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Pretest probability of coronary artery disease as a factor for optimizing invasive diagnostics in routine clinical practice

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According to the European Society of Cardiology guidelines, patients with chest pain requires the calculation of pretest probability (PTP) of coronary artery disease (CAD), followed by the identification of diagnostic tactics.

Aim. To analyze the registry of patients with stable CAD in order to assess the frequency of PTP calculation, as well as the validity of diagnostic tactics choice depending on its level.

Material and methods. The data of the registry of patients with stable CAD for the periods from 2012 to 2014 and from 2017 to 2019 were analyzed. We assessed the number of CAD patients, proportion of men, and distribution of patients depending on angina functional class. In addition, data on PTP calculation, as well as distribution of patients and diagnostic strategy selected depending on its value was analyzed. To assess differences (p) in pairwise comparisons, Student's t-test was used. Differences were considered significant at $p<0,05$. Statistical analysis was performed using Microsoft Office Excel 2010 (Microsoft, USA) and STATISTICA 6.0 (StatSoft Inc., USA).

Results. In 2017-2019, the number of detected CAD cases and proportion of men increased. In both time periods, an insufficient level of calculating PTP of CAD remains. In patients with intermediate PTP, 15-85% of priority tactics are invasive interventions, and with high PTP, the percentage of invasive methods does not reach the proper level, which does not correspond to modern guidelines for the management of CAD patients and leads to misappropriation of funds and healthcare resources.

Conclusion. According to medical records, PTP can be determined in less than half of patients. In CAD patients with intermediate PTP, non-invasive studies are not carried out in full, since coronary angiography is preferred. In patients with a high PTP, invasive diagnostics is insufficient.

Keywords: coronary artery disease, pretest probability, coronary angiography, non-invasive testing, registry.

Relationships and Activities. The study was carried out within the state assignment of the Ministry of Health of Russia "Development of technology for the rational use of myocardial revascularization in patients with coronary artery disease based on typical clinical models of patients using registries" (AAAA-A19-119021190052-3).

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The use of any diagnostic and therapeutic intervention in a particular patient should be based on the predominance of potential benefits over risks [1]. Therefore, to help a practitioner, risk assessment scales for various events are developed to justify approaches to diagnosis and treatment [2]. One of these methods is assessing pretest probability (PTP) of coronary artery disease (CAD), which determines the indications for invasive and non-invasive tests in order to clarify the need for coronary revascularization in a particular patient [3, 4]. The target group for PTP evaluation and subsequent invasive examination are patients with chest pain, without prior coronary events, and having lower coronary risks than patients with previous events [5]. Therefore, it is especially important to evaluate the benefits of PTP introduction into real clinical practice, in contrast to the previous empirical appointment of invasive tests [5].

The aim of the study was to analyze the registry of patients with stable CAD in order to assess the frequency of PTP calculation, as well as the validity of diagnostic tactics choice depending on its level.

Material and methods

To achieve this aim, the registries of patients who were hospitalized in 2012-2014 and 2017-2019 in several Russian cardiac surgical centers were analyzed. Information about patients was sequentially entered into the registry at the time of discharge on the basis of medical records. The primary analysis involved the data of patients aged 30 years and older with a record of CAD, with the exception of cases with a myocardial infarction (MI) within prior 3 months and previous coronary artery bypass grafting.

Based on the registry data, the mean age of patients was calculated, presented as M±SD (mean ± standard deviation), as well as absolute and relative values (presented as a percentage of total number) of the following parameters: number of men; presence of angina and its class; presence of myocardial infarction; use of exercise electrocardiography (ECG), stress echocardiography, computed tomography angiography, coronary angiography (CAG), percutaneous coronary intervention (PCI); estimation of PTP and the distribution of patients depending on its value. PTP was calculated on the basis of 2013 European Society of Cardiology (ESC) guidelines on the management of stable CAD [4]. To do this, using the nomogram proposed in the clinical guidelines (Table 1), sex, age and chest pain characteristics indicated in a patient's medical records were compared. As a result, for each patient, the probability of stable CAD was determined in percent. If PTP was <15%, further specific diagnostic tests (non-invasive stress and imaging techniques, and CAG) were not indicated. At PTP 15-85%, echocardiography and at least one non-invasive stress test (exercise ECG, stress echocardiography) or computed tomography angiography was determined. At PTP >85%, the diagnosis of CAD was considered verified and any non-invasive diagnostic tests or coronary angiography could be performed.

Next, a pairwise comparison of calculated indicators was made with each other. Student's t-test was used to assess statistical differences (p). Differences were considered significant at $p<0,05$.

The next step was the assessment of diagnostics implementation (echocardiography, CAG, PCI) according to the distribution into groups depending on PTP value (<15%, 15-85%, >85%), or the absence of PTP data. For these indicators, both absolute and relative values (percentage of the total number of CAD patients) were also calculated, followed by an assessment of the significance of differences between patients from the 2012-2014 and 2017-2019 registers.

Statistical analysis was performed using Microsoft Office Excel 2010 (Microsoft, USA) and STATISTICA 6.0 (StatSoft Inc., USA).

The study was performed in accordance with Good Clinical Practice and Declaration of Helsinki principles. The study protocol was approved by the ethics committees of all participating clinical centers. Written informed consent was obtained from all participants prior to enrollment in the study.

Table 1

PTP of stable CAD depending on the type of chest pain [4]

Age, years	Classic angina		Atypical angina		Non-anginal chest pain	
	Men	Women	Men	Women	Men	Women
30-39	59%	28%	29%	10%	18%	5%
40-49	69%	37%	38%	14%	25%	8%
50-59	77%	47%	49%	20%	34%	12%
60-69	84%	58%	59%	28%	44%	17%
70-79	89%	68%	69%	37%	54%	24%
>80	93%	76%	78%	47%	65%	32%

Table 2

Characteristics of CAD patients included in the registry in 2012-2014 and 2017-2019

Parameter	2012-2014	2017-2019	p
Total number in registry	52529	16832	
Total number with CAD	15151 (28,8%)	5780 (34,3%)	<0,001
Men	6984 (46,1%)	3268 (53,54%)	<0,001
Mean age	69,02±11,4	64,84±11,27	0,018
Diagnosis of “angina pectoris”, of which:	7833 (57,7%)	3088 (53,42%)	<0,001
— class I	1305 (16,66%)	191 (6,19%)	<0,001
— class II	2986 (38,12%)	1663 (52,88%)	<0,001
— class III	1368 (17,46%)	745 (24,13%)	<0,001
— class IV	16 (0,2%)	11 (0,36%)	0,630
— no data available	2158 (27,55%)	478 (15,48%)	<0,001
Prior MI	4732 (60,41%)	2726 (47,16%)	<0,001
PTP estimated	3783 (24,97%)	2510 (43,43%)	<0,001
PTP not estimated	11368 (75,44%)	3271 (56,59%)	<0,001
PTP categories:			
<15%	77 (2,04%)	9 (0,36%)	0,56
15-85%	3424 (90,51%)	2303 (91,75%)	0,077
>85%	282 (7,45%)	197 (7,85%)	<0,001
Exercise ECG	622 (4,11%)	282 (4,88%)	0,001
Stress echocardiography	15 (0,1%)	11 (0,19%)	0,099
CT angiography	1 (0,01%)	3 (0,05%)	0,074
CAG	1903 (12,56%)	1215 (21,02%)	<0,001
PCI	979 (6,46%)	1160 (20,07%)	<0,001

Note: data are presented either as the mean and standard deviation (M±SD), or the absolute number of persons and their proportion (percentage) — n (%). Significant differences (p) are highlighted in color.

Abbreviations: CAD — coronary artery disease, MI — myocardial infarction, CAG — coronary angiography, CT — computed tomography, PTP — pretest probability, PCI — percutaneous coronary intervention, ECG — electrocardiography.

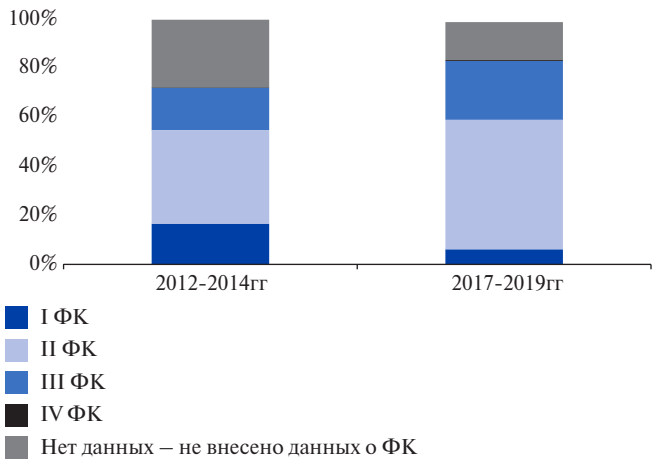

Figure 1. Distribution of patients depending on angina FC in 2012-2014 and 2017-2019.

Results

During the primary analysis of registry data, the main parameters described earlier were calculated. Characteristics and statistical differences between groups depending on the date of registry completion (2012-2014 and 2017-2019) are presented in Table 2.

In the registry of 2017-2019 (Table 2), a record of CAD in discharge summary was revealed by 5,5% more often than in the registry of 2012-2014 (p<0,001). In addition, it was noted that in the period from 2017 to 2019, on average, CAD was more often detected in women (p<0,001), while the age of CAD patients has become younger (p=0,018).

It was shown that in 2017-2019, a record of exertional angina became less common in the diagnosis by 4,3% (p<0,001). At the same time, a change in the distribution of angina class among patients was revealed (Figure 1).

The percentage of patients with MI decreased by 13,3% in 2017-2019 compared to 2012-2014 (p<0,001).

Favorable is the fact of an increase in estimating PTP in 2017-2019 by 18,5% (p<0,001). The distribution of patients into groups depending on

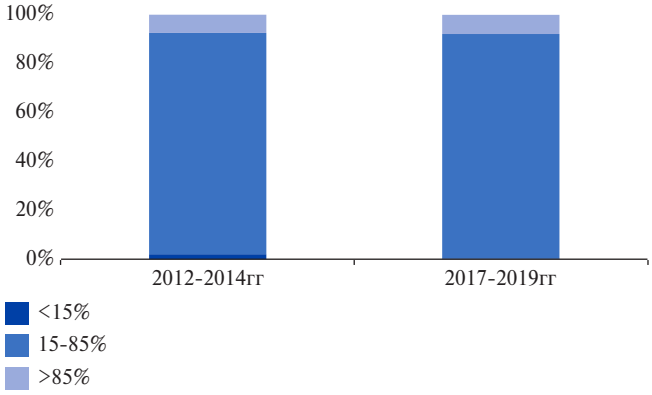

Figure 2. Distribution of CAD patients depending on the PTP value in 2012-2014 and 2017-2019.

PTP value is shown in Figure 2. Age distribution, according to the World Health Organization criteria, is presented in Table 3. The largest proportion of patients both in the 2012-2014 and 2017-2019 registers belonged to the age group of 60-74 years and had an intermediate PTP. The age group of 45-59 years was the second largest, while the age group of 75-90 years was third in intermediate PTP category according to both analyzed registers. Together, these three age groups (45-90 years old) with intermediate PTP values (from 15 to 85%) made up 97% of the 2012-2014 sample and 88% of the 2017-2019 sample.

The next important factor was the number of instrumental investigations. Both in 2012-2014 and 2017-2019, the percentage of using diagnostic methods remained low (Table 2).

Next, we analyzed the results of investigations in CAD patients with calculated PTP (Table 4).

In the period from 2017 to 2019, the number of diagnostic measures performed in patients with PTP 15-85% increased significantly (Table 4). At the same time, the analysis of performed examinations in patients with PTP >85% did not revealed such unambiguous results. It was shown that in patients in the period from 2017 to 2019, non-invasive tests were performed much less frequently (by 40%) (p<0,001), while invasive interventions — more often as follows: CAG (by 15%; p<0,001) and CAG followed by percutaneous intervention (by 17%; p<0,001). Unfortunately, it was not possible to assess the diagnostics quality in patients with PTP <15% due to the small number of patients in this group in both periods.

Table 3

Detailed age structure among patients with estimated PTP

PTP	Age group	2012-2014 (n=3783)	2017-2019 (n=2510)	p
<15	18-44	7 (9%)	4 (44,4%)	0,611
	45-59	69 (89,6%)	5 (55,5%)	0,0003
	60-74	0	0	-
	75-90	0	0	-
	>90	1 (1,3%)	0	-
	Total	77	9	
15-85	18-44	37 (1,1%)	58 (2,52%)	<0,001
	45-59	1119 (32,7%)	487 (21,1%)	<0,001
	60-74	1869 (55,4%)	1266 (55%)	0,7653
	75-90	670 (19,6%)	464 (20,1%)	0,6415
	>90	29 (0,8%)	28 (1,2%)	0,1282
	Total	3424	2303	
>85	18-44	0	0	-
	45-59	0	0	-
	60-74	112 (39,7%)	93 (47,2%)	0,69
	75-90	169 (59,9%)	98 (49,7%)	0,275
	>90	1 (0,4%)	6 (3%)	0,204
	Total	282	197	

Note: data are presented as the absolute number of persons and their proportion (percentage) — n (%). Significant differences (p) between the 2012-2014 and 2017-2019 registries are highlighted in color.

Abbreviation: PTP — pretest probability.

Discussion

The analysis of registry data of patients with stable CAD demonstrated the position of practitioners regarding the assessment of CAD probability in a particular patient and the use of non-invasive and invasive diagnostic methods. Despite the recommendations to assess PTP to select the most appropriate cost-benefit diagnostics, physicians tend to use CAG as the gold standard strategy, which is also the most expensive method.

The study showed that in 2017-2019 CAD was detected more often than in 2012-2014. Currently, it is necessary to assess PTP for a more accurate diagnosis of CAD and determine the further tactics of managing such patients [4, 6]. Currently, in the Russian and foreign literature, the correspondence of coronary obstructions expected by PTP to real findings are widely discussed [5, 7]. Approaches are being developed to improve predictive models [5, 7, 8]. However, the limitations of existing PTP models do not imply their exclusion from clinical practice. On the contrary, the experience of practical PTP application to select the management of patients with stable CAD can serve to improve the healthcare provision. Thus, the wider practical use of PTP will help to avoid unjustified non-invasive and invasive testing in cases where the probability of obstructive CAD is low. In addition, this can make possible to

Table 4

Performed diagnostic measures in patients, depending on the PTP of CAD

	PTP, 2012-2014				PTP, 2017-2019						
Parameter	<15%	15-85%	>85%	NA	<15%	15-85%	p_1	>85%	p_2	NA	p_3
Total	77 (0,5%)	3424 (90,5%)	282 (1,86%)	11368 (75,44%)	9 (0,4%)	2303 (91,8%)	-	197 (7,9%)	-	3271 (56,6%)	-
LVEF determined	67 (87,0%)	902 (2,34%)	202 (71,63%)	2402 (21,13%)	4 (40%)	1366 (59,3%)	-	155 (79%)	-	1162 (35,5%)	-
LVEF <50%	10 (13%)	131 (3,83%)	30 (10,6%)	346 (3,0%)	2 (20%)	300 (22%)	-	42 (27%)	-	240 (20,7%)	-
NIT performed (exercise ECG or stress echocardiography or CT angiography)	0 (0%)	119 (3,48%)	121 (42,9%)	6 (0,1%)	1 (10%)	140 (6,08%)	<0,001	6 (3%)	<0,001	4 (0,12%)	-
CAG performed	63 (81,82%)	594 (17,4%)	77 (27,3%)	1267 (11,2%)	2 (20%)	677 (29,4%)	<0,001	83 (42,1%)	0,008	449 (13,7%)	0,012
PCI performed	22 (28,57%)	339 (9,9%)	98 (34,8%)	565 (4,97%)	2 (20%)	605 (26,27%)	<0,001	82 (41,6%)	0,131	468 (14,3%)	<0,001
CAG+PCI	22 (28,57%)	227 (9,9%)	53 (18,8%)	329 (2,89%)	2 (20%)	496 (21,54%)	<0,001	70 (35,5%)	<0,001	318 (9,72%)	<0,001
NIT+CAG	0 (0%)	8 (0,23%)	47 (16,7%)	95 (0,84%)	1 (10%)	20 (0,86%)	<0,001	0 (0%)	-	38 (1,16%)	0,102
NIT+PCI	0 (0%)	16 (0,47%)	50 (18,4%)	157 (1,38%)	0 (0%)	17 (0,74%)	0,329	1 (0,5%)	-	26 (0,79%)	0,02

Note: data are presented as the absolute number of persons data are presented as the absolute number of persons and their share (in percent) — n (%). Statistically significant differences (p) are highlighted in color — n (%). Significant differences (p) are highlighted in color; p_1 reflects the significance of differences between groups with PTP of 15-85%, p_2 — between groups with PTP >85%; p_3 — significance of differences between group with uncertain PTP (NA).

Abbreviations: CAG — coronary angiography, CT — computed tomography, LV — left ventricle, NIT — non-invasive testing, PTP — pretest probability, EF — ejection fraction, PCI — percutaneous coronary intervention, ECG — electrocardiography.

conduct non-invasive testing in all patients who need to confirm ischemia to consider treatment for CAD, and depending on therapy effectiveness, to perform CAG with subsequent myocardial revascularization.

It is noteworthy that in the period from 2017 to 2019, physicians more often followed the recommendations for managing CAD patients as follows: the percentage of patients with estimated PTP increased (Table 2). However, as we can see, in 2012-2014 and 2017-2019, the proportion of patients with calculated PTP was less than half of the total number of CAD patients (Table 2). Considering that sex and age in the study group were known in all patients, the main reason for PTP non-determination was insufficiently detailed description of chest pain characteristics.

According to ESC guidelines, among patients with intermediate PTP (15-85%), stress tests should be used to clarify the diagnosis, including with visualization [4]. Based on our results, these non-invasive techniques (stress echocardiography, exercise ECG) were performed rarely both in 2012-2014 and 2017-2019 (Tables 2, 4). At the same time, physicians are increasingly using invasive diagnostics to verify the diagnosis (Table 4). Perhaps this approach is associated with the doctor's desire to exclude as much as possible the possible errors of non-invasive techniques and get an unambiguous answer about coronary pathology. Nevertheless, according to ESC colleagues, non-invasive tests, firstly, are quite safe for patients, and secondly, they provide an accurate assessment of cardiovascular functional status, which generally allows avoiding the excessive use of high-tech interventions [9].

It may also be associated with scheduled hospitalizations for PCI in patients who are not sufficiently examined to rule out non-coronary chest pain at the prehospital stage. Indeed, practical healthcare provides limited opportunities for additional examination of patients with non-coronary chest pain in the conditions of cardiology department, limiting the number of patients who, according to healthcare care, can undergo an extended examination [3]. Practitioners who are familiar with the difficulties of rereferring patients between various departments may unconsciously

or even consciously choose not the rational tactics of examining a patient with chest pain, proposed in the guidelines, but the narrowly focused strategy of cardiology examinations.

At the same time, according to our results, for patients with PTP >85% who are recommended invasive diagnostic methods [4], these interventions are performed in less than half of the cases in both studied periods, while non-invasive testing is carried out quite often, especially in the period from 2012 to 2014 (Table 4). According to the NICE guidelines, this category of patients does not need diagnostic tests at all, and the diagnosis of CAD can be considered established [10]. Obviously, the recommendations for invasive CAG in such patients, provided by the consensus documents of both the ESC and the ACC/AHA, imply using CAG data in such patients immediately in order to select surgical tactics for interventions on coronary vessels [11]. In this group, indeed, according to our analysis, one third of patients underwent coronary stenting, but this number is clearly not enough to cover the need for interventions for all suspected obstructions in this group. Thus, according to the CONFIRM study, the actual incidence of obstructive stenosis in patients with high PTP during CAG was up to 40% [12].

This demonstrates that, in general, physicians do not have a clear idea of the need for certain interventions, which entails both misappropriation of health care funds for complex interventions, and a failure of risk-benefit balance for a patient. In addition, it was previously shown that with adequate drug therapy, intracoronary interventions can be avoided [13], which once again emphasizes the importance of timely PTP assessment and considering the advisability of high-tech diagnostic and treatment methods. Therefore, physicians are advised to be more careful in determining PTP in patients with chest pain when choosing a diagnostic strategy. In intermediate or high PTP, at least one non-invasive exercise test should be performed to detect ischemia before CAG. Prior to CAG, in all patients with probable CAD (positive exercise test, PTP >65%), optimal medical therapy for CAD (statins, antiplatelet agents, at least one first-line anti-ischemic drug: beta-blocker or calcium antagonist) should be prescribed and an exercise test should be performed. This will reduce the performance of non-therapeutic interventions performed. Wider use of non-invasive testing will eliminate the mechanistic approach to myocardial revascularization (treatment of stenosis), shifting the focus to treating impaired myocardial function (treatment of verified ischemia).

Conclusion

The study demonstrated that, despite the increase in the proportion of patients with estimated PTP, this procedure is still performed in less than half of the cases. Further analysis showed that in patients with an intermediate PTP of 15-85%, the recommended methods of non-invasive examination are not used enough — invasive coronary interventions are preferred. In addition, in patients with a high PTP >85%, invasive diagnostic interventions, which to a greater extent determine the further surgical tactics required for this group of patients, are insufficiently performed. Thus, in modern healthcare there is an unjustified use of both diagnostic and therapeutic resources, which increase a risk in patients with both intermediate (risk related to diagnostic intervention) and high PTP (risk of adverse cardiovascular events).

Relationship and Activities. The study was carried out within the state assignment of the Ministry of Health of Russia "Development of technology for the rational use of myocardial revascularization in patients with coronary artery disease based on typical clinical models of patients using registries" (AAAA-A19-119021190052-3).

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