Stress echocardiography vs coronary computed tomography angiography for the detection of obstructive coronary artery disease in patients aged ⩾70 years with suspected stable coronary artery disease

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Aim. To compare stress echocardiography and coronary computed tomography angiography (CTA) in the diagnosis of stable coronary artery disease (CAD) in patients aged ⩾70 years.

Material and methods. The study included 390 patients aged ⩾70 years with suspected stable CAD, which underwent elective coronary artery angiography (CAG). Initially, patients for whom stress echocardiography and CTA is appropriate was determined. After that diagnostic accuracy of both methods in the detection of obstructive CAD was evaluated in patients with atypical angina and non-anginal chest pain.

Results. Among 111 patients with atypical angina and non-anginal pain which underwent stress echocardiography and had unequivocal results, 69 (62%) patients had obstructive CAD. Stress echocardiography has sensitivity of 89%, specificity of 95%, positive likelihood ratio (LR+) of 17,8, and negative likelihood ratio (LR-) of 0,1. Positive result increased probability of obstructive CAD from 62% to 95%, while negative result reduced probability to 16%. Among 82 patients with atypical angina and non-anginal pain which underwent CTA, 48 (59%) patients had obstructive CAD. CTA has sensitivity of 100%, specificity of 88%, LR+ of 8,3, and LR- of 0,3. Positive result increased post-test probability of obstructive CAD from 59% to 86%, while negative result reduced post-test probability to 0%.

Conclusion. Stress echocardiography and CCTA has comparable diagnostic accuracy in the detection of obstructive CAD in patients aged ⩾70 years with atypical angina and non-anginal pain. Stress echocardiography has a greater diagnostic value of positive result; CTA has a greater diagnostic value of negative result.

Key words: older adults, coronary computed tomography angiography, stress echocardiography, stable coronary artery disease.

Relationships and Activities: none.

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The algorithm for diagnosing stable coronary artery disease (CAD) at the first stage involves a clinical assessment of pretest probability, which is most often carried out taking into account age, sex and characteristics of chest pain [1, 2]. Determining the pretest probability is a key moment in deciding on further actions. According to the 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes [3], in the case of an equal opportunity to carry out stress imaging or computed tomography angiography (CTA), both methods are considered as the first-line. Of the imaging stress techniques, stress echocardiography with exercise is the most appropriate method for diagnosing obstructive CAD in older patients. Exercise stress echocardiography is more accurate than exercise ECG [4]. Older patients often have ECG changes that requires preventing stress tests. Unlike myocardial perfusion scintigraphy, patients are not exposed to radiation. There are few studies on the accuracy of exercise stress echocardiography and CTA in the diagnosis of stable CAD in patients of older age. There is no data on the question of how great is the difference between exercise stress echocardiography and CTA in the diagnosis of obstructive CAD in such patients. The aim of this study was to compare stress echocardiography and coronary computed tomography angiography (CCTA) in the diagnosis of stable CAD in patients aged ⩾70 years.

Material and methods

The study protocol was approved by the local ethics committee. All patients signed informed consent.

This prospective, non-randomized, comparative study included 390 patients ⩾70 years of age who were hospitalized with suspected stable CAD and who underwent an elective coronary angiography (CAG). The study did not include patients with suspected myocardial infarction or unstable angina, a history of myocardial infarction or myocardial revascularization, hypertrophic and dilated cardiomyopathy, atrial fibrillation or atrial flutter, frequent (>5 per minute) premature beats, pulmonary embolism, severe valvular heart disease, congestive heart disease.

Among men, 81 (47%) patients had typical angina, 65 (37%) patients — atypical angina pectoris; 28 (16%) patients had nonanginal pain or exercise dyspnea, which was regarded as equivalent to angina. Among women, 52 (24%) patients had typical angina pectoris, 113 (52%) — atypical angina pectoris, 51 (24%) — nonanginal pain. The quantitative assessment of CAD was carried out visually and using the Xcelera software (Philips, Netherlands). A decrease in the diameter of left coronary artery and/or one of the main coronary arteries by ⩾50% was considered hemodynamically significant [5].

At the first stage, the frequency of obstructive CAD detection was assessed depending on sex and the nature of chest pain, as well as the contingent of patients in whom stress echocardiography and CTA for the diagnosis of stable CAD was inappropriate was determined. Such a contingent included patients in whom the obstructive CAD detection rate exceeded 85%. At the second stage, the diagnostic accuracy of stress echocardiography and CTA was assessed in detecting obstructive CAD in patients with a detection rate of ⩽85%. The sensitivity was calculated = TPR/(TPR+FNR), where TPR is a true positive rate, FNR — a false negative rate; specificity = TNR/(TNR+FPR), where TNR is a true negative rate, FPR — a false positive rate; positive predictive value (PV+) = TPR/(TPR+FPR); negative predictive value (PV-) = TNR/(NR+FNR); predictive accuracy (PA) = TPR+TNR/(TPR+FPR+TNR+FNR); positive likelihood ratio (LR+) = sensitivity/(1-specificity); negative likelihood ratio (NLR-) = (1-sensitivity)/specificity. The posttest probability was calculated as follows:

$$\text{posttest probability} = \frac{(\text{pretest probability}/[1-\text{pretest probability}]) \times PV}{\text{pretest probability}/[1-\text{pretest probability}]) \times PV + 1} \quad [6].$$

Exercise stress echocardiography on a semi-reclining ergometer (Ergoline, Germany) was performed in 179 patients. Echocardiography was performed on an ultrasound system Philips iE33. The patient had a continuous stepwise increasing load, starting from 25 W. The increase at each load stage with a duration of 3 min was 25 W. Echocardiography was recorded at rest, during exercise and at the 3rd, 6th, 12th minutes of the recovery [7]. Echocardiographic images were recorded in 5 heart sections: parasternal long axis view, short axis papillary muscle view, in the apical 4-, 3- and 2-chamber views. Local left ventricular (LV) contractility was analyzed by studying clips at rest and at the load peak. Local contractility was studied using 16-segment model [8]. The contractility of each of the segments was assessed using a 4-point scale, where 1 — hypokinesis, 2 — hypokinesis, 3 — akinesis, 4 — dyskinesis. The index of impaired local LV contractility was calculated as the ratio of the sum of asynergy points to the number of assessed segments. The criteria for a positive test were the appearance of transient local contractility disorders, such as a decreased amplitude of wall motion, a decreased systolic thickening in ⩾2 segments, a decreased contractility of initially hypokinetic myocardium, decreased global LV contractility, no increase in ejection fraction, LV dilatation, even without clinical and ECG criteria for myocardial ischemia. Without LV contractility deterioration in the scar area at the load peak, the test results were considered negative. There were following criteria for stopping test: angina attack; ischemic ECG abnormalities; a patient's refusal to continue the exercise; submaximal age-related heart rate (HR); severe arrhythmias; pronounced blood pressure increase. The submaximal age-related HR was 85% of the maximum age-related heart rate, which was calculated using the formula: 208-(0,7×age) [9].

CTA was performed on an Aquilion 64 CT scanner (Toshiba, Japan) with ECG gating. The study did not include patients with an adverse reaction to iodine-based contrast agents, blood creatinine levels >1,5 mg/dL and/or glomerular filtration rate <40 ml/min, weight >100 kg. Patients with a heart rate >70 bpm received beta-blockers to achieve a heart rate of <70 bpm. The CTA protocol included native and arterial phases: phase 1 (native) was performed before contrast agent administration; phase 2 (arterial) was performed in a spiral mode, providing 64 slices 0,5 mm thick in 400 ms with continuous movement of the table with the patient. The current and voltage across the tube were 400 mA and 120 kV, respectively. A contrast agent (optiray-350 or omnipaque-350) at a dose of 100-150 ml (1,5 ml per kg of body weight) was injected intravenously 5 ml/s with an automatic syringe. The assessment of coronary arteries permeability was carried out by analyzing the heart images on transverse tomographic sections. For a detailed assessment of the coronary system state, a multi-plane and three-dimensional image reconstructions with a semi-automatic calculation of stenosis degree were performed. Coronary arteries were assessed according to the American Heart Association [10]. The degree of coronary stenosis was determined according to the following parameters: a patent coronary artery — no stenosis or stenosis <50%; hemodynamically significant stenosis — stenosis >50%; coronary artery occlusion. Image quality was assessed according to the following parameters: excellent — image without artifacts; good — minor artifacts due to coronary artery motion, step artifacts or moderate calcification; poor — pronounced artifacts due to coronary artery motion, step artifacts and/or calcification, preventing the assessment of artery lumen. Arteries <2 mm in diameter were not included in the study. Only excellent and good quality images were used to evaluate the diagnostic CTA.

The data obtained were processed using the Statistica 6.0 program. Quantitative data are presented as mean±standard deviation. To test statistical hypotheses on distribution, the Shapiro-Wilk W-test was used. For a comparative analysis of both groups, nonparametric statistics were used: Fisher's exact test and Yates's chi-squared test — for comparison of qualitative traits; Mann-Whitney U-test — for comparison of quantitative traits. The differences were considered significant at p<0,05. The risk of bias was assessed according to the QUADAS tool [11].

Results

According to CAG data, obstructive CAD was detected in 81 (100%) men and 46 (88%) of 52 women with typical angina and in 44 (68%) of 65 men and 48 (42%) of 113 women with atypical angina. It was also revealed in 4 (14%) of 28 men and 11 (22%) of 51 women with nonanginal pain. Due to the fact that, with a high (>85%) detection rate of obstructive CAD, its non-invasive diagnosis is inexpedient [1], the analysis of diagnostic significance of stress echocardiography and CTA in patients with typical angina was not carried out. The probability of obstructive CAD detection in men and women with atypical angina and nonanginal pain was 42% (95% confidence interval (CI), 36-48%).

Stress echocardiography was performed in 134 patients with atypical angina and nonanginal pain. The test did not achieve the diagnostic criteria in 23 (17%)

Table 1

Patient characteristics

	Stress echocardiography (n=111)	CTA (n=82)
Age, years	75±5	75±5
Men/women	58 (51%)/53 (49%)	32 (39%)/50 (61%)
Hypertension	111 (100%)	82 (100%)
Dyslipidemia	111 (100%)	82 (100%)
Diabetes	20 (18%)	22 (27%)
Smoking	26 (23%)	23 (28%)
Positive family history	22 (20%)	21 (26%)
Without MCA lesion	42 (38%)	34 (41%)
With MCA lesion	69 (62%)	48 (59%)
Single-vessel lesion	36 (32%)	15 (31%)
Two-vessel lesion	38 (34%)	16 (33%)
Three-vessel lesion	37 (33%)	17 (35%)
LMCA	5 (5%)	3 (6%)

Note: LMCA — left main coronary artery, MCA — main coronary artery; p>0,05 for all.

patients. Nighty two patients with atypical angina and nonanginal pain were referred for CTA. The study was impossible in 10 (11%) patients due to severe coronary calcification (Agatston score >400). Patients in whom stress echocardiography achieved the diagnostic criteria did not differ in characteristics from patients who underwent CTA (Table 1).

Among 111 patients in whom stress echocardiography achieved the diagnostic criteria, 69 (62%) patients had obstructive CAD (p>0,05 compared with patients with atypical angina and nonanginal pain who underwent CAG). In 62 patients, the test was positive, in 7 patients — negative. The sensitivity in obstructive CAD diagnosis was 89% (95% CI, 80-95). Of 111 patients, 42 (38%) patients did not have obstructive CAD. In 40 patients, the test was negative; in 2 patients — positive. The specificity was 95% (95% CI, 83-99). PV+ was 97% (95% CI, 89-99), PV- — 85% (95% CI, 71-93), PA — 92% (95% CI, 87-95%), LR+ — 17,8 (95% CI, 4.8-42), LR- — 0,1 (95% CI, 0,01-0,2). A positive result increased the likelihood of obstructive CAD from 62% to 95%, while a negative result reduced it to 16%.

Among 82 patients who underwent CTA, 48 (59%) patients had obstructive CAD. The sensitivity of CTA in the diagnosis of obstructive CAD was 100%. In 30 (88%) of 34 patients without obstructive CAD, the CTA indicated the absence of disease, in 4 (12%) patients — the presence. The specificity of CTA in the diagnosis of obstructive CAD was 88% (95% CI, 80-92). PV+ was 92% (95% CI, 89-99), PV- — 100%, PA — 95% (95% CI, 78-99), LR+ — 8,3 (95% CI, 3,9-12,5), LR- — 0. A positive CTA increased the probability of obstructive CAD from 59% to 86%, while a negative result reduced it to 0%. In comparison with CTA, stress echocardiography is less sensitive and has a lower PV- in the diagnosis of obstructive CAD in patients with atypical angina and nonanginal pain (Table 2). The difference was revealed in the values of LR+ and LR- of both diagnostic methods. The risk of bias, according to the QUADAS tool, was 9, which is a low value.

Discussion

According to the results, in men and women ⩾70 years old with typical angina, the detection rate of obstructive CAD is high (>85%) — 100% and 88%, respectively. With this detection rate, non-invasive diagnostic examination is not indicated. In this regard, the analysis of diagnostic accuracy of stress echocardiography and CTA in identifying obstructive CAD in patients with typical angina has not been performed. The high pretest probability of obstructive CAD in men ⩾70 years old with typical angina is stated in the ESC guidelines [1]. According to these guidelines, the probability of obstructive CAD in women 70-79 years old with typical angina is 68%, which is less than in the present study. In the UK guidelines, women of similar age with typical angina have a pretest probability of >90% [12], which is consistent with the present study.

According to the study results, the sensitivity and specificity of CTA in the diagnosis of obstructive CAD in patients ⩾70 years of age with atypical angina and nonanginal pain is 100% and 88%, respectively. Similar values were obtained in studies that included patients with an intermediate pretest probability regardless of age. In a study by Meijboom WB, et al. (2007), the sensitivity and specificity of CTA were 100% and 84%, respectively [13]. According to a meta-analysis of 18 studies, the sensitivity and specificity of CTA in the diagnosis of obstructive CAD is 98% (95% CI, 97-99%) and 82% (95% CI, 79-84%), respectively [14]. According to this study, the sensitivity and specificity of stress echocardiography in the diagnosis of obstructive CAD in patients ⩾70 years of age with atypical angina and nonanginal pain is 89% and 95%, respectively. These values are slightly higher than in meta-analyzes,

Table 2

Diagnostic accuracy of stress echocardiography and CTA in obstructive CAD detection

	Sensitivity	Specificity	PV+	PV-	PA	LR+	LR-
CTA	100%	88%	92%	100%	95%	8,3	0
Stress echocardiography	89%	95%	97%	85%	92%	17,8	0,1
p	0,0007	0,12	0,21	0,0003	0,4	0,02	0,004

which included patients regardless of age. According to these meta-analyzes, the sensitivity of exercise stress echocardiography was 83-85%, while the specificity — 82-84% [15, 16]. According to this study, exercise stress echocardiography is a less sensitive test in the diagnosis of obstructive CAD than CTA. Both samples have comparable specificity, which is consistent with the results of the above studies.

According to the present study, the PV+ and PV- of CTA in the diagnosis of obstructive CAD is 92% and 100%, respectively; the PV+ and PV- of exercise stress echocardiography — 97% and 85%, respectively. PV+ and PV- depends on the incidence of the diagnosed disease among the examined patients. This pattern makes it impossible to compare these indicators in studies with different incidence of the disease. In the present study, the frequency of obstructive CAD detection among patients who underwent CTA and stress echocardiography did not differ, which made it possible to compare the indicators.

To assess how the test result changes the initial data on the probability of disease, it is most appropriate to use LR+ and LR- [17]. LR+ indicates the ratio of TP and FP results, while LR- — the ratio of FN and TN results. According to the LR values, it is possible to estimate how significant the increase or decrease in the posttest probability is (Table 3) [18]. According to the results of this study, the LR+ and LR- of CTA were 8,3 and 0, respectively. This LR+ value indicates moderate differences between the pretest and posttest probability of obstructive CAD, while the LR- value — pronounced differences. Comparable values of these parameters were obtained in studies that included patients with intermediate pretest probability regardless of age. In the study by Meijboom WB, et al. (2007) [13], the LR+ and LR- of the CTA result were 6,38 and 0, respectively; in the ACCURACY trial [19] — 5,56 and 0,06, respectively. According to the results of this study, the LR+ and LR- of stress echocardiography were 17,8 and 0,1, respectively. This LR+ value indicates a pronounced difference between the pretest and posttest probability of obstructive CAD, while the LR- value — moderate difference. LR+ (11,34) and LR- (0,17) of exercise stress echocardiography in the study by Banerjee A, et al. (2012) [4] are close to the values obtained in the presented study.

Table 3

Differences between pretest and posttest probability

Difference	LR+	LR-
Not significant	<2	<0,5
Low	2-5	0,5-0,2
Moderate	5-10	0,1-0,2
High	>10	<0,1

According to the results of this study, a positive CTA increases the likelihood of obstructive CAD from 59% to 86%, while a negative result reduces the likelihood to 0%. A positive stress echocardiography increases the likelihood from 62% to 95%, while a negative result reduces the likelihood to 16%. In the first case, the changes in the posttest probability are so pronounced that they allow changing the initial intermediate probability to a high (>85%) or low (<15%). Such an increase in the likelihood with a positive CTA result allows to establish obstructive CAD, while a decrease in the probability with a negative result allows to conclude that there is no obstructive CAD. Similar results have been demonstrated by Meijboom WB, et al. (2007) [13]. A positive CTA increased the likelihood of obstructive CAD to 88%, while a negative result reduced the likelihood to 0%. An increase in the probability with a positive result of stress echocardiography also allows to ascertain the obstructive CAD, and a decrease in the probability with a negative result gives strong grounds to rule out it. Changes in the obstructive CAD likelihood depending on stress echocardiography result in the present study are consistent with the changes in likelihood that are reported in the meta-analysis [4]. A positive result of exercise stress echocardiography increases the likelihood of obstructive CAD from 49% to 92%, while a negative result reduces the likelihood to 16%.

Conclusion

Stress echocardiography and CTA has comparable diagnostic accuracy in the detection of obstructive CAD in patients aged ≥70 years with atypical angina and non-anginal pain. Stress echocardiography has a greater diagnostic value of positive result; CTA has a greater diagnostic value of negative result.

Relationships and Activities: none.

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