And the reduction of this parameter by 1.0 mmol/L was accompanied by 16–22% reduction in risk of the major cardiovascular events according to Cholesterol Treatment Trialists' Collaboration (2015).

Consequently, the outpatient records analyzed at the first two stages of the study contained very few lifestyle interventions documented. The more detailed results of the dynamics over that study period regarding a non-pharmacological treatment were published in the earlier paper about the patients with stable angina (Fitilev et al. 2017). Some positive trends identified in 2011 and 2018 were still inadequate, although certain non-pharmacological interventions regarding lifestyle risk factors became more frequent at the third stage compared with the second stage. We detected an increase in frequency of dietary counseling (mainly salt restriction) – 97.5% versus 66.1% ($p < 0.05$); BP self-monitoring recommendations – 57.3% versus 14.1% ($p < 0.05$); advice on smoking cessation – 63.9% versus 9.0% ($p < 0.05$), although only 20.4% of smokers were referred to a special program in 2018. Advice on physical activity, on the contrary, was given less frequently – 7.8% in 2018 versus 14.7% in 2011 ($p < 0.05$). In view of the revealed inadequate counseling on diet and physical activity, high prevalence of overweight and obesity in coronary patients (Table 2) was not much of a surprise. It seems that primary care physicians underestimate the role of lifestyle interventions in improving the prognosis of patients with SCAD (Artinian et al. 2010; Janssen et al. 2013).

To be fair, one could not exclude that the recommendations were given by physicians orally. But as practice shows the absence of "paper trail" in most cases was followed by no real actions. For instance, the RELIF study revealed that, according to doctors, they provided advice on lifestyle interventions to almost all patients. However, according to patients, every fifth subject received no recommendations at all (Oganov et al. 2007).

This opinion was also indirectly confirmed by an interesting fact we identified working with the Russian system of electronic medical records called Unified Medical Information Analytical System (EMIAS) at the third stage of the study. Physician consultation templates uploaded in EMIAS were developed by the doctors themselves. Thus, even in the same healthcare facility, a cardiologist consultation template might differ depending on the specialist. This approach contradicted the standardization principle itself. In addition, some templates lacked pre-defined fields or sections to register information regarding cardiovascular risk factors (diet status and dietary recommendations, alcohol and smoking status, interventions

to promote smoking cessation, level of physical activity and relevant advice, family history). At the same time, the fields for registration of BP and anthropometric parameters were pre-specified in most templates. And as a result, there were high recording rates of these parameters revealed in 2018 (Table 3).

Thus, measures for the identification and non-pharmacological modification of lifestyle risk factors are crucial regarding the efficacy of pharmacotherapy. In the comprehensive quality improvement program of the American College of Cardiology – *The Guidelines Applied in Practice* (*GAP*) *Initiative* – the set of quality indicators included not only pharmacological interventions (target improvement levels at discharge for acetylsalicylic acid – 95%, beta-blockers – 87%, ACE inhibitors – 78%), but also non-pharmacological strategies, like advice on smoking cessation (target improvement level – 75%) and dietary counseling (Mehta et al. 2004).

The fact that still many patients in the 2018 cohort were not achieving target levels of BP and lipids prompted attention to another important determinant of the efficacy of pharmacotherapy – medication adherence. In this regard, medication adherence was measured in the patients with SCAD at the third stage of the study. Accurate answers to all the questions of MMAS-8 were obtained from 386 patients. According to the points scored, all the subjects were referred to adherent (8 points) and non-adherent (less than 8 points) (Fig. 1). In general, the results were consistent with the data from the 2003 WHO report that anounced medication adherence to long-term pharmacotherapy to be approximately 50% (De Geest and Sabate 2003). Later systematic reviews and meta-analyses of medication adherence in patients with CVD highlighted this serious problem. The prevalence of suboptimal adherence to pharmacological treatment was approximately 40–50% (Chowdhury et al. 2013; Khatib et al. 2019).

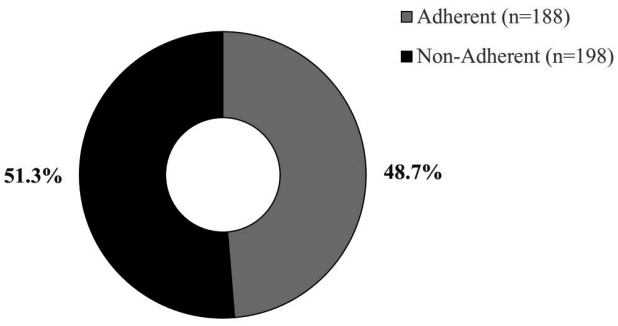

Figure 1. Medication adherence in patients with stable coronary artery disease in 2018.

Our results were also consistent with the existing Russian data. Within the framework of the national CVD registry PROFIL, medication adherence was measured using the MMAS-8 (n = 130). Only 40% of patients were adherent to treatment (Lukina et al. 2018). Another study in patients with hypertension and SCAD examined in outpatient healthcare facilities of Moscow reported the level of non-adherence (3 points or less by 4-item MMAS) to prescribed drug therapies being at 61% (Fofanova et al. 2017).

In fact, we have identified, or rather confirmed, for the studied patient population another significant reason for the inefficacy of the management of SCAD. In this regard, the persisting inadequate level of BP and lipids control (Table 2) was quite expected. In foreign studies, it has been repeatedly demonstrated that by addressing support to non-adherent patients, it was possible to improve risk factor control. Thus, the UMPIRE study reported 21% higher medication adherence in patients with SCAD in the intervention group compared with the control group (odds ratio 1.33; 95% confidence interval (CI) 1.26–1.41; $p < 0.001$) due to a polypill strategy. Better adherence was accompanied by decreased systolic BP (-2.6 mm Hg; 95% CI -4.0 – -1.1 mm Hg) and LDL cholesterol (-4.2 mg/dl; 95% CI -6.6 – -1.9 mg/dl) (Thom et al. 2013). The SPREAD study demonstrated that the efforts to improve medication adherence and modify lifestyle in patients after acute coronary syndrome led to a decrease in average systolic BP (124.4 versus 128.0 mm Hg; $p = 0.002$) and BMI (24.4 versus 25.0 kg/m^2, $p < 0.0001$) in the intervention group compared with the control group (Xavier et al. 2016). It became obvious that the identification of the risk group of non-adherent patients might also be a reserve for increasing the effectiveness of therapeutic interventions, and the standardization of this process by means of appropriate SOPs might improve the quality of medical care.

Conclusion

Over the 7-year period (2011–2018), the primary care physicians' adherence to the guideline-recommended pharmacotherapy of SCAD increased up to 82.9% that corresponded to the international requirements of developed countries. Consequently, the control of certain modifiable cardiovascular risk factors improved. The target levels of BP were reached in 58.3% (+20.7%) of coronary patients, total cholesterol – in 33.0% (+16.0%), and LDL cholesterol – in 23.3% (+12.2%). Nevertheless, there were no grounds to consider those parameters as satisfactory. The study exposed two critical problems that largely determined such a situation. First, the attention of primary care physicians to cardiovascular risk factors and the rates of non-pharmacological interventions remained poor throughout the study. Secondly, medication non-adherence was disregarded in patients' medical records, but was identified in 51.3% of patients.

Thus, further increase in efficacy of evidence-based pharmacological therapy in primary care practice might be provided by implementation of SOPs regarding the registration and modification of cardiovascular risk factors. As part of the standardization of this process, it is reasonable to incorporate specific fields for recording information about cardiovascular risk factors into the electronic consultation template of a cardiologist and general practitioner in EMIAS and make these pre-defined fields obligatory for completion (inability to move to the next section of the template without

entering relevant data). From a technical perspective, this does not present any difficulties. Other SOPs to implement should cover the processes of identification of non-adherent patients and promotion of medication adherence.

Conflict of interest

The authors declare no conflict of interest.

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